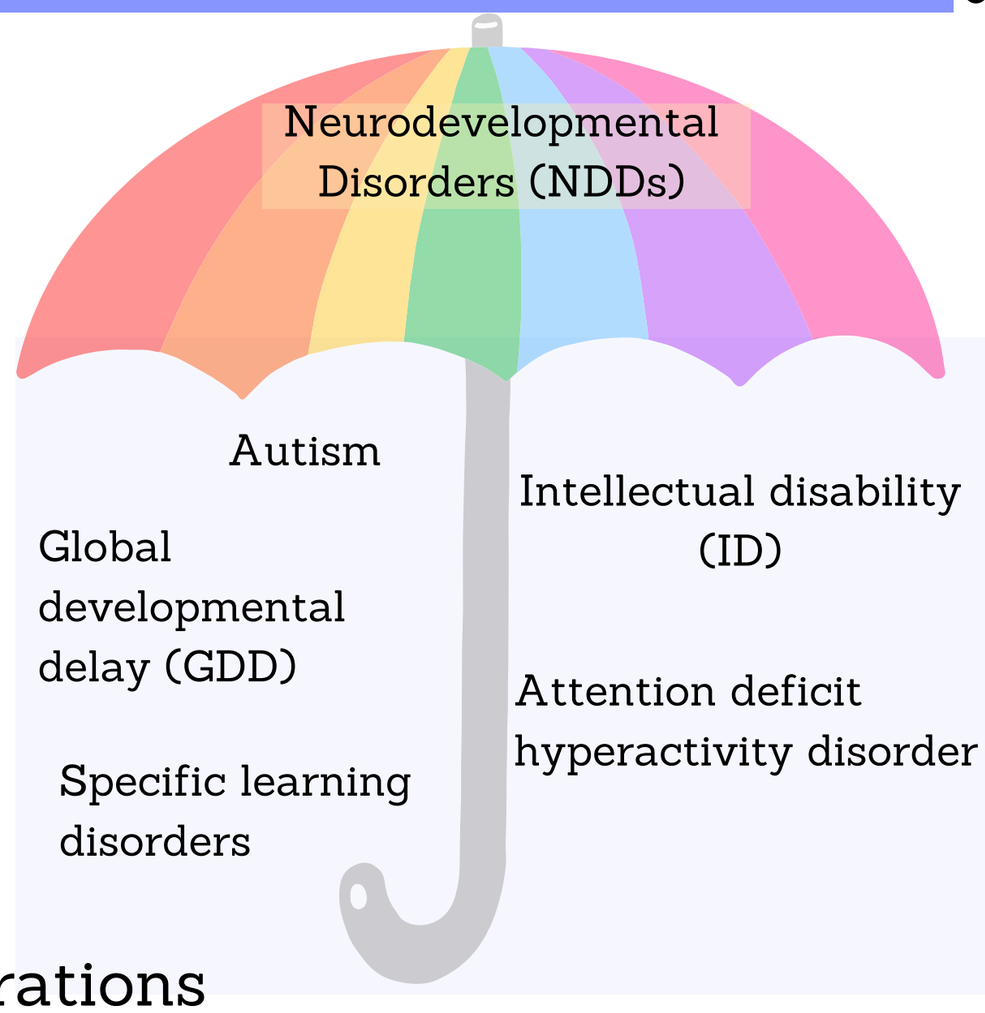
GECKO
Genetics Education Canada: Knowledge Organization
Centre d'éducation en génétique canadien: Connaissances organisées
POINT OF CARE TOOL

GENETIC TESTING FOR NEURODEVELOPMENTAL DISORDERS

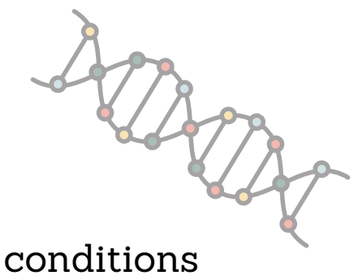
INFORMATION FOR INDIVIDUALS AND FAMILIES

A diagnosis of a neurodevelopmental disorder is made and your healthcare practitioner is offering genetic testing...

Neurodevelopmental disorder (NDD) is an umbrella term for conditions where differences in brain development lead to learning, behavioural, social, motor, and/or communication challenges. Everyone with an NDD is unique and will have individual strengths and support needs.



Who is offered genetic testing?



In Canada genetic testing is typically offered to <u>all</u>:

- autistic individuals
- individuals with unexplained GDD and/or ID
- individuals with any other NDD <u>plus</u> other health conditions

Potential benefits

A genetic diagnosis may:

- Explain why someone has developmental differences. This could increase feelings of empowerment, and decrease feelings of guilt.
- Support access to resources, like making connections to other individuals/families or access to research studies.
- Inform medical management e.g. which medications to use or avoid, whether extra screening should be offered such as cancer screening for Cowden syndrome.
- Provide an idea about possible future care needs.
- Provide information about the chance future children could have similar developmental differences.

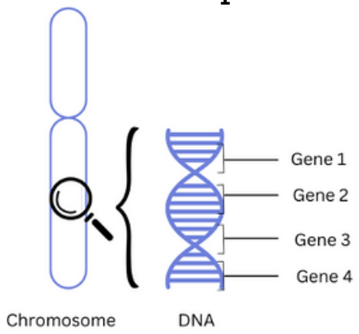
Considerations

- Genetic test results will not confirm or rule out an NDD diagnosis.
- A genetic test does not always find answers.
- Finding out about a genetic diagnosis might not be useful for medical care.
- There is a chance that the genetic results are unclear or surprising.
- For some people the information from genetic testing can cause anxiety, confusion, or stress.

Some common questions about genetic testing

- Will this test be used for research?
  - No, the testing offered is a clinical test for the benefit of the individual, family and healthcare team. There may be an offer to participate in a research study at a later time, but that would be separate, and explicit consent from the individual/substitute decision maker would be required.
- Who will have access to the test results?
  - The individual/substitute decision maker(s), healthcare practitioners in the patient's circle of care, and others who have explicit consent from the individual/substitute decision maker(s). The individuals/substitute decision maker(s) can refuse or take back consent at anytime.
  - In Canada, the collection, use and disclosure of health information is protected under <u>provincial and federal laws</u>.
- What about discrimination?
  - Genetic information (clinical or research) is protected under the federal Genetic Non-Discrimination Act, It applies to everyone in Canada and no third party can access genetic test results and use them against that person or their family members. <u>More can be read here.</u>

What do genes have to do with NDD?



- DNA is a set of instructions inside every cell of our body
- Genes are pieces of DNA that act like recipes.
- They are important instructions to the body for growing, developing and staying healthy.
- In our genomic library, there about 21,000 genes.
- Many genes play a role in how the brain develops and works.
- A chromosome is a DNA structure made up of a string of genes.
- Most (99.9%) DNA is the same from person to person, but everyone has variation/differences in their genes and this is why everyone is unique.
- Most of the time, differences in our DNA do not have any harmful effects.
- Some genetic variants can cause the person to have health issues or developmental differences, or a higher risk for these.
- Some genetic variants may cause someone to have an NDD or make them more likely to have an NDD.
- Genetic variants may be passed on from parent to child or may happen out of the blue for the first time.

<u>More about genetics at www.genome.gov > About Genomics.</u>

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What are the next steps?

Genetic testing is usually done on a blood sample. Talk with your healthcare practitioner if blood draws are challenging, as helpful approaches, such as coordinating with other routine bloodwork so only one poke is needed, can be explored. There are online resources that have some helpful tips.

surreyplace.ca > Resources > Blood Draw Toolkit

autism speaks > Toolkit >Provider guide to blood draw

1 First-tier genetic testing:

likely offered before an appointment with a Genetics specialist

a CHROMOSOMAL MICROARRAY

Chromosomal microarray (CMA) is a type of test that looks for differences in the *amount* of genetic information someone has.

CMA is a helpful test to find out if someone's medical condition(s) or developmental difference(s) could be caused by tiny extra or missing pieces of DNA, or by a whole extra or missing chromosome.

b FRAGILE X SYNDROME TESTING

Some people may also be offered testing for a condition called fragile X syndrome (FXS). FXS is more common in those whose sex assigned at birth is male. Often people with FXS will have additional physical or health features or a suggestive family history.

Many people who have FXS will also have an NDD, but most people with a NDD will not have FXS.

c GENOME SEQUENCING

Some people may also be offered genome sequencing (GS). This is a test that reads through each letter of all the genes in the genomic library to look for differences that could cause a gene to not work properly.

Currently this is only a first-tier test in Ontario for certain indications but may be offered as a second-tier test in other provinces.

2 Second-tier genetic testing:

When first-tier genetic testing does not find an answer, a geneticist (a doctor who specializes in genetic conditions) may offer further genetic testing, unless the only reason for testing was a diagnosis of autism. A referral would be needed to meet a geneticist.

What kind of CMA or GS results might be reported?

Positive

A genetic variant known to be associated with NDDs has been found.

This allows for relatives to be offered genetic testing.

These results may help guide medical management, predict the course of a condition.

A referral to a geneticist will be offered to explain results and discuss follow up.

Negative

also known as uninformative

No genetic variation known to affect health or development was found.

This does not rule out a possible a genetic cause.

A referral to a geneticist will be offered for consideration of 2nd-tier testing, *unless* a diagnosis of autism was the only reason for testing.

Variant of unclear significance

also called a VUS

A genetic variation was found, but there is not enough available information to know what it could mean.

A referral to a geneticist will be offered to discuss this result and for consideration of 2nd-tier testing.

Incidental finding

also called secondary finding

A genetic variation was found which may lead to a medical recommendation, but it is not related to NDD.

This may have implications for the individual and their relatives.

A referral to a geneticist will be offered for follow-up and consideration of 2nd-tier testing.

What kind of FXS results might be reported?

These results can be tricky to understand. Your doctor and genetics specialist can help.

Positive

Also called a full 'mutation'

This confirms a diagnosis of FXS.

A referral to a geneticist will be offered to explain results and discuss follow up.

Negative

This is a 'normal' result and rules out FXS as the underlying cause.

A referral to a geneticist will be offered for consideration of 2nd-tier testing, unless CMA results are also negative and a diagnosis of autism was the only reason for testing.

Other

May be called intermediate or 'premutation'

This is not a normal result, but also not *positive*.

This rules out FXS as the underlying cause but could be important for relatives, affecting family planning and adult health.

A referral to a geneticist will be offered for follow-up and possibly for consideration of 2nd-tier testing