Institute of Psychiatry

at The Maudsley

KING'S College LONDON
Founded 1829

TS 2000 Study
Annual Newsletter 2010

Hello to All

You haven't heard from us in a while, so we thought sending our annual newsletter would be the best way to let you know how the research is progressing.

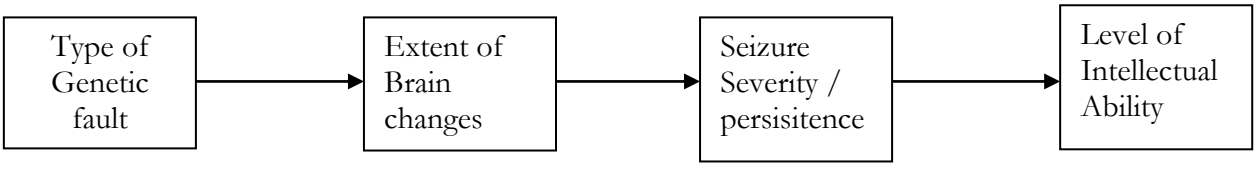
Research Update

Now that we have good quality information for most of the TS 2000 children, we have been able to embark on a detailed analysis of these data. We have been analysing data on the initial symptoms that lead to the diagnosis of TS and how the diagnosis was made. We are also looking at the seizure histories, results of genetic testing and the detailed brain scan findings to see how these may have affected intellectual disability. Several research papers are currently being written on these data, and we hope to have these published by early next year.

Summary of findings so far

Having successfully completed the first phase of the study, we want to take the opportunity to tell you about some of the key findings.

This study has shown the value of genetic testing for confirming the diagnosis. Genetic testing identifies the genetic defect in 90% of TS cases and should be more widely used for confirming the diagnosis, particularly in young children, in whom diagnosis of TS can be difficult. The commonest initial presentation of TS in this study was with seizures in infancy or early childhood. This was the first sign of TS in 62% of children. The second most common presentation, seen in 17% of babies, was the identification of abnormalities at routine antenatal ultrasound examination, particularly rhabdomyomas in the heart. This study has shown that diagnosis of TS before onset of epilepsy is becoming increasingly common (in one fourth of cases with TS), raising difficult questions about whether children should be monitored for early detection of seizures and whether there would be any benefit from starting treatment with anticonvulsants before seizures begin. This study has also emphasized the importance of kidney scans in all newly diagnosed cases for early detection of polycystic kidney disease, a rare complication of TS. About 65% of cases in this study showed some degree of intellectual disability. One of the key findings from our research is that the risk of intellectual disability is influenced by genetic factors, the extent of brain changes and the severity of seizures. In comparison to mutations in the TSC1 gene, TS caused by generic changes in the TSC2 gene tends to be associated with a greater number of cortical tubers throughout the brain. More extensive brain involvement tends to cause a higher frequency & severity of seizures. This in turn is associated with a higher risk of learning problems. The following figure summarises this key finding: which has a correlation with brain involvement as illustrated in the diagram below.



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Future Plans

John Yates retired in April 2008 but has been continuing to work on the study helping with the analysis and publication of the study data. Cathy MacLean has moved to a new post at Cambridge University, but in her spare time is also helping out to complete this phase of the study. Having worked for so many years on the TS 2000 Study the whole study team are committed to completing the first phase and publishing the results. Michelle Clifford has returned to Ireland to take up a consultant post there, but remains in touch. Patrick Bolton, based at the Institute of Psychiatry and the Maudsley Hospital in London, is now leading the TS 2000 Study and is busy planning the next stage of the research.

Phase two of the study will involve further follow up of the TS 2000 children to chart their progress. At follow up, we will be aiming to complete further assessments of all children in terms of their cognitive & behaviour development which will help us understand their areas of strengths & weaknesses. All the children in the study are now old enough to allow these detailed assessments, and adding these results to all the data we now have on the children should give us a much better understanding of the factors that lead to some children with TS having developmental and behavioural problems whilst others do not. Currently, we are also seeking funding for more in-depth brain imaging and brain wave (EEG) studies for all children and we will update you on progress with this. We will therefore be contacting you again soon to request that you help us in collecting further information on your children. We would be grateful if you could update us with any change in your contact details.

Thank You!

The data we collect from this study is a very important way to learn more about the natural history of Tuberous Sclerosis and how we can improve the outcome for affected children. We would like to take this opportunity to thank you again for participating in this study and to wish you a merry Christmas and happy New Year.

With Best Wishes,

Cathy MacLean
Study Co-ordinator

Professor John Yates
Emeritus Professor of Medical Genetics, University of Cambridge

Professor Patrick Bolton
Professor of Child & Adolescent Psychiatry and Honorary Consultant, Institute of Psychiatry, London

If you need to Contact us:

Cathy MacLean
TS 2000 Study
Box 279, Addenbrooke's Hospital
Cambridge, CB2 0QQ
Tel: 01223 348 450
Email: cm329@cam.ac.uk

Professor Patrick Bolton
Child & Adolescent Psychiatry
Box P046
The Institute of Psychiatry
De Crespigny Park
London, SE5 8AF
Tel: 0207 848 5325