



## Psychiatric and Behavioural Issues in Adults with Tuberous Sclerosis Complex

Although Tuberous sclerosis complex (TSC) is a disorder involving many different parts of the body, it is well known that the brain is one of the major organs affected. Despite this, it is only recently that we have started to understand more clearly the effects that TSC has on the brain.

### Commonly asked questions

Many parents of a child with TSC, particularly as the child gets older, express the desire for information about what the future might hold. Although there is limited information available as yet, one of the purposes of this Fact Sheet is to examine the available research that has followed up children with TSC into adulthood to try and answer some of these questions.

Many adults with TSC, particularly those who have no learning disabilities, report feelings of anxiety, depression and/or anger and often question whether such feelings are related to TSC. In this Fact Sheet, we will also examine the evidence for this and will review the possible treatment options.

### What happens when children with TSC grow up?

Some of the best descriptions of behaviour in TSC were published in 1932 in Critchley and Earl's report of autistic behaviour in TSC. Critchley and Earl (1932) studied 29 residents of mental institutions and reported that unusual hand movements, bizarre attitudes and unusual repetitive movements (stereotypies) were frequently observed in people with TSC. After Critchley and Earl, there were no further systematic studies of psychiatric or behavioural

problems in TSC for the next 50 years. Despite this, occasional small studies were performed and an analysis of these studies revealed that three behaviours predominated: autism or autistic-like behaviours, hyperactive or impulsive behaviours and aggressive or uncooperative behaviours (Smalley et al., 1992).

More systematic studies began again in the 1980's and 1990's. In a large postal survey of 300 people with TSC, 80% were found to have learning difficulties or developmental delay and 93% had a history of epileptic seizures (Hunt 1993). In addition, parents reported that 56% had demonstrated behaviour that caused problems to others including disruptive behaviours, hyperactivity, socially impaired behaviour, repetitive and aggressive behaviours. While the age of this sample ranged from 6 months to 74 years, 40% were aged 15 years and over.

In a later study, Hunt and colleagues (1998) attempted to look at the outcome for children with TSC when they became adults. Data on 23 children with TSC aged 8-14 years, all of whom had mild or profound learning disability, were collected using parental interviews. All case notes were reviewed (Hunt & Dennis, 1987) and data were recorded on seizures, development and behaviours at age 5 years, giving individual personal profiles. After 10 years, the same 23 children were followed-up using parental interviews and data were recorded on a variety of measures including abilities and behaviour (Tables 1-2). Hunt and colleagues (1998) found that there was no deterioration in intellectual functioning mobility or speech when people with TSC were followed up. However, parents reported that the major problem area in TSC was in speech and communication and, for the great majority, communication did not improve with age. However, one child without speech at age 5 years, who was given intensive music therapy, had almost normal speech at age 20 years, could read both words and music, and had even sung with the local cathedral choir!

**Table 1** Abilities recorded at age 5 and as adults for 23 people with tuberous sclerosis (N = 23)

Abilities	Age 5	Age 18+
<b>Intellectual disability</b>		
None	2	0
Mild	2	2
Moderate	1	7
Severe	18	14
<b>Mobility</b>		
Walk unsupported	19	19
Walk with support	1	2
Not walk	3	2
<b>Speech</b>		
Normal for age	4	5
Structure good, content restricted	1	4
Simple words or echolalia	5	1
No speech	13	13

**Table 2** Behaviour problems recorded at age 5 and as adults for 23 people with tuberous sclerosis (N = 23)

	Age 5	Age 18+
No behaviour problems	2	5
Autism or autistic traits	17	10
Hyperactivity	14	5
Rage outbursts/aggressive	6	7
Destructive outbursts	9	3
Self-mutilation	3	3
Shouts (no speech)	4	7
Pica	4	2
Little emotional response	6	5

Parents also reported that there were fewer behaviours that caused family problems as their children had grown into adulthood, although 80% of parents still reported some problems. The biggest change was a drop in reports of hyperactive behaviour from 60% of the children reported as being more active than their peers to only 22% of the adults. Similarly, while 74% of the children studied were found to have some autistic features, only 43% of the adults had autistic traits.

One of the most important findings of this study, the first of its kind to follow up children with TSC into adulthood, was that there was little evidence of gross deterioration of actual intellectual ability between age 5 years and adult life in people with TSC. There was a steady increase in developmental skills among some of those assessed to have severe intellectual disabilities at age 5 years and moderate disabilities by age 18 years. In addition, there was a decrease in

behaviours associated with autism, behaviours which had been very prominent at age 5 years. Although hyperactive and destructive behaviours had also decreased greatly, reports of “blank” behaviour showing little emotional response remained constant in some individuals as did rage outbursts and aggression in others.

There are very few published reports of other psychiatric disorders occurring in adults with TSC and those that exist tend to be reports of isolated case reports of psychosis. Heckert and colleagues (1972) reviewed cases of psychosis in TSC reported to 1972 and reported 11 cases from various sources with diagnoses of schizophrenia, paranoia, hallucinations or delusions. However, there is no strong evidence that TSC has a specific relationship to psychosis and it is likely that the psychosis observed in some people with TSC is related to epilepsy or the presence of cortical tubers in isolated individuals.

In a much more sophisticated study of a large extended family where affected family members had a mutation of the TSC2 gene, 77% of people with TSC (both children and adults) were found to have a psychiatric disorder. These disorders included anxiety disorder (59%), mood disorder (35%) and attention deficit and hyperactivity disorder (13%) (Smalley et al., 1994).

### **Will children with TSC have to live in hospital when they grow up?**

Many parents of children with TSC worry that their children will not be able to live independently when they grow up. Although there is no way to completely predict the future for each individual child, it is generally considered that the more severe the learning difficulties/disability, the more likely that supported/supervised accommodation will be required. As about 50% of people with TSC do not have learning disability (a full scale IQ of greater than 70), it would be expected that the majority of these would not require supported accommodation. Where more severe learning disability occurs, some people may benefit from short-term supported accommodation although, for the most severely affected people, long-term supported accommodation may be required.

### **Brain abnormalities in TSC**

There is now considerable interest in the relationship between learning disability, psychiatric disorder, behaviour and the brain lesions seen in

TSC. It seems clear that the severity of the learning disability is closely related to the number of cortical tubers seen. In addition, the risk of cognitive impairment is also associated with the type and age of onset of epilepsy. Recently, Jones and colleagues (1999) reported preliminary evidence to suggest that learning disability was significantly more frequent in people with sporadic TSC2 rather than TSC1 mutations. In view of this, the TSA is currently funding further research to examine for more detailed genotype-phenotype correlations in people with TSC.

Is there any evidence that the presence of psychiatric disorder is associated with the presence of brain lesions? Bolton and Griffiths (1997) reported that involvement of the temporal lobe was associated with autism. Eight of nine people with TSC and autism or atypical autism had tubers in the temporal lobes compared with none in a group of nine people with TSC without autism. Future research will need to examine whether there are any correlations between other psychiatric and behavioural disorders and the presence of brain lesions in TSC individuals.

Although there is good evidence for an association between the presence of cortical tubers and learning disability, epilepsy and autism, few studies have examined whether people with TSC who have normal intelligence have specific cognitive impairments. Recently however, Harrison and colleagues (1999) reported that, in a series of seven children and adults with TSC and normal intelligence, people with TSC had significantly more cognitive deficits (errors in the ability of the brain to process information) than a control group of people without TSC. In other words, even those people with TSC who have an IQ in the normal (non-disabled) range may have some difficulty in performing certain tasks. Therefore, although approximately 50% of people with TSC are of normal intelligence, some of these people are still at risk of specific cognitive deficits. Full neuropsychological testing (i.e. testing by a clinical neuropsychologist) should therefore be performed on all TSC individuals whether or not they are thought to have a learning disability.

### **What are the treatment options?**

The treatment of psychiatric and behavioural disorders in both children and adults requires a well co-ordinated multidisciplinary approach. Specific studies of the effectiveness of psychiatric

and psychological treatments in TSC have yet to be performed. However, the available evidence suggests that standard psychiatric and psychological treatments with appropriate modifications to take account of the nature of the disease, are effective. If any adult with TSC experiences feelings of depression, anxiety, persistent feelings of anger, or indeed unusual experiences such as hearing voices or developing unusual or bizarre beliefs, they should seek an appointment with their General Practitioner as soon as possible. After such an assessment, the General Practitioner will then be able to advise on the most appropriate course of action. In many cases, no further action may be required. However, in some cases, a course of medication or counselling may be recommended. For more serious conditions, referral to specialised psychiatric or psychological services may be necessary. It is important to remember that, even if the psychiatric or behavioural problems are a consequence of TSC, there are many possible treatment options available and the available evidence suggests that treatment works just as well as in people without TSC.

### **Why are some people with TSC aggressive?**

Aggressive behaviour in people with TSC is often described, and can be a particularly difficult to manage when children with TSC enter adolescence and adulthood. The most important factor in managing aggression in people with TSC is to try and identify an underlying cause. Many people become aggressive because they become frustrated with certain things and are unable to articulate their needs accurately. Some people with TSC may become aggressive because of an underlying psychiatric disorder that has not been identified. In addition, aggressive behaviour can sometimes be a side-effect of some forms of medication. In view of this, consistent aggressive behaviour should be assessed by the General Practitioner who will then be able to advise on further management.

### **Conclusions**

It is well known that children with TSC have high rates of pervasive developmental disorders (including autism and atypical autism), attention deficit/hyperactivity disorder, epilepsy, learning disability and sleep disorders. The majority of research performed in this area has been confined

to children with TSC, or has included both children and adults in the study sample without separating the sample into separate age bands. Despite this, the available evidence suggests that, in a proportion of children with TSC, such disorders persist into adulthood. In addition, adults with TSC are also reported to have increased rates of anxiety and mood disorders. This suggests that the feelings of anxiety, depression and/or anger that many adults report may be a consequence of their TSC rather than a “normal” reaction to stress or difficult circumstances.

Future research will need to focus much more on long-term follow-up of adults with TSC to determine the true prevalence of psychiatric and behavioural disorders in this group. In addition, future studies combining molecular genetics, comprehensive neuropsychological assessment and structural brain imaging will lead to a much greater understanding of the neurobiological mechanisms underlying the psychiatric and behavioural disorders observed in people with TSC.

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