

Epilepsy Genetics Service
Kings College Hospital & St Thomas's
Hospital, London

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Epilepsy Genetics Team

Professor Deb Pal

Dr Elaine Hughes

Dr Ruth Williams

Dr Karine Lascelles

Stephanie Oates (Specialist Genetic Counsellor)

Service

We run bi-monthly clinics for children and families affected by Complex Epilepsies to try and identify the genetic cause behind each condition. Currently we know of 102 genes that are involved in causing many different types of epilepsy, and if we are able to identify the genetic cause in your child, then we may be able to give more tailored advice on prognosis and treatment, as well as implications for the wider family and risks for future children. However, we still have a lot more to learn, and therefore cannot always identify the reason why your child has epilepsy.

How can I get a referral to your Service?

Have a discussion with your doctor as to whether this would be a suitable referral for you/your family. If they agree, then ask them to make a referral directly to Professor Deb Pal in the Paediatric Neurosciences department at either Kings College Hospital or St Thomas's (Evelina London Children's) Hospital. It would be helpful if your doctor could provide up to date contact details (telephone/email) for you as we always try to contact newly referred families before the appointment.

What can I expect at my appointment?

Before the appointment:

After you have been referred to our service, you should receive a phone call from Stephanie Oates, the specialist genetic counselor for this clinic. She will have a chat with you about your appointment, answer any questions you may have and ask about health conditions in your family tree. If you have any other relatives affected by epilepsy, it would be helpful if you could bring further information about them to the clinic appointment.

During your appointment:

- You should allow up to 1 hour for your visit.
- You will see Prof Pal and/or Stephanie Oates.
- We will ask about your child's health and perform a neurological examination.
- We may want your child to have further tests at another appointment. We may discuss medication with you.
- We may also ask further questions about your relatives and their health.
- We will discuss the possibility of genetic testing and the potential advantages and disadvantages of this if your child has not already had this.
- If you want to proceed with genetic testing, we can arrange this and further follow-up for your results.
- If your child has already had genetic testing we can discuss the meaning of their results and help interpret them for you.
- We can also discuss the possibility of taking part in any research studies or clinical trials that your child/your family might be eligible for.
- We will let you know about relevant patient groups or internet resources.

Epilepsy Gene Testing Options

There are currently two different types of genetic test options that are routinely available through our service: Array-CGH and Gene Panel testing.

Array CGH testing

Your chromosomes (the structures that carry your genetic information – DNA - that tell your body how to develop and function) can be examined under a microscope against a comparison set of chromosomes to look for small missing or extra pieces ("imbalances", also known as deletions or duplications). From this, the gene content of any such imbalance can be established. About 55% of epilepsies can be explained by a chromosomal imbalance, also known as a "copy number variant, or CNV." Array CGH (comparative genomic hybridization) can be performed on blood or prenatal samples. Results take about 6-8 weeks to come back.

Gene Panel Testing

It is possible to test for pathogenic mutations (disease causing changes) in lots of genes that are associated with epilepsy, all

at the same time. Currently we offer testing for up to 102 genes that have been associated with many different types of epilepsy. We all carry these genes, so it is not the gene itself that causes epilepsy, rather the mutation within it that stops the gene from doing its job properly.

Your Epilepsy Specialist will know which type of epilepsy your child has and, if appropriate, may request gene panel testing. As with Array CGH, this test can also be performed on blood or prenatal samples. The DNA sequence from each relevant gene is then isolated and read letter by letter to look for any unexpected changes.

We all have changes in our genes that don't cause anything serious to happen, it's just part of what makes us all different. So whatever changes are found, the laboratory will then analyse it/them carefully to see if it/they might be pathogenic (disease causing), benign (not disease causing, and just part of the normal background variation we all have) or a variant of uncertain significance (not enough evidence to classify it one way or the other).

Pathogenic gene mutations can be found in 25-30% of epilepsies sent for gene panel testing overall, although the age at which symptoms began, and the type of epilepsy can significantly affect the chance of finding a mutation.

Results usually take 4-6 weeks to come back.

Advantages and Disadvantage of Genetic Testing

If your child has already been diagnosed with epilepsy, then genetic testing will not change their diagnosis in any way, but if a mutation is found, it may suggest an alternative treatment that is appropriate to better manage symptoms.

There can be advantages and disadvantages to having a genetic test, depending on your point of view, including:

Advantages

Finding a potential reason for your child's diagnosis and the most suitable treatment for them, as well as the potential to get involved with specific research.

Disadvantages

Finding a potential reason for your child's diagnosis – as it sometimes change how you feel about their condition, yourself or your family e.g. for some people it can trigger feelings of anxiety, anger and guilt.

Genetic Counselling

Genetic counselling is a communication process, which aims to help individuals, couples and families understand and adapt to the medical, psychological, familial and reproductive implications of the genetic contribution to specific health conditions.

This process integrates the following:

- Interpretation of family and medical histories to assess the chance of disease occurrence or recurrence.
- Education about the natural history of the condition, inheritance pattern, testing, management, prevention, support resources and research.
- Counselling to promote informed choices in view of risk assessment, family goals, ethical and religious values.
- Support to encourage the best possible adjustment to the disorder in an affected family member and/or to the risk of recurrence of that disorder

(Resta et al, (2006) A new definition of genetic counselling: NSGC task force report, J Gen Counselling)

It is important to consider all this before going ahead with genetic testing so you are fully aware of what it can or cannot tell you and how it might affect your child and your family. We always review these issues in our clinic and for more in-depth discussion; our genetic counselor can see you in clinic or speak with you over the phone.