Current Research Studies

Biomarker Development Efforts Continue

We continue to develop new collaborations and to seek additional funding to support our research by applying artificial intelligence for the continued development of brain MRI and quantitative EEG as biomarkers to improve the clinical diagnosis, monitoring and prognosis of patients with SWS, and to determine their ability to predict treatment responses. Refer to Figure 1 to learn more about these biomarkers. For more information, please reach out and we are happy to share a copy of our recently published review on this topic:

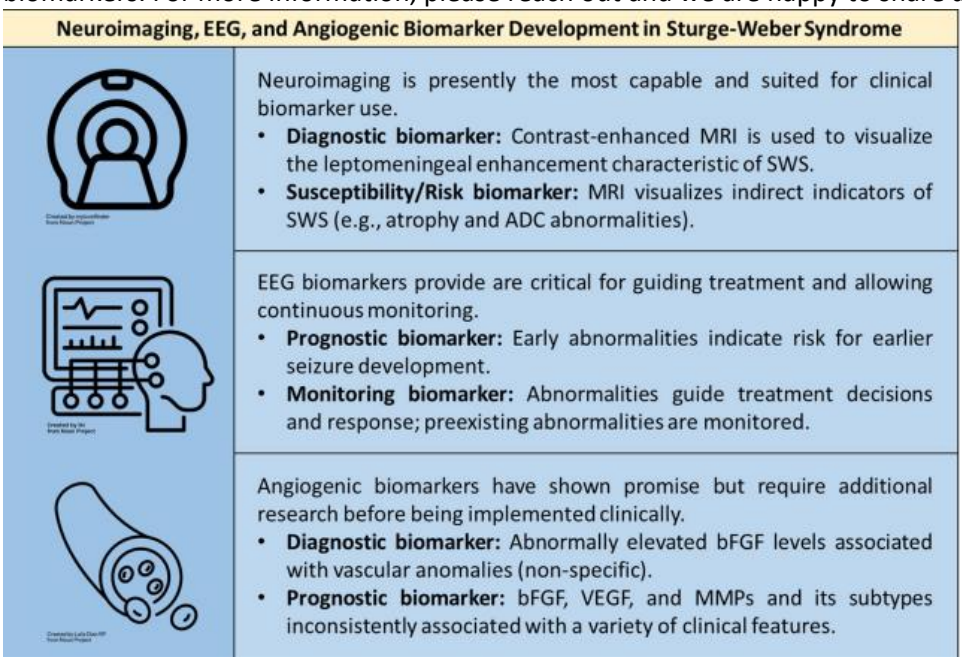

Figure 1: Biomarkers used in SWS, including MRI, EEG, and angiogenic biomarkers. While all these biomarkers are non-invasive and affordable, MRI and EEG biomarkers have shown the most clinical relevance related to SWS. Urine biomarkers still require further research to support their regular use in clinical settings (Gupta *et al. Journal of Neurodevelopmental Disorders*).

Biomarker Development in Sturge-Weber Syndrome (2025) Gupta SS, Joslyn KE, McKenney KD, Comi AM. Biomarker development in Sturge-Weber syndrome. *J Neurodev Disord*. 2025;17(1):50. Published 2025 Aug 25. doi:10.1186/s11689-025-09640-6

This review summarizes past, ongoing, and future research needed to explore both diagnostic and prognostic biomarkers aimed to improve clinical care for SWS. SWS requires multidisciplinary monitoring and management, and early identification of the disease can help improve neurological outcomes. The recent advancements in biomarker research may contribute to earlier diagnoses and better prognosis and allow for improved monitoring of treatment response. See Figure 2 to better understand the progression of SWS over a lifetime. Biomarkers, coupled with clinical data, may allow for

presymptomatic treatment initiation in infants with SWS, an important avenue of future research.

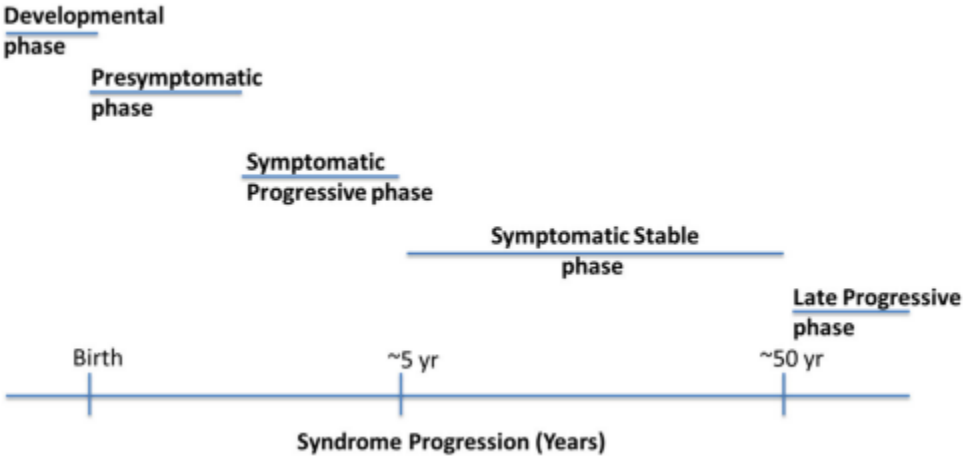

Figure 2: Typical SWS progression over a lifetime (Valery & Comi, *Annals of the Child Neurology Society*).

Outcomes in Adults with SWS

Katharine E. Joslyn, Catherine Stephan, Bernard A. Cohen, Stacy J. Suskauer, Courtney L. Kraus, Nara D. Sobreira, Anna L. Grossberg, Anne M. Comi, Andrew T. Zabel

Due to the highly variable nature of SWS, long-term outcomes in adulthood are not well understood. We created a clinical needs assessment and sent it to all adult patients older than 18 years old with SWS to better understand the long-term vocational, educational, overall health and wellbeing, and medical and neurological outcomes in adulthood. Currently, we are gathering data to formulate analyses with the intention of publishing our results.

Infant Monitoring Device Usage in Infants with Sturge-Weber Syndrome

Figure 3: Sleeping SWS infant being monitored using an infant monitoring device to detect seizures during the night (created using Microsoft 365 Copilot).

Katharine E. Joslyn, Ashley N. Eisenberg, Veronica M. Lee, Linda Rozell-Shannon, Anne M. Comi

In this study, we created a clinical questionnaire to gauge parental experience using infant monitoring devices (IMD), like the Owlet and Nanit, and assessed their utility for detecting seizures in infants with SWS. Overall, parents reported having a positive experience using an IMD for their child at risk for or diagnosed with SWS brain involvement. In a subgroup of patients with brain involvement and a history of seizures, parents also reported being able to detect first seizures via an IMD. This study supports the use of IMDs to monitor and detect first seizures in infants with or at risk for SWS; however, continued prospective research is needed with a larger and more diverse sample size.

Sturge-Weber Syndrome Acute Crisis (SWAC) Index

Kieran D. McKenney, Luther G. Kalb, Adrienne M. Hammill, Anne M. Comi

In this study, we developed the Sturge-Weber Acute Crisis (SWAC) index based on clinical care guidelines and practical experience. This measure, capable of quantifying neurologic symptoms during an SWS acute crisis, was evaluated for its practical application. The SWAC was retrospectively applied to a prospective drug trial, with SWAC scores assigned for every acute crisis during 6-month baseline and treatment phases. It was found that six of 10 subjects experienced 670 acute crises. This study supports the use of the SWAC index, which helped reflect clinical experience of site-PIs, quantified the severity of SWS acute crises, and enabled stronger comparison of baseline and treatment responses. Further studies with the SWAC index to explore its clinical uses as an acute crisis outcome measure for treatment trials in SWS are needed.

Seizure Susceptibility In SWS Mouse Model

Nicholas Truver, Solomon Comi, Anne Comi

We recently published a mouse model of SWS, where mice express the GNAQ gene variant responsible for many cases of SWS. SWS mice brains have unique cell culture characteristics that we are studying in terms of seizure susceptibility and effects. The data collected informs our understanding of seizures in relation to SWS, and supports the further development of our mouse model to study SWS outcomes and treatments.

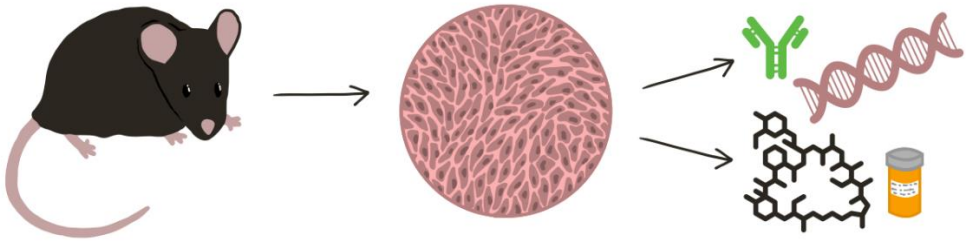

Figure 4: Cell culture in SWS mouse model studied in terms of endothelial cell function. Data collected will contribute to developing novel treatments (created using Notability).

Gene Therapy

We are currently developing a gene therapy to stop expression of the p.R183Q gene variant. Currently, we are testing the delivery system to ensure the treatment reaches the correct target tissues. We hope this therapy will be able to slow, stop or even reverse the progression of SWS.

Glaucoma Pilot Studies

We will measure axial length and intraocular pressure in mice with SWS. Axial length measures how long the eye is, front to back, and higher values are linked to nearsightedness. Intraocular pressure is a measure of the fluid pressure inside the eye. High pressure is linked to glaucoma. We hope to gain a better understanding of the progression of glaucoma and vision problems over the lifespan in patients with SWS.

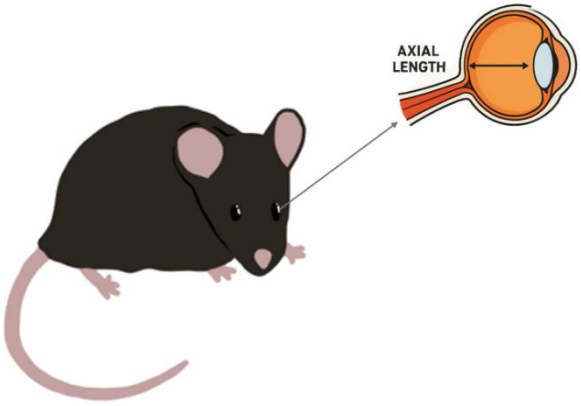

Figure 6: Axial length measured in an SWS mouse model (created using Notability and Microsoft 365 Copilot).

Completed Research Studies

New Clinical Drug Trials for Older Patients with Sturge-Weber Syndrome

Cannabidiol (Epidiolex): Cannabidiol (CBD) is a cannabinoid with no psychoactive properties which has been implicated to have anticonvulsant, antioxidant, anti-inflammatory and neuroprotective properties. Early pilot trials have suggested that CBD is well tolerated in older patients and may improve cognitive function, mood, and overall quality of life in patients with SWS. Preclinical trials have suggested interconnected molecular pathways between SWS and CBD, leading to the idea that CBD may be effective in addressing SWS brain involvement.

We have published the following manuscripts related to CBD:

Kaplan EH, Offermann EA, Sievers JW, Comi AM. Cannabidiol Treatment for Refractory Seizures in Sturge-Weber Syndrome. *Pediatr Neurol*. 2017;71:18-23.e2. doi:10.1016/j.pediatrneurol.2017.02.009

Smegal LF, Vedmurthy P, Ryan M, et al. Cannabidiol Treatment for Neurological, Cognitive, and Psychiatric Symptoms in Sturge-Weber Syndrome. *Pediatr Neurol*. 2023;139:24-34. doi:10.1016/j.pediatrneurol.2022.10.014

Joslyn KE, Truver NF, Comi AM. A Review of Sturge-Weber Syndrome Brain Involvement, Cannabidiol Treatment and Molecular Pathways. *Molecules*. 2024;29(22):5279. Published 2024 Nov 8. doi:10.3390/molecules29225279

Sirolimus: SWS is thought to arise from a somatic activating mutation in the GNAQ. Studies have suggested that this genetic mutation may cause hyperactivation of the mammalian target of rapamycin (mTOR) pathway. Sirolimus is an inhibitor of the mTOR pathway that has been studied in other vascular anomalies. It is therefore a potentially promising therapy in SWS. We have published one clinical trial, which showed that sirolimus was well-tolerated in SWS patients and may pose benefits to cognitive impairment. Future randomized control trials of sirolimus in SWS patients are needed to further understand its potential benefits.

We have published the following manuscript related to sirolimus:

Sebold AJ, Day AM, Ewen J, Adamek J, Byars A, Cohen B et al. Sirolimus Treatment in Sturge-Weber Syndrome. *Pediatric neurology.* 2021 Feb;115:29-40. doi: 10.1016/j.pediatrneurol.2020.10.013

Retrospective Analysis of Presymptomatic Treatment In Sturge-Weber Syndrome.

Valery CB, Iannotti I, Kossoff EH, et al. Retrospective Analysis of Presymptomatic Treatment In Sturge-Weber Syndrome. *Ann Child Neurol Soc*. 2024;2(1):60-72. doi:10.1002/cns3.20058

Presymptomatic treatment initiated prior to the onset of seizures may delay the onset of seizures and improve neurologic outcomes in patients with Sturge-Weber syndrome. This recent retrospective analysis using clinical data from two SWS centers explored seizure outcomes in presymptomatically treated patients (before seizure onset) compared to patients treated after the onset of seizures. Results of the study revealed that presymptomatic treatment is promising for children with SWS brain involvement diagnosed prior to the onset of seizures. Further prospective drug trials are needed to

determine long-term outcomes.

R183Q GNAQ Sturge-Weber Syndrome Leptomeningeal and Cerebrovascular Developmental Mouse Model.

Solomon C, McCann M, Singh P, Nemeth C, Comi AM. R183Q GNAQ Sturge-Weber Syndrome Leptomeningeal and Cerebrovascular Developmental Mouse Model. *J. Vasc. Anom.* **5**, e099 (2024).

In this study, a mouse model of SWS in brain endothelial cells during development was created. Brain endothelial cells line blood vessels that supply blood to the brain. We inserted two mutated DNA sequences into mice. The GNAQ p.R183Q variant is the gene responsible for most cases of SWS. The other gene, Tet, controls when and in which cells the mouse can produce mutant GNAQ. When mice are given doxycycline, an antibiotic, in their food or water, the Tet gene is turned on in all cells that produce Tie2. Tie2 is a protein found on the outer surface of endothelial cells. The Tet gene produces a molecule that turns on production of the mutant GNAQ protein. A mouse needs to have both the Tet gene and the GNAQ p.R183Q gene to produce the mutant GNAQ protein. Creating a mouse model allows us to research more subjects in a shorter time than if we were to study only human patients. Mice with the p.R183Q variant had higher amounts of P-S6, indicating greater activity of the mTOR pathway, which is involved in cell growth and metabolism. A set of these mice were injected with Evans blue, a dye that cannot cross the blood-brain barrier under normal conditions. The blood-brain barrier controls which molecules are allowed to pass from the bloodstream into the brain. Mice expressing the p.R183Q variant showed more severe Evans blue staining in their brains, indicating that the blood-brain barrier was not functioning correctly. Another set of mice were injected with kainate, a drug that causes seizures. Seizure activity was monitored, and brain tissues were analyzed for protein markers. Xgal staining stains cells that express the Tet gene and in mutant mice. It was found that Xgal staining in the leptomeninges increased after seizures. This finding indicates that production of the GNAQ p.R183Q protein increased after seizures.

Sturge-Weber syndrome: updates in translational neurology.

Solomon C, Comi A. Sturge-Weber syndrome: updates in translational neurology. *Front Neurol*. 2024;15:1493873. Published 2024 Dec 2. doi:10.3389/fneur.2024.1493873

This review discusses recent updates in SWS research, and how mouse and cell models of SWS led to the development of new treatment options. Many cases of port-wine birthmark (PWB) and SWS are caused by a mutation in the GNAQ gene that changes the behavior of brain endothelial cells, the cells that line blood vessels throughout the brain. Tools like MRI and Neuroscore help clinicians evaluate how SWS is affecting individual patients. Mouse and cell models allow researchers to figure out what changes are happening to affected cells and tissues to make them work differently than normal cells. Mouse models have already helped identify multiple proteins that are important for blood vessel development and blood-brain barrier function that are disrupted in SWS. Recent clinical research has focused on early diagnosis, biomarker development, presymptomatic treatment, and development of new treatment strategies. Pilot studies of cannabidiol and sirolimus show that these drugs may reduce seizure frequency and improve cognitive outcomes.

Genetic testing in the evaluation of individuals with clinical diagnosis of atypical Sturge-Weber syndrome.

Yeom S, Cohen B, Weiss CR, et al. Genetic testing in the evaluation of individuals with clinical diagnosis of atypical Sturge-Weber syndrome. *Am J Med Genet A*. 2023;191(4):983-994. doi:10.1002/ajmg.a.63106

In this case series, 12 SWS patients with atypical features underwent germline and/or somatic genetic testing. Atypical features included extensive capillary malformation on the body in addition to the face, overgrowth of extremities, absence of neurologic signs and symptoms, and family history of vascular malformations. It was found that five patients had a somatic GNAQ or GNA11 pathogenic variant, with other patients found to have variants in other genes such as RASA1, EPHB4, and KIT. Our findings from this study suggest that SWS patients with atypical characteristics may have somatic variants in genes besides GNAQ or GNA11. Broad germline and somatic genetic testing may have important implications for improved medical care, prognosis, and trial eligibility.

Study Protocol: retrospectively mining multisite clinical data to presymptomatically predict seizure onset for individual patients with Sturge-Weber.

Vedmurthy P, Pinto ALR, Lin DDM, Comi AM, Ou Y; BCH-KKI SWS Pre-symptomatic Biomarker Working Group. Study protocol: retrospectively mining multisite clinical data to presymptomatically predict seizure onset for individual patients with Sturge-Weber. *BMJ Open*. 2022;12(2):e053103. Published 2022 Feb 4. doi:10.1136/bmjopen-2021-053103

In this study, clinical SWS data from two national centers were retrospectively collected to develop presymptomatic biomarkers. This data included MRI and neurocognitive outcome data for SWS patients who underwent a brain MRI before two years old. Presymptomatic treatment initiated before seizure onset in 0–2-year-olds may delay or prevent the onset of seizures by two years old, therefore improving neurocognitive outcomes. The proposed work from this protocol would be one of the largest and most comprehensive multisite databases for presymptomatic treatment approach of this disease.

Multicenter Research Data of Epilepsy Management in Patients With Sturge-Weber Syndrome.

Smegal LF, Sebold AJ, Hammill AM, et al. Multicenter Research Data of Epilepsy Management in Patients With Sturge-Weber Syndrome. *Pediatr Neurol*. 2021;119:3-10. doi:10.1016/j.pediatrneurol.2021.02.006

In this study, we analyzed a large multi-center database with a focus on neurological drug treatment in different demographic and SWS characteristic groups. 268 patients with brain involvement and a history of seizures were selected from a research data registry generated from a multi-center cross-sectional questionnaire. Associations between medication use and variables such as sex, ethnicity, and brain, skin and eye involvement were examined. It was found that the most commonly used medications were levetiracetam, low-dose aspirin, oxcarbazepine, and phenobarbital. Lamotrigine was more frequently used in adults than children. More severely affected patients were on a greater number of antiseizure

medications. Longitudinal studies are needed to further investigate medication use in patients with SWS.

Quantitative EEG improves prediction of Sturge-Weber syndrome in infants with port-wine birthmark.

Gill RE, Tang B, Smegal L, Adamek JH, McAuliffe D, Lakshmanan BM, et al. Clin Neurophysiol. 2021;132(10):2440-6.

Diagnosing brain involvement in infants with a facial port-wine birthmark is complicated due to the low sensitivity of neuroimaging at a young age. We have been developing quantitative EEG (qEEG) as a safe tool to screen infants with a facial port-wine birthmark for brain involvement and for monitoring neurologic progression. This involves a routine EEG that is analyzed in a special way to evaluate abnormal asymmetry in power. qEEG may be a useful biomarker for SWS brain involvement, especially for young patients, as an alternative to MRIs or CTs. The purpose of our most recent study was to determine whether qEEG can improve early screening of SWS brain involvement in at-risk infants with a V1 facial port-wine birthmark and to determine if it will help us safely monitor response to treatment.

Identification of a Mosaic Activating Mutation in GNA11 in Atypical Sturge-Weber Syndrome.

Thorpe J, Frelin LP, McCann M, et al. Identification of a Mosaic Activating Mutation in GNA11 in Atypical Sturge-Weber Syndrome. *J Invest Dermatol*. 2021;141(3):685-688. doi:10.1016/j.jid.2020.03.978

Based on targeted next-generation sequencing, five individuals with SWS but negative for GNAQ R183Q mutations were identified. Whole exome sequencing was performed to identify potential causal mutations. Additional patients with pathologic GNA11 mutations and features that overlap with SWS are needed to determine if they all display a milder neurologic phenotype than the typical SWS patient with a GNAQ R183Q mutation.

Suicide Screening in Sturge-Weber Syndrome: An Important Issue in Need of Further Study.

Sebold AJ, Ahmed AS, Ryan TC, et al. Suicide Screening in Sturge-Weber Syndrome: An Important Issue in Need of Further Study. *Pediatr Neurol*. 2020;110:80-86. doi:10.1016/j.pediatrneurol.2020.03.013

This study explored clinical factors associated with suicide risk in patients with SWS, an underexplored topic. Although SWS patients are vulnerable to risk factors for suicide, including chronic illness and physical differences, frequency of suicidal ideation and attempts and clinical factors associated with suicide risk is unknown. Outpatients eight years and older underwent a suicide risk screening during nursing triage using a standardized suicide screening tool. Suicide screening results, demographic variables, and medical history for SWS patients were used for retrospective within- and between-group analysis. In the combined sample of SWS and neurologically-involved patients, a positive suicide risk screen was related to SWS diagnosis. This study showed that people with SWS may be at greater risk of suicidal thoughts or behaviors than those with other neurological conditions. Further study of suicide risk in SWS patients is needed.

Quality of Life in Children With Sturge-Weber Syndrome.

Harmon KA, Day AM, Hammill AM, et al. Quality of Life in Children With Sturge-Weber Syndrome. *Pediatr Neurol*. 2019;101:26-32. doi:10.1016/j.pediatrneurol.2019.04.004

We assessed the utilization of the National Institutes of Health Quality of Life in Neurological Disorders (Neuro-QoL) in pediatric patients with Sturge-Weber syndrome. 22 subjects filled out the Pediatric Neuro-QoL and 21 participants also filled out the Brain Vascular Malformation Consortium Database Questionnaire containing data pertaining to SWS-related medical history, medications, comorbidities, and family history. This study showed that cognitive function quality of life was significantly lower in pediatric patients with SWS compared to control subjects. A younger age of seizure onset was associated with lower cognitive function Neuro-QoL even after controlling for extent of brain, skin, or eye involvement. The results of this study suggest that targeting cognitive function Neuro-QoL in treatment trials and reiterate the prognostic value of early seizure onset. In addition, sex-related differences were noted, which should be further studied.

Hypothesis: Presymptomatic Treatment of Sturge-Weber Syndrome With Aspirin and Antiepileptic Drugs May Delay Seizure Onset.

Day AM, Hammill AM, Juhász C, et al. Hypothesis: Presymptomatic treatment of Sturge-Weber Syndrome With Aspirin and Antiepileptic Drugs May Delay Seizure Onset. *Pediatr Neurol*. 2019;90:8-12. doi:10.1016/j.pediatrneurol.2018.04.009

Efforts should be made to identify neuroprotective interventions that could positively impact outcome in early stages of the disease. We hypothesized in this paper that low-dose antiepileptic drugs and aspirin may be effective in delaying seizure onset in SWS infants. This hypothesis is supported by lower seizure scores and older age of seizure onset in the presymptomatically-treated infants. Four of the infants treated presymptomatically with antiepileptic drugs and aspirin had yet to develop seizures at ages 14-39 months.

Physical and Family History Variables Associated with Neurological and Cognitive Development in Sturge-Weber Syndrome.

Day AM, McCulloch CE, Hammill AM, et al. Physical and Family History Variables Associated With Neurological and Cognitive Development in Sturge-Weber Syndrome. *Pediatr Neurol*. 2019;96:30-36. doi:10.1016/j.pediatrneurol.2018.12.002

The variability in clinical presentation of SWS makes accurate prognosis of the disease difficult. It was hypothesized in this paper that greater extent of physical factors, presence of genetic factors, and age of seizure onset might be associated with increased symptom severity and greater need for surgery in SWS patients. 277 participants with SWS brain involvement completed a questionnaire, and it was found that the extent of brain and skin involvement and the age of seizure onset impacts disease prognosis. An important suggestion that arose from this study is the idea that family history may contribute to the

development of common comorbidities, supporting the hypothesis that genetic factors contribute to SWS variability.

Gαq and hyper-phosphorylated ERK expression in Sturge-Weber syndrome leptomeningeal blood vessel endothelial cells.

Wellman RJ, Cho SB, Singh P, et al. Gαq and hyper-phosphorylated ERK expression in Sturge-Weber syndrome leptomeningeal blood vessel endothelial cells. *Vasc Med*. 2019;24(1):72-75. doi:10.1177/1358863X18786068

Brain tissue samples from SWS patients and epilepsy controls were analyzed in this study. Staining with hematoxylin and eosin, which are used to analyze the structure and organization of the tissue, showed SWS brain tissue had thin, disorganized blood vessels and areas of calcification in the cerebral cortex. Antibody staining showed decreased CD34 and larger leptomeningeal vessels in SWS brain samples than in epilepsy controls. CD34 is a marker found on cells lining small blood vessels to signal vessel growth and formation. Decreased CD34 suggests that SWS tissue may be more prone to blood vessel growth and inflammation. Antibody staining for ERK and phospho-ERK (p-ERK) showed that a larger percent of ERK was present as p-ERK in SWS leptomeningeal tissue compared to in epilepsy controls. ERK is a protein in the MAPK signaling pathway, which is involved in regulating cell growth, and p-ERK is the active form of ERK. A larger proportion of p-ERK suggests higher MAPK activity, leading to abnormal growth signaling that interferes with normal vascular development. These findings suggest that leptomeningeal vessels, the blood vessels found in the inner layer of tissue surrounding the brain, are affected by SWS.

Anticonvulsant Efficacy in Sturge-Weber Syndrome.

Kaplan EH, Kossoff EH, Bachur CD, et al. Anticonvulsant Efficacy in Sturge-Weber Syndrome. *Pediatr Neurol*. 2016;58:31-36. doi:10.1016/j.pediatrneurol.2015.10.015

SWS patients are often prescribed one or several seizure medications, or anticonvulsants. This study examined these different anticonvulsants, their side effects, and the associated clinical outcomes. Individuals with epilepsy due to SWS were analyzed to determine which anticonvulsants provided optimal seizure control and which resulted in the fewest side effects. 108 records from one center were retrospectively analyzed for SWS brain involvement, epilepsy, SWS neuroscores, and currently used anticonvulsants. Of the 14 anticonvulsants that had been employed, the most used agents were oxcarbazepine and levetiracetam. It was found that carbamazepine and oxcarbazepine were associated with better seizure control than levetiracetam in this SWS cohort and so they may be preferred as the initial therapy. When used as an adjunctive therapy, topiramate was effective in this limited analysis without a clear increased incidence of glaucoma.

Aspirin use in Sturge-Weber syndrome: side effects and clinical outcomes.

Lance EI, Sreenivasan AK, Zabel TA, Kossoff EH, Comi AM. Aspirin use in Sturge-Weber syndrome: side effects and clinical outcomes. *J Child Neurol*. 2013;28(2):213-218. doi:10.1177/0883073812463607

This study summarized our experience with the side effects and outcomes of low-dose aspirin usage in a large number of children with SWS, suggesting that low-dose aspirin is generally safe and useful in the treatment of patients with SWS. This study further addresses the side effects and outcomes of low-dose aspirin usage in SWS. 58 subjects on aspirin with brain involvement were analyzed in a retrospective chart review, which were evaluated for brain involvement, age at first seizure, and side effects. This cohort's clinical experience adds significant support for low-dose aspirin use to optimize neurodevelopmental outcomes in Sturge-Weber syndrome with minimal side effects.

Importance of utilizing a sensitive free thyroxine assay in Sturge-Weber syndrome.

Siddique L, Sreenivasan A, Comi AM, Germain-Lee EL. Importance of utilizing a sensitive free thyroxine assay in Sturge-Weber syndrome. *J Child Neurol*. 2013;28(2):269-274. doi:10.1177/0883073812463606

This study described 5 children with SWS on anticonvulsants suspected to have hypothyroidism and the importance of using the free T4 assay to accurately diagnose this condition. Central hypothyroidism is more prevalent in SWS than in the general population. We routinely evaluated thyroid function in 5 children with SWS on anticonvulsants and diagnosed with hypothyroidism based on thyroid function testing. All 5 patients were eventually tested utilizing the more accurate free thyroxine equilibrium dialysis assay. Results indicated that only 2 of the 5 patients who exhibited the most severe symptoms had true hypothyroidism. This case series demonstrated the benefits of using the free thyroxine by equilibrium dialysis when testing SWS patients on antiepileptic medications. This testing algorithm is more cost-effective and improves the quality of care by providing an accurate diagnosis more quickly. In addition, we proposed consideration of this testing method in any patient taking anticonvulsants, particularly oxcarbazepine.

Increased choroidal thickness in patients with Sturge-Weber syndrome.

Arora KS, Quigley HA, Comi AM, Miller RB, Jampel HD. Increased choroidal thickness in patients with Sturge-Weber syndrome. *JAMA Ophthalmol*. 2013;131(9):1216-1219. doi:10.1001/jamaophthalmol.2013.4044

With the recent development of enhanced depth imaging spectral-domain optical coherence tomography (SD-OCT), it is now possible to measure choroidal thickness in patients with Sturge-Weber syndrome and detect abnormalities that are not visible as part of the fundus examination. The advent of enhanced depth imaging SD-OCT has allowed us to quantify choroidal thickness in the posterior pole, even in eyes with a markedly thickened choroid, such as those found in individuals with SWS. Spectral-domain OCT has a much higher resolution (5-10 µm) than B-scan ultrasonography (150 µm) and can be used to distinguish between the retina and the choroid. Furthermore, enhanced depth imaging SD-OCT can detect choroidal thickness in eyes without clinically apparent choroidal abnormalities. This study demonstrated that optical coherence tomography can quantify eye involvement with the vascular malformation in SWS and may be useful as a biomarker in clinical care and drug trials.

Urine biomarkers in Sturge-Weber syndrome

Sreenivasan AK, Bachur CD, Lanier KE, et al. Urine vascular biomarkers in Sturge-Weber syndrome. *Vasc Med*. 2013;18(3):122-128. doi:10.1177/1358863X13486312

This study showed that urine biomarkers correlate with the severity of neurologic involvement in SWS and can be developed as a biomarker for clinical care and drug trials in SWS. This study investigated the use of urinary matrix metalloproteinase (MMP)-2, MMP-9, vascular endothelial growth factor (VEGF), and basic fibroblast growth factor (bFGF) levels to non-invasively monitor the progression of SWS. The results suggested that MMP-2 and MMP-9 levels may be useful in assessing SWS progression, as well as indicating which patients might benefit from more aggressive treatment, while bFGF levels may be useful in judging the efficacy of neurologic treatment in SWS.

Case report of subdural hematoma in a patient with Sturge-Weber syndrome and literature review: questions and implications for therapy.

Lopez J, Yeom KW, Comi A, Van Haren K. Case report of subdural hematoma in a patient with Sturge-Weber syndrome and literature review: questions and implications for therapy. *J Child Neurol*. 2013;28(5):672-675. doi:10.1177/0883073812449514

In this paper, we present a toddler with SWS who developed a subdural hematoma in the setting of a mechanical fall with minor head trauma. This paper discusses the possible role of aspirin in contributing to, or perhaps protecting against, intracranial hemorrhage in patients with SWS.

Sturge-Weber syndrome and port-wine stains caused by somatic mutation in GNAQ.

Shirley MD, Tang H, Gallione CJ, et al. Sturge-Weber syndrome and port-wine stains caused by somatic mutation in GNAQ. *N Engl J Med*. 2013;368(21):1971-1979. doi:10.1056/NEJMoa1213507

In this study, the entire genome was sequenced from samples of affected and unaffected skin from three SWS patients. This showed 1,294 places where at least one affected sample differed in DNA sequence from the same patient's unaffected sample; 658 of these variations were present in two or three of the three affected samples. Functional annotation, where a computer analyzes a gene sequence to predict the gene's function, left us with one variant: GNAQ c.548G→A. This means that the 548th letter in the coding sequence of the GNAQ gene changed from a G to an A, which changed the 183rd position in the protein sequence from R to Q (p.R183Q). The GNAQ c.548G→A gene variant was tested for in DNA sequences from skin and brain tissue samples of SWS patients, brain samples from patients with no vascular malformation, and brain samples from patients with cerebral cavernous malformation, a vascular malformation unrelated to SWS. 88% of SWS patients tested positive for the c.548G→A variant in brain or skin samples. All patients without a vascular malformation and all patients with an unrelated vascular malformation tested negative for this variant. An additional aspect of this study was introducing the normal GNAQ gene, the p.R183Q variant, and a different p.Q209L variant found in uveal melanoma, into stem cells. ERK and SRE were measured. ERK is a protein in the MAPK signaling

pathway, which is involved in regulating cell growth. Cells that received the p.R183Q variant showed increased growth signaling compared to the normal gene, but not as much as p.Q209L. SRE is a sequence of DNA that regulates the production of growth factors. Cells that received the p.R183Q variant showed increased SRE activity compared to normal controls, but not as much as p.Q209L.

A needle in a haystack: Sturge-Weber syndrome gene discovery.

Comi AM, Marchuk DA, Pevsner J. A needle in a haystack: Sturge-Weber syndrome gene discovery. *Pediatr Neurol*. 2013;49(6):391-392. doi:10.1016/j.pediatrneurol.2013.07.009

This manuscript summarizes the story behind the scientific discovery of the somatic mutation that causes Sturge-Weber syndrome.

Updates and future horizons on the understanding, diagnosis, and treatment of Sturge-Weber syndrome brain involvement.

Lo W, Marchuk DA, Ball KL, Juhász C, Jordan LC, Ewen JB, **Comi A**; Brain Vascular Malformation Consortium National Sturge-Weber Syndrome Workgroup. *Dev Med Child Neurol.* 2012 Mar; 54(3):214-23. doi: 10.1111/j.1469-8749.2011.04169.x. Epub 2011 Dec 23.
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This review summarizes the efforts of the Brain Vascular Malformation Consortium over the last several years to make inroads into the understanding, diagnosis, and treatment of Sturge-Weber syndrome. This review shows that the increasing number of reports dealing with SWS over the last decade reflects progress in the diagnosis and understanding of neurological involvement. The proliferation of centers and advocacy groups to care for patients with SWS and to stimulate research has aided the development of new insights into the clinical manifestations and the pathophysiology of neurological progression, and the development of novel hypotheses to direct future research. This review summarizes important new knowledge and presents new research directions that are likely to provide further insights, earlier diagnosis, improved treatments, and possibly, prevention of this syndrome.

Survey of aspirin use in Sturge-Weber syndrome.

Bay MJ, Kossoff EH, Lehmann CU, Zabel TA, Comi AM. Survey of aspirin use in Sturge-Weber syndrome. *J Child Neurol*. 2011;26(6):692-702. doi:10.1177/0883073810388646

This study showed a significant relative reduction in both self-reported seizure frequency and stroke-like episodes after starting aspirin. It also suggested that low-dose aspirin can be safely used in these patients. In this study, an internet-based questionnaire was designed to assess the frequency of use, effectiveness, and safety of aspirin treatment in SWS. 34 of 98 subjects who completed the survey reported using aspirin. The mean number of reported stroke-like episodes and the median number of seizure episodes per month decreased after starting aspirin.

A pilot study of the modified Atkins diet for Sturge-Weber syndrome.

Kossoff EH, Borsage JL, Comi AM. A pilot study of the modified Atkins diet for Sturge-Weber syndrome. *Epilepsy Res*. 2010;92(2-3):240-243. doi:10.1016/j.eplepsyres.2010.09.008

This study explored how a modified Atkins diet (MAD) could be used as a treatment for epilepsy in patients with SWS. The MAD is a dietary treatment that does not restrict fluids or calories. Theoretically, this is safer than the ketogenic diet for children with SWS. Five children aged 4-18 years old with SWS and at least one monthly intractable seizure were started prospectively on the MAD for 6 months. All children included had urinary ketosis and seizure improvement, including three with greater than 50% seizure reduction.

Effect of a single application of pulsed dye laser treatment of port-wine birthmarks on intraocular pressure.

Quan SY, Comi AM, Parsa CF, Irving ND, Krakowski AC, Cohen BA. Effect of a single application of pulsed dye laser treatment of port-wine birthmarks on intraocular pressure. *Arch Dermatol*. 2010;146(9):1015-1018. doi:10.1001/archdermatol.2010.223

This study examined the optimal timing and use of laser in treating patients with or at risk for SWS. No evidence of worsening eye pressures was noted immediately following laser treatments compared to just prior to the laser eye treatment. In this study, we investigated to what extent a single application of laser therapy might affect intraocular pressure. Pressures before and after laser treatment were measured to determine any pressure differences in 15 patients included in the study. The results of the study concluded that a single laser application to a port-wine birthmark did not appear to show any clinically relevant changes in intraocular pressure. Further longitudinal studies are needed in a broader range of patients to explore this treatment in more detail.

Behavioral and psychiatric features of Sturge-Weber syndrome.

Turin E, Grados MA, Tierney E, Ferenc LM, Zabel A, Comi AM. Behavioral and psychiatric features of Sturge-Weber syndrome. *J Nerv Ment Dis*. 2010;198(12):905-913. doi:10.1097/NMD.0b013e3181fe75ee

This study included a small group of outpatients (n=16, aged 3-34 years old) with SWS seeking medical services to report their behavioral and psychiatric features. It was found that problems with mood, attention, sleep, learning, and substance use were common. Disruptive behavior disorders and their association with medical conditions should be further investigated.

Neuropsychological features and risk factors in children with Sturge-Weber syndrome: four case reports.

Zabel TA, Reesman J, Wodka EL, et al. Neuropsychological features and risk factors in children with Sturge-Weber syndrome: four case reports. *Clin Neuropsychol*. 2010;24(5):841-859. doi:10.1080/13854046.2010.485133

In this paper, four cases were presented of children between 8-9 years old, illustrating the broad range of physiological involvement and associated neuropsychological functioning in SWS. Findings argue against the idea of a "typical" SWS neuropsychological presentation. This report highlights a preliminary collection of disease status and severity factors thought to impact neuropsychological presentation in SWS.

Psychiatric findings in individuals with Sturge-Weber syndrome.

Suskauer SJ, Trovato MK, Zabel TA, Comi AM. Psychiatric findings in individuals with Sturge-Weber syndrome. *Am J Phys Med Rehabil*. 2010;89(4):323-330. doi:10.1097/PHM.0b013e3181ca23a8

This study summarized psychiatric findings and recommendations for 30 individuals aged 4 months to 55 years with SWS and brain involvement. The patients were retrospectively reviewed, looking at presence or absence of motor, cognitive, and behavioral concerns and need for orthoses, spasticity management, and therapy services.

Sturge-Weber syndrome: ear, nose, and throat issues and neurologic status.

Irving ND, Lim JH, Cohen B, Ferenc LM, Comi AM. Sturge-Weber syndrome: ear, nose, and throat issues and neurologic status. *Pediatr Neurol*. 2010;43(4):241-244. doi:10.1016/j.pediatrneurol.2010.05.010

This study determined what types of ENT issues most affect patients with SWS and identified symptoms and issues that should be screened for and evaluated in order to optimize neurologic outcome.

An infantile-onset, severe, yet sporadic seizure pattern is common in Sturge-Weber syndrome.

Kossoff EH, Ferenc L, Comi AM. An infantile-onset, severe, yet sporadic seizure pattern is common in Sturge-Weber syndrome. *Epilepsia*. 2009;50(9):2154-2157. doi:10.1111/j.1528-1167.2009.02072.x

The young age of onset and frequently intractable nature of seizures associated with SWS have been well-reported in large studies. However, many clinicians also anecdotally describe prolonged but sporadic seizure clusters. In this study, we analyzed data over a 5-year period from 77 children and adults with SWS in relation to sporadic seizure clusters. Sporadic seizure clusters were common and complicated the management of these patients.

Use of quantitative EEG in infants with port-wine birthmark to assess for Sturge-Weber brain involvement.

Ewen JB, Kossoff EH, Crone NE, et al. Use of quantitative EEG in infants with port-wine birthmark to assess for Sturge-Weber brain involvement. *Clin Neurophysiol*. 2009;120(8):1433-1440. doi:10.1016/j.clinph.2009.06.005

This was an observational study of qEEG results from eight infants with facial port-wine birthmarks (PWB) (four had SWS brain involvement). We recorded standard clinical EEGs and then derived a measure of asymmetry. This threshold was validated through a study of an additional nine infants with PWB (five with SWS brain involvement). Quantitative EEG was able to distinguish between those infants with and those without brain involvement and should be further developed as a biomarker for the early screening of SWS brain involvement in at-risk infants.

Hemiparesis is a clinical correlate of general adaptive dysfunction in children and adolescents with Sturge-Weber syndrome.

Reesman J, Gray R, Suskauer SJ, et al. Hemiparesis is a clinical correlate of general adaptive dysfunction in children and adolescents with Sturge-Weber syndrome. *J Child Neurol*. 2009;24(6):701-708. doi:10.1177/0883073808329529

This study sought to identify neurologic correlates of adaptive functioning in individuals with Sturge-Weber syndrome. Hemiparesis identified on neurologic exam correlated with the presence of impaired general adaptive dysfunction, suggesting that hemiparesis when noted on clinical exam should trigger neuropsychological evaluation to address more global functional needs.

Sturge-Weber syndrome with cerebellar involvement.

Smith Pearl M, Abdalla WM, Lin DD, et al. Sturge-Weber syndrome with cerebellar involvement. *J Neuroradiol*. 2009;36(1):57-60. doi:10.1016/j.neurad.2008.07.008

SWS typically presents with angiomas involving the face, ocular choroid, and ipsilateral supratentorial leptomeninges. Posterior fossa involvement is extremely rare. In this paper, we presented two patients with simultaneous supra- and infratentorial involvement. Magnetic resonance imaging (MRI) and digital subtracted angiography (DSA) findings are discussed. The importance of this study is that it highlights the occurrence of lesser-known cerebellar brain involvement in SWS so that this aspect is not overlooked in patients.

Central hypothyroidism and Sturge-Weber syndrome.

Comi AM, Bellamkonda S, Ferenc LM, Cohen BA, Germain-Lee EL. Central hypothyroidism and Sturge-Weber syndrome. *Pediatr Neurol*. 2008;39(1):58-62. doi:10.1016/j.pediatrneurol.2008.03.018

Previous investigations have revealed an increased prevalence of growth hormone deficiency in SWS patients, presumably secondary to involvement of the hypothalamic-pituitary axis. We have continued to screen for hormonal abnormalities in SWS patients, specifically from our multidisciplinary center for patients with this condition. In this paper, we describe 2 children with SWS and brain involvement who were evaluated and diagnosed with central hypothyroidism at our center based on clinical and laboratory findings. This paper stresses the need to test thyroid function in patients with SWS and treat deficiency if present. This problem had not been previously described in the context of SWS.

Transcranial Doppler ultrasound in children with Sturge-Weber syndrome.

Jordan LC, Wityk RJ, Dowling MM, DeJong MR, Comi AM. Transcranial Doppler ultrasound in children with Sturge-Weber syndrome. *J Child Neurol*. 2008;23(2):137-143. doi:10.1177/0883073807307079

Transcranial Doppler ultrasound is a noninvasive vascular assessment technique proved useful in the management of pediatric disorders predisposed to stroke, and may have similar utility for Sturge-Weber syndrome. Eight children with Sturge-Weber syndrome had velocities measured in the major cerebral arteries via the Stroke Prevention Trial in Sickle Cell Anemia methodology. Velocities and pulsatility indexes were compared between the unaffected and affected sides. All subjects had reduced velocity on the affected side; the mean middle cerebral artery percentage difference was 20% (95% CI, 15%-25%). Pulsatility index was increased on the affected side; mean middle cerebral artery pulsatility index percentage difference, 34% (95% CI, 15%-53%). Six subjects also had reduced posterior cerebral artery velocity on the affected side. Side-to-side differences in middle cerebral artery and posterior cerebral artery velocities correlated with severity of MRI asymmetry (Spearman rho = 0.88, P = .02). Decreased arterial flow velocity and increased pulsatility index in the middle cerebral artery and posterior cerebral artery suggests a high resistance pattern that may reflect venous stasis and may contribute to chronic hypoperfusion of brain tissue. Further study of Transcranial Doppler in children with Sturge-Weber syndrome is indicated. Overall, this research found that Transcranial Doppler is a safe way to measure blood flow abnormalities in SWS, suggesting that it may be useful for tracking response to treatment in a clinical trial or monitoring progression in SWS.

Quantitative EEG asymmetry correlates with clinical severity in unilateral Sturge-Weber syndrome.

Hatfield LA, Crone NE, Kossoff EH, et al. Quantitative EEG asymmetry correlates with clinical severity in unilateral Sturge-Weber syndrome. *Epilepsia*. 2007;48(1):191-195. doi:10.1111/j.1528-1167.2006.00630.x

This research found that decreased power by quantitative EEG (qEEG) analysis on the affected brain side of patients with SWS correlated with the severity of neurologic involvement. These findings indicated that qEEG was likely to be useful for the early diagnosis of SWS and for monitoring progression and treatment response in a clinical trial. qEEG provides an objective measure of EEG asymmetry that correlates with clinical status and brain asymmetry seen on MRI. These findings support the conclusion that qEEG reflects the degree and extent of brain involvement and dysfunction in SWS.

Sturge-Weber syndrome and epilepsy: an argument for aggressive seizure management in these patients.

Comi AM. Sturge-Weber syndrome and epilepsy: an argument for aggressive seizure management in these patients. *Expert Rev Neurother*. 2007;7(8):951-956. doi:10.1586/14737175.7.8.951

Based on available literature, our research, and our clinical experience, this paper argues that early aggressive seizure management is important to the long-term neurodevelopmental outcome in SWS. Several controversies exist in the management of seizures and other neurologic impairments in SWS.

Continued efforts are needed to develop a multicentered network for SWS clinical trials. This paper emphasizes that future research should be focused on this goal and on studies to improve our understanding of the causes and molecular neuropathology of SWS.

Self-reported treatment patterns in patients with Sturge-Weber syndrome and migraines.

Kossoff EH, Balasta M, Hatfield LM, Lehmann CU, Comi AM. Self-reported treatment patterns in patients with Sturge-Weber syndrome and migraines. *J Child Neurol*. 2007;22(6):720-726. doi:10.1177/0883073807304008

Migraines are common in patients with SWS, yet treatment options are poorly described. In this study, an internet-based questionnaire was completed anonymously by 104 SWS patients, 74 of whom reported experiencing migraines. SWS patients with migraines were found to be using triptans and preventative agents, and self-reporting good efficacy. This research highlighted several important findings, including the underuse of migraine prophylactic medications and the safe effective use of triptans for migraines in some patients with SWS.

Update on Sturge-Weber syndrome: diagnosis, treatment, quantitative measures, and controversies.

Comi AM. Update on Sturge-Weber syndrome: diagnosis, treatment, quantitative measures, and controversies. *Lymphat Res Biol*. 2007;5(4):257-264. doi:10.1089/lrb.2007.1016

This review summarizes the recent and evolving literature on current and needed tools for diagnosis and monitoring of SWS and treatment trends, and highlighted key research questions and directions. Recent advances in neuroimaging have provided important insights into the progression of neurologic injury that occurs because of impaired blood flow. Important limitations exist, however, as currently the early diagnosis and exclusion of SWS is impaired by the poor sensitivity of imaging in the newborn period and early infancy. Several important controversies complicate our ability to care for these patients, and include the questions of ideal timing of surgery, whether seizures themselves contribute to the neurologic injury, and what the role of low-dose aspirin should be. This review summarizes several recent advances in our understanding of the mechanisms of brain injury in SWS, new measures for quantifying neurologic involvement, and new approaches and controversies in the management of the neurologic complications.

Myoclonic-astatic epilepsy in a child with Sturge-Weber syndrome.

Ewen JB, Comi AM, Kossoff EH. Myoclonic-astatic epilepsy in a child with Sturge-Weber syndrome. *Pediatr Neurol*. 2007;36(2):115-117. doi:10.1016/j.pediatrneurol.2006.08.006

This paper highlights the importance of being aware that patients with SWS can have generalized drop seizures that worsen with some anticonvulsants and need to be properly diagnosed with EEG and properly treated with an anticonvulsant that covers both focal and generalized seizures. This describes a case of a child with SWS and left occipital leptomeningeal angioma who developed focal seizures at 6 years old. The child responded initially to oxcarbazepine, but after 7 months of seizure freedom,

developed typical myoclonic-astatic seizures associated with generalized electrographic discharges that worsened as oxcarbazepine was increased. The seizures and electroencephalogram improved dramatically in 3 weeks as the oxcarbazepine was withdrawn and valproic acid was initiated. This case demonstrates the importance of recognizing that children with epilepsy due to focal lesions can develop secondary bilateral synchrony which can be aggravated by medications that are effective for partial seizures. In such cases, treatment with a broad-spectrum antiepileptic may be advantageous.

Oromaxillofacial osseous abnormality in Sturge-Weber syndrome: case report and review of the literature.

Lin DD, Gailloud P, McCarthy EF, Comi AM. Oromaxillofacial osseous abnormality in Sturge-Weber syndrome: case report and review of the literature. *AJNR Am J Neuroradiol*. 2006;27(2):274-277.

This paper reported an unusual bony tumor of the upper jaw associated with SWS so that if this situation occurs again, doctors know how to approach it. We reported a case of a 17-month-old child affected by SWS who had unusually rapid overgrowth of the left frontal, temporal, orbital, and maxillary regions. CT angiography illustrated osteohypertrophy with periostitis and associated soft tissue hypertrophy directly corresponding to the distribution of the cutaneous port-wine stain. Extended maxillectomy was performed because of rapid growth and clinical debilitation, with surgical pathology revealing juvenile ossifying fibroma.

Advances in Sturge-Weber syndrome.

Comi AM. Advances in Sturge-Weber syndrome. *Curr Opin Neurol*. 2006;19(2):124-128. doi:10.1097/01.wco.0000218226.27937.57

This review article summarizes recent advances in diagnosis and treatment of SWS. New magnetic resonance sequences may be useful for the early diagnosis of SWS, and perfusion magnetic resonance imaging, single photon emission computed tomography imaging, and positron emission tomography imaging studies are suggesting that decreased brain blood flow combined with altered hemodynamics during prolonged seizures may contribute to the neurologic declines in SWS.

Growth hormone deficiency in Sturge-Weber syndrome.

Miller RS, Ball KL, Comi AM, Germain-Lee EL. Growth hormone deficiency in Sturge-Weber syndrome. *Arch Dis Child*. 2006;91(4):340-341. doi:10.1136/adc.2005.082578

This research demonstrated for the first time that growth hormone deficiency occurs in SWS with higher prevalence compared to the general population and requires treatment. Records of 19 patients with suspected growth hormone deficiency, identified from a registry of 1,653 patients with SWS, were reviewed. It was found that 9 patients had growth hormone deficiency.

Dynamic MR perfusion and proton MR spectroscopic imaging in Sturge-Weber syndrome: correlation with neurological symptoms.

Lin DD, Barker PB, Hatfield LA, Comi AM. Dynamic MR perfusion and proton MR spectroscopic imaging in Sturge-Weber syndrome: correlation with neurological symptoms. *J Magn Reson Imaging*. 2006;24(2):274-281. doi:10.1002/jmri.20627

This work demonstrated that perfusion MR deficits correlate with the severity of neurologic impairment in SWS, indicating that it will likely be useful for tracking response to treatment in a clinical trial and neurologic progression. In this study, six consecutive patients with diagnosed SWS underwent MRI using a 1.5 Tesla scanner. A pediatric neurologist evaluated the neurological scores, and the imaging results were correlated with neurological scores using nonparametric correlation analysis. In SWS, MR perfusion imaging indicates cerebral hypoperfusion predominantly due to impaired venous drainage, with only the most severely affected regions in some patients also showing arterial perfusion deficiency. The extent and severity of the perfusion abnormality and neuronal loss/dysfunction reflect the severity of neurological symptoms and disability. These parameters may be useful as quantitative measures of disease burden; however, further studies in larger numbers of patients are required to confirm the preliminary findings reported in this study.

Quantitative analysis of cerebral cortical atrophy and correlation with clinical severity in unilateral Sturge-Weber syndrome.

Kelley TM, Hatfield LA, Lin DD, Comi AM. Quantitative analysis of cerebral cortical atrophy and correlation with clinical severity in unilateral Sturge-Weber syndrome. *J Child Neurol*. 2005;20(11):867-870. doi:10.1177/08830738050200110201

This study validated the new SWS neuroscore against measurements of brain atrophy, indicating that the SWS neuroscore should be useful for research and as an outcome measure for clinical trials. In this study, 18 subjects with unilateral SWS received a neurologic examination and submitted previous magnetic resonance imaging (MRI) films. A blinded investigator assigned clinical severity scores based on seizures, hemiparesis, visual field cut, and cognitive impairments. Computer-aided analysis of MRIs produced laterality scores for cortical volume asymmetry. A significant relationship existed between clinical severity and laterality scores (Spearman's rho = -0.804; $P < .001$). Laterality scores also correlated well with hemiparesis subscores and weakly with cognitive impairment subscores (Kendall’s tau b; $P < .05$). Using this simple, computer-aided analysis, cortical volume asymmetry correlated with clinical status. This method offers the advantages of relative simplicity, objectivity, and wide applicability to films from outside institutions, as would be encountered in clinical practice.

Sturge-Weber syndrome associated with other abnormalities: a medical record and literature.

Comi AM, Mehta P, Hatfield LA, Dowling MM. Sturge-Weber syndrome associated with other abnormalities: a medical record and literature review. *Arch Neurol*. 2005;62(12):1924-1927. doi:10.1001/archneur.62.12.1924

This paper reported a series of patients with SWS and other malformations, tumors, or abnormal conditions. This information was used to search databases and suggest a gene locus that may have some role in the etiology of SWS. Medical records of 28 SWS patients were retrospectively reviewed, noting main features of SWS and accompanying unexpected abnormalities. A literature review was also conducted of abnormalities associated with SWS. In this paper, we proposed that some patients with SWS may have disorders of cholesterol biosynthesis or carbohydrate glycosylation.

Sturge-Weber syndrome: altered blood vessel fibronectin expression and morphology.

Comi AM, Weisz CJ, Highet BH, Skolasky RL, Pardo CA, Hess EJ. Sturge-Weber syndrome: altered blood vessel fibronectin expression and morphology. *J Child Neurol*. 2005;20(7):572-577. doi:10.1177/08830738050200070601

This research studied how the extracellular matrix molecule fibronectin is expressed in the brain and skin tissue of individuals with SWS. It showed evidence of abnormal expression in the brain. Fibronectin has important roles in the blood-brain barrier, in blood vessel function, and in the innervation of blood vessels. This paper discusses new hypotheses regarding the pathogenesis of SWS.

Comorbidity of epilepsy and headache in patients with Sturge-Weber syndrome.

Kossoff EH, Hatfield LA, Ball KL, Comi AM. Comorbidity of epilepsy and headache in patients with Sturge-Weber syndrome. *J Child Neurol*. 2005;20(8):678-682. doi:10.1177/08830738050200080901

This research showed that in older children and adults with SWS, headaches are an important and undertreated neurologic problem requiring additional study and new treatment options. A questionnaire was mailed to 190 patients with reported comorbid epilepsy and headache as identified by the Sturge-Weber Foundation. The median age at headache onset was 8 years, with a median of three headaches per month. Fifty-eight percent felt that headaches were an equal or greater problem. Ibuprofen and acetaminophen were the most frequently tried abortive medications; 22% had tried sumatriptan. Only 22% reported a neurologist suggesting the use of an anticonvulsant as a preventive agent. Subjects with a family history of headaches had an earlier age at headache onset (7.5 vs 11 years; P = .02), and those with a family history of seizures were more likely to report behavior problems (69% vs 33%; P = .02). Subjects reporting learning problems or hemiparesis had an earlier age at seizure onset. Migraine-like headaches can be as significant a problem as epilepsy for patients with SWS. Despite this, triptans and prophylactic medications (including anticonvulsants) were used in less than half of the patients. Correlations of family history with both age at symptom onset and behavior problems suggest that genetic substrate could be one factor determining the variable neurologic manifestations seen in Sturge-Weber syndrome.

Early characteristics of Sturge-Weber syndrome shown by perfusion MR imaging and proton MR spectroscopy imaging.

Lin DD, Barker PB, Kraut MA, Comi A. Early characteristics of Sturge-Weber syndrome shown by perfusion MR imaging and proton MR spectroscopic imaging. *AJNR Am J Neuroradiol*. 2003;24(9):1912-1915.

This research reported on the new MR perfusion imaging showing in SWS that the abnormal vasculature results in severely impaired venous drainage from the involved region, resulting in arterial perfusion deficits in that region. This paper reported the case of a 9-month-old boy with SWS and new onset of seizures. Perfusion MR imaging showed early changes compatible with impaired venous drainage in the affected hemisphere, whereas proton MR spectroscopic imaging revealed a focal parietal area of elevated choline without significant alteration of N-acetylaspartate levels. The perfusion and subtle metabolic abnormalities are comparable with the extent of the overlying leptomeningeal enhancement, illustrating the early pathophysiological manifestation of this disease.