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Quality of Life in Children With Sturge-Weber Syndrome

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Abstract

Aim: 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, a rare neurovascular disorder which frequently results in seizures, brain atrophy, calcification, and a range of neurological impairments.

Methods: Subjects were seen clinically and consented for research. All 22 patients filled out the Pediatric Neuro-QoL. The Neuro-QoL subscores were converted to T-scores to compare with the referenced control population. Twenty-one participants also filled out the Brain Vascular Malformation Consortium Database Questionnaire containing data pertaining to Sturge-Weber syndromeerelated medical history, medications, comorbidities, and family history. All data were analyzed with a significance threshold of $P < 0.05$.

Results: Cognitive function quality of life was significantly lower ($P < 0.001$) in pediatric patients with Sturge-Weber syndrome compared with referenced control subjects. Male gender ($P = 0.02$) was associated with lower cognitive function Neuro-QoL. The extent of skin ($R = -0.46$, $P = 0.04$), total eyelid port-wine birthmark ($R = -0.56$, $P = 0.007$), eye ($R = -0.58$, $P = 0.005$), and total Sturge-Weber syndrome involvement ($R = -0.63$, $P = 0.002$) were negatively correlated with cognitive function NeuroQoL. A younger age at seizure onset was associated with lower cognitive function Neuro-QoL (hazard ratio = 0.90, $P = 0.004$) even after controlling for extent of brain, skin, or eye involvement. Antidepressant use was associated with lower cognitive function Neuro-

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QoL ($P = 0.005$), and cognitive function Neuro-QoL was negatively correlated with depression Neuro-QoL; however, after adjusting for depression this relationship was no longer significant.

Conclusions: The results suggest 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.

Keywords

Sturge-Weber syndrome; Port-wine birthmark; Vascular malformation; Leptomeningeal enhancement; G protein subunit alpha q; National Institutes of Health Toolbox; Quality of life in neurological disorders

Introduction

Sturge-Weber syndrome (SWS) is a rare neurocutaneous disorder, characterized by vascular malformations in the brain, skin, and eye, that affects about one in 20,000 to 50,000 individuals. SWS exists as a spectrum disorder, ranging from isolated brain or eye involvement to skin, eye, and brain involvement. Most patients present with the facial capillary malformation (port-wine birthmark [PWB]) in combination with leptomeningeal capillary malformation. Patients with SWS may present with the following symptomology: seizures, strokes or stroke-like episodes, headaches, migraines, cognitive disability, attention problems, and glaucoma. A somatic nonsynonymous mutation in G protein subunit alpha q has been identified in both SWS-related and isolated PWBs alike.[1] The G protein subunit alpha q mutation may result in endothelial dysfunction, potentially bringing about the vascular remodeling found in SWS. Given the varying extents of involvement, it is hypothesized that the extent of involvement results from when the mutation arises in embryonic development.

Published prospective and retrospective drug studies in SWS have used seizure frequency, magnetic resonance imaging (MRI) score, PWB score, and neurological score as outcome measures. However, the importance of assessing quality of life changes, both in terms of the impact of the disease process itself and in response to treatment, is increasingly being recognized; a 2018 consensus article identified the need for measures of quality of life in the research and clinical care of patients with SWS.[2] One previously published prospective drug trial in SWS assessed global "quality of life" using a Likert scale; however, a more detailed assessment of the impact of SWS on quality of life would be useful.

The goal of this study was to assess utilization of the National Institutes of Health's (NIH) Pediatric Quality of Life in Nurological Disorders (Neuro-QoL) measure in patients with SWS. The primary aim of the Neuro-QoL was to standardize how studies assess the physical, mental, and social well-being of children with neurological conditions.[3] The pediatric Neuro-QoL has been used in research studying the effects of epilepsy, muscular dystrophy, and traumatic brain injury on children.[4–6] By providing a standardized assessment of quality of life of patients with SWS, providers can better address patients' needs and clinical trials can target outcomes important to patients and their families.[7]

Subjects and methods

Subjects for this study were seen clinically at three centers in the Brain Vascular Malformation Consortium (BVMC): the Kennedy Krieger Institute, Cincinnati Children's Hospital Medical Center, and Boston Children's Hospital. The BVMC is a part of the NIH Rare Diseases Clinical Research Network (RDCRN). The Johns Hopkins Institutional Review Board (IRB), each sites' local IRBs, and the NIH approved this study. For the RDCRN, the NIH reviews and approves the protocol before submission to the IRB to ensure it corresponds to the main grant and to also review for scientific purposes. All subjects provided informed consent. The inclusion criterion for these aims of the BVMC protocol was the presence of SWS brain involvement, as confirmed by the review of contrast-enhanced brain MRI.

The Neuro-QoL questionnaire is provided by the NIH Toolbox. The question sets vary by age; there is a pediatric-specific form for patients aged between 8 and 18 years (Appendix 1). The pediatric Neuro-QoL contains sets of questions related to the following areas: anger, anxiety, pain, social relations, stigma, depression, cognitive function, and fatigue. Study staff was available to help with questions.

The raters at each site prospectively evaluated the neurological severity in each patient during routine clinical visits. The neurological severity was evaluated using a previously published scale, which contains scoring for the severity of seizures, hemiparesis, visual field cut, and cognitive function, for a total score of up to 15 (Appendix 2).[8] Each age group (infant and preschool, child, and adult) contains variations in the scoring system.

Similarly, the raters evaluated the PWB severity in each patient during routine clinical visits. The extent of the PWB was evaluated using a previously published scale.[9] The provider scored the PWB for extent and severity (color, hypertrophy, and blebbing) for a total score of up to 37 (Appendix 3).

The BVMC Database Questionnaire was completed by 21 of the 22 pediatric participants. The questionnaire included data related to seizure onset, comorbidities, family history, medications, and laterality of brain, skin, and eye involvement (Appendix 4). For the participant that did not complete the questionnaire, study staff completed a medical record review to obtain brain involvement and medications data. Of note, the questionnaire included a question asking whether the child displayed a PWB involving the first division of the trigeminal nerve (V1 distribution), defined as the forehead and eyelid region. We will use the term "upper face" rather than V1 distribution to reflect more recent understanding of the pathogenesis of SWS in relation to embryonic vasculature of the face.[10]

Both the Neuro-QoL and the BVMC Database Questionnaire were filled out by the patient alone, by the patient with the help of a parent, or by the parent alone. For the participant that did not complete the BVMC Database Questionnaire, study staff completed a medical record review to obtain brain involvement and medications data.

Laterality of brain, skin, and eye involvement was obtained from the BVMC Database Questionnaire for the 21 participants that completed it. Involvement was scored in the

following manner: 0 for no involvement, 1 for unilateral involvement, and 2 for bilateral involvement. The study's inclusion criteria required participants to have brain involvement; therefore total SWS involvement scores ranged from 1 (unilateral brain involvement only) to 6 (bilateral skin, eye, and brain involvement) (Appendix 5).

Given the disparity between the age at BVMC Database Questionnaire completion and age at Neuro-QoL completion among some patients, study staff completed a record review to update medication, eye involvement, and brain involvement (unilateral, bilateral, side, and lobe of involvement) data from the questionnaire. Study staff updated eye involvement through a record analysis of glaucoma medication use or reference to the presence of glaucoma, glaucoma surgery, or eye involvement in neurology or ophthalmology clinic notes. Self-reported laterality of brain involvement was also verified by study staff with MRI source documentation (contrast-enhanced MRI discs or reports), as required for enrollment. This neuroimaging review was done without knowing about Neuro-QoL scores.

All the data obtained were uploaded into the RDCRN database by study staff at their respective sites. Data were cleaned by the University of California San Francisco and the Kennedy Krieger Institute in cooperation with the participating sites to detect and correct any inaccurate or incomplete data points using source documentation, clinic notes, and patient contact, if necessary.

Statistical methods

To analyze the Neuro-QoL data, the raw scores for each section of the questionnaire were transformed to a T-score as described in the National Institute of Neurological Disorders and Stroke User Manual. These T-score distributions rescale raw scores to standardized scores with a mean of 50 and a standard deviation (S.D.) of 10; therefore if a person has a T-score of 60, their score is one S.D. above the average of the referenced populations. For pediatric participants, a general reference population was used for all measures except stigma and pain. These measures were referenced against a clinical population that consisted of children diagnosed with neurological disorders, such as epilepsy and muscular dystrophy. As a note, a higher T-score represents more of the concept being measured. For example, if the patient has a T-score for cognitive function Neuro-QoL measurement that is greater than 50, then they reported a higher cognitive function quality of life.

All data were analyzed using SPSS (Statistical Package for Social Sciences) Version 25 (SPSS Inc, Chicago, IL, USA). To compare the Neuro-QoL subscores' T-scores to the mean of 50 from the reported control subjects, a *t* test was used. For the correlations between extent of skin, eye, and total SWS involvement and cognitive function Neuro-QoL, a Spearman's correlation was used. For age at seizure onset (a time-to-event variable), a Cox regression was used to assess associations (hazard ratio). A Cox regression was used to assess the association of the hazard rate of seizure onset with Neuro QoL both unadjusted and adjusted for forms of SWS involvement. A linear regression was used to assess the association of antidepressant use and cognitive function Neuro-QoL after adjusting for depression Neuro-QoL. A confidence interval was reported for this measure. For any remaining associations (e.g., upper face PWB distribution versus cognitive function Neuro-QoL), Mann-Whitney *U* test was used. The significance level for all analyses was $P < 0.05$.

Results

The population consisted of 10 males (45.45%) and 12 females (54.54%). The median age of the set at time of Neuro-QoL completion was 12.64 years with a range of 8.76 to 17.49 years (Table 1). The participants included 14 White (66.64%), three Black or African American (13.64%), two Asian (9.09%), and three with two or more races (13.64%). One (4.55%) of the participants reported an ethnicity of Hispanic, Latino, or Spanish origin. On the basis of the 2010 United States census, this distribution is similar to that of the US population.

At the time of Neuro-QoL completion, the patients were taking between 0 and 3 antiepileptic drugs (AEDs) (Table 1). The most common AED used by the patients was oxcarbazepine (59.09%). The next most common AED used was levetiracetam (31.82%). Six (27.27%) patients took one AED, six (27.27%) took two AEDs, five (22.73%) took three AEDs, and five (22.73%) took 0 AEDs (one underwent hemispherectomy allowing him to wean off AEDs, two weaned off AEDs after several years of seizure freedom, one never experienced seizure onset, and one had only one seizure in medical history and was never on AEDs).

Neuro-QoL domains

Neuro-QoL is plotted in Fig 1. The results for most of the Neuro QoL domains were similar to the referenced control populations. However, the cognitive function Neuro-QoL subscale was significantly lower (mean T-score 40.62 ± 7.77; $P < 0.001$) in the SWS pediatric population compared with the referenced control population; therefore further analyses focused on this measure. A trend for increased anger quality of life (more anger) was noted (mean T-score 53.36 ± 7.69; $P = 0.05$).

Gender

Male gender was associated with lower cognitive function Neuro-QoL (mean T-score 36.62 ± 6.51 for males versus 43.95 ± 7.34 for females; $P = 0.02$) (see Fig 2). Male gender was also associated with a greater extent of glaucoma (median 1, range of 0 to 2 in males versus median 0, range 0 to 1 in females; $P = 0.03$) and a greater extent of total SWS involvement (median 4, range 1 to 5 in males versus median 2, range 1 to 5 in females; $P = 0.03$); however, there was no difference between genders in the extent of skin and brain involvement. There were trends noted among male gender with increased cognitive function subscore of their neuroscores (median 3, range 1 to 3 in males versus median 2, range 0 to 3 in females; $P = 0.07$) and increased total neuroscores (median 5.5, range 3 to 9 in males versus median 4, range 0 to 7 in females; $P = 0.06$).

Extent of Total SWS, Brain, Skin, and Eye Involvement

The extent of total SWS involvement negatively correlated with cognitive function Neuro-QoL (see Table 2; $R = -0.63$, $P = 0.002$). The extent of the PWB negatively correlated with cognitive function Neuro-QoL (see Table 2; $R = -0.46$, $P = 0.04$). In particular, the presence of an upper face PWB distribution was associated with a lower cognitive function Neuro-QoL (mean T-score of 47.35 ± 2.29 in those without an upper face PWB distribution versus

39.25 ± 8.00 in those with an upper face PWB distribution; $P = 0.03$). Total eyelid involvement ($R = -0.56$, $P = 0.007$) and the extent of eye involvement (see Table 2; $R = -0.58$, $P = 0.005$) correlated with lower cognitive function Neuro-QoL. The presence of glaucoma was associated with lower cognitive function NeuroQoL (mean T-score of 44.98 ± 6.42 in those without glaucoma versus 36.98 ± 7.39 in those with glaucoma; $P = 0.02$).

Age at seizure onset

In a Cox regression survival analysis, a younger age at seizure onset was associated with a lower cognitive function Neuro-QoL (hazard ratio = 0.90, $P = 0.004$) (see Fig 3). The association between cognitive function Neuro-QoL and age at seizure onset remains significant after adjusting for differences because of the extent of skin ($P = 0.006$), eye ($P = 0.03$), brain ($P = 0.008$), or total SWS involvement ($P = 0.02$).

Medications

Antidepressant use was associated with lower cognitive function Neuro-QoL (mean T-score 32.86 ± 5.84 in those taking antidepressants versus 42.90 ± 6.80 in those not taking antidepressants; $P = 0.01$). This association did not control for differences between the groups on antidepressants and off antidepressants. The group on antidepressants exhibited an earlier age at seizure onset (median age 0.21 years, range 0.17 to 1.50 years in those taking antidepressants versus median age 1.13 years, range 0.33 to 16.92 years in those not taking antidepressants; $P = 0.04$) and an increased extent of glaucoma involvement (median 1, range 1 to 2 in those taking antidepressants versus median 0, range 0 to 2 in those not taking antidepressants; $P = 0.03$). There were no significant differences between the groups of patients on antidepressants and off antidepressants in terms of extent of skin, brain, and total involvement. Cognitive function Neuro-QoL was negatively correlated with depression Neuro-QoL ($R = -0.594$, $P = 0.004$). After adjusting for depression Neuro-QoL, antidepressant use was not significantly associated with cognitive function Neuro-QoL (95% confidence interval −12.13 to 5.93, $P = 0.5$).

Other analyses

No disorders indicated in the comorbidities or family history sections of the BVMC Database Questionnaire were significantly associated with the cognitive Neuro-QoL. None of the neuroscore domains were significantly correlated with the cognitive function Neuro-QoL measure.

Discussion

This is the first study to measure quality of life outcome measures in SWS. Understanding which quality of life domains are most impacted is important because it provides both targets and outcome measures for future treatment trials. Intellectual disability is present in about one-half of all patients with SWS.[7,11,12] The presence of epilepsy alone in patients with SWS has been shown to negatively affect neurocognitive status.[13–15] The cognitive function Neuro-QoL measure was significantly lower in the SWS pediatric population compared with the referenced control population. The cognitive function quality of life

measure is likely to be useful for clinical monitoring and for future clinical trial outcome measurement.

Within the SWS pediatric population, males were significantly more likely than females to report lower cognitive function Neuro-QoL. The largest study on SWS to date found that males with SWS that experienced seizure onset at age less than or equal to 6 months were more likely to experience stroke-like episodes.[16] Sex-related differences have been extensively studied outside the SWS literature. In terms of stroke, males are more likely to experience ischemic episodes at a younger age.[17–20] Males have a higher incidence of epilepsy and an increased lifetime risk of developing epilepsy.[21–23] Furthermore, males with epilepsy are at an increased risk of premature death, including sudden unexpected death in epilepsy.[24–27] In addition, quality of life studies in adults have demonstrated sex-related differences after stroke and in epilepsy.[28,29] Sex-related differences in quality of life in SWS require further study to confirm this difference and to determine its cause.

Greater extent of total SWS involvement correlated with lower cognitive function quality of life. It is hypothesized that the greater the extent of SWS involvement, the earlier the somatic mutation likely occurred in fetal development. The earlier the somatic mutation occurs, the earlier the mutant progenitor and the more cell types likely to be impacted by the somatic mutation. These data provide some support for this hypothesis, but it requires an animal model or tissue studies for further investigation.

In the general SWS population, roughly 86% present with unilateral brain involvement and 14% present with bilateral.[30] In this study, the breakdown of unilateral and bilateral brain involvement is relatively similar. It is hypothesized that cognitive deficits occur as a result of the underlying SWS pathophysiology: abnormal vascular function, response to seizures, and impaired cerebral blood flow, leading to brain injury, atrophy, and calcification. Patients with bilateral SWS brain involvement experience worse cognitive outcomes than those with unilateral involvement.[30–33]

Of those diagnosed with SWS brain involvement, about 5.5% to 7% typically present with no PWBs, 63% with unilateral, and 31% with bilateral.[11,34] In this study, there are a greater proportion of participants with no PWBs and relatively similar numbers with unilateral and bilateral PWB involvement. A greater extent of the PWBs correlated with lower cognitive function Neuro-QoL. In addition, an upper face PWB distribution was associated with lower cognitive function Neuro-QoL. As noted widely in the SWS literature, the greater the size of the PWB, especially with respect to an upper facial distribution, the greater the likelihood of SWS brain involvement diagnosis.[10,35–38] In this study, a greater eyelid involvement correlated with lower cognitive function Neuro-QoL. A positive correlation between upper eyelid involvement and extent of brain involvement has been described in the SWS literature[36,37] Glaucoma has been reported in 30% to 70% of patients with SWS.[30] The number of participants in this study with unilateral or bilateral glaucoma falls in the middle of that range. An increased glaucoma extent also correlated with lower cognitive function Neuro-QoL as well. As children age, visual demands in school escalate; therefore the presence of glaucoma may interfere with their ability to read and learn.[39] In a study of 1154 adults with glaucoma, spoken reading speed was significantly lower in patients with bilateral

glaucoma with advanced field loss.[40] Although the correlation between glaucoma extent and cognitive function Neuro-QoL has not yet been reported in the SWS literature, abnormal imaging, defined as the presence of leptomeningeal angiomatosis on MRI, has been shown to be a predictor for increased glaucoma risk.[10]

Neurological presentation in the form of seizures typically presents in 85% of patients with SWS. In particular, seizure onset occurs by age 1 year in 75%, by 2 years in 86%, and by 5 years in 95% of patients with SWS who have seizures.[7,31] On average, participants in this study experienced seizure onset later; the median age at seizure onset was 1.00 years with a range of 0.17 to 16.92 years. A younger age at seizure onset was associated with a poorer cognitive function Neuro-QoL in the study set. This association remained significant even after adjusting for differences because of the extent of skin, eye, brain, or total SWS involvement. It is generally accepted that an earlier onset of seizures in SWS confers a worse neurological and developmental prognosis.[13,31,41–44] Early seizure onset can also have a particularly profound negative effect on the intelligence quotient as well.[13,44] In a small neuropsychological case study of four patients with SWS, little to no seizure activity was associated with preserved cognitive function.[32] Given that the patient population experienced later ages at seizure onset overall compared with what is reported in the literature for patients with SWS, one would expect that typical population of patients with SWS would report an even lower level of cognitive function Neuro-QoL.

Antidepressant use was associated with lower cognitive function quality of life, and depression quality of life was negatively correlated with cognitive function quality of life. Those on antidepressants reported an earlier age at seizure onset and an increased extent of glaucoma, although there were no significant differences between the groups in terms of extent of skin, brain, and total SWS involvement. However, given that antidepressant use was not significantly associated with cognitive function Neuro-QoL after adjusting for depression Neuro-QoL, we do not have any evidence that antidepressant use per se negatively affects cognitive function quality of life. The lowered cognitive function Neuro-QoL in subjects on antidepressants may have occurred as a result of the underlying mood disorder rather than the medications; alternatively, we can hypothesize that early seizures may increase the risk of both depression and cognitive dysfunction. Given these confounds, further study is required to ascertain the relationship between antidepressants use and cognitive function.

Limitations

SWS is a rare disorder and therefore the number of subjects in this study limits its power and the conclusions that can be derived. A larger longitudinal study may demonstrate other helpful quality of life measures or demonstrate that measures change over time. Given that SWS is defined as a spectrum disorder, there is a high degree of phenotypic variation among patients. There are a wide range of symptoms associated with SWS and with the low prevalence rate of SWS in the general population; it is difficult to assemble a cohort of patients with similar manifestations. Although the subjects were limited to those with confirmed brain involvement, participation was not limited on the basis of other SWS characteristics, such as the presence of a PWB.

In addition, given that a number of the participants are rather young or have some degree of cognitive impairments, the parents of the participants either assisted them in filling the questionnaire out or filled the questionnaire out for them. In these cases, the scores reflect the perception of cognitive function Neuro-QoL of parents rather than the subjects. Several neuropsychological tests also assess parental perception. This limitation is inherent in any quality of life measure used in young children or patients with cognitive impairments and should be further evaluated with future larger studies with tools that also objectively measure cognition. Neuropsychological testing quantitatively assesses function, whereas the Neuro-QoL focuses more on the impact of functional impairments on quality of life. It is meant to be complementary to quantitative measures of function, rather than a replacement for neuropsychological testing, and future studies should consider including both.

Conclusions

These data summarize the first study of the NIH's Neuro-QoL measure in patients with SWS. The results suggest targeting cognitive function Neuro-QoL in treatment trials and reiterate the prognostic value of early seizure onset. As in this study, the Neuro-QoL measurement may prove useful for assessing the quality of life in patients with SWS across clinical settings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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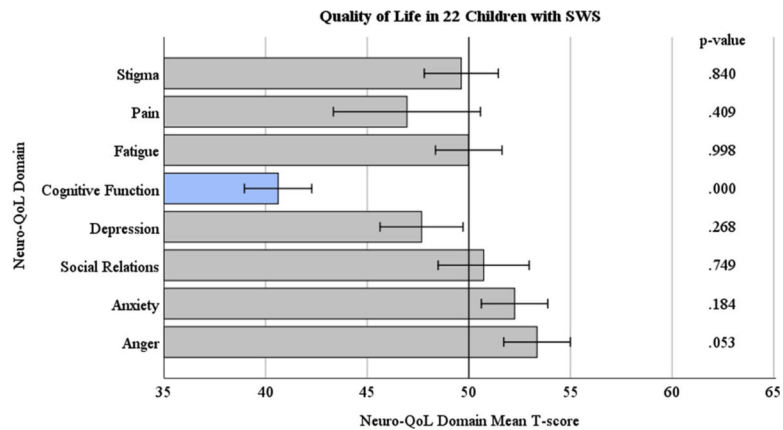
Quality of Life in 22 Children with SWS

FIGURE 1.
Neuro-QoL T-scores and standard error bars for pediatric patients with SWS in various domains. A higher T-score represents more of the concept being measured, and they are standardized to have a standard deviation of 10 with 50 representing the mean value in the reference population (see text for description). P values compare the mean value in the patients with SWS with the mean in the reference population. In pediatric patients with SWS, cognitive function Neuro-QoL is significantly lower compared with referenced control subjects. Neuro-QoL, quality of life in neurological disorders; SWS, Sturge-Weber syndrome. The color version of this figure is available in the online edition.
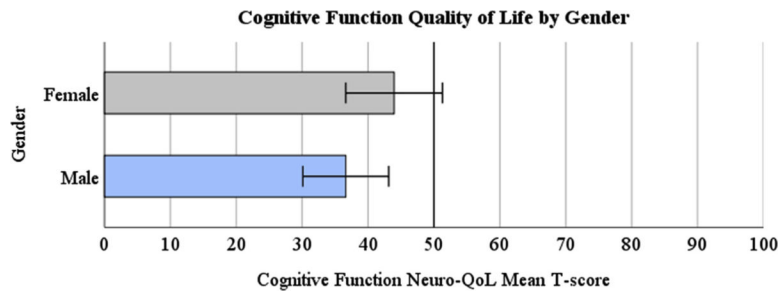
FIGURE 2.
Cognitive function Neuro-QoL domain T-scores and standard error bars for pediatric patients with SWS by gender. A higher T-score represents more cognitive function Neuro-QoL, and it is standardized to have a standard deviation of 10 with 50 representing the mean value in the reference population (see text for description). The P value compares the mean value in the male patients with SWS with the mean in the female patients with SWS. In pediatric patients with SWS, cognitive function NeuroQoL is significantly lower in males compared with females. Neuro-QoL, quality of life in neurological disorders; SWS, Sturge-Weber syndrome. The color version of this figure is available in the online edition.

Cognitive Function Quality of Life by Age at Seizure Onset

FIGURE 3.

Cognitive function Neuro-QoL domain T-scores for pediatric patients with SWS by age at seizure onset (in years). A higher T-score represents more cognitive function Neuro-QoL, and it is standardized to have a standard deviation of 10 with 50 representing the mean value in the reference population (see text for description). In pediatric patients with SWS, an earlier age at seizure onset is associated with lower cognitive function Neuro-QoL. Neuro-QoL, quality of life in neurological disorders; SWS, Sturge-Weber syndrome. The color version of this figure is available in the online edition.
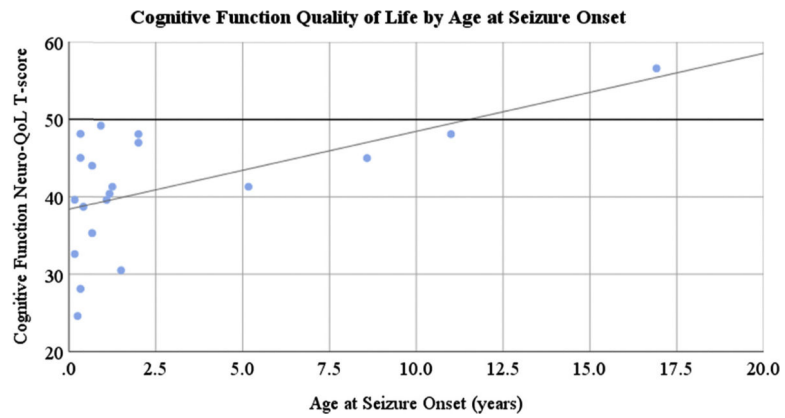
TABLE 1.

Demographics and Clinical Data of 22 Children With Sturge-Weber Syndrome

No.	Sex	Race	Ethnicity	Age at Neuro-QoL	Cog. Fxn. Neuro-QoL	Age at Seizure Onset	Extent of BI	AEDs
1	F (female)	2	2	8.76	41.3	5.17	L FTPO	CLB, LEV
2	M (male)	2, 3, 5	2	10.23	28.1	0.33	L TPO, R O	LEV, OXC
3	M	5	2	10.62	39.6	0.17	L FTPO	None[*]
4	F	5	2	10.95	39.6	1.08	R FTPO	LCM, LEV, OXC
5	M	5	2	11.27	24.6	0.25	L TPO	CLB, LTG, TPM
6	M	5	2	11.79	38.7	0.42	R TPO	LEV, VPA, OXC
7	F	5	2	11.98	41.3	1.25	L FTPO	OXC
8	M	3	2	12.22	45	8.58	L FT	None[†]
9	M	5	2	12.38	44	0.67	L FTPO	VPA, LEV
10	M	5	2	12.41	40.4	1.17	R FTPO	OXC
11	M	5	2	12.55	37	N/A[‡]	L TO	LTG, OXC
12	F	5	2	12.72	47	2.00	R TPO	LEV, OXC, TPM
13	M	5	2	13.72	33.5	N/A	L FTPO, R FTPO	None[§]
14	F	4, 5	2	13.91	48.1	11.00	R PO	OXC, TPM
15	M	3	2	14.02	35.3	0.67	L TPO, R O	OXC
16	F	5	1	14.15	30.5	1.50	L TPO	None[‖]
17	F	1, 5	2	15.03	49.2	0.92	L TPO	FBM, OXC, TPM
18	F	3	2	16.13	32.6	0.17	R FTPO	None[¶]
19	F	5	2	16.15	48.1	0.33	L FTPO	OXC
20	F	2	2	16.94	48.1	2.00	R TO	OXC
21	F	5	2	17.16	56.6	16.92	R FTPO	ZNS
22	F	5	2	17.49	45	0.33	L FTPO, R F	LEV, OXC

Abbreviations:

AEDs = antiepileptic drugs

BI = brain involvement

CLB = clobazam

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DB = Cog. Fxn. Neuro-QoL (cognitive function domain of the Neuro-QoL T-score)

F = frontal

FBM = felbamate

L = left

LCM = lacosamide

LEV = levetiracetam

LTG = lamotrigine

Neuro-QoL = quality of life in neurological disorders

O = occipital

OXC = oxcarbazepine

P = parietal

R = right

T = temporal

TPM = topiramate

VPA = valproic acid

ZNS = zonisamide

Patients are listed from the youngest to the oldest by the age (in years) at completion of the Neuro-QoL Questionnaire.

Race: 1, American Indian or Alaska Native; 2, Asian; 3, Black or African American; 4, Native Hawaiian or Other Pacific Islander; 5, White. Ethnicity: 1: Hispanic, Latino, or Spanish Origin. 2: Not Hispanic, Latino, or Spanish Origin.

*
Hemispherectomy, weaned off AEDs in October 2015.

†
Only one seizure in medical history, never on AEDs.

‡
Age at seizure onset data not available.

§
No history of seizures, never on AEDs.

‖
Weaned off AEDs in March 2014 after 2 years of seizure freedom.

¶
Weaned off AEDs in 2007 after 5 years of seizure freedom.

TABLE 2.

Cognitive Function Neuro-QoL Domain T-Scores for Pediatric Patients With SWS by Extent of Total SWS (the Sum of a Subject's Brain, Skin, and Eye Involvement Scores), Brain, Skin, and Eye Involvement

Sturge-Weber Extent	Extent of Involvement	n	%	Cog. Fxn. Neuro-QoL (Mean T-score ± S.D.)	R	P-Value
Total SWS involvement	0	0	0.00	N/A	−0.63	0.002
	1	4	19.05	47.35 ± 2.29		
	2	5	23.81	45.38 ± 7.07		
	3	4	19.05	38.18 ± 6.66		
	4	5	23.81	35.86 ± 6.95		
	5	3	14.29	36.10 ± 10.45		
	6	0	0.00	N/A		
Brain involvement	None	0	0.00	N/A	N/A	0.1
	Unilateral	18	81.82	41.76 ± 7.62		
	Bilateral	4	18.18	35.48 ± 7.05		
Skin involvement	None	4	19.05	47.35 ± 2.29	−0.46	0.04
	Unilateral	11	52.38	40.27 ± 8.09		
	Bilateral	6	28.57	37.37 ± 8.22		
Eye involvement	None	10	47.62	44.98 ± 6.42	−0.58	0.005
	Unilateral	9	42.86	38.17 ± 6.87		
	Bilateral	2	9.52	31.65 ± 9.97		

Abbreviations:

Neuro-QoL = quality of life in neurological disorders

SWS = Sturge-Weber syndrome

A higher T-score represents more cognitive function Neuro-QoL, and it is standardized to have a standard deviation of 10 with 50 representing the mean value in the reference population (see text for description). An increased extent of skin, eye, and total SWS involvement correlated with lower cognitive function Neuro-QoL. Extent of brain involvement was not significantly associated with cognitive function Neuro-QoL.