

Background

Individuals who have two or more copies of the Methyl CpG Binding Protein 2 (*MECP2*) gene, located on the Xq28 chromosome, have been found to share a distinct clinical phenotype known as *MECP2* duplication syndrome¹. The majority of cases are diagnosed using an Array CGH (comparative Genomic Hybridization) test which has the capacity to detect sub-microscopic duplications and deletions².

Over the last decade more than a hundred cases have been reported in the medical literature but the incidence and prevalence are unknown, as no population-based studies have been undertaken³. Patients diagnosed with *MECP2* duplication syndrome present with a range of general indications such as developmental delay, intellectual disability, dysmorphic features, multiple congenital anomalies, autism, epilepsy, short stature, or failure to thrive^{3,4}. While the syndrome is mostly identified in males, females have also been reported with a phenotype that has some similarities but is distinct to that of males and with a wide range of severity⁵.

This study will improve our understanding of the core clinical features of *MECP2* duplication syndrome and concomitantly increase awareness of it among clinicians. This is important since the majority of affected males reported to date inherited the duplication from their mother and mothers with more than one affected child have been reported. In addition, since microarray is being performed so frequently, it is also important that those who order the tests are able to interpret and counsel families appropriately.

Objectives

The study aims to:

1. generate population-based estimates of incidence and prevalence of *MECP2* duplication syndrome in Australia;
2. describe the core clinical features of *MECP2* duplication syndrome; and
3. raise awareness in the clinical community of this rare syndrome

Case definition

Please report any child in your care aged up to 15 years for whom genetic testing has confirmed the presence of a genomic duplication that includes the *MECP2* gene.

Clinical features reported to have occurred in *MECP2* duplication syndrome include:

1. infantile hypotonia;
2. intellectual impairment commonly with absence of speech;
3. epilepsy;
4. recurrent respiratory infections;
5. progressive spasticity; and
6. autistic behaviours such as repetitive hand movements and abnormal social development.

Affected individuals may also have distinctive features such as microcephaly, depressed nasal bridge, thick lips and tapering fingers.

Importantly, the presence or absence of these clinical features does not define the case definition which is genetically based.

Reporting instructions

Please report any child fulfilling the genetic case definition whom you have seen in the last month and whom you have not already reported to the APSU.

Investigators

Professor Helen Leonard, *Telethon Institute for Child Health Research, UWA*

Dr Jenny Downs PhD, *Telethon Institute for Child Health Research, Perth*

Dr Alison Anderson PhD, *Telethon Institute for Child Health Research, Perth*

Dr Cathy Kiraly-Borri, *Princess Margaret Hospital for Children, Perth*

Dr Ashleigh Murch, *PathWest Laboratory Medicine, Perth*

Dr Carolyn Ellaway, *Western Sydney Genetics Program, Children's Hospital at Westmead, Sydney*

Dr David Amor, *Victorian Clinical Genetics Services, Royal Children's Hospital, Melbourne*

Dr Michael Gattas, *Brisbane Genetics, Brisbane*

Dr Elizabeth Thompson, *SA Clinical Genetic Services, Women's and Children's Hospital, Adelaide*

Any questions should be directed to:

Professor Helen Leonard

Telethon Institute for Child Health Research

PO Box 855 West Perth WA 6871

Tel: 08 9489 7790 or mobile 0419 946 956

Fax: 08 9489 7704

Email: hleonard@ichr.uwa.edu.au

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5. Shimada, S., Okamoto, N., Ito, M., Arai, Y., Momosaki, K., Togawa, M., et al. 2013. MECP2 duplication syndrome in both genders. *Brain and Development*, 35, 411-419.