



## The Tuberos Sclerosis Association

This document can be found at [www.tuberous-sclerosis.org](http://www.tuberous-sclerosis.org)

It reports on a presentation at a meeting of the TS Alliance in San Diego in July 2001.

### TSA Alliance Family Conference, San Diego, July 2001

In the USA our sister organisation, the TSAAlliance ([www.tsalliance.org](http://www.tsalliance.org)), directs their research programme through their Centre Without Walls, led by Dr Vicky Whittemore. In 2000-2001, the CWW funded \$1million of research in TSC, and in addition there was \$3million of TSC research undertaken through the US Government National Institutes of Health. Researchers from the CWW came to the Family conference in San Diego to tell parents about research in progress or planned.

David Kwiatkowski, a clinical geneticist from Boston explained the work on whether TSC1 or TSC2 produced different problems. They looked at 16 measures of TSC from severity of learning disability to kidney problems. Learning disability was far more common in TSC2 (70%) than in TSC1(13%). TSC1 was also milder than TSC2 for a wide range of the effects on other organs of the body as well as the brain. There were still 17% of people in whom the mutation, whether TSC1 or TSC2 had not been identified, but in these people 7 out of 16 measures were less severe than those with identified mutations. In these people mosaicism may be present, that is, some of their body cells will have normally functioning TSC genes, some will have mutated TSC genes. If there are less than 30% of cells affected, milder symptoms could be predicted and there would be less risk of passing TSC on to children.

Peter Crino , a neurologist from Philadelphia, had looked at GABA and Glutamate within and outside the cortical tubers in the brains of people with TSC. GABA has an inhibitory effect on neurons, and damps down electrical activity, whereas Glutamate excites activity. The number of binding sites for Glutamate was much increased in the tubers, and the number of GABA binding sites was much decreased., and this meant there was an increase in excitatory activity and at the same time a decrease in inhibitory response. The result was that the normal GABA/Glutamate balance was off in TSC tubers and this is why the epilepsy is so difficult to control. More potent pro-GABA and anti-glutamate drugs were needed in TSC, and ways to target the tubers more directly.

Petrus de Vries, a psychiatrist from Cambridge, has just been given a CWW grant to follow up the attention studies he recently completed. He tested 20 children and adults and 55% had ADHD (Attention Deficit Hyperactivity Disorder) but 90% had some neuropsychological attention deficits. This meant that most children with TSC who did not show ADHD could still be having attentional problems at school. His grant would

enable him to study this further with the aim of developing strategies to treat these deficits.

David Gutman who is a neurologist explained that as well as neurons in the brain, there are the network of supporting glial cells. Glial cells (astrocytes) provide insulation for the neurons, promote the formation of the synapses where one neuron passes a signal to the next, provide nutrients to neurons, replenish the neurotransmitter pool and scavenge for toxins. The dysfunction in TSC was associated with an increased number of abnormal glial cells.