

STARS: Studies, Trials and Assessments after Research Studies

Cerebral palsy

The aim of the Cerebral Palsy Research Group is to determine whether cerebral palsy has a genetic basis and whether genetic susceptibility for cerebral palsy is triggered by environmental risk factors during pregnancy and early life.

The incidence of cerebral palsy in Australia, 2.5 cases in every 1000 births, has not changed in 50 years. This is despite a 6-fold increase in caesarean delivery which should have reduced cerebral palsy if the main assumed cause, problems in labour, was correct. It is now thought that probably less than 2% of cases are directly related to problems in labour.

The financial cost of cerebral palsy in Australia alone is over \$5 billion per year. There is no cure for cerebral palsy and no proven method to prevent it. A better understanding of the causes of cerebral palsy is essential to allow preventive measures to be formulated and tested.

Led by Professor Alastair MacLennan, the South Australian Cerebral Palsy Research Group changed its name to the Australian

Collaborative Cerebral Palsy Research Group when it set up the world's largest genetic and epidemiological study of cerebral palsy with collaborators throughout Australia. DNA was extracted from over 4,200 buccal swabs from case and control families throughout Australia. The study examined 35 candidate genes that may be associated with cerebral palsy through their influence on fetal or maternal inflammatory responses, thrombophilia or an increased risk of preterm labour. A large amount of epidemiological information was collected from state perinatal data sets, state cerebral palsy registers and maternal questionnaires. These data were linked to the genetic data. The results will be offered for publication in 2011.

This large Australian gene-association study of individual gene mutations has led in 2010 to an international collaboration with colleagues in the United States who have access to new second-generation genetic technology that allows much more detailed analyses of the human genome and the common variations of large submicroscopic segments of chromosomes that may predispose to neurological developmental disorders. These have been associated recently with autism, epilepsy

and intellectual disability, but until now cerebral palsy has not been studied for these genetic variations. We are building up a large biobank of buccal and blood-derived DNA from cerebral palsy families to study potential genetic changes found by these increasingly sophisticated and expensive technologies, either through collaboration with our US collaborators or, if future funding permits, in Adelaide.

The three-year buccal swab DNA national study successfully finished recruitment in 2010, and all genetic and epidemiological data were entered into our databank for ongoing analyses. Scientific papers concerning these results are being prepared for submission for publication in 2011. Michael O'Callaghan, PhD student, has completed his thesis based on the gene-association study and, on behalf of the research group, published the study protocol and a systematic genetic literature review of this area. Gai McMichael started her master's thesis based on the new second-generation genetic methodologies, and has also published on improved methodology to extract viral DNA from stored neonatal blood spots. These data can also be linked with the same cases and controls.



Professor Alastair MacLennan
and Matthew Reinertsen