CURRENT EVENTS

See what is happening in the SynGap World!

SynGAP Awareness Day June 21, 2019
T-Shirt Fundraiser
Opening May 1st - May 27th
https://try.bonfire.com/syngap/

Rocking For SynGap
June 1st - June 21st
Dance or Donate and Tag 3 Friends!
https://www.mightycause.com/organization/Bridge-The-Gap-Syngap-Education-And-Research-Foundation

Houston Family Meetup
August 15-16 Tentative Date - DATE CHANGE PENDING due to Venue availability

Baltimore Family Meetup
November 8-10
FDA Externally Led Meeting Pending

BTG 5 Year Anniversary Celebration
November 9, 2019
Location TBA
### Methods

The Bridge the Gap Education and Research Foundation, in partnership with the National Organization for Rare Disorders and support from the US Food and Drug Administration, launched the SYNGAP1 (MRD5) patient registry in 2017. The registry contains 13 surveys covering diagnostics, disease, treatment, care management, and quality of life. As of December 2018, 105 patients have provided data for 717 survey submissions.

The pediatric quality of life survey has 62 respondents and questions that cover the impact of the disease on the participant’s life in the 4 weeks preceding their responses. Respondents in the survey were less than 18 with a median age of 4 years at diagnosis (mean of 5.18 years), 61% (38/62) female, and mostly resided in the US (56%, 35/52).

### Trends in Functional Impairment

**FUNCTIONAL IMPAIRMENT IN THE PAST FOUR WEEKS**

During the past 4 weeks, to what degree were the following functions impaired?

<table>
<thead>
<tr>
<th>Function</th>
<th>Normal</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hearing (n=54)</td>
<td>81%</td>
<td></td>
<td>17%</td>
<td>2%</td>
</tr>
<tr>
<td>Vision (with usual glasses) (n=46)</td>
<td>74%</td>
<td>20%</td>
<td>7%</td>
<td></td>
</tr>
<tr>
<td>Feeding (n=53)</td>
<td>74%</td>
<td>25%</td>
<td>2%</td>
<td></td>
</tr>
<tr>
<td>Mobility (n=54)</td>
<td>24%</td>
<td>67%</td>
<td>7%</td>
<td>2%</td>
</tr>
<tr>
<td>Educational Achievement (n=54)</td>
<td>11%</td>
<td>81%</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Communication (n=46)</td>
<td>30%</td>
<td>30%</td>
<td>30%</td>
<td>39%</td>
</tr>
</tbody>
</table>
The importance of finding trends in Real World Data, such as the data we collect in the registry helps paint a picture of what is occurring over the spectrum of the disorder. This information is used to help find measurable endpoints and bio-markers that can be used in clinical trial design. This information gets us one step closer to finding treatments.
SYNGAP1 SCIENCE FRONTIER

Latest New on SYNGAP1 Research for Families

The quarterly SYNGAP1 Science Frontier brings you close to the frontiers of breakthrough discoveries in the field of SYNGAP1. Each article features a single study and summarizes its highlights in an easy-to-understand language. Spend 3 minutes to keep yourself informed of the exciting research on SYNGAP1!

Early this year, Dr. Vlaskamp and others published a study on the largest cohort of SYNGAP1 patients to this day. The study compiled the genetic mutations found in 57 SYNGAP1 patients and detailed information on their epilepsy, developmental delay, and other symptoms. Click here to read a quick summary of the study’s highlights and learn more about the experiences of other SYNGAP1 children!

ABOUT THE AUTHOR

Shaowen (Sarah) Ju is a researcher of SynGAP at the Huganir Lab of the Johns Hopkins University School of Medicine. In the laboratory, she works on developing treatments for SYNGAP1-related disorders by targeting SYNGAP2, a natural antisense transcript of SYNGAP1 found in human. Shaowen also sees SYNGAP1 patients by shadowing Dr. Constance Smith-Hicks at the Kennedy Krieger Institute. Seeing how keen families are to learn about SYNGAP1, she volunteered to write articles for Bridge the Gap ERF to keep families informed of ongoing research in the field.
In January of 2019, a study was published in Neurology detailing the spectrum of symptoms and features observed in 57 patients with SYNGAP1-related intellectual disability. This is the largest cohort of SYNGAP1 patients studied in literature, with 39 patients recruited from Dr. Vlaskamp's and others' practices in Australia, Italy, the Netherlands, and China and 27 patients from the SYNGAP1 Facebook group. Based on the predicted potential of these genetic changes for causing disease, 57 out of 66 patients were included in the final analysis.

Information about patients' symptoms and features were collected from:
- A standardized epilepsy questionnaire
- Medical records
- EEG
- Neuroimaging (e.g. MRI)
- Seizure videos and video-EEG data (if available)

Developmental Delay

The results found developmental delay in 96.4% of patients and reported the ranges and the median ages at which individuals met their developmental milestones (Figure 1). Median age is the age of the individual in the “middle” of a dataset, indicated by the white vertical lines in Figure 1. For example, the age at which SYNGAP1 patients first sat up ranged from 4 months to 2.5 years with a median age of 9 months (Figure 1).
Epilepsy

The study showed that 98.2% of all patients in the cohort had seizures and 61.4% had multiple seizure types. In most cases, developmental delay preceded seizure onset, which ranged from 4 months to 7 years with a median age of 2 years (Figure 1). Among those with seizures, 17.8% became seizure-free at a median age of 7.5 years (Figure 1). The study also revealed two distinctive types of seizures in SYNGAP1 patients: chewing induced reflex seizures, which were observed in 25% of the cohort, and a novel type of seizure characterized by eyelid myoclonia evolving to a myoclonic-atonic or atonic seizure, which affected 22.8% of the cohort.

Comorbidities

In addition to developmental delay and epilepsy (a neurological disorder marked by recurrent seizures), SYNGAP1 patients also experience other difficulties. The study showed the percentages of some common comorbidities observed in the cohort, such as behavioral problems, high pain threshold, hypotonia (low muscle tone), and autism spectrum disorder (Figure 2). These results highlighted the spectrum of cognitive, social, behavior, and sensory difficulties associated with SYNGAP1-related disorder.
The survey revealed that communication was the most severely impaired function compared to hearing, vision, feeding, mobility and educational achievement. None of the respondents had normal levels of communication in the past four weeks and more than 1/3 (39%, 20/46) reported severe impairment.

In contrast, hearing, vision (with usual glasses), and feeding were the least impaired in both severity and prevalence, with 74-81% respondents answering normal, 17-25% mild, 2-7% moderate, and none severe.

Interestingly, mobility and educational achievement had the greatest range in severity of impairment, with individuals who had normal functioning to severe impairment. Compared to mobility, for which 2/3 (67%, 36/54) respondents answered mild, educational achievement was more severely impaired, with most (81%, 44/54) respondents answering moderate.
Our journey started when our daughter, Jadyn, didn't do well at her 9 month check-up as a baby. She wasn't eating and her muscle tone started to tighten up. That is when we were referred to a neurologist, and the mystery began. The first neurologist we saw kept telling us that everything was fine. Jadyn was just a little delayed but not to worry. It wasn't until she was 2 that he decided to do an in office EEG that showed seizure activity. Then began our long road of seizure medications (that didn't work) until we looked for more answers with Texas Children's Hospital. The doctor there ordered genetic testing that lead to the diagnosis of the SynGap1 mutation. Jadyn is now a healthy 6 year old girl. Her seizures have finally been controlled after trying her 7th medicine, Lamictal. She is still non-verbal and cannot eat solid foods. Her behavior is mild, but she doesn't interact with others very much. Jadyn does have sensory issues, such as chewing on clothing/hair and spinning objects. Fidget spinners are the best! We have also had to "Jadyn Proof" our house because she is such a climber! She sure keeps us on our toes!

Jadyn has a little brother who is 18 months younger than her. He doesn't ask questions about why Jadyn doesn't talk or play, but does understand that she is special. Having a unique household has it's challenges at times. Jase, her brother, is now in tee-ball and games are a challenge. Basic family outings take more planning and preparing. But we put our best foot forward and make things a new normal for us. Jadyn has taught us how to be a stronger family and that love comes in many special ways.