MEDICOVER
GENETICS

PEDIATRIC GLOBAL DELAY

Define&Decide

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Physician Information

WHAT IS GLOBAL DELAY DEFINE&DECIDE

DEFINE

Global developmental delay and intellectual disability (GDD/ID) affect up to 3% of children <5 years old and is defined as a delay in ≥2 developmental domains*. Up to 40% of GDD/ID cases are caused by genetic factors, including chromosomal abnormalities in 25% of cases, and monogenic disorders in up to 10% of cases. Up to two-thirds of children with GDD do not have a single group of symptoms that can point towards a specific diagnosis; therefore, several genetic tests are often required to define the cause of GDD/ID.

Our tests **combine chromosomal analyses and (comprehensive) gene panels** associated with many different disorders with overlapping features.

DECIDE

Having a diagnosis can help you decide on early rehabilitation services (if possible) and treatment options and identify associated medical risks, thereby improving the patient's clinical outcome and preventing further complications. Our genetic counselling can help guide management options and reproductive decisions based on recurrence risks.

*Developmental domains include physical, cognitive, speech/language, social and emotional

WHO COULD BENEFIT FROM THIS TEST

- Children <5 years with a significant delay in ≥2 developmental domains*
- Children with an autism spectrum disorder
- Children with dysmorphic features

IMPORTANCE OF GETTING TESTED

GDD/ID disorders often require lifelong support and/or treatment and may have a profound impact on the lives of children and their families. Identifying the cause can provide a prognosis, refine treatment options, evaluate recurrence risks and provide closure to the diagnostic journey, which can improve the psychological outcomes for the child and their families.

MEDICAL GENETIC COUNSELLING

We provide expert medical interpretation of the results for the specialist as well as for the patient, where needed. Our goal is to provide the patient with a better understanding of the results and the ability to make a more informed decision.

GLOBAL DELAY SYNDROMES

GREIG CEPHALOPOLYSYNDACTYLY

RETT • SOTOS • KABUKI • COFFIN-SIRIS

CHARGE • LEOPARD • SHPRINTZEN

SEGAWA • CORNELIA DE LANGE

WILLIAMS-BEUREN • COFFIN-LOWRY

PELIZAEUS-MERZBACHER • SECKEL

SIMPSON-GOLABI-BEHMEL

COSTELLO • DIGEORGE • WEAVER

MECP2 DUPLICATION • ROBINOW

BECKWITH-WIEDEMAN • ANGELMAN

RUBINSTEIN-TAYBI • SILVER-RUSSELL

LUJAN-FRYNS • PITT-HOPKINS

PHELAN-MCDERMID • MOWAT-WILSON

MICRODUPLICATION 22q11.2

SMITH-MAGENIS • MILLER-DIEKER

DIAGNOSTIC PROCESS

STEP 1

Patient history, **physical examination** and **sensory evaluation** should be conducted for each child with suspected GDD/ID

STEP 2

Following a clinical evaluation, **genetic counselling** is recommended with one of our counsellors

STEP 3

Molecular genetic analysis of the patient's genome

WE OFFER TWO OPTIONS TO TEST FOR GDD/ID:

OPTION 1: Stepwise Analysis

First, a genome-wide screen for **deletions/duplications** is performed. If none are detected, another **genetic counselling session** is conducted and one of our **gene panels** will be recommended by our genetic counsellor.

OPTION 2: Simultaneous Analysis

Screening for **deletions/duplications** and **gene panel sequencing** are performed **at the same time**. Performing both steps simultaneously saves time and resources for the patient.

STEP 4

All cases are finalized with a **medical report** and **genetic counselling**

OUR TESTS

SCREENING OF DELETIONS, DUPLICATIONS AND ANEUPLOIDIES

Microarray comparative genomic hybridization (microarray CGH) is used for genome-wide screening of deletions (loss of genetic material) and duplications (gain of genetic material) and does not require prior knowledge of precise genetic aberrations. This method will not detect chromosomal structural changes that do not result in deletions/duplications, such as translocations or inversions, ring chromosomes or low-level mosaicism.

GENE PANELS

- 63 genes — Autism Spectrum Disorders
- 43 genes — Brain Malformations, Comprehensive
- 9 genes — Brain Malformations, Lissencephaly
- 19 genes — Brain Malformations, Pontocerebellar Hypoplasia
- 8 genes — Brain Malformations, Tubulinopathies
- 10 genes — Coffin-Siris Syndrome
- 43 genes — Congenital Disorders Of Glycosylation
- 7 genes — Cornelia De Lange Syndrome
- 21 genes — GPI Anchor Deficiency
- 179 genes — Intellectual Disability
- 66 genes — Macrocephaly
- 30 genes — Microcephaly
- 11 genes — Overgrowth Syndromes
- 14 genes — Pediatric Neurotransmitter Disorders
- 20 genes — RASopathies, Comprehensive
- 3 genes — Rett Syndrome
- 22 genes — Rett Syndrome And Related Disorders

- Fragile X syndrome analysis is available upon request
- Interpretation of the molecular genetic results relies on having an accurate clinical picture of the patient

WHAT ARE THE POSSIBLE OUTCOMES OF THE TEST

A molecular genetic diagnostic report outlining the results of the sequencing analysis is provided. Changes in DNA sequences (variants) can be detrimental and lead to a disorder causing GDD/ID. We will report on the following types of variants:

Pathogenic and likely pathogenic variants: the genetic cause of the observed symptoms has been identified and may help determine the right treatment and management plan.

Variants of unknown significance: there was not enough evidence to classify the variant as either pathogenic or neutral. Annual variant reclassification and testing family members is recommended.

It is important to note that a negative result does not guarantee the absence of a disorder or that the disorder does not have a genetic cause. Genetic testing is an evolving field and may not detect all variants or there may not currently be enough evidence to classify all variants that lead to an inherited disease.

TECHNICAL DETAILS

Microarray CGH: DNA is isolated, digested with restriction enzymes, labeled with 180K probes and hybridized with a reference DNA for 24-40 hours. The microarray is washed and scanned, and results are analyzed using a specialized software that identifies deletions and/or duplications in the patient sample with a functional resolution of 50kb.

Gene panel sequencing: DNA is isolated and next generation sequencing is performed on all coding exons and conserved intronic regions. Single base pair changes, small deletions and duplications, and copy number variants (CNV) are identified. Sequencing runs result in a Quality Score of >30 (accuracy >99.9%) in at least 75% of all bases with a coverage of >20-fold. CNV detection sensitivity is 76.99% and precision is 62.59% (with GC limitation between 0.4 and 0.6 per target, sensitivity is 77.04% and precision is 84.10%). Variant classification is performed following ACMG guidelines (Richards et al. 2015, Genet Med 17:405; Kearney et al. 2011, Genet Med 13:680).

WHY US

- A network of laboratories and medical institutions makes us **a leader in genetic testing** in Germany with foundations dating back to 1998
- A clinical team comprised of scientists, physicians and medical geneticists, several with **>20 years of experience** in genetic testing, assuring meaningful and comprehensive genetic tests
- **Up-to-date diagnostic algorithms**
- Expertise in gene variant analysis ensuring **"no variant left behind"**
- Cutting-edge technology in sequencing and laboratory methods allows for **short turnaround times**
- **Quality** assessed by several certifying bodies, including EFI, DIN EN ISO 15189 accreditation for medical laboratories, DIN EN ISO/IEC 17025 accreditation for testing and calibration laboratories and a generally valid GMP (Good Medical Practice) certificate
- **Data privacy** is your right and our priority

HOW TO ORDER THE TEST FOR YOUR PATIENT

1. Complete Global Delay Test Order Form
2. A sample is collected at the nearest blood drawing point
3. Analysis is performed in our laboratory
4. A medical report is delivered
5. Genetic counselling is available upon request

Step 3-4 takes 15-25 working days

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Contact info

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