



Behaviour and learning in Tuberous Sclerosis: Guidelines for assessments needed, when to do them, and recommended available tests.

“...behavioural disorders are underrecognised, underdiagnosed and often not treated in TSC” Behavioral and Psychiatric Panel, NIH TSC Consensus Conference, Annapolis USA, 1998

Background to Guidelines

Clinical guidelines for physical aspects of TSC were put together in 1998 but behavioural and cognitive aspects of TSC were not covered in detail. These new guidelines were first published in 2005, and have been written by a panel of experts in TSC and are endorsed by the Tuberous Sclerosis Association (UK) and the TSAAlliance (USA). The aim was to produce clinical guidelines for cognitive and behavioural assessments of individuals with TSC using evidence from research studies. The panel included parents of individuals with TSC, psychiatrists, psychologists, paediatricians, and special needs teachers. The research evidence and the consensus clinical guidelines were published in full in July 2005, in the journal, *European Child and Adolescent Psychiatry*: de Vries P, Humphrey A, McCartney D, Prather P, Bolton P, Hunt A. Consensus clinical guidelines for the assessment of cognitive and behavioural problems in Tuberous Sclerosis. *European Child and Adolescent Psychiatry*. 2005 Jul;14(4):183-90. The information and Tables in this short summary are reproduced from the journal paper with the permission of the publishers.

What are the problems in Tuberous Sclerosis?

Tuberous sclerosis (TSC) is a multi-system genetic disorder characterised by benign tumours in a wide range of organs including the central nervous system. In over two-thirds of cases diagnosis is made when a baby starts to have epileptic seizures in the first year of life. These are caused by tubers in the cortex (CT) which also interfere with learning and behaviour. Nodules are also present around the ventricles (SEN), and these can occasionally grow (SEGAs) and need to be removed..

Difficult to control epilepsy is a major medical concern to doctors, but less attention is paid to the behavioural and neuropsychiatric problems also associated with TSC such as Autism Spectrum Disorders (ASD) and Attention Deficit Hyperactivity Disorder (ADHD) although these are often of equal concern to families. There is often little or no clinical assessment or intervention offered for problems in these areas, in spite of the fact that these can lead to significant difficulties in daily life, and disrupt educational and occupational progress.

Rationale for the Guidelines

Research has shown that TSC is a brain disorder with a high prevalence of cognitive and behavioural difficulties. Some of these difficulties, such as ASD or ADHD, will have clear social consequences and require intensive help and support. Others, such as attention or memory deficits could easily be missed in a normally intelligent child and quite severe educational problems can follow. It is therefore important to know if a child or adult with TSC has such difficulties or not. If a child is routinely checked for problems known to be associated with TSC, backed up by accepted assessment tests, this would then enable a child to be offered, from the beginning, an individual remedial programme if it is required. It can never be good practice to put such a child or adult, without assessment, into a situation where they fail and only after failure assess them and offer help. Routine checks would minimize the risk of added complications developing, thus avoiding not only expensive and protracted interventions but also the emotional trauma induced in a child or adult who fails.

What do the Guidelines offer?

Around 45% of individuals with TSC will have some learning disabilities ranging from a profound handicap to mild learning problems. But even children in mainstream schools can have problems with attention and memory that need to be assessed as they could be causing educational difficulties. In addition around 50% of people with TSC show behaviour problems associated with the Autism Spectrum Disorder (ASD) and/or Attention Deficit Hyperactivity Disorder (ADD). These guidelines offer advice on the assessments recommended to be performed at various stages in a child or adult's life in two broad areas: firstly, assessments of learning difficulties to enable maximum support to be given for future cognitive development; and secondly, behavioural assessments to diagnose problems that require psychiatric or psychological help. The stages when assessments are recommended are common to all children and adults with TSC. However, the tests administered, the subsequent educational

programmes developed and any clinical treatment offered should remain tailored to the individual, their age and the standard tests used locally and nationally.

The guidelines recommend areas that should be targeted in the context of TSC, but are not meant to imply limiting assessments only to those areas. The guidelines are intended as advice to professionals who have individuals with TSC in their care, and as guidance to individuals, parents and caregivers about stages when assessments should be sought.

Summary of cognitive and behavioural difficulties in TSC

Tuberous sclerosis (TSC) is associated with a range of serious behavioural and cognitive difficulties in individuals with and without learning disability. Table 1 summarises these difficulties in TSC. The range of behavioural problems include sleep disturbance, aggressive behaviours, specific phobias, self-injury, temper tantrums, depressed mood and anxiety. In particular, there is strong evidence for high rates of ADHD, autism and ASD, and these can also occur at the same time as developmental disorders. Similar to the physical manifestations of TSC, there is great variability in the occurrence and severity of these problems between individuals, even in identical twins. Developmental disorders, socially unaware and disruptive behaviours are most often seen in childhood and adolescence, whereas in adulthood high rates of anxiety symptoms and depressed mood are reported.

Intellectual abilities in TSC divide individuals approximately into two groups. Around 55% function within the normal range of IQ (>80) while the rest have moderate to profound handicaps, with about 30% with global intellectual ability in the severe to profoundly impaired range (IQ<21) These cognitive deficits can be apparent by one year of age and if present, the children did not show any evidence of ‘catch-up’ in development by 30 months of age.

In some children with TSC developmental outcome and progress may be associated with the severity of seizure disorder and its control. Those with intellectual impairments are more likely to have ASD, or disruptive behaviours but neither learning disability nor epilepsy are necessary or sufficient to explain the high rates of these behavioural disorders. There is also a high prevalence of significant language delay, even in those with normal intelligence.

Among children and adults with TSC who have normal intelligence, there is increasing evidence of specific cognitive deficits in attentional and executive skills, even in individuals without criteria for ADHD such as impulsivity or hyperactivity. People with problems in executive control processes may be inefficient and even inept in doing tasks that require planning, organisation, monitoring and judgement. Memory skills may also be impaired in normally intelligent adults with TSC, particularly in retrieval of information already stored in the memory. All these problems could also happen in people with moderate to profound intellectual disability who cannot be evaluated on the tests available at present.

In the more able group, parents report significant difficulties in academic performance such as in reading, writing and arithmetic although these have not been researched in TSC. There were also reports that adults had difficulties in occupational functioning, such as in establishing a career or vocation, and in the ability to ‘multi-task’ in the workplace. These problems can lead to very high rates of low self-esteem, and the consequent high burden of care and stress on families. In some areas, difficulties are reported in obtaining appropriate services from statutory and non-statutory agencies such as educational authorities, social services departments, health care professionals or insurance companies due to the lack of understanding of the problems specific to TSC that have been identified by research.

Table 1. Cognitive and behavioural problems associated with Tuberous Sclerosis

Cognition	Behaviour
<p>Global cognitive deficits: mental retardation(WHO)/learning difficulties</p> <p>Specific cognitive deficits:</p> <ul style="list-style-type: none"> • Social-communication deficits • Receptive and expressive language deficits • Attentional deficits (selective attention, sustained attention and attentional switching) • Executive deficits (planning, poor sequencing, perseveration) • Memory deficits (working memory, episodic memory) <p>Motor deficits</p> <ul style="list-style-type: none"> • Motor abnormalities (fine motor, gross motor, movement disorders) 	<p>Autism, Asperger’s and other autism spectrum disorders (ASD)</p> <p>ADHD and related disorders</p> <p>Aggression, rage outbursts and temper tantrums</p> <p>Negativity (temporary resistance to change)</p> <p>Emotional lability</p> <p>Depressive disorders</p> <p>Anxiety disorders</p> <p>Sleep disorders</p> <p>Epilepsy-related psychotic disorders</p>

Panel recommendation I: Perform regular assessment of cognitive development and behaviour to identify and treat emerging difficulties and to establish a baseline for evaluating any later changes.

Assessments should be tailored to the presentation of problems shown by each individual and performed at the recommended ages, as shown in Table 2. The pre-school assessments should be routinely done to identify developmental and behavioural impairments that otherwise can be difficult to identify in young children and to establish a baseline measure against which any future changes may be compared. Extra assessments may be necessary if new clinical concerns emerge as the child develops. Evaluations should use neuropsychological and behavioural tools appropriate to the developmental level of the individual so that these results can be interpreted against those of the population at large.

It may not be necessary or appropriate to assess for every area of difficulty in every individual at every age. Global cognitive, motor and language development will be very important in infants and young children, but emotional problems and skills needed for independent living will be more relevant to adolescents and adults. Assessment of the various areas will involve different professionals such as developmental or community paediatricians, speech and language therapists, clinical or educational psychologists and psychiatrists in child and adolescent, adult and learning disability services. These cognitive and behavioural profiles will be useful to the local multidisciplinary care team, in planning the services needed by the person with TSC and will enable a review of longitudinal progress and response to treatment and support.

Panel recommendation II: Perform a comprehensive assessment when there are changes in cognitive development or behaviour to identify and treat the underlying causes of neurobehavioural change

Changes in behaviour (e.g. increased aggression, withdrawal or change in sleep patterns), regression in development (e.g. loss of language or motor skills), deterioration of academic or vocational abilities or changes in physical manifestations (e.g. change in seizures, vision) should always be assessed and appropriately investigated. Regression and deterioration of functional abilities are not characteristics of TSC, but may result from a range of biological, psychological and social factors such as seizures, pain, renal failure, medications, onset of a psychiatric illness or changes in the routine or environment of an individual with severe learning difficulties. In a small but significant minority of individuals, subependymal giant cell astrocytomas (SEGAS) may develop and produce complications. In such circumstances there may be an associated deterioration in behaviour and intellectual ability or potentially the emergence of specific cognitive impairments. It is recommended that investigations of these changes include a comprehensive physical and

neurological review, functional analysis of behaviour, neuropsychological evaluation and appropriate special investigations such as biochemical profile, EEG and MRI.

Consensus Panel Guidelines

The consensus guidelines for routine cognitive and behavioural assessments are presented in Table 2 and recommend assessments at set stages. For each assessment stage, the age range for the assessment is given and the general purpose of assessment are outlined. Specific concerns to pay attention to in TSC are also listed for each stage. Even if an early assessment is within normal limits, re-assessment should be performed when the individual is moving into a new educational or social environment. Any subtle deficits identified should be recorded and taken into account by educators, families and other relevant professionals should problems arise.

Table 2. Consensus guidelines for cognitive and behavioural assessments and post-assessment interventions in Tuberous Sclerosis. The table shows the regular timepoints for assessment of all individuals with TSC.

Assessment stage	Age range for assessment	General purpose of assessment	General areas to assess	* Areas of particular concern in TSC:	*Behavioural and learning problems of particular concern in TSC
At diagnosis		Initial assessment of cognitive and behavioural profile	As listed for chronological age		
Infancy	Birth – 12 months	To perform a baseline assessment for regular monitoring of development	Global standardised assessment of infant development	Impact of seizure onset and treatment on development	
Toddler	1y – 2y11m	To identify early developmental delay or developmental disorders	Global cognitive ability and adaptive behaviours Specific skills: <ul style="list-style-type: none"> • Gross and fine motor skills • Social-communication skills 	Quality of eye-contact, joint attention, reciprocity	Autism and Autism Spectrum Disorders (ASD) Severe aggressive outbursts Severe Sleep Problems
Pre-school	3y to school entry	Evaluation of cognitive and behavioural profile to ensure the provision of appropriate educational programmes	Global cognitive ability Specific cognitive skills: <ul style="list-style-type: none"> • Receptive and expressive language • Social communication skills • Attentional-executive skills • Visuospatial skills • Motor skills 	Uneven profile of abilities Poor expressive language Poor reciprocity, peer interaction Poor regulation of affect and impulse Poor bilateral co-ordination	Autism and ASD ADHD and related disorders Self-injurious behaviour

Early school years	6y – 8y	Monitoring the child's ability to make appropriate educational progress	<p>Global cognitive abilities</p> <p>Specific cognitive skills:</p> <ul style="list-style-type: none"> • Receptive and expressive language • Social communication skills • Memory • Attentional-executive skills • Visuospatial skills <p>Motor skills</p>	<p>Best time to establish baseline to assess whether specific cognitive skills and scholastic performance is discrepant from global intellectual abilities</p> <p>Poor expressive language and word retrieval</p> <p>Rote learning difficulties</p> <p>Selective attention, sustained attention difficulties</p>	<p>Specific scholastic difficulties (reading, writing, spelling, mathematics)</p> <p>ADHD and related disorders</p> <p>Peer problems</p> <p>Aggressive behaviours</p>
Middle school years	9y – 12y	Complete review of child's abilities, specific learning difficulties and behavioural problems in preparation for the transition to secondary education	<p>Global cognitive abilities</p> <p>Specific cognitive skills :</p> <ul style="list-style-type: none"> • Receptive and expressive language • Social communication skills • Memory • Attentional-executive skills 	<p>Subtle deficits of social-communication, unusual interests</p> <p>Poor short-term memory, episodic memory</p> <p>Planning, organisational abilities, multi-tasking difficulties</p>	<p>Asperger's Syndrome</p> <p>Peer problems</p> <p>Scholastic difficulties (reading, writing, spelling, mathematics)</p>

Adolescence	13y – 16y	Determining individual needs and the support required for transition into adult life	Global cognitive abilities Specific cognitive skills • Attentional-executive skills Vocational assessment with knowledge of cognitive strengths and weaknesses Adaptive behaviour and daily living skills	Poor judgement, decision making	Depressive disorders Anxiety disorders Peer problems
Adults	18y+	<u>Newly diagnosed adults:</u> assessment of cognitive, behavioural and vocational profile, determining bio-psycho-social needs	Global cognitive abilities Specific cognitive skills: • Attentional-executive skills • Memory	Difficulty with integrational skills Working memory, episodic memory problems	Depressive disorders Anxiety disorders Epilepsy-related psychotic disorders
Adults (follow-up)	18y+	Monitoring for emergence of psychiatric problems or changes in existing cognitive and behavioural difficulties	<u>Dependent adults:</u> Annual review of social care needs and support <u>Independent adults:</u> Vocational advice Genetic counselling as appropriate Review if problems arise	Pay particular attention to <i>change</i> in cognitive abilities or behaviour Pay particular attention to <i>change</i> in cognitive abilities, vocational performance and behaviour	Depressive disorders Anxiety disorders Epilepsy-related psychotic disorders

Abbreviations: ASD = autism spectrum disorders; ADHD = attention deficit hyperactivity disorder

* Many features listed in these columns can present at any age, but are listed here at stages most commonly associated with the emergence of such difficulties in TSC

Neuropsychological tests

There is a wide range of neuropsychological tests in general use in different countries, with some that are routine in pre-school or school settings, and others that are more specialized tools derived from research studies. Some of the tests most often used in the UK are shown in Table 3 but those used will depend on local resources and preferences. However the areas of potential difficulty will not vary and it is important that these are assessed appropriately.

Table 3 -Tests for Clinical Assessment of Cognition and Behaviour

The following tests should be readily available in the UK for use by appropriately qualified clinical or educational psychologists. Approximate ages of suitability are given in brackets.

<u>AGE 0-4 years, Infants and pre-school</u>	
General	
<u>Readily available</u>	<u>Age range of test</u>
Bayley Scales of Infant Development –2 nd Edition	1-42 months
Griffiths (general development)	0-8 years
Vineland Adaptive Behavior Scales (communication and social skills)	0-12 years
Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III)	2 yrs 6m to 7 yrs 3m
NEPSY (to assess general neuropsychological development)	3-12 years
Leiter, Snijders-Oomen (non-verbal intellect)	2 yrs 11m to 20 years
<u>Sometimes available</u>	
Mullens Scales of Early Learning	0-3 years
Beery VMI (visual and motor skills)	2-18 years
Pre-school - language development	
Reynell Developmental Language Scales III	15m to 7 yrs 6m
Preschool Clinical Evaluation of Language Fundamentals (CELF-Preschool)	3-7 years
Pre-school - behaviour	
CHAT (Autism - first general screening)	1yr 6m – 3 years
<u>AGE 5-17 years</u>	
Children – Global cognition/intelligence	
Wechsler Intelligence Scale for Children – 4 th edition (WISC-III/IV)	6 yrs – 16 yrs 11m
Ravens Progressive Matrices	5-11 years
Children – Visuospatial and motor skills	
<u>Readily available</u>	
Kaufman KABC-II	3-18 years
<u>Sometimes available</u>	
Wide Range Assessment of Visual Motor Abilities (WRAVMA)	3-17 years
Children –Language	
Clinical Evaluation of Language Fundamentals (CELF-3)	6-16 years
Children – Memory	
<u>Readily available</u>	
Children's Memory Scale	5-16 years
Doors and People	5-11years
Wide Range Assessment of Memory and Learning-2 (WRAML-2)	5-90 years
<u>Sometimes available</u>	
Benton Visual Retention Test	8years -Adult

Children – Attention and concentration

Test of Everyday Attention for Children (TEACh)
NEPSY

6-16 years
3-12 years

Children – Formal scholastic skills

Wechsler Objective Language Dimensions (WOLD)
Wechsler Objective Reading Dimensions (WORD)
Wechsler Objective Numerical Dimensions (WOND)
Wechsler Individual Achievement Test (WIAT-II)

6 yrs – 16 yrs 11m
6-16 years
6yrs - 16 yrs 6m
4yrs -16yrs 6m

Children – Higher 'executive' function/'logic'

Tower of London
NEPSY

7-15 years
3-12 years

Autism and ASD

Readily available

Childhood Autism Rating Scale (CARS)

2- 18 years

Sometimes available

Autism Diagnostic Interview- Revised , ADI-R
Autism Diagnostic Observation Schedule ADOS Modules

2years -Adult
Single words – fluent adult

Behavioural difficulties (for the carer to complete regarding the child)

Sometimes available

Social Communication Questionnaire (SCQ)
Strengths and Difficulties Questionnaire
K-SADS Psychopathology

6 years +
3-16 years
6-18 years

ADULTS 18+ years**Adults – Global cognition/intelligence**

Wechsler Adult Intelligence Scale- Third Edition (WAIS-III)
Ravens Progressive Matrices

16-89 years
6yr-Adult

Adults – Visual, spatial and motor skills

Readily available

Visual Object and Space Perception battery (VOSP)

18+

Sometimes available

Grooved Pegboard tasks
Benton Visual Retention Test (BVRT)
Rey Complex Figure Test copying

6-89 years
8yr -Adult
Child to Adult

Adults – Memory

Readily available

Doors and People
Rivermead Behavioural Memory Test (RBMT-II)

18-80 years
16-96 years

Sometimes available

Wechsler Memory Scale-Third Edition (WMS-III)
Rey Complex Figure Test recall

16 – 89 years
Child - Adult

Adults – Attention and concentration

Test of Everyday Attention, TEA
Behavioural Inattention Test BIT –unilateral neglect

18-80 years
19-83years

Adults – Higher 'executive' functionSometimes available

Hayling and Brixton tests	<i>18-80 years</i>
Behavioural Assessment of the Dysexecutive Syndrome (BADS)	<i>16-87 years</i>
Verbal fluency (COWAT)	<i>Adult</i>
Wisconsin Card Sorting test (WCST)	<i>6yrs5m – 89 years</i>
Trail making tests	<i>8-89 years</i>

Adults –Behaviour

SADS/M-SADS Psychopathology	<i>Adult</i>
Beck –Depression, anxiety	<i>13-80 years</i>

The clinical diagnosis of psychiatric disorders should be made according to established international diagnostic criteria such as ICD-10 and DSM-IV. A range of supplemental tools such as interviewer-based schedules, observational schedules and behavioural rating scales are available to aid the diagnostic process by clinicians.

Post-assessment interventions

These clinical guidelines do not present information on specific post-assessment interventions but if specific difficulties are identified at any of the assessment stages, the child or adult should be managed or referred as clinically appropriate. Management strategies are likely to involve a range of clinical specialities and multi-agency involvement. Table 4 lists a range of possible outcomes of neurobehavioural assessments.

Table 4 Possible outcomes of neurobehavioural assessment of individuals with tuberous sclerosis.

1. Arrange further detailed evaluations (including functional analysis of behaviour, physical review and special investigations)
2. Enroll child in community programme for early intervention
3. Develop specific therapeutic programme for a child's developmental needs (pre-school, primary school, secondary school and post-school)
4. Statutory assessment of special educational needs before the child begins formal education
5. Perform an annual review of progress and educational needs
6. Refer to social services departments and other agencies for respite and/or daily living support
7. Liaison with children's disability teams
8. Refer for or provide appropriate psychological support and psychiatric intervention including psychopharmacology
9. Assess support required for vocational training and daily living in adult life
10. Provide support for parents and carers

TSC Behaviour Consensus Panel Members

These consensus guidelines were compiled at the TSC Brain/Behaviour Workshop held January 10-12th 2003 in Cambridge, UK and financially supported by the Tuberous Sclerosis Association (UK) and the Tuberous Sclerosis Alliance (USA)

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Tuberous Sclerosis Association



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