

TS 2000 Study

Annual Newsletter 2011-12

Hello to All

You haven't heard from us for about a year, so we thought we would send our annual newsletter in time for Christmas, to let you know how the research is progressing and to invite you to participate in our £50.00 Christmas Prize Draw (see enclosed details).

Research Update

Last year, we updated you with the findings from the phase 1 of the study. This included a summary of the common findings in tuberous sclerosis, importance of genetic testing and the predictive value of some of the key elements of tuberous sclerosis. I am delighted to say that the findings regarding the features of tuberous sclerosis at first diagnosis have been published (Yates et al., 2011) in the Journal "Archives of Diseases in Childhood". This paper reported that diagnosis is being made increasingly early and that genetic testing is can be very useful to confirm a suspected diagnosis. The paper also highlighted the need for regular check ups to look for any of the complications that may develop in tuberous sclerosis.

We also explained in the Newsletter some results from phase 1 about the development of intellectual disability in tuberous sclerosis. These indicated that TSC2 as compared to TSC1 mutation is more likely to result in more brain changes (cortical tubers in various parts of the brain). The extent of brain involvement was associated with a higher frequency & severity of seizures. This was associated with more learning problems. A paper describing these findings (Bolton et al., in submission) has now been submitted for publication and shortly, we hope to hear that it has been accepted.

Since we last wrote to you, Dr Charles Shepherd from the TS clinic in Belfast, has contacted us to help gather more information about the TS 2000 children that have developed a SEGA (subependymal giant cell astrocytoma), one of the main complications that can develop in the brain. Some of you may have received a letter from him. If not and SEGA has been a problem in your child, please let us know and we can alert Dr Shepherd.

This year, we have started on phase 2 of the TS 2000 study. Phase 2 aims to follow-up all the children in TS 2000 to see how they have been progressing since they were originally assessed. We hope to learn more about the types of problems that develop as children grow up. We are very keen to find out about the development of each and every child in the TS 2000 study, because we want to get as accurate a picture as possible about the 'natural history' of tuberous sclerosis.

To begin phase 2, we are contacting families and inviting them to complete questionnaires by post and 'on line' regarding their cognitive & behaviour development. We are also asking for details about seizures, medical investigations and other medical updates. As part of this survey, we are asking teachers to also provide information about the child's progress and behaviour at school. The findings will help us further understand areas of strengths & difficulty. So far, we have received a large number of response and we are very delighted that so many teachers have helped by successfully completing the questionnaires. Please send them our thanks.

The added information we now have on the children is providing us with a much better understanding of the factors that lead to some children with TS having developmental and behavioural problems whilst others do not. As a token of our appreciation, we are sending **£10 vouchers** for the children of families who have completed the questionnaires.

The Research Team

A few colleagues have joined the research team to help with Phase 2.

Dr Chhitij Srivastava, a child psychiatrist has been helping to co-ordinate the collection of the questionnaires. Some of you who have attended the TS clinic at the Institute of Psychiatry and Maudsley hospital may remember him. He has recently completed writing a report about children with TS who show a regression and loss of skills after the onset of seizures and hopes that this will be published shortly. The report shows that regression can occur quite late in development (around 22 months of age).

Dr Shonima. Viswanathan has also helped to collect information, as part of an MSc in child psychiatry. For her dissertation, she made a preliminary investigation of the frequency of (attention deficit / hyperactivity (ADHD) in a subset of children from the TS 2000 study. The findings confirmed that children with tuberous sclerosis complex are at high risk for developing ADHD with 64.7% showing ADHD traits and 52.9% meeting criteria for a diagnosis of ADHD. She found that the higher the intellectual ability of the child, the less the chances of developing ADHD. We need to learn much more about why ADHD develops in children with TS, so that we can develop the best ways of treating and helping children.

Dr Stephen Hopkins has recently joined the team and will be helping to contact families to gather the remaining questionnaires.

News from the 2011 International Conference on TS

This year, the International conference on TS was held in Belfast and was hosted by Dr Charles Shepherd and Dr Patrick Morrison. A number of families were able to attend the meeting and gave very moving accounts of the trials and tribulations they have experienced. It was also a joy to learn how well some have been fairing after such very difficult times.

One of the undoubted highlights of the meeting was the promising results from the clinical trials of drugs (known as mTOR inhibitors) in the treatment of TS. The early indications are that these drugs may have a very important role to play in treating aspects of TS such as the kidney complications and the management of inoperable SEGAS. The very exciting findings from these studies highlighted however how valuable it is to have good quality information about the natural history of TS, so there was a lot of interest in the progress that is being made in the TS 2000 study. Professor Patrick Bolton presented the findings from the TS 2000 study with regard to intellectual development in TS. The findings from the TS 2000 study showed important differences to those from a study of adults from the Wessex region, that Patrick Bolton, Finbar O'Callaghan, John Osborne and colleagues conducted some 9 years ago (Joinson et al., 2003). Profound and severe intellectual disabilities were more common in the adults from Wessex study than in the children in the TS 2000 study. The findings raise the possibilities that either children with TS decline in intellectual function as they grow older or that improvements in the treatment

of epilepsy have led to less severe intellectual impairments. Over the last 20-30 years. It is clear that it will be important to determine which of these explanations is correct.

Future Plans

Currently, we are seeking funding to visit and assess children in order to get a more in-depth picture. We will hopefully therefore be contacting you again soon to request that you help us in collecting this further information on your children. As always, we would be grateful for any update and change to your contact details.

Thank You!

We would like to take this opportunity to thank you again for participating in this study. The data we collect from this study is a very important way to learn more about the natural history of Tuberous Sclerosis.

With Best Wishes,



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Bolton P, Clifford M, Maclean M, Humphrey A, Le Marechal K, Higgins J, et al. Intellectual Development in the UK Tuberous Sclerosis 2000 Cohort study: Risk Factors & Correlates. in submission.

Joinson C, O'Callaghan FJ, Osborne JP, Martyn C, Harris T, Bolton PF. Learning disability and epilepsy in an epidemiological sample of individuals with tuberous sclerosis complex. *Psychol Med* 2003; 33: 335-44.

Yates JR, Maclean C, Higgins JN, Humphrey A, le Marechal K, Clifford M, et al. The Tuberous Sclerosis 2000 Study: presentation, initial assessments and implications for diagnosis and management. *Arch Dis Child* 2011.