

# STXBPI related disorders / encephalopathy / developmental and epileptic encephalopathy

## Patient journey



### First symptom

**Timeline:** From the 1st day of life up to 1 year

#### Clinical signs / Symptoms

Seizures

- >80% present with seizures in the 1st year of life with neonatal onset seizures in about half.
- Seizure onset at later age has been reported.
- Seizure types at onset are mainly focal motor/ tonic, epileptic spasms, clonic, focal-to-bilateral tonic-clonic.
- Seizures may occur in clusters

Developmental delay

- Present in all individuals and usually observed within the 1st year of life.
- May be the presenting symptom in patient with no/late onset seizures.

### Diagnosis

**Timeline:** Usually < age 2 years, depending on the availability of genetic testing

#### Clinical signs / Symptoms

Seizures

- Different types of epileptic seizures can be present: focal or generalized motor seizures are most frequent, but absences and focal impaired awareness seizures can occur later. Status Epilepticus can occur.
- About 1/3 of patients become seizure free in the first years of life; 2/3 develop drug-resistant epilepsy. Prolonged periods of seizure remission with later relapse can occur.

Developmental delay

- Present in all patients and usually observed within the 1st year of life.
- Developmental trajectories differ on individual basis, but delayed speech and motor development is usually clear from early age.
- Periods of developmental stagnation or regression can occur at different ages and do not always correlate with epileptic activity.
- Developmental outcomes differ significantly between individuals: some need wheelchair, others can walk independently; language is severely impaired in up to 80% of individuals.
- Intellectual disability is present in all the individuals, ranging from mild-moderate to profound.
- Behavioral problems including autistic features are seen in more than half of the patients.
- Movement disorders are frequent including tremor and ataxia.
- Other recurrent comorbidities are gastro-intestinal problems and orthopedic issues.
- People with STXBPI-RD will be life-long partially or totally dependent.

### Treatment

**Timeline :** life long

#### Clinical signs / symptoms

Seizures

- Epileptic seizures are often difficult to treat. No specific anti-seizure treatment has been proven to be superior and treatment needs to be individualized to the specific seizure types of the individual.
- Ketogenic diet has been reported to maintain seizure freedom in some.
- Epilepsy surgery should not be excluded given the genetic diagnosis, especially in presence of clear focality and intractable seizures.
- Treatments should aim at controlling seizure and reducing side effects, especially in infancy and childhood, when seizures can contribute to the developmental impairment.
- Seizures resolve in childhood in about one third of individuals. Seizure recurrence at later age is possible and needs to be monitored.

Developmental delay

- An early multi-disciplinary rehabilitation plan, including physiotherapy, speech therapy, occupational therapy, and behavioral is important to maximize the developmental potential and needs to be tailored to the needs of each individual patient.

### Follow-up

**Timeline:** 2-16 years

#### Clinical signs / symptoms:

- Epileptic seizures may be intractable, may be in remission, or may have relapsed.
- Behavioral problems may manifest.
- Movement disorders may manifest, such as tremor and ataxia.
- Sleep disturbances can be present.
- Orthopedic issues may occur.

### adult / transition

**Timeline:** 16 years and up

#### Clinical signs / symptoms:

- Epileptic seizures may be intractable, may have remitted, or may have relapsed.
- Behavioral problems may change.
- Movement disorders are present.
- Sleep disturbances can be present.
- Orthopedic issues are common.
- Adolescents and adults with STXBPI-RD are partially or totally dependent for activities of daily living and need continuous support.
- Possibilities of daycare or residential care need to be discussed with the parents.
- When reaching adulthood, legal issues such as a legal guardian for when the patients become of age should be discussed.
- The transition from pediatric to adult care may cause lack of appropriate support for the patient and the caregivers.

### Identifying patient needs

- Parents need to have basic information on epilepsy and epileptic seizures.
- Parents need to be informed about how seizures need to be managed and have an individualized emergency protocol.
- Parents need to be informed their child could have cognitive disability and developmental delay (if not already identified).
- Parents need to know how to access early habilitative interventions (e.g. psychomotricity).

### Ideal results / support

- Parents concerns are taken seriously, they are given explanations, and reassurance.
- Caregivers are given instructions on how to manage epileptic seizures and an individualized emergency protocol is provided (rescue medication and when to go to the hospital).
- Rehabilitation plan is provided.

### Identifying patient needs

- Parents need to be offered genetic testing and counselling.
- Parents need an explanation of the diagnosis and possible prognosis, with psychological support.
- Parents should understand that developmental and epilepsy outcomes are different from child to child.
- Parents need to have a plan to manage epileptic seizures.
- Parents need to be trained on how to keep the child safe (falls, prolonged seizures, fever...).
- Parents need to have access to early rehabilitation within a multidisciplinary team to maximize the development potential and reduce comorbidities.
- Parents should be informed about STXBPI family groups and associations in their country and worldwide, for support, networking, and information.
- Parents need to be informed about ongoing clinical studies on STXBPI
- Parents need to know what social assistance is available from the government.

### Ideal results / support

- Genetic diagnosis and consultancy, with explanation of causes and recurrence risk.
- Professional support is offered to help parents cope with the diagnosis and the family is directed to the parent support group and/or the association.
- Parents receive clear instructions, emergency protocols, explanation of risks and how to minimize them.
- Parents receive clear information about possible clinical studies in which their child can participate with in-depth information on risk and benefits.
- It is important for the family to know how important education and rehabilitation are for the development of the child and this should be closely monitored.
- The family is given a document summarizing the social benefits available and offered for the type of disease according to their country/region.

### Identifying patient needs

- Parents need counselling and professionals' help.
- Parents need information on prescribed medications, side effects, on side-effect monitoring in the long term.
- Parents need medical help /advice on non-epileptic symptoms, especially related with severe motor and cognitive impairment.
- Advice on pre-school/school/aid.
- Access to clinical trials for new treatment opportunities.
- Other family members, like siblings of the affected individual, need counselling.

### Ideal results / support

- Regular consultations are offered with a health-care professional.
- Up-to-date information is available for parents any time, including research initiatives.
- Parents are informed on medication side effects and monitoring.
- Parents are provided with a treatment strategy for non-epileptic symptoms.
- Parents are offered support to find a school / daily assistance and care.
- A multi-disciplinary team works with the patient on the physical, communication and occupational domains, adjusting the strategy based on patient's needs.

### Identifying patient needs

- Parents need evidence-based information on additional symptoms and comorbidities that may arise.
- Parents needs and expectations change over time and need to be re-evaluated and discussed.
- Evidence-based therapies (psychomotricity, speech therapy, postural re-education, behavioral therapy) need to be tailored to the patient's needs and age.
- Siblings' wellbeing and needs have to be evaluated and discussed, and support provided.

### Ideal results / support

- Monitoring above mentioned issues and if possible, offering any treatment.
- Needs and expectations are discussed and strategies are planned.
- Availability of home and/or institutional care at the highest level.
- Defining a rehabilitation program (psychomotricity, speech therapy, postural re-education, behavioral therapy) tailored to the patient's needs and age.
- Siblings' needs are adequately addressed.

### Identifying patient needs

- Parents need counselling and support in the transition to adulthood.
- Monitoring and treating comorbidities and new symptoms that may arise.
- Parents need additional support when caring for an adult person.

### Ideal results / support

- Plan the transition process from child to adult specialist.
- Setting up of a rehabilitation plan for maintenance and prevention of comorbidities.
- Occupational therapy / day-care centers / residential centers.
- Re-evaluate the family's needs and concerns.
- Provide the family with support and advice on later stages of adulthood and in case of the primary caregivers became unable to provide care.