

Support and Information



Understanding Chromosome & Gene Disorders

Rare Chromosome Disorder Support Group,

The Stables, Station Road West, Oxted, Surrey RH8 9EE, United Kingdom

Tel: +44(0)1883 723356

info@rarechromo.org | www.rarechromo.org

Join UniqUe for family links, information and support.

UniqUe is a charity without government funding, existing entirely on donations and grants. If you can, please make a donation via our website at www.rarechromo.org/donate Please help us to help you!

Websites

<http://floatingharborsyndromesupport.com/>

<https://floatingharborsyndrome.com/>

Facebook

<https://www.facebook.com/FHSglobal/>

<https://www.facebook.com/groups/121319221297807/>

UniqUe lists external message boards and websites in order to be helpful to families looking for information and support. This does not imply that we endorse their content or have any responsibility for it.

This information guide is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. Information on genetic changes is a very fast-moving field and while the information in this guide is believed to be the best available at the time of publication, some facts may later change. UniqUe does its best to keep abreast of changing information and to review its published guides as needed. The text was written by Dr Alice Gardham, Specialty Registrar in Clinical Genetics, North East Thames Clinical Genetics Service, and Dr Jane Hurst, Consultant in Clinical Genetics, Great Ormond Street Hospital for Children, London, UK, and the guide was compiled by UniqUe. The guide was updated by Dr Lara Menzies, Specialty Registrar in Clinical Genetics, and Dr Jane Hurst, Consultant in Clinical Genetics, Great Ormond Street Hospital for Children, London, UK in 2020.

2016 Version 1 (PM)

2020 Version 2 (AP)

Copyright © UniqUe 2020

Rare Chromosome Disorder Support Group
Registered in England and Wales

Charity Number 1110661
Company Number 5460413



Understanding Chromosome & Gene Disorders

Floating-Harbor syndrome



rarechromo.org

What is Floating-Harbor syndrome and how is it caused?

Floating-Harbor syndrome is a genetic condition that causes short stature, speech and language delay, and characteristic facial features. It is named after the two hospitals where it was first described – the Boston Floating Hospital and Harbor General Hospital in California.

Genes are instructions that have important roles in our growth and development. They are made of DNA and are packaged into structures called chromosomes. Floating-Harbor syndrome is caused by an alteration (mutation) in the SRCAP gene which means that the gene does not function correctly. The SRCAP gene is on chromosome 16 within a band called p11.2. We all have two copies of the SRCAP gene – one on the chromosome 16 inherited from our mother and one on the chromosome 16 inherited from our father. The SRCAP gene is important in regulating cell growth and division and is important for normal development. An individual only needs to have one altered copy of the SRCAP gene to be affected by Floating-Harbor syndrome. This is known as 'autosomal dominant inheritance'.

Most common features

All children with Floating-Harbor syndrome are short and have speech and language delay, although the severity can vary. Other typical features include:

- Characteristic facial features such as a prominent nose
- Mild to moderate learning disability
- Minor problems with hearing and eyesight
- Minor problems with genitalia such as undescended testes
- Kidney problems

“ We found that describing speech 'delay' is misleading, as it implies that the ability to speak fluently will come in time. He has limited vocabulary, and unclear pronunciation to all but those who know him well. ”

“ She is very independent and likes to have a go at everything. She does struggle with some things, such as formal learning and especially maths, but she tries very hard. She is very fond of her tablet and likes to edit videos on it. ”

“ The other thing which has impacted most on us as a family is behaviour, described as 'hyperkinetic'. He has displayed classic ADHD behaviour and can be challenging. On the plus side he is a sociable, mostly happy young man with a big character, who is loved by everyone who gets to know him. ”



“ She is a lively member of the family, it is certainly quiet when she is not around! She has an infectious laugh and you can't help joining in when she starts giggling! She is a stickler for rules, and likes to make sure everyone is abiding by them. ”

References

Nikkel *et al.*, The phenotype of Floating-Harbor syndrome: clinical characterization of 52 individuals with mutations in exon 34 of *SRCAP*. Orphanet Journal of Rare Diseases 2013, 8:63

Nowaczyk MJM, Nikkel SM, White SM. Floating-Harbor Syndrome. 2012 Nov 29 [Updated 2013 Jan 24]. In: Pagon RA, Adam MP, Ardinger HH, *et al.*, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2016.

Available from: <http://www.ncbi.nlm.nih.gov/books/NBK114458/>

Hood *et al.*, Mutations in SRCAP, encoding SNF2-related CREBBP activator protein, cause Floating-Harbor syndrome. Am J Hum Genet. 2012 Feb 10; 90 (2):308-13

Reschen *et al.*, Floating-Harbor syndrome and polycystic kidneys associated with SRCAP mutation. Am J Med Genet A. 2012 Dec;158A(12):3196-200.

Menzies L *et al.*, Intracranial vascular pathology in two further patients with Floating-Harbor syndrome: Proposals for cerebrovascular disease risk management. Eur J Med Genet. 2019 Oct 9:103785.

Management recommendations

At diagnosis

- Full clinical examination including examination of heart and genitalia
- Full developmental assessment by community pediatrician
- Feeding management if necessary
- Kidney and urinary tract ultrasound scan
- EEG (measurement of brain's electrical activity), if seizures are suspected
- Eye check
- Hearing check
- Dental check
- Endocrine (hormone specialist) review to consider growth hormone and thyroid hormone measurements

After diagnosis

- Long-term follow-up by a community paediatrician
- Speech and language therapy usually required
- Physiotherapy, and occupational therapy if needed
- Regular eyesight and hearing checks may be recommended
- Regular dental checks
- Annual blood pressure check and treatment of high blood pressure if found
- At least one further kidney scan in early adulthood to check for kidney cysts
- We do not yet have enough information to know whether all young adults with FHS should have a screening investigation called an MRA (magnetic resonance angiogram) scan of the brain and neck to check for brain aneurysms. For anyone with FHS and high blood pressure and/or kidney cysts, an MRA scan should be considered. This could be requested by a GP or a neurologist. It is also important to make sure that high blood pressure is monitored and treated.
- If acute neurological symptoms occur such as persistent severe headaches, limb weakness or a suspected seizure (epileptic fit), urgent medical attention should be sought to consider whether this is secondary to a brain aneurysm
- Further endocrine review if signs of early puberty or if growth velocity (speed of growth) slows
- Follow-up in genetics clinic as required

How many people have this condition?

Floating-Harbor syndrome is a rare condition with about 100 affected individuals reported in the medical literature. The gene for Floating-Harbor syndrome was only identified in 2012. Until this time, a diagnosis of Floating-Harbor syndrome was made based on clinical features of the condition alone. Now a genetic test is often offered to confirm the diagnosis. The increased availability of genetic testing for Floating-Harbor syndrome means that it is likely that more children and adults will be diagnosed with Floating-Harbor syndrome in the future.

Why did this happen?

When children are conceived, their parents' genetic material is copied in the egg and sperm that makes a new child. The copying method is not perfect and occasionally random gene alterations occur for the first time. Such gene alterations, therefore, are not found in the child's parents. In the vast majority of families that we know about so far, the SRCAP gene alteration happened 'out of the blue' (this is what you may hear a geneticist referring to as a 'de novo' change). On rare occasions, one parent will have the Floating-Harbor syndrome too and if this is the case, the gene alteration has been inherited from the affected parent.

Can it happen again?

Provided that neither parent is found to carry the same SRCAP change as their child, the chance of having another child with the same genetic change would be considered extremely low (less than 1%). The reason why there is some residual risk of recurrence is due to a rare phenomenon called 'gonadal mosaicism'. This is when a parent carries a genetic change, but it is limited to a small cluster of egg or sperm cells. The genetic change would not, therefore, be detected on this parent's blood test. If either parent has the same SRCAP gene alteration as their child (and therefore also has Floating-Harbor syndrome), every time that they have a child in the future there will be a 50% (1 in 2) chance of having another child with Floating-Harbor syndrome.



Development

■ Growth

Most babies with Floating-Harbor syndrome have a low birth weight and are slow to gain weight and height. Average adult height is 140-155cm. Head size is usually normal. X-rays in early life may show that the bones are slow to develop (delayed bone age). Some children have low levels of growth hormone and may benefit from growth hormone injections to improve their growth.

“ She is now 13 and has been on growth hormone injections since she was 4, having been diagnosed with FHS age 3. She is due to stop taking it when she is 14, an event that she is looking forward to immensely! ”

■ Sitting, moving, walking

Children do not usually have a delay in reaching their motor milestones such as sitting, crawling and walking.

■ Speech

All children with Floating-Harbor have some degree of speech and language delay and this can be severe. Some children do not learn to speak. Receptive language skills (understanding spoken language) are usually stronger than expressive language skills (speaking or signing). Children with Floating-Harbor syndrome sometimes have a distinctive high pitched or 'nasal' voice.

■ Learning

Children usually have mild to moderate learning disability. Most attend a mainstream school but receive extra support with their learning.

■ Behaviour

Behavioural problems such as temper tantrums, attention deficit-hyperactivity disorder (ADHD) and anxiety are more common in childhood but often improve with age.

Medical concerns

Minor vision problems such as a squint or being long-sighted are common.

Minor hearing problems such as glue ear may be present. Treatment is needed if this affects how well the child can hear as good hearing is important for speech development.

Seizures/epilepsy have been reported in a small number of individuals with Floating-Harbor syndrome.

Gastrointestinal problems including gastro-oesophageal reflux which can be severe and may require treatment with medications or occasionally tube feeding. Constipation is also common and may need medical treatment.

Kidney problems such as hydronephrosis (swollen kidneys caused by a build-up of urine), kidney cysts or a missing kidney can occur. These can usually be picked up on a kidney ultrasound scan. Kidney problems can lead to high blood pressure which may need treatment.

Possible increased risk of brain aneurysms (a swelling of a blood vessel in the brain). Four adults with FHS have been found to have brain aneurysms and individuals with FHS *may* be more likely to develop aneurysms than the general population. Aneurysms may not cause any symptoms but some may rupture (burst) and cause problems such as a stroke. A special type of brain and neck scan (MRA – magnetic resonance imaging with angiography scan) can identify aneurysms, and it is possible to have treatment for an aneurysm to prevent rupture from occurring.

Genital abnormalities including undescended testes and hypospadias (the opening of the urethra through which a boy passes urine is not correctly positioned on the tip of the penis) are common. Boys may need an operation to correct these.

Early puberty may occur (before eight years of age in a girl or nine years of age in a boy).

Minor hand abnormalities such as short fingers or broad thumbs are common but do not usually cause any health problems.

Dental problems such as a delay in losing milk teeth, dental decay and small teeth are often seen but may not cause any health problems. Brushing teeth twice a day and avoiding sugary snacks and drinks is important to prevent tooth decay.