An Australian population study of factors associated with MRI patterns in cerebral palsy

Sue Reid, PhD1,4 Charuta Dagia, MBBS2 Michael Ditchfield, MBBS3 John Carlin, PhD1,4 Elaine Meehan BSc1 Dinah Reddihough, MD1,2,4

1Murdoch Childrens Research Institute, Melbourne, 2Royal Children’s Hospital, Melbourne, 3Monash Children’s Hospital, Melbourne, 4University of Melbourne, Australia

Background and aims
Magnetic resonance imaging (MRI) provides information about the nature and timing of the brain injury in cerebral palsy (CP).

The aims of our study were to
1. describe the distribution of brain MRI patterns in a large population sample of children with CP, and
2. examine associations between MRI patterns and selected antenatal, perinatal, and clinical variables.

Methods
Children born between 1999 and 2006 (n=884) were identified, and demographic, birth and clinical data were extracted from the Victorian Cerebral Palsy Register, a population-based Register of persons born in Victoria, Australia, since 1970 with a diagnosis of cerebral palsy. Children with brain lesions acquired after day 28 of life were excluded.

Of the 884 eligible children:
• 230 (26%) had no known imaging
• 60 (7%) had scans unavailable for assessment
• 1 had poor quality imaging that was unable to be assessed
• 593 (67%) had scans assessed and classified by one of two paediatric radiologists blinded to clinical information and previous reports.

The scans were classified into six major categories:
• White matter injury (WMI), a pattern frequently seen in children born before 34 weeks’ gestation, but also seen in term-born children
• Cerebral gray matter injury (GMI) affecting the cortex/subcortex and/or deep gray matter bilaterally. GMI has been described following acute hypoxic-ischaemic, inflammatory, or metabolic insults in infants born near term
• Brain malformations
• Focal vascular insults, the most common of which is infarction in the territory of the middle cerebral artery
• Miscellaneous lesions
• Normal scans

For children classified to a single MRI pattern, the frequencies of variables previously reported to be associated with CP were compared between patterns and with population or control frequencies.

Results
Most MRI scans (82%) showed a single pattern of abnormality, 5% had dual abnormalities and 13% were normal.

The distribution of MRI patterns is shown in the graph for 563 children with a single classification. White matter injury was the most common pattern (45%), followed by gray matter injury (14%), normal imaging (13%), malformations (10%), focal vascular insults (9%), and miscellaneous patterns (7%).

White Matter Injury
The strongest risk factors for white matter injury were preterm and multiple birth. WMI comprised the highest proportion of spastic diplegia, and the lowest frequency of epilepsy.

Gray Matter Injury
Grey matter injury was associated with term delivery, male sex, an Apgar score below 4, intubation or more than 10 minutes to establish respiration and neonatal seizures. Clinically, GMI was associated with dyskinesia, severe motor impairment and epilepsy.

Focal Vascular Insults
Small for gestational age and primiparity were risk factors for focal vascular insults. The majority of children were born at term, had spastic hemiplegia and mild motor impairment.

Malformations
Malformations were associated with multiparity and near term birth. Clinically, there were often multiple comorbidities.

Conclusions
This is the largest known population cohort of children with cerebral palsy and assessed MRI.

We found that:
• known risk factors for cerebral palsy had differentially strong associations with specific pathogenic patterns
• clinical features were associated with particular neuropathological patterns.

Cerebral palsy is an umbrella term.
• Further exploration of causal pathways to cerebral palsy will be facilitated by stratification on MRI patterns.
• Defining particular phenotypes will also be useful for counselling families.