Translational Centre for Speech Disorders
Centre of Research Excellence

Kleefstra syndrome

Fact sheet

What is Kleefstra syndrome?

Euchromatic history lysine methyltransferase 1 (*EHMT1*), plays a significant role in turning off other genes. *EHMT1* is found on chromosome 9 at the location 9q34.3.

Deletions of and variations in the *EHMT1* gene cause Kleefstra syndrome; a rare condition with a recognisable but heterogeneous phenotype, including a spectrum from average cognition to severe intellectual disability, speech and language disorders, epilepsy, autism, distinct facial features, sleep disturbance, vision and hearing impairment, and cardiac, renal, and urological conditions.[1]

Speech and Language

The terms 'speech' and 'language' are often used interchangeably; yet, they are categorised differently by a speech pathologist, with has implications for therapy:

Speech is focused on speech sounds. This includes sound accuracy, articulation, voicing, resonance (e.g., nasality), and prosody (e.g., stress and rhythm).

Language involves the understanding and use of words (vocabulary) and sentences (grammar).

What are the associated health and medical conditions seen in Kleefstra syndrome?

- Feeding difficulties: in infancy and early childhood, some children might need a nasogastric tube to support their nutrition. Some individuals with large genetic deletions (>1Mb) have a gastrostomy tube.[2]
- Vision & hearing: several individuals also have vision and hearing impairments, and many require glasses and/or hearing aids[1,2]
- Intellectual disability: most individuals have mild to severe intellectual disability, although there are some individuals with average cognition.[2]
- Sleep disturbances: for example, frequent and early waking.[2]
- Fine & gross motor delays and disorders: many individuals seek support from occupational and physiotherapists to support fine and gross motor development.[2]
- Heart: approximately one-third of individuals have cardiac (heart) defects.[1,2]
- Behavioural difficulties: these include diagnoses of autism spectrum disorder, attention deficit hyperactive disorder and anxiety.[2]
- Some individuals experience regression (loss of previously acquired skills) in adolescence and adulthood.[1-3]
- Epilepsy: about 1/10 individuals have epilepsy and take medication to control seizures.[2]

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What are the common speech and language features in children with Kleefstra syndrome?

If a child begins speaking most will exhibit features of dysarthria, a neuromotor speech disorder and/or Childhood Apraxia of Speech (CAS), a motor speech disorder affecting speech planning and programming. These motor speech conditions can occur at the same time in the same person.[2] Other common speech disorders include phonological delay and disorder, and articulation disorder. Articulation disorders may be impacted by facial features, such as dental issues or underbites.[1] Many individuals learn to use single, spoken words but some individuals may not learn to combine words to create sentences. As many individuals have limited and/or unclear verbal speech, several individuals use augmentative and alternative communication (AAC), such as sign language, communication books or speech generating devices.[2]

At what age do individuals with Kleefstra syndrome begin speaking?

The age at which children say their first words is very delayed compared to typically developing children. Most children say their first when they are older than 18 months old (for typically developing children this occurs around 12 months old). For those that learn to combine words into sentences, this usually occurs around 4-5-years-old (in typical development this happens at around 2-years-old). Some individuals acquire few if any spoken words (often referred to as non-/minimally verbal/vocal or non-speaking) and rely on other forms of communication (such as AAC).[1,2] Even for those individuals who learn to speak, they may need to use AAC whilst their speech is still developing or because their speech is unclear due to dysarthria and/or CAS.

How can speech pathologists/therapists support children with Kleefstra syndrome?

There is no research on speech and language interventions that are specifically designed for individuals with Kleefstra syndrome. At present an individualised approach should be taken to assessment and management to ensure therapies are tailored to and optimised for each child.

Due to delayed speech and language milestones in Kleefstra syndrome, alongside motor speech disorders in individuals who use speech, AAC should be implemented as early as possible for individuals with Kleefstra syndrome. AAC interventions often involve approaches such as Key Word Sign (e.g., Makaton, Baby Sign), communication books and boards, and speech generating devices. Speech generating devices (also known as voice output communication aides, electronic AAC or high-tech AAC) can enable the individual to communicate using an electronic voice when selecting icons or pictures on a digital screen. Speech generating devices can be on a dedicated electronic device, or be a specialised application on a general device, such as an iPad®. Some individuals with Kleefstra syndrome become very proficient users of sign language and speech generating devices.[2] Additionally, some individuals use more than one AAC system, or use an AAC system alongside speech. For adolescents and adults who have experienced regression, AAC can be helpful to support communication when there is a loss of speech and language skills.[2]

Assessment/evaluation

Important domains for a speech pathology assessment include:

- Speech production skills: to evaluate for specific speech diagnoses (e.g., dysarthria, CAS)
- Expressive, receptive and pragmatic language skills
- Feeding and swallowing abilities
- Augmentative and alternative communication (AAC), e.g., speech generating devices
- Literacy, e.g., reading and writing

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The types of assessment tools used will vary depending on the child's individual profile and developmental age. Assessment may be required at an initial diagnosis and throughout childhood and adolescence. The goal of assessment will be to understand the nature and severity of speech and language challenges, then make recommendations for appropriate therapies when needed. Speech and language therapies should be tailored to the type of speech and language disorders that an individual may presents with.

Do individuals attend mainstream school?

Some individuals attend mainstream school settings, whilst other individuals attend specialist school settings. A child's education setting is dependent on an individual child's support needs, alongside supports the education system around the child can offer.

How does speech develop over time in Kleefstra syndrome?

As aforementioned, some individuals with Kleefstra syndrome may experience regression in the adolescent and adult years, whilst others have not experienced regression.[2] There are adults who may use AAC well into adulthood, either because they are minimally verbal or because they have very unclear speech. However, there are other adults with Kleefstra syndrome who will use speech to converse independently.[2]

Further information and support:

- For more information on speech and language research in Kleefstra syndrome. https://www.geneticsofspeech.org.au/media/edud0cye/summary-expanding-the-phenotype-of-klfs-speech-language-and-cognition-in-103-individuals-86.pdf
  French, Spanish and Portuguese versions are also available on our website.
- For information and support on Kleefstra syndrome: https://kleefstrasyndrome.org https://www.idefine.org/ https://idefine-europe.org/
- More information on dysarthria: Dysarthria Fact Sheet
- More information on CAS: CAS Fact Sheet
- More information on AAC: AAC Fact Sheet
- Apraxia kids information support group: Support Group Website

References:

1. Kleefstra, T., de Leeuw, N. (2023). Kleefstra syndrome. *GeneReviews*. https://www.ncbi.nlm.nih.gov/books/NBK47079/

2. Morison, L. D., Kennis, M. G., Rots, D., Bouman, A., Kummeling, J., Palmer, E., ... & Morgan, A. T. (2024). Expanding the phenotype of Kleefstra syndrome: speech, language and cognition in 103 individuals. *Journal of Medical Genetics*, *61*(6), 578-585. doi: 10.1136/jmg-2023-109702.

3. Vermeulen, K., Staal, W. G., Janzing, J. G., van Bokhoven, H., Egger, J. I., & Kleefstra, T. (2017). Sleep disturbance as a precursor of severe regression in Kleefstra syndrome suggests a need for firm and rapid pharmacological treatment. *Clinical Neuropharmacology*, *40*(4), 185-188.

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