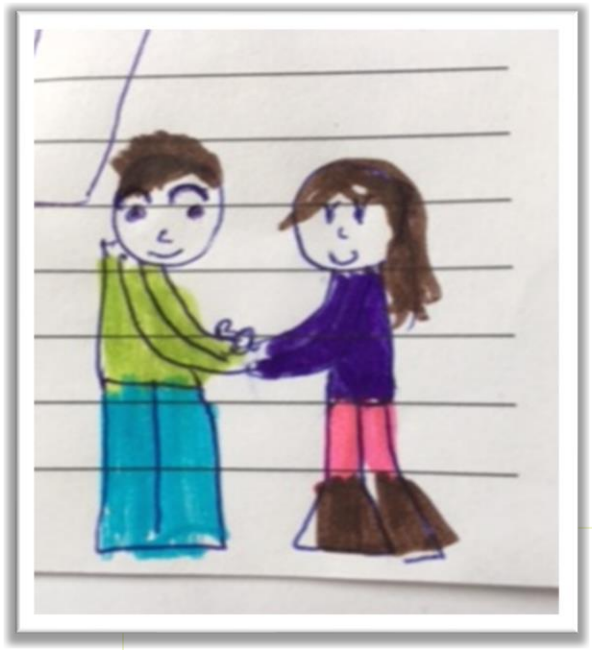

SYNGAP1

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SYNGAP1 – normal function

- The SYNGAP1 gene provides instructions for making a protein, called SynGAP, that plays an important role in nerve cells in the brain.
- SynGAP is found at the junctions between nerve cells (synapses) where cell-to-cell communication takes place.
- Connected nerve cells compose the "wiring" in the circuitry of the brain.
- Synapses are able to change and adapt over time, rewiring brain circuits, which is critical for learning and memory.
- SynGAP helps regulate synapse adaptations and promotes proper brain wiring.
- The protein's function is particularly important during a critical period of early brain development that affects future cognitive ability.

Source : https://ghr.nlm.nih.gov/condition/syngap1-related-intellectual-disability

Effects of SYNGAP1 mutations

- De novo mutations in the SYNGAP1 gene have been found to cause SYNGAP1-related intellectual disability; with Epilepsy, Hypotonia and Speech Impairment in combination, being significant other symptoms (see next slide).
- SYNGAP1 (working title for this disorder) is a Neurological disorder.
- It is also a Genetic disorder as the genetic change which causes the disorder is known. This only identified since 2009.
- A disorder is defined as 'rare' in Europe when it affects fewer than 1 in 2,000.
- SYNGAP1 is considered both a Rare Disorder and a Rare Disease; these titles can be used interchangeably for the purposes of understanding this document.
- There is currently no cure or treatment to reverse or contain / improve the disorder as researchers and clinicians are still trying to understand it's underlying and intricate biology.

Common symptoms of SYNGAP1 mutations…

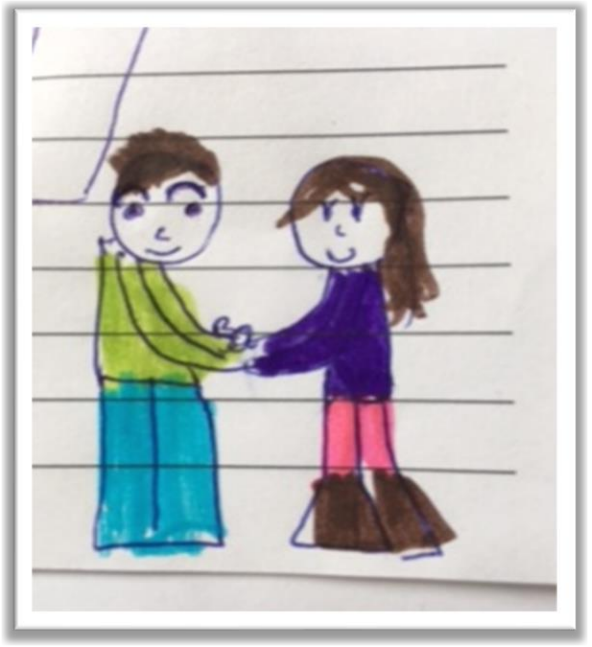
Not all of these symptoms will be present in every affected person. However, to date the most commonly described symptoms are:

- Intellectual Disability – can vary across the range, mild to severe
- Global Development Delay – onset in infancy
- Hypotonia (low muscle tone)
- Spectrum of Epilepsies – usually difficult to achieve seizure control
- Speech Delay - both receptive and expressive, can remain non verbal
- Delayed development of motor skills
- Language Disorder - Apraxia
- Autism Spectrum Disorders
- Sensory Perception Disorders
- Sleep Disturbances
- Constipation
- Joint, Spine and Gait issues – likely linked to low muscle tone.

What makes SYNGAP1 different

- Some of the symptoms are shared with other disorders but the underlying cause of the symptoms differ.
- The severity and onset of the symptoms can vary from patient; it is considered a spectrum disorder.
- It has a genetic basis meaning that the gene that causes the disorder has been identified.
- It has an emerging collection of symptoms, but there may be insufficient unique clinical characteristics to enable an early clinical diagnosis.
- There is a long journey of research and analysis ahead to further inform on SYNGAP1, and the points made here are reflective of that journey.

- Our family life is built on the foundations of Acceptance and Hope, Patience and Protection, Guidance and Gratitude, Health and Happiness, and Laughter and Love.
- There is presently no cure for SYNGAP1.
- As we are at the very start of our research journey, we have everything to play for in relation to treatments and cures.



- I hope we can Connect Local and Collaborate Global to better enable our ROI Syngap1 families.
- Email address: syngap1roi@gmail. com
- Family Awareness Contact : Michele Giblin
- Contact number ROI 087 793 7168
- There are many great SYNGAP1 resources available though home pages and Facebook groups, including
  - https://www.bridgesyngap.org
  - https://www.syngapglobal.net
  - https://www.syngapresearchfund.org