SCN2A INFORMATION SHEET #1

What is SCN2A?

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- *SCN2A* is a **gene.**
- It tells the body to produce a protein called **Nav1.2.**[1]

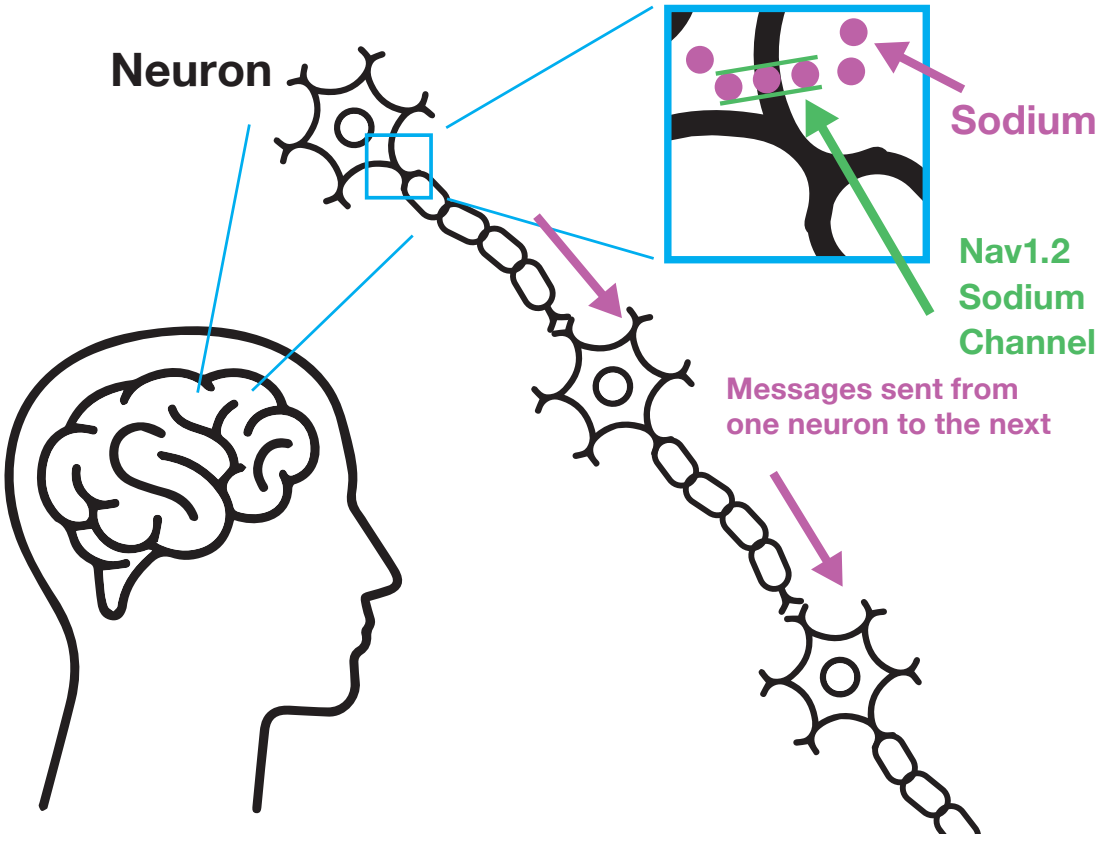
What does Nav1.2 do?

- Nav1.2 is an important **sodium channel** in the brain.
- This channel lets a chemical called **sodium** into brain cells **(neurons)**.
- The movement of sodium tells the neurons to 'fire', which sends messages between neurons and to the rest of the body.

In short...

SCN2A is a gene that tells the body to produce an important protein called ***Nav1.2***

Nav1.2 is a sodium channel that is found in brain cells (neurons)



How do changes in the *SCN2A* gene affect Nav1.2? [2-6]

Changes in the genetic code of the *SCN2A* gene can affect the way the Nav1.2 channel works.

- **If the channel lets in more sodium than usual, it may become overactive.**
  - > An **overactive** channel can cause brain cells to fire **more frequently** than usual. More messages are sent.
  - > Changes in *SCN2A* that cause the channel to become **more** active are called **gain of function variants.**
- **If the channel lets in less sodium than usual, it may become underactive.**
  - > An **underactive** channel can cause brain cells to fire **less frequently** than usual. Fewer messages are sent.
  - > Changes in *SCN2A* that cause the channel to become **less** active are called **loss of function variants.**

For more information about these changes, see Information Sheet #2 “What does gain of function and loss of function mean? ”

What impact could this have? [4-7]

- A change in the *SCN2A* gene can cause a range of conditions that affect the way the brain works (neurodevelopmental conditions).
- Some individuals are more affected than others.
- Symptoms include:
  - > Seizures
  - > Developmental delay and/or intellectual disability
  - > Movement disorders
  - > Autism spectrum disorder (ASD)
  - > Gastrointestinal problems (e.g. constipation, reflux)
  - > Problems with sleep.

The combination and severity of symptoms seen in individuals with *SCN2A*-related conditions varies widely. Most individuals fall into one of two broad categories. These may be further divided according to the age the seizures start and the type and severity of symptoms.

SCN2A-related conditions with epilepsy [7]

Self-limited neonatal / infantile epilepsy

(previously called benign familial neonatal/infantile seizures [BFNIS])

- The changed gene is usually inherited from a parent.
- Seizures start between 0–4 months of age and usually stop before the child is about 1 year old.
- Seizures generally respond to treatment.
- Most individuals have no other symptoms – there is usually no developmental delay or intellectual disability.

Severe neonatal/early infantile

- Also known as early onset developmental and epileptic encephalopathy (DEE).
- Seizures start before 3 months of age, usually during the first week after birth, and may be difficult to treat.
- Seizures usually continue into childhood but may reduce in frequency from 2–4 years of age.
- Most children have developmental delay and intellectual disability, ranging from moderate to very severe.
- Many children have movement disorders in the first few months of life, which may be severe.
- Other problems include low or high muscle tone, and gastrointestinal problems such as reflux and constipation.

Intermediate neonatal/early infantile

- Treatment-resistant seizures start soon after birth or in the first few months of life.
- Seizures may stop, become less frequent and/or respond to medication after 12 months of age.
- Individuals may have normal or moderately impaired development.
- Other symptoms may include ASD, mild movement disorders and gastrointestinal symptoms.

Mid-late infancy onset phenotype

- Also known as later onset DEE.
- Seizures start between the ages of 3–15 months and are usually not the first symptom of the condition.
- Children may have developmental delay, movement disorders, severe vomiting and/or failure to thrive before seizures start.
- Development may regress (go backward) when seizures start. Most individuals have moderate-severe developmental delay / intellectual disability.
- Other symptoms include ASD, movement disorders, high or low muscle tone, and gastrointestinal problems.

Childhood-onset phenotype

- Seizures start after the child is 1 year old, sometimes as late as 17 years.
- Development may be normal before the first seizure, and may later regress.
- Most individuals have developmental delay / intellectual disability or ASD.

SCN2A-related conditions without epilepsy

Intellectual disability and/or ASD

- A wide range of intellectual disability may be seen.
- Some individuals have a period where their development regresses.
- Other symptoms include low muscle tone and gastrointestinal problems.

Episodic ataxia

- Individuals with episodic ataxia have recurring periods of poor coordination and balance. During these episodes, they may also experience other symptoms including dizziness, nausea/vomiting, migraine, slurred speech and muscle weakness.
- The episodes may last from minutes to several hours.
- Frequency varies - from daily to once yearly.
- Symptoms usually start between the ages of 10 months and 14 years.
- Many individuals also have seizures.
- Individuals usually have normal development or mild developmental delay / intellectual disability.

More information

- Unique
- Children's Hospital of Philadelphia
- Centre for Genetics Education
- Human Disease Genes

References

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4. Centre for Genetics Education. Health conditions caused by changes in the SCN2A gene. Available at https://www.genetics.edu.au/SitePages/SCN2A.aspx. Accessed 17 July 2022.

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7. Howell KB, Palmer EE, Hildebrand M. SCN2A. Professionals: Clinical characteristics. Available at https://humandiseasegenes.nl/scn2a/professionals/clinical-characteristics. Accessed 17 July 2022.