SETBP1 Haploinsufficiency Disorder (SETBP1-HD)

Resource Guide

SETBP1 SOCIETY

About this Resource Packet

This information was collected from the following 2 recent publications and represents data from 44 individuals:

- Morgan, A., Braden, R., Wong, M. M. K., Collin, E., Amor, D., Liegeois, F., Srivastava, S., Vogel, A., Bizaoui, V., Ranguin, K., Fisher, S. E., & van Bon, B. W. (2021). Speech and language deficits are central to SETBP1 haploinsufficiency disorder. *European Journal of Human Genetics*. 29:1216-1225
- Jansen, N. A., Braden, R. O., Srivastava, S., Otness, E. F., Lesca, G., Rossi, M., Nizon, M., Bernier, R. A., Quelin, C., van Haeringen, A., Kleefstra, T., Wong, M. M. K., Whalen, S., Fisher, S. E., Morgan, A. T., & van Bon, B. W. (2021). Clinical delineation of SETBP1 haploinsufficiency disorder. *European Journal of Human Genetics.* 29: 1198-1205

The information represents 34 individuals with SETBP1 haploinsufficiency disorder, also known as SETBP1 disorder and SETBP1-HD, in the *Clinical delineation of SETBP1 haploinsufficiency disorder* publication and 31 individuals with SETBP1 -HD in the *Speech and language deficits are central to SETBP1 haploinsufficiency disorder* publication. Some individuals are represented in both publications and efforts were not taken to try to match up data between the 2 publications. Data is pulled from either publication depending on the type of data presented.

This resource packet is designed to be useful for parents of children with SETBP1-HD and for education specialists, medical specialists, and therapists working with children with SETBP1-HD.

SETBP1 Haploinsufficiency Disorder

SETBP1 haploinsufficiency disorder is a genetic neurodevelopmental disorder characterized by moderate to severe speech impairment, motor developmental delay, a wide range of intellectual functioning (from normal IQ to severe ID), hypotonia and behavior problems. Commonly reported behavioral characteristics are attention deficit and hyperactivity. Other reported clinical signs include young-onset vision impairment, autism spectrum disorder, anxiety, seizures, gastrointestinal issues, genital anomalies, and sleep problems. There is wide variability in how severely individuals may be affected.

SETBP1-HD Characteristics

Developmental Delay

Speech Disorder*

Motor Planning/ Programming Deficits

>95%

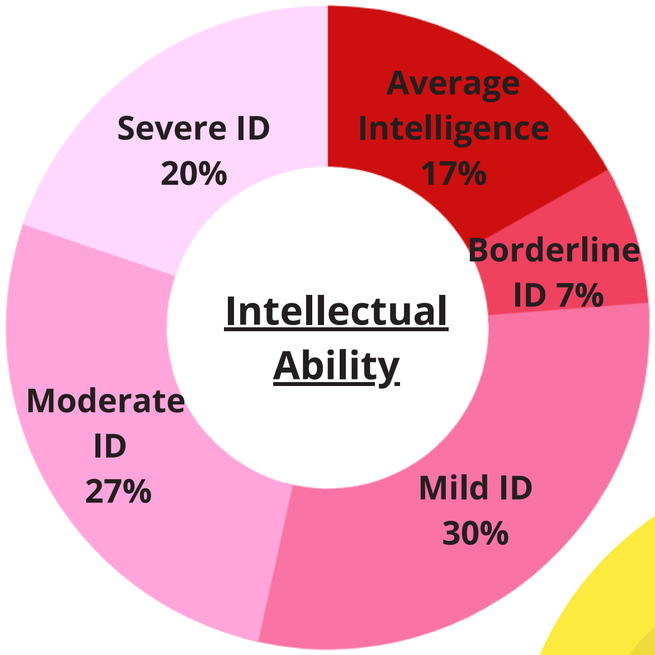
Intellectual Disability (ID)

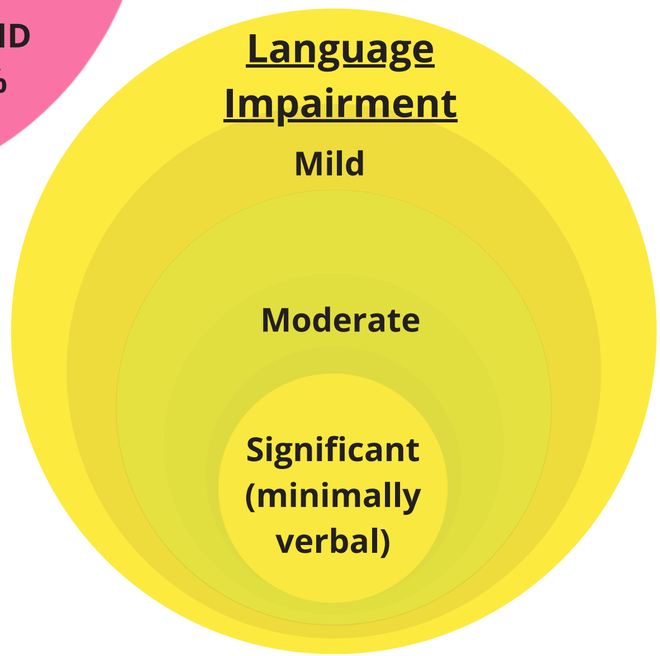
Childhood Apraxia of Speech (CAS)

Behavior Challenges

Fine/Gross Motor Delay

>75%





Sensory Sensitivities

Reading and/or Writing Disorders

Anxiety

Seizures

Recurrent Ear Infections

Gastrointestinal Issues

Minor Facial Differences**

Eczema/ Other Skin Issues

>20%

Attention or Concentration Deficits/ADHD

Hypotonia

Social Skills Deficits

Feeding Difficulties

Restricted Interests

Vision Impairment

Autistic Traits/ Autism (ASD)

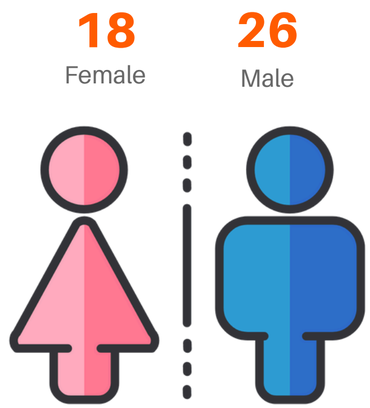
>50%

*At a young age, this may first present as a speech delay. **Broad nasal bridge, ptosis, epicanthal folds, blepharophimosis, full nasal tip, hypertelorism, and high palate

Participation

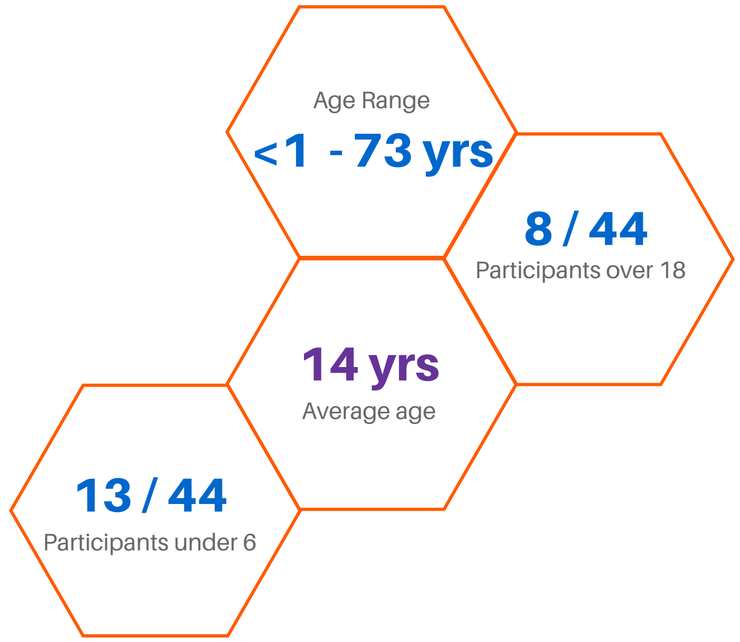
Total Males and Females

Among the 44 participants, there are 26 males and 18 females who have SETBP1 haploinsufficiency disorder represented in this guide.



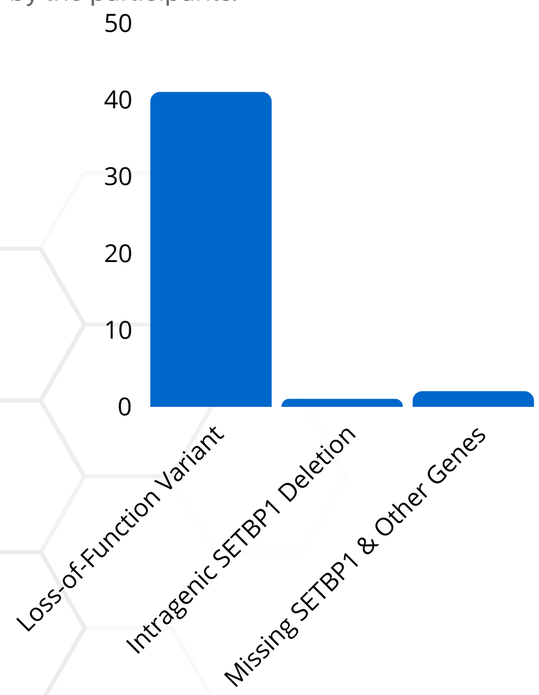
Age Range

The average age is 14 years old. Ages range from 8 months old to 73 years old with 13 of the 44 participants under 6 and 8 over 18.



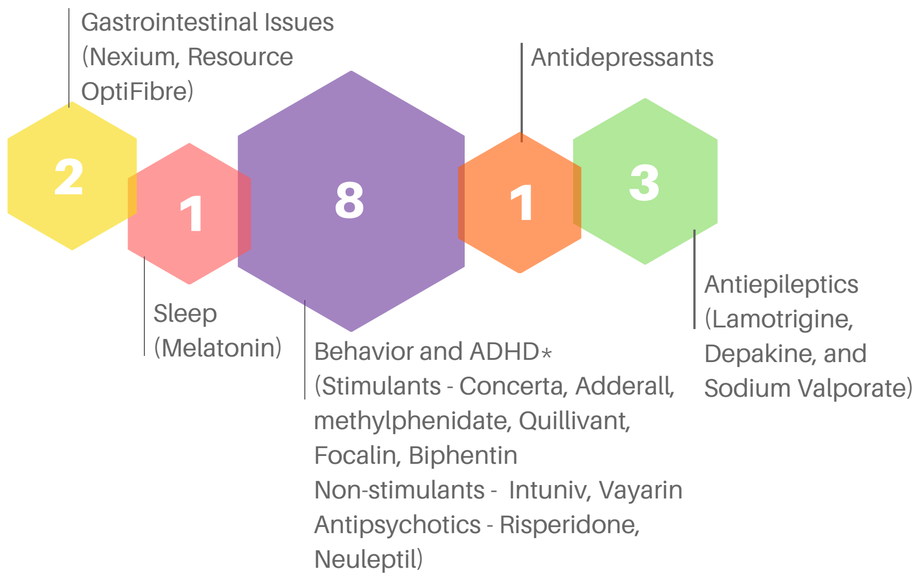
Genetic Changes

The following SETBP1 changes were represented by the participants.



Medications Noted

The following medications were noted by 13 individuals included within this study. The numbers represent the number of people who reported taking that type of medication. This portion is informational and no medications should be tried or adjusted without physician support and guidance.



*7 of the 8 individuals are boys

Where We Live

Countries Represented

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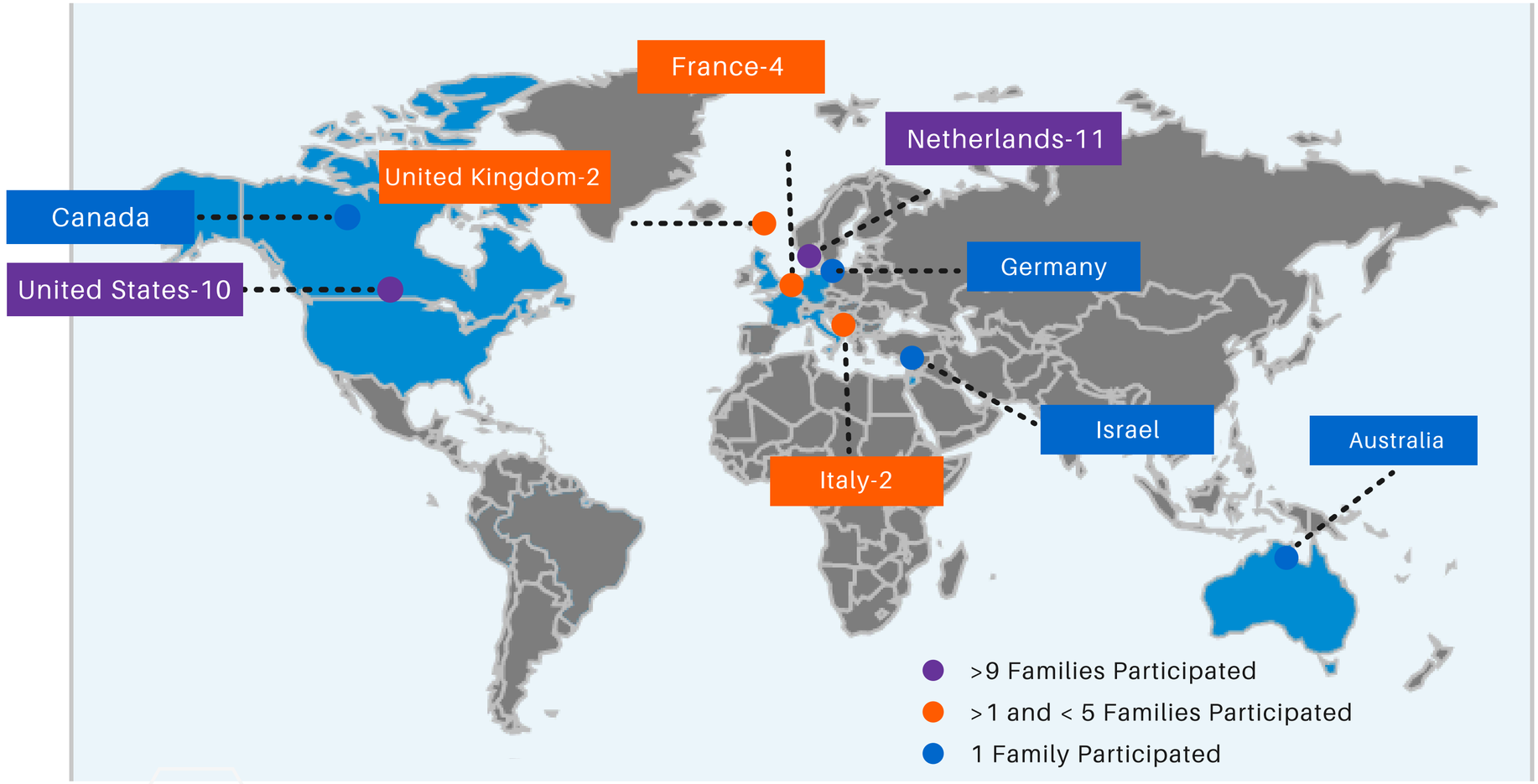
The location for 33 participants was noted in the publications. The individuals represent 9 countries.



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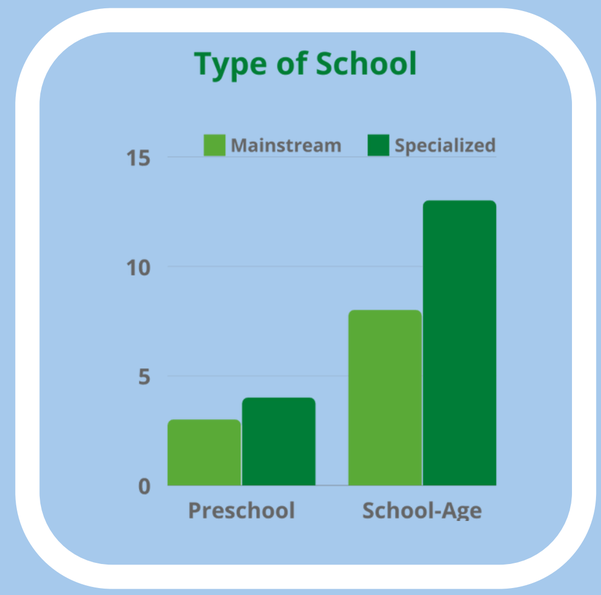
Intervention Needs

This document represents the educational, therapeutic, and behavioral needs for individuals with SETBP1 haploinsufficiency disorder.

These interventions may be needed regardless of a formal diagnosis of intellectual disability, autism spectrum disorder, or attention-deficit/hyperactivity disorder.

86% **required learning support across all settings**



LEARNING IMPACT

BEHAVIOR PLAN FOR

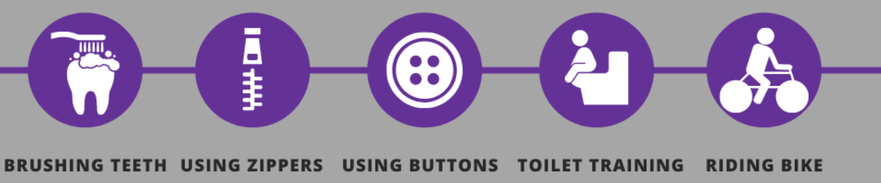
- Autistic traits
- limited social skills
- restricted interests
- sensory sensitive
- Attention Deficits
- Anxiety
- Aggression

Not all symptoms may be present

21% **reported seizure activity**

12% **reported official ASD diagnosis**

PERSONAL CARE



CHILD WILL NEED

speech-motor therapies to develop verbal speech starting at an early age

phonological interventions for

- literacy awareness
- language comprehension
- language production

94% **required occupational or physical therapy**

Speech & Language Findings

EARLY INTERVENTION

Multi-Modal Communication Approach*

Speech therapy coupled with augmentative and alternative communication (AAC) device support

OR

sign language support

Intensive therapy as often as 4 sessions per week

*Supports language acquisition prior to speech development

OTHER AREAS TO ADDRESS

- Social Skills
- Phonological Awareness
- Literacy Support
- Language Comprehension
- Language Production
- Articulation
- Consistent speech-motor therapy

23%

had a frenectomy due to tongue-tie

SPEECH DIAGNOSES

- Childhood Apraxia of Speech (CAS)
- Phonological Disorder
- Dysarthria
- Articulation Disorder
- Dysfluency

> "CHILDREN WILL NEED SPEECH-MOTOR THERAPIES TO DEVELOP VERBAL SPEECH"

> "EARLY SPEECH INTERVENTION APPEARS TO BE CRITICAL FOR ALL WITH SETBP1 LOF VARIANTS WHO PRESENT WITH SEVERE SPEECH DISORDER, WITH BEST EVIDENCED APPROACHES FOR SPEECH APRAXIA KNOWN TO INVOLVE INTENSIVE THERAPY AS OFTEN AS FOUR SESSIONS PER WEEK"

SETBP1 neurodevelopmental disorders

Changes in the SETBP1 gene are associated with 2 distinct genetic neurodevelopmental disorders, as well as, variants of uncertain molecular impact which are classified as SETBP1-related disorders.

	SETBP1 HAPLOINSUFFICIENCY DISORDER	SCHINZEL-GIEDION SYNDROME SGS*		SETBP1-RELATED DISORDERS
	SETBP1 DISORDER SETBP1-HD	CLASSICAL	ATYPICAL	UNKNOWN MOLECULAR IMPACT
DESCRIPTION	a neurodevelopmental disorder consisting of moderate to severe speech impairment, mild motor developmental delay, a wide range of intellectual functioning (from normal IQ to severe ID), hypotonia in childhood and behavior problems	a severe multi-system disorder consisting of recognizable facial characteristics, neurological problems (including severe intellectual disability, intractable epilepsy, cerebral blindness, and deafness) and various congenital anomalies	a milder form than classical Schinzel-Giedion Syndrome	a SETBP1 change that is not identified as causing SGS or SETBP1 haploinsufficiency disorder. 1. It is not yet known if the SETBP1 change is contributing to the individual's challenges 2. SETBP1 is causing challenges for the individual but the reason is not known
CAUSE	A loss of function (LoF) change in one copy of the two SETBP1 genes causing the body to not produce enough of the SETBP1 protein. This type of change is referred to as a loss of function change/variant.	A gain of function (GoF) change in one copy of the two SETBP1 genes causing the body to accumulate too much of the SETBP1 protein. This type of change is referred to as a gain of function change/variant.	A gain of function (GoF) change in one copy of the two SETBP1 genes causing the body to produce/accumulate too much of the SETBP1 protein. This type of change is referred to as a gain of function change/variant.	A change in one copy of the two SETBP1 genes with one of the following outcomes: 1.It is not known whether the SETBP1 change is impacting the body. This change is called a Variant of Unknown Significance (VUS). 2. It is not known how the SETBP1 change is impacting the body.
INHERITANCE	Most Often De Novo (Not inherited from parents) Possibility exists of germline or low-grade somatic mosaicism inheritance	Most Often De Novo (Not inherited from parents) Possibility exists of germline or low-grade somatic mosaicism inheritance	Most Often De Novo (Not inherited from parents) Possibility exists of germline or low-grade somatic mosaicism inheritance	De Novo (Not Inheritied) OR Inherited from either parent
LOCATION	Variants located throughout the SETBP1 gene, which is located on chromosome 18 A deletion may include part or all of the SETBP1 gene	SETBP1 variant located within a specific region (residues 868 to 871 of the SETBP1 protein). The SETBP1 gene is located on chromosome 18.	SETBP1 variant located in close proximity but outside of the classical SGS specific region. The SETBP1 gene is located on chromosome 18.	Variants located throughout the SETBP1 gene, which is located on chromosome 18, and not within the SGS atypical or classical region.

*Additional SGS info from Acuna et al 2017 & Banfi et al 2021