



Behaviour and Learning Disability in Tuberous Sclerosis

Introduction

How are the TSC genes involved?

Tuberous Sclerosis (TSC) is estimated to occur in 1 in 6000 individuals in the population at birth (1). About two thirds of cases are 'sporadic', that is "out of the blue", and neither the baby's father nor mother are found themselves to have TSC after full genetic testing. In the remaining third of cases the baby has inherited either the TSC1 or TSC2 gene from their father or mother since anyone with either TSC gene has a 1 in 2 chance of passing it on to any baby they conceive. Recent genetic work has found more *inherited* cases of tuberous sclerosis linked to a faulty TSC1 gene, and more *sporadic* cases to a faulty TSC2 gene (2). In addition, the learning disability and epilepsy associated with growths in the brain known as *cortical tubers* are less frequent in people with TSC1 mutations than in people with TSC2 mutations (3).

Parents are often only diagnosed with TSC after their child has been found to have it because they developed an obvious problem, such as infantile spasms, an early form of epilepsy. Their child can go on to develop severe learning disability and very challenging behaviours, all related to TSC, whereas the parent is not noticeably affected. It is this wide variation in physical and intellectual abilities that is so striking in tuberous sclerosis.

Does everybody with TSC have learning problems?

A survey in the Wessex region of the UK (4) where the IQ of people with TSC was tested found 55% with normal intellect and 45% with *learning disability*, the majority of whom had profound retardation with an IQ less than 20. But people

with TSC and normal intellect could be at risk from learning difficulties and the mean IQ of 93.6 of the group was slightly below the mean IQ of 105.6 for their siblings without TSC. There were also *significant language* deficits in normal intellect TSC children, but no increased rate of specific disorders of reading, spelling or maths.

Epilepsy, tubers and learning disability

How do cortical tubers in the brain affect epilepsy and learning disability ?

The faulty TSC1 and TSC2 genes produce abnormal growths of tissue in the brain as well as in other organs such as the skin or kidneys. In the brain, the major functional problems of TSC such as epilepsy, learning disability, autism and attention deficit disorders are assumed to be associated with the cortical tubers.

Does the epilepsy cause the retardation and behavioural problems?

A common form of early seizures in TSC is *infantile spasms*, and these are associated with later learning disability and autism. But it should not be thought that the epilepsy or learning disability causes the behaviour that is so characteristic of TSC. Instead, it is probable that the *number* and *position* of the cortical tubers themselves cause the learning disability and at the same time put the child at risk of behavioural problems. The *more* tubers there are, the more likely the child is to have epilepsy and learning disability. The *earlier* the epilepsy starts and particularly if early infantile spasms are present, is significantly related to lower intellectual ability (4).

What is the relationship between tubers, IQ scores and epilepsy?

One study found a statistically significant relationship between the total number of tubers and IQ, with a fall of IQ related to an increase in the number of tubers(5). In addition, the study found that people *with* epilepsy had more tubers than those *without* but this was not statistically

significant. However those *with* epilepsy had an average IQ of 85.8, and those *without* an average IQ of 105.3 which was significant. But it was not the epilepsy alone that produced the learning problems, since even after the epilepsy was taken into account, the number and position of the tubers remained the significant factor.

Epilepsy, tubers and behaviour problems

How common are behavioural problems in TSC?

It has been found that around a quarter of children with TSC will have behaviours that add up to make a diagnosis of *autism*, with a further quarter having fewer problems which nevertheless satisfy a diagnosis of *pervasive developmental disorder* (PDD). Although the majority of autistic children with TSC will also be learning disabled, aspects of PDD, autism or Asperger's syndrome can affect those with no learning problems. More than half of all children with TSC will also have attention and overactive behaviours that cluster together under a diagnosis of *Attention Deficit Hyperactivity Disorder* (ADHD).

What difference does the position of the tubers make?

Although behavioural problems in TSC are associated with structural brain abnormalities, such as cortical tubers, more so than with epilepsy, it is undoubtedly the case that an early onset of epilepsy can increase behaviour problems. But so also can the position of the tubers. A study in the Anglia Region of the UK (6) found that if a child had one or no *frontal* lobe tubers with a late onset of epilepsy, or no epilepsy at all, then they made normal intellectual progress. More than one tuber in the *frontal* lobe and an early onset of seizures increased the likelihood of learning disability. Similar tubers in the *temporal* lobe of the brain, even with early onset of epilepsy, did not predict learning disability, but in this case there was a worse outcome for *autism*.

Can some kinds of epilepsy produce unusual behaviours?

Since the brain controls the sensory and behavioural functions of the body as well as the motor functions, *non-convulsive seizures* occur if there is epileptic activity in the parts of the brain which do not control movement. In one of these kinds of non convulsive seizures there is often first

an '*aura*', in which strange sensations are felt, or there can be feelings of fear or *déjà vu*, or apparent hallucinations of sights, sounds, smells or tastes. Emotional outbursts of anger or uncontrollable sadness can also occur. The aura is followed by altered awareness when there can be a state of *confusion* which can continue for some time. If the electrical activity spreads into the part of the brain controlling movements *automatisms* can occur and these are automatic repetitive behaviours such as sniffing, swallowing or fumbling with clothes. If the seizure does not progress further into an obvious tonic or clonic motor seizure, the person will instead then feel very tired and sleepy. Unless these complex partial seizures progress to obvious motor movements they can be misunderstood as behaviour problems or sometimes even psychotic states such as 'atypical schizophrenia' are diagnosed.

What is non-convulsive epilepsy?

If these states go on for some time they are called *non-convulsive status epilepticus*. A *convulsive status epilepticus* episode can be easily recognised and help obtained, but the signs of non-convulsive status may not be obvious and can be mistaken for behaviour problems, particularly if the person has severe learning disability and no speech. An EEG of a person in such a state will show either continuous abnormal brain activity across the whole brain (when it is called *absence status epilepticus*) or in just one part of the brain (when it is called *complex partial status epilepticus* CPSE).

What kinds of behaviour result from non-convulsive status epilepticus?

In CPSE people can appear confused and have difficulty responding to what is said to them, they seem to be half asleep, drugged or 'like a zombie'. Alternatively there can be changes or fluctuation in behaviour for no apparent reason, such as sudden unexplained outbursts of aggression or noisy 'high' behaviour in someone who does not normally behave that way. Sometimes there can be strange or bizarre movements or actions. There can be a change or loss of speech with drooling or dribbling, and subtle small twitches and jerks. These symptoms of CPSE can be more difficult to recognise if a person is mentally retarded and already has a behaviour problem such as autism, but parents and carers who know them well are usually the first people to recognise these changes.

Non-convulsive status epilepticus is more likely to occur in people whose other epilepsies are difficult to control and the states can go on for days, weeks and even months if unrecognised. An EEG will soon confirm or exclude the diagnosis and appropriate medication, such as diazepam or clobazam can be given. Although this kind of status epilepticus is not dangerous or life-threatening it can have a bad effect on a person's memory or intellectual ability if it goes on for weeks and months. Some people with tuberous sclerosis who begin seizures in adult life can first appear to hallucinate or lose abilities if non-convulsive status is not recognised and treated.

Are there sleep problems in TSC?

Over 60% of people with TSC report *sleep problems*. These are also known to be associated with epilepsy that is not totally under control (7), and indeed the best indication that epilepsy in TSC is controlled is now thought to be a normal sleep EEG pattern. The major sleep disturbances found are difficulty relaxing into sleep or waking several times in the night. These problems are associated with abnormal sleep recordings on *polysomnography*, with many spikes instead of the slow wave patterns found in normal sleep (8). It is important therefore that a 24 hour EEG is performed if a child would appear to have controlled epilepsy but still has major sleep problems.

Autism and learning disability in TSC

Is autism associated with TSC?

Thirty years ago it was common for autism in learning disabled children to be ignored and their unusual behaviour put down to their intellectual delays. 'All' learning disabled children walked round on tiptoe in circles, flapped their fingers, played for hours with a piece of shining paper. Twenty years ago most clinicians dismissed the idea that you could have tuberous sclerosis and autism - tuberous sclerosis was an inherited disease due to growths in the brain, and autism was a totally different psychiatric disorder. Nowadays there are an increasing number of educational programmes for autistic children, 70% of whom are mentally retarded, and tuberous sclerosis is one of the medical conditions most recognised as associated with both learning disability and autism.

What affect does autism have on IQ scores?

Recent research on autism and learning disability in children with TSC in the Anglia region of the UK (6) found that those *without* autism showed a normal distribution of IQ scores in a bell curve. However in those *with* autism there were more profoundly learning disabled children than moderately or mildly learning disabled children. The summation of these two groups across *all* intelligence scores produced the very unusual *bimodal* distribution of IQ that has been noted before in TSC with two peaks of scores instead of one.

How is autism diagnosed?

Whole textbooks and research groups are devoted to the study of autism (see Fact Sheet 32: *Tuberous Sclerosis Complex and Autism Spectrum Disorder* by Dr Patrick Bolton). The behaviours that lead to a diagnosis are grouped in three categories. In each category both the actual and the mental age of the person must be taken into account since autism is a developmental disorder and expressed in different ways at different stages of development. The three areas are:

Qualitative impairment in reciprocal social interaction. Does your child's head turn when they hear their name? Does your small child try to get your attention when they see something that interests them? If you point to something, do they look the way you are pointing or are they 'in a world of their own'? Does your child smile when someone smiles at them? If you are hurt or sad, do they show sympathy?

Qualitative impairment in verbal and non-verbal communication, and in imaginative activity. If your child cannot speak, are they still able by body language to let you know they want something? Does your child echo back phrases they hear? Do they talk to other children as they 'pretend' play together? Can you hold a 'to and fro' conversation with them or does such talk consist of a series of responses which are the same every time? Do they talk over and over again on the same topic? Are they aware that other adults are bored after 10 minutes detailed description of different bus routes or the biographies of film stars?

Markedly restricted repertoire of activities and interests. Does your small child need to examine closely the picture on their beaker every time you

offer them juice? Does your child insist on licking the glass of the fish tank at home or is the problem one of keeping them from licking the wing mirrors of cars in supermarket car parks? Are they fully toilet trained at school but you can't get them out of the pampers at home? Will they only watch the latest video if they have first seen all the others in the order they have been brought into the house? Can they tell you about every moon landing and space capsule, but still not put the washing machine on the right cycle?

Do all people with autism behave the same way?

There are some myths about autistic behaviour that don't apply as children get older. For instance, many people wrongly believe that the major criteria for autism is *gaze aversion*, not looking at someone when they talk to you, however brief the peek. But experiments have shown that autistic children spend less time looking at everything, however it is only the human beings that complain. In fact, many autistic children with TSC do the opposite of gaze avert, they stare for a disconcerting long time at the person talking. Their eye contact is '*bizarre*' rather than '*aloof*'.

Can people with autism recognise emotions?

Another myth is that people with autism do not express emotion, that they do not form attachments to other people. Any parent will tell you that their autistic child has as many happy giggling sessions or temper tantrums as other children. Where they have difficulty is in recognising that these emotions also exist in other people and this causes them problems. If you don't pick up that another person is irritated by your behaviour, it is possible that you may be shouted at without understanding why, and so you don't learn from the experience. If you see someone smiling at you, but don't understand that it is in a special way that means they like you, it is difficult to make friends.

How are the problems of learning disability separated from those of autism?

If the majority of children with autism are also learning disabled, both of which conditions are regarded as developmental disorders, how do professionals tell which problem contributes most to a particular behaviour? The short answer is that nothing is black or white. The most widely used test of general intelligence is the Wechsler Scales of Intelligence (WISC) which consists of

many different sub-tests of cognitive ability. An ideal 'normal' child shows an exact average for their age group that is even across all the sub-tests. A child with learning disability or a gifted child will show the same even spread, although their average score will be below or above that of the 'normal' child of their age.

But a child with a neurological problem such as TSC often scores widely differently on various sub-tests, depending on how their brain is handicapped. An autistic child will also have a variable set of sub-test scores, but two opposite poles of *worst* and *best* performance have been found, even in autistic children with normal intelligence. Their worst scores are on sub-tests of communicative abilities, where it is important not only to give a correct answer to the question, but also one that is relevant. An example often quoted is '*What should you do if you cut yourself?*' Autistic answer '*Bleed*'. Their best scores are in copying patterns where little social or verbal communication is required, and it is just these tests that a non-autistic retarded child finds very difficult. In summary an autistic child does best on the tests that do *not* require the wider context of the question to be taken into account and the child with learning disability does best on those tests that do.

Can this be done in TSC?

The situation in TSC is still under investigation but will be more complicated since no two children with TSC will have exactly the same number and position of cortical tubers. The most useful information so far has come from the results of research with those children with few cortical tubers, where it may be easier to separate autism from learning disability (6). But if frontal lobe tubers were to be responsible for the learning disability and temporal lobe tubers for the autism, the difficulty comes in recognising how these problems interact in those children who have many tubers in both frontal and temporal lobes, and who are profoundly learning disabled. It could also be possible in TSC that the problems do not lie in the actual tubers but in how well the neurons between the tubers are working.

Is autism in TSC different?

Is autism in TSC different in any way from non-TSC autism? The short answer from research is '*no*' so far as the kinds of autistic behaviour seen, and '*maybe*' in that autism in TSC may lessen as

the child matures into an adult to a greater extent than autism in non-TSC people. In a comparison of behaviours in 23 children with TSC at age five and age 18, 74% had autistic traits at age five but only 43% at age 18 (9). Exactly the same kinds of educational and social programmes used to teach autistic children also apply to those who have TSC and autism.

Can autism be helped?

Autism is a *developmental* disorder, so changes may occur over time. Since the behaviour can be helped by a variety of special teaching programmes, it is important that your child is assessed by a psychiatrist or psychologist as early as possible so that the information can be included when you decide on the most appropriate education they need. In general a structured environment and consistency between school and home is recommended. Language should be as simple and direct as possible - metaphors and ambiguities will not be understood. There is no 'magic pill' to cure either autism or learning disability in TSC, but the best control of the epilepsy with a drug that has few side effects will certainly help lessen problems. Parents and carers are in the best position to understand and interpret the oddities of language that can occur since they know the child's history, and they also know how to avoid any stimuli that cause great distress such as the sound of a vacuum cleaner or dogs. As with any handicap, children can be taught to compensate for their disability, but with TSC it is also important to remember that the underlying *neurological* cause will be *life long*.

Attention Deficit Hyperactivity Disorder (ADHD) and learning disability in TSC

Is ADHD associated with TSC?

ADHD and attention problems are discussed fully in Fact Sheets 33 and 34: *Attention Deficit Hyperactivity Disorder (ADHD) and Tuberous Sclerosis Complex* by Dr David Dunn and Dr William Kronenberger and *How the tuberous sclerosis brain pays attention* by Dr Petrus de Vries. ADHD is defined by the problems of *hyperactivity*, *impulsive behaviour* and *inattention* that are present in different situations. So far there has been less research in TSC on the overactive and attention related behaviour as opposed to the autism, but for many parents,

particularly parents of younger children, these can be the major cause of stress in the family. Although there are often severe language deficits in TSC with around 50% of those with learning disability having no speech (10), this is not matched by any physical disability with 78% of the same group having no walking problems. So parents have to be constantly vigilant as their child wanders around creating aimless, but not deliberate, chaos.

How common is hyperactivity TSC?

In a similar study of 265 children under age 17 years with TSC (11) 60% of those who had learning disability were reported to be *overactive* as opposed to 32% of those who had normal intellectual abilities, with a rate of 50% in the whole group. The overactivity reported fell to 12% for those people without epilepsy, and to 7% for those who had neither learning disability nor epilepsy. There were similar figures for *restlessness*, 60% of those with learning disability as opposed to 36% of those without, with an overall rate of 52%. Again this fell to 32% in people without epilepsy but still affected 22% of those with normal intellect and no seizures.

There can be a decrease in hyperactive behaviour during teenage years and in the study of 23 people at age 5 and age 18 (9), 61% were hyperactive at age 5, but only 22% at age 18.

How common is impulsive behaviour in TC?

Another of the criteria for ADHD is impulsive behaviour and this was reported for 48% of the whole sample. Rates varied from 54% in people with learning disability, 33% in those without, 24% in those without epilepsy and was still present in 19% of those with neither epilepsy nor retardation. Since the prevalence rate of ADHD in the general child population is 3-6%, it is obviously much higher in TSC, even among people who apparently have no intellectual problems or epilepsy.

Are there other attention problems in TSC?

It should also be remembered that attention problems can be experienced by children who are *not* hyperactive and this may affect their learning ability throughout life. If a child with TSC and attention problems is also autistic they may not be aware of the effects of these problems on their ability to keep up with other children at school.

However, if they are not autistic and are of normal intelligence, and their attention problems mean they are falling behind other children in classwork, their self esteem starts to fall, and emotional problems can begin. Treatment of these problems is discussed in the Fact Sheets mentioned previously.

Aggression and learning disability in TSC

How common is aggressive behaviour in TSC?

Although parents and teachers may be aware of the learning disability and autism of children with TSC, the problem that will bring them in conflict with outside agencies is their aggressive behaviour. Rates of aggressive behaviour are high, and those reported range from 33% in one UK survey to 54% in a survey of people on the NTSA Registry. In the UK survey (10) 33% of people with TSC had temper tantrums or rage outbursts, 28% would attack other people, and 29% self-injure themselves. But these were almost exclusive groups, with only 5% who would attack both others and self-injure. For people with learning disability these figures were higher, and 96% of anger control problems were in this group, 95% of those who attacked others and 97% of self-injurious behaviour.

In a US survey (12), using the Overt Aggression scale which measures both verbal and physical aggression at four levels of severity, (none, mild, moderate and severe), aggression was recorded for 54% of 353 people with TSC, but in the majority of cases it was assessed to be only mild aggression.

In the comparison survey of 23 children at 5 and 18 years (9), aggressive outbursts remained at the same level, as did self-mutilation, although destructive outburst decreased.

What contributes to aggressive outbursts?

The triggers for aggressive outbursts vary from person to person, but epilepsy, disrupted sleep, medication, lack of communication skills, autism and ADHD are all associated with this problem behaviour so the high rates are understandable. In addition in some people these rage attacks are so unpredictable ('Jeckyll and Hyde behaviour') that neurologists consider they could be associated with complex partial seizures and might therefore be lessened by better seizure control. Anger management programmes can help those who can

understand their behaviour, and other behaviour management techniques such as 'time out' can work for people with more limited understanding of cause and effect.

Special Educational Needs services in the UK

To get the specialist help that many children with TSC need for their learning disability and autism, they will need to have a Statement of Special Educational Needs (SEN). Pre-school children with obvious developmental delays often attend opportunity playgroups or special nurseries, but some children's needs may not be identified until they have been in mainstream school for a couple of years. These will be the children who have attention problems and it can be only when they begin to be verbally or physically aggressive to children or staff that the implications of their TSC are taken seriously by the LEA (Local Education Authority). Other children with more severe learning disabilities may have the contribution of autism to their behaviour misread as 'wilful' naughtiness as they wander around the class making high pitched noises because they are distressed by all the bustle of the stimulating environment. If they are then sent out a peaceful corridor until they 'quieten down' they will have achieved their aim of reducing stress!

A Statement should be sought by parents or the school if they are concerned that the child will not progress unless they have more 1 to 1 help, as the LEA then provides extra money to the school to provide the help. In the first part of the process the LEA first decide, on the advice of an educational psychologist and school reports, whether to do the full Statutory Assessment required before a Statement will be made. Parents can submit information for inclusion in this process. The draft statement is sent to the parents for acceptance or challenge before it is officially made.

The Special Educational Needs and Disability Bill requires all LEAs to provide parents of children with Special Educational Needs with advice and information and a means of resolving any disputes with schools and the LEA. If differences cannot be resolved locally and have to be taken to the Special Needs Tribunal, the LEA now has a set time in which to comply with any tribunal decision. Disability Discrimination rights will now be extended to the provision of education in schools, Further Education, Higher and Adult education.

The discrimination duties in education now fall under the jurisdiction of the SEN Tribunal who have the power to secure 'educational redress' for children experiencing discrimination.

Conclusion

There are problems affecting behaviour associated with Tuberous Sclerosis and the major ones are autism or PDD, attention deficits, ADHD and disruptive behaviours (see Fact Sheets mentioned) such as aggression. All these problems occur more frequently in younger children, in individuals with learning disability and in individuals with epilepsy. Not all the problems will occur together in any one person. But when they do it is essential to obtain professional assessment of the contributions made by the various elements so that appropriate treatment or education can be given. If the professionals say they don't know much about tuberous sclerosis, give them information about it to help them understand. The days of major tranquillizers being used as chemical straight-jackets should be over. There is much advice now available on autism and ADHD and what applies to individuals without TSC with these problems also applies to individuals with TSC. Use it!

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