



# TS 2000 Study

## Annual Newsletter 2016

### **Hello everyone!**

It's been a year since we were last in touch, so we want to update you about our progress on the TS 2000 study and associated projects. Thank you for your ongoing participation.

### **Phase 2 is complete!**

We completed Phase 2 of the study in late 2015. Phase 2 followed up the children in TS 2000 to see how they had developed since they were originally assessed. We wanted to get as much information as possible about the 'natural history' of Tuberous Sclerosis, and in particular whether children were at increased risk of neurodevelopmental disorders such as Attention Deficit Hyperactivity Disorder (ADHD) and autism spectrum disorder (ASD).

Between 2013 and 2015 we carried out in-depth assessments of behaviour and cognition. We asked parents to complete an interview about their child's behaviour, communication and play, and complete questionnaires about aspects of communication, social interaction, 'adaptive' abilities in day-to-day life, activity levels and attention. We also asked children and young people with TS to take part in a range of assessments, tasks and games. These were designed to assess intellectual ability, social understanding, language, planning, memory, attention and thinking style. We also saw a sample of families to assess siblings who are *unaffected* by TS to act as a comparison group. We saw around 90 of the original 125 TS 2000 families and 30 siblings, and contacted over 90 doctors, accessing around 70 digital brain scans. We are very grateful for your time and all of your hard work!

### **Findings from Phase 2**

The findings from Phase 2 confirmed there is a high risk for ASD and ADHD in TS. We found that around 4 in every 10 children and young people with TS met clear-cut criteria for ASD and a further quarter of all children had possible ASD. We also found that among those children who did not meet criteria for ASD, a significant proportion showed traits of ASD. Around 2 in every 10 children showed no evidence of autistic difficulties, indicating that the prognosis for some children with TS is good. In terms of ADHD, we found that almost 40% of the children and young people with TS scored highly on our measure of ADHD, indicating that a significant

proportion of young people with TS have difficulties with attention, hyperactivity, and impulsivity.

We have also been using statistical modelling techniques to map 'risk pathways' to ASD and ADHD in TS. We found that the gene (TSC1 or TSC2) affected by mutation was important in the risk pathway to ASD, with TSC2 mutations resulting in greater numbers of cortical tubers. In turn, more tubers increased the severity of seizures in the first two years of life, and higher seizure severity increased the risk for ASD, as well as intellectual impairment, later in life. Different risk pathways seem to be involved in ADHD in TS. We found that current epilepsy severity was associated with higher levels of current ADHD symptoms, while the severity of seizures in the first two years of life increased the likelihood that children with TS would show increased variability in their responses during cognitive tasks, which is often reported in children and young people with ADHD without TS. In turn, this increased variability was associated with higher ADHD symptoms.

We presented these findings from Phase 2 at several scientific conferences this year, including the Tuberous Sclerosis Complex International conference in Lisbon, Portugal, the International Meeting for Autism Research in Baltimore, USA, and the European Network for Hyper-Kinetic Disorder (the European conference for ADHD research, Eunethydis) in Berlin, Germany. We are working to publish these findings in scientific journals soon and will keep you up to date with results as they are published.

### **Phase 3 has begun!**

We began seeing families for Phase 3 of the study earlier this year. In Phase 3 we are examining brain activity using EEG to see if different brain processes are associated with different outcomes in TS, including ASD, ADHD, epilepsy, and intellectual impairment. EEG is a non-invasive technique which records electrical brain activity ('brain waves') from electrodes (sensors) placed on the head. We are using a state-of-the-art EEG system (see the picture below) which, unlike clinical EEGs, lets us record brain activity without using gel and without having to 'glue' on each electrode separately. In our EEG system, we use a net which contains all of the electrodes and is simply

soaked in warm water and then placed on the head. We are finding that this is much easier for children and young people with TS to tolerate wearing than the clinical-style EEG systems. While they are wearing the net, we show the young person with TS a set of pictures and video clips, and ask them to complete some simple computer-game type tasks. We have tasks that are suitable for all abilities and ages. The tasks help us understand more about the brain processes in TS.



At the beginning of 2016 we started inviting TS 2000 participants to visit our research centre in London to take part in Phase 3. So far almost 40 of the young people with TS have visited us in London, as well as a sample of unaffected siblings. We hope to see the remaining TS 2000 participants in 2017.

If you have not yet taken part in Phase 3, or would like more information about the project, please contact Dr Lizzie Shephard ([elizabeth.1.shephard@kcl.ac.uk](mailto:elizabeth.1.shephard@kcl.ac.uk)). We will reimburse participants and their families for travel, meals and other expenses during the trip to London, and can offer accommodation for long-distance travel.

#### **MRI brain scans**

In 2016 we began inviting some participants to London to have a state-of-the-art MRI brain scan. We are using new MRI techniques to study how different parts of the brain are connected to each other, as well as visualizing cortical tubers, SEGAs, and other lesions. These scans help us understand more about the structural brain changes that occur in TS. We are hoping to conduct some more MRI brain scans in 2017. Our team might have already been in touch to find out if you are interested in a MRI scan, but you can also contact Dr Lizzie Shephard for more information ([elizabeth.1.shephard@kcl.ac.uk](mailto:elizabeth.1.shephard@kcl.ac.uk)). We will also pay all expenses for the visit to London for the scan.

#### **Our Research Team**

We are welcoming new members to the TS 2000 and saying goodbye to others. The study coordinator, Dr Fiona McEwen, left the team earlier in 2016 for a new position at Queen Mary University of London, where she is setting up a new project studying Syrian refugee

children. Dr Charlotte Tye was awarded a Junior Fellowship award from the Tuberous Sclerosis Association in 2015 and is now running a new study of infants with TS at King's College London – the Early Development in Tuberous Sclerosis study (EDiTS study). She is looking at how brain activity, measured using EEG, can help predict which infants will develop problems with social interaction, communication, and attention. She is currently looking for babies with TS ages 10 months or younger to take part in the study. EDiTS study assessments are conducted in the baby's home to make taking part as easy as possible for families. You can find out more about the EDiTS study on the study website ([www.edits-study.org](http://www.edits-study.org)) and by contacting Dr Tye by email ([charlotte.tye@kcl.ac.uk](mailto:charlotte.tye@kcl.ac.uk)). Drs McEwen and Tye remain involved in TS 2000 and are currently helping to analyse data and publish results.

Dr Lizzie Shepard joined the team in late 2015 and is running the Phase 3 EEG study. She has previously worked with infants at risk for autism spectrum disorder and children with ADHD and has expertise in using EEG techniques to study brain activity. Students and visiting researchers from abroad currently on placement with the team – Nina Friedrich, Dr Rosa Savino, Dr Gellan Ahmed – are currently providing invaluable support with data collection and administration.

#### **Contact details**

If any of your contact details have changed we'd really appreciate it if you could let us know.

#### **Thank You!**

We would like to take this opportunity to thank you again for participating in this study.

**With Best Wishes,**



**Professor Patrick Bolton & the TS 2000 Study Team**

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

#### **If you need to Contact us:**

TS 2000 (Lizzie Shephard), PO80, Institute of Psychiatry,  
Psychology & Neuroscience, 16 De Crespigny Park,  
London, SE5 8AF

Tel: 020 7848 5272, Email: [ts2000@kcl.ac.uk](mailto:ts2000@kcl.ac.uk) , Website:  
[www.tuberoussclerosis2000.co.uk](http://www.tuberoussclerosis2000.co.uk)