



The Australian Cerebral Palsy Research Study

NEWSLETTER July 2011

An Update from the Principal Investigator

Our national buccal swab study is drawing to a close with recruitment and analysis complete and publications currently under review. This study was the largest study in the world looking at epidemiological and gene associations and their interactions in cerebral palsy families and control families. DNA from both child and mother were analysed. So many, many thanks to all our collaborators around Australia and of course our families who volunteered to give us detailed pregnancy information and their cheek swabs. The initial results of the study have been presented in the UK at Perinatal Medicine (Harrogate June 14-17th) and the abstract is attached. Michael O'Callaghan presented the paper and it won the best oral presentation award. We also congratulate Michael as he has just been awarded his PhD based on this work.

We shall update you with more publications in due course.

Team update

Two members of our team – Jessica Broadbent and Catherine Gibson – are currently on maternity leave and have had lovely baby girls.

Peta Watts joins us part time in WA to assist with blood collections for our latest project.

Dr Michael O'Callaghan leaves us for six months to work in Auckland on an Endeavour fellowship before returning in to the South Australian Cerebral palsy research group in 2012.

Thanks

Thank you to all of our collaborators who have played such an important role in the project over the last three years. We are continuing to work together in the research projects below and have renamed this collaboration as The Australian Collaborative Cerebral Palsy Research Group. We have also been able to collaborate with two major genetic laboratories in the US, Emory University and Washington State.

Current and future research

With rapid advances in gene technology it is now possible to study in greater detail the exome (the protein coding part of the genome) and the whole genome. This is opening up a new universe of exciting genetic information with many potential genetic alterations in functional areas of the genome that will have to be validated as pathogenic or non-pathogenic. These new studies require blood derived DNA and we are continuing



From Left: Corinne Reynolds, Alastair MacLennan, Gai McMichael, Michael O'Callaghan.

our interstate collaboration to collect triplicates of blood from mother, father and child in cerebral palsy families. We thank Neuroscience Research Australia and Steve Turner for their support of this bio-bank. Even more valuable are DNA samples from families with more than one family member with cerebral palsy. Our buccal swab study has helped identify some of these families. So our current efforts are to build up a large biobank of DNA from cerebral palsy families and to seek funding for these expensive but elucidating genetic tests. At the same time we collect extensive epidemiological information from these families and continue to look for interaction between genetic susceptibility and environmental triggers such as prematurity, intrauterine growth restriction and perinatal infection.

Kind regards

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The University of Adelaide.*

On behalf of the South Australian Cerebral Palsy Research Team: Catherine Gibson, (Cerebral Palsy Foundation Fellow), Gai McMichael (PhD candidate), Jessica Broadbent (Research Assistant), Corinne Reynolds (Research Assistant), and Michael O'Callaghan.

Overleaf:
Epidemiological and Genetic Associations with Cerebral Palsy



The Australian Cerebral Palsy Research Study

The Australian Cerebral Palsy Research Study Epidemiological and Genetic Associations with Cerebral Palsy

Michael E. O'Callaghan, Alastair H. MacLennan, Catherine S. Gibson, Gai L. McMichael, Eric A. Haan, Jessica Broadbent, Kevin Priest, Paul N. Goldwater, Jodie N Painter, Grant W Montgomery, Peter A Baghurst, Gus Dekker for the Australian Collaborative Cerebral Palsy Research Group.

Introduction

The Australian Cerebral Palsy Research Study assessed established and novel epidemiological and genetic risk factors for cerebral palsy (CP) along with their interactions.

Methods

Epidemiological data were collected by maternal questionnaire and linkage to state-based perinatal repositories and CP registers. Buccal swabs from 587 case and 1,154 control mother-child pairs provided DNA for assessment of 35 single nucleotide polymorphisms (SNPs).

Results

Epidemiological associations with CP included: maternal infection during pregnancy (OR 1.55, 95% CI 1.26-1.91), small for gestational age (<10th centile, OR 4.35, 95% CI 2.92-6.48), gestational age <32 weeks (OR 59.20, 95% CI 28.87-121.38), multiple birth (OR 6.62, 95% CI 4.00-10.95), a relative with CP (OR 1.61, 95% CI 1.12-2.32), breech position (OR 2.48,

95% CI 1.76-3.49), male gender (OR 1.68, 95% CI 1.38-2.06), previous miscarriage (OR 2.30, 95% CI 1.38-3.82) and illicit drug use (OR 2.22, 95% CI 1.14-4.30). Iatrogenic heat in labour was not associated with CP outcome. No association with CP was found for 34 of the 35 SNPs studied; there was a marginal association with fetal carriage of Prothrombin gene mutation in hemiplegics born at term with a reported infection during pregnancy ($p=0.0589$, OR 4.52, 1.70-12.03 after Bonferroni correction). Multivariable analysis of CP subtypes showed family history of CP to be a risk factor in quadriplegia (OR 3.27, 95% CI 1.13-9.45) and those born at term (OR 2.38, 95% CI 1.40-4.06).

Conclusions

The largest risk factors for CP were preterm birth, small for gestational age and multiple birth. Family history, male gender and one SNP associations suggest a genetic contribution for some cases of cerebral palsy, with a possible interaction with antenatally acquired infection.

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