Guidelines for the assessment of cognitive and behavioural issues in TSC

tsa
tuberous sclerosis association

Tuberous Sclerosis Complex (TSC) is a multi-system genetic disorder caused by mutations in one of the tumour suppressor genes TSC1 or TSC2. It is characterised by abnormal growths in a wide range of organs including the skin, kidneys and central nervous system. In more than two-thirds of cases, diagnosis is made when an infant presents with seizures in the first year of life. In the brain, features include cortical tubers (CT), subependymal nodules (SEN), subependymal giant cell astrocytomas (SEGA) and widespread grey and white matter abnormalities. Intractable epilepsy is a major medical concem to doctors. Often, less attention is paid to the behavioural and neuropsychiatric problems also associated with TSC such as Autism Spectrum Disorders (ASD), Attention Deficit Hyperactivity Disorder (ADHD) and Anxiety Disorder.

Together with the intellectual and leaming disabilities, behavioural and neuropsychiatric problems are often of greatest concem to families. Unfortunately, there is generally little or no clinical assessment or intervention offered for problems in these areas, in spite of the fact that these problems can lead to significant difficulties in daily life and disrupt educational and occupational progress.

Development of guidelines and behavioural evaluation in TSC.

Although clinical guidelines for physical aspects of TSC were- established at a consensus conference in Annapolis, MD, in 1998, no specific guidelines were given on which behavioural and cognitive aspects to assess in TSC. To address this situation, a consensus conference was convened in 2003 in Cambridge (UK) with the financial support and endorsement of the Tuberous Sclerosis Association (UK) and the Tuberous Sclerosis Alliance (USA). The aim was to produce clinical guidelines for cognitive and behavioural assessments of individuals with TSC using up-to-date evidence from research studies. The panel included parents of individuals with TSC, psychiatrists, neuropsychologists, psychologists, paediatric neurologists, and special education teachers. The research evidence and the consensus clinical guidelines were published in full in July 2005 (de Vries et al., 2005). The information and Tables in this short summary are reproduced from the j oumal paper with the permission of the publishers.

Guidelines previously established for the assessment of the clinical manifestations of TSC included very little detailed advice on neurodevelopmental testing. However, the growing body of literature substantiates the very high prevalence of cognitive and behavioural problems in individuals with TSC that warrants as much emphasis on assessment and treatment as the physical problems.

The guidelines presented here offer advice on the assessments that should be performed at various stages in a child or adult's life in two broad areas: (l) neurocognitive assessments to enable maximum support to be given for future cognitive development, and (2) behavioural assessments to diagnose problems that require psychiatric and/or psychological intervention. 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, age and the local and national context. The guidelines recommend areas that are to be targeted in the context of TSC, but are not meant to imply limiting assessments only to those areas.

The guidelines presented here are a consensus based on the best available evidence in the field. All peer reviewed publications relating to cognition and behaviour in TSC were used in the preparation of these guidelines and references are given in the full paper (de Vries et al, 2005).

Unlike other disabling conditions such as Down's syndrome or Fragile-X syndrome, many aspects of

cognition and behaviour in TSC have received little systematic research so far and, in particular, areas such as language and academic skills lack full research. 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 are to be sought.

Summary of cognitive and behavioural difficulties in TSC

TSC is associated with a range of serious behavioural and cognitive difficulties in individuals with and without intellectual disability. Table 1 summarizes these difficulties in TSC. The range of behavioural problems include sleep disturbance, aggressive behaviours, specific phobias, self-injury, temper tantrums, depressed mood and anxiety disorder. In particular, there is strong evidence for high rates of ADHD and ASD, and intellectual disability (IQ<70). Similar to the physical manifestations of TSC, there is great variability in the occurrence and severity of these problems between individuals, even in monozygotic (identical) twins. Developmental disorders, socially unaware and disruptive behaviours are most often seen in childhood and adolescence, whereas in adulthood high rates of anxiety and mood disorder are reported.

Intellectual assessments in TSC divide individuals approximately into two groups. Around 55% function within the normal range of IQ (>80) while the rest have some degree of intellectual disability (ranging from mild to profound). About 30% of individuals with TSC have global intellectual ability in the profoundly impaired range (IQ<21). A study of early cognitive development in a clinic-based sample of infants with TSC found that intellectual disabilities are frequently apparent by one year of age and that these 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 correlated with the severity of their epilepsy and its control. Those with intellectual disability 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 in individuals with TSC. 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 behavioural signs of ADHD such as impulsivity or hyperactivity People with problems in executive control processes may be inefficient and even inept in managing tasks that require planning, organization, monitoring and judgment. Memory skills may also be impaired in normally intelligent adults with TSC, particularly in retrieval of encoded memories. All these problems could also occur in people with moderate to profound intellectual disability who cannot be evaluated on the tests available at present.

In the more moderately affected 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 to a 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, or health care providers or insurance companies due to the lack of understanding of the problems specific to TSC that have been identified by research.

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.

Therefore, it is important to know if a child or adult with TSC has such disabilities 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 plan if it were required. It can never be good practice to put such children or adults, 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.

Consensus recommendations

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 are to be performed at the recommended ages, as shown in Table 2. The pre-school assessments are to 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 are very important in infants and young children, but emotional problems and skills needed for independent living are more relevant to adolescents and adults. Assessment of the various areas will involve different professionals such as community paediatricians, speech and language therapists, clinical or educational psychologists, psychiatrists in child, adolescent, and 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 or 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 disabilities. In a small but significant minority of individuals, SEGAs may develop and produce complications either through invasion of surrounding cerebral tissue or through blockage of the flow of cerebrospinal fluid through the foramen of Munro, producing increased pressure on the brain. In such circumstances there may be an associated deterioration in behaviour and intellectual ability or, potentially, the emergence of specific cognitive impairments.

Investigations of these changes should therefore 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 recommend assessments at set stages and are presented in Table 2. For each assessment stage, the age range for the assessment is given and the general purpose of assessments is outlined. Specific concerns to pay attention to in TSC are also listed for each stage. Even if an early assessment is within normal limits, reassessment hould 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.

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 U.S.A. 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 areas are assessed appropriately.

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 specialities and multi-agency involvement. Table 4 lists a range of possible outcomes of neurobehavioural assessments.

Table 1. Cognitive and behavioral problems associated with TS

Cognition	Behavior
Global cognitive deficits: mental retardation (WHO)/learning difficulties • Specific cognitive deficits: • 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) Motor deficits: Motor abnormalities (fine motor, gross motor, movement disorders)	Autism, Asperger's and other autism spectrum disorders (ASD) ADHD and related disorders Aggression, rage outbursts and temper tantrums Negativity (temporary resistance to change) Emotional lability Depressive disorders Anxiety disorders Sleep disorders Epilepsy-related psychotic disorders

Table 2. Consensus guidelines for cognitive and behavioural assessments in TSC. The table shows the regular time points foe 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 standardized 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: 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 programs	Global cognitive ability Specific cognitive skills: 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	Global cognitive abilities Specific cognitive skills: Receptive and expressive language Social communication skills Memory Attentional-executive skills Visuospatial skills Motor skills	Best time to establish baseline to assess whether specific cognitive skills and scholastic performance is discrepant from global intellectual abilities Poor expressive language and word retrieval Rote learning difficulties Selective attention, sustained attention difficulties	Specific scholastic difficulties (reading, writing, spelling, mathematics) ADHD and related disorders Peer problems Aggressive behaviours
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	Global cognitive abilities Specific cognitive skills: Receptive and expressive language Social communication skills Memory Attentional-executive skills	Subtle deficits of social-communication, unusual interests Poor short-term memory, episodic memory Planning, organizational abilities, multi-tasking difficulties	Asperger's Syndrome Peer problems Scholastic difficulties (reading, writing, spelling, mathematics)
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 behavior and daily living skills	Poor judgment, decision making	Depressive disorders Anxiety disorders Peer problems
Adults	18y+	Newly diagnosed adults: 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	Dependent adults: Annual review of social care needs and support Independent adults: Vocational advice Genetic counseling as appropriate Review if problems arise	Pay particular attention to change in cognitive abilities or behaviour Pay particular attention to change in cognitive abilities, vocational performance and behaviour	Depressive disorders Anxiety disorders Epilepsy-related psychotic disorders

Abreviations: 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.

Table 3. Suggested Instruments for Neuropsychological Evaluation of Individuals with TSC (Compiled by Penny Prather, Ph.D)

Stage	Age	Developmental assessment	Global cognitive abilities	Attention (regulation)	ECPs	Social communication	Memory	Language	Visual/ Spatial	Motor	Academic
Infancy	Birth to 12 mos	Bayley or Mullen		Bayley structured observation (supplemented by clinical observation[i])		Social adjustment interview (Vineland) [ii]					
Toddler	1 to 2,11	Bayley or Mullen		Bayley structured observation		Vineland					
	2-2,11	Bayley or Mullen	WPPSI-III[1]	Bayley structured observation		Vineland					
Preschool	3-5		WPPSI-III (with Bayley or Mullen as alternative, if appropriate[iii]	Questionnaire[iv] Attention questionnaire (BRIEF) [v]	Attention questionnaire (BRIEF)	Vineland		PPVT-III EOWPVT[vi]	VMI		
Early school years	6-8		WISC-IV	Attention questionnaire (BRIEF) Continuous Performance Test (CPT) [vii]	Attention questionnaire (BRIEF) WISC-III Mazes (7+: Tower of London) (8+, Trails)	Vineland Relevant subtests, WISC-IV	WRAML or CMS	BNT Word fluency, NEPSY	VMI ROCF	By observation Grooved pegboard or Purdue pegboard	WIAT-II GORT-4 TOWL-III
Middle school years	9-12		WISC-IV	Attention questionnaire (BRIEF) CPT	Attention questionnaire (BRIEF) Tower of London WCST Trails	Vineland Relevant subtests, WISC-IV	WRAML or CMS	BNT Word fluency, NEPSY	VMI ROCF	Grooved pegboard or Purdue pegboard	WIAT-II GORT-4
Early adolescence	13 to 15		WISC-IV	Attention questionnaire (BRIEF) CPT	Attention questionnaire (BRIEF) Tower of London WCST Trails	Vineland Relevant subtests, WISC-IV	WRAML or CMS	BNT Word fluency, FAS	VMI ROCF	Grooved pegboard or Purdue pegboard	WIAT-II GORT-4
Later adolescence	16 to 18		WAIS-III	Attention questionnaire (BRIEF; Brown ADD Scales)	Attention questionnaire (BRIEF) WCST Trails	Vineland Relevant subtests, WAIS-III	WRAML or WMS-III	BNT Word fluency, FAS	VMI ROCF	Grooved pegboard or Purdue pegboard	WIAT-II GORT-4
Adults	18+		WAIS-III	Attention questionnaire (BRIEF; Brown ADD Scales)	Attention questionnaire (BRIEF) WCST Trails	Vineland Relevant subtests, WAIS-III	WMS-III	BNT Word fluency, FAS	ROCF	Grooved pegboard or Purdue pegboard	GORT-4 (?math)

1 WPPSI-III: description, age range, AND re choosing between Bayley vs. Mullen for 2 to 3 years of age

Behavioural questionnaires:

General: BASC

Attention: BRIEF

Social communication, Daily living skills: Vineland Adaptive Behaviour Scales (administered to parent/caregiver)

Autism: Autism Diagnostic Interview- Revised (Western Psychological Services, USA)

Autism Diagnostic Observation Schedule (ditto)

Childhood Autism Rating Scale (CARS)

i "By observation" is just that – a clinical impression based on observing of a child's behaviour in the context of formal testing. Formal measures of attention and executive control processes are not generally available for children under age 6, and even than, are neither specific to nor sufficient in characterizing regulatory systems. Consequently, the observations and impressions of an experienced clinician and, when possible, of a child's teacher and parents tend to be the most relevant information for assessing Behavioural regulation and for assessing (in younger children) or supplementing formal assessment of (in older children) executive control processes.

ii Questionnaire, Social domain:
The Vineland is a useful and familiar instrument for assessing "real life" skills, including social communication skills.

Where appropriate (based on clinical observation and/or referral concerns), other potentially relevant questionnaires include:
Childhood Autism Rating Scale (CARS)
Autism Diagnostic Interview- Revised, ADI-R (Western Psychological Services, USA)
Autism Diagnostic Observation Schedule ADOS

Note, however that these questionnaires require specialized training that most psychologists/neuropsychologists
will not have had (and so may involve referral to an appropriate specialist).

iii In most instances, it will be most appropriate to administer the Bayley or Mullen test to children under age 3. Occasionally the WPPSI-III may be more appropriate for a child who is between 2 and 3 years of age; and often, though not always, it is likely to be the more appropriate test to use with children who are between ages 3 and 6.

iv Relevant questionnaires for attention and regulation: BRIEF; BASC

v Attention questionnaires: While there are a number of different attention measures available, the recommendation is for use of the Behavioural Rating Inventory for Executive Functions (BRIEF), currently available for children from ages 3 through adolescence.

vi The PPVT-III and EOWPVT are measures of receptive and expressive language respectively. These tests may be administered by a psychologist/neuropsychologist or by a speech pathologist (and if a child is scheduled for both types of evaluation, it is most likely that they would be administered by the speech pathologist). Of note, unlike the WPPSI-R, the current edition of the WPPSI (the WPPSI-III) includes subtests to assess receptive and expressive language that are very similar in format to the PPVT and EOWPVT, so that it is less likely that the latter tests would be administered as part of a cognitive or neuropsychological evaluation that includes administration of the WPPSI-III.

vii Continuous Performance Test (CPT): There are many different versions of CPTs (e.g. the TOVA, the Connors CPT), and all serve the same purpose, which is assessment of sustained attention. Not all clinicians/clinics have a CPT available, but if possible, this can be a very useful instrument in combination with age-appropriate attention questionnaires, both in identifying any potential concerns with regulation of attention, and (if relevant) in following the effectiveness of specific interventions in addressing attentional difficulties.

Table 4. Possible outcomes of neurobehavioural assessment of individuals with TSC.

1. Arrange further detailed evaluations (including functional analysis of behaviour, physical review and special investigations)
2. Enrol child in community program for early intervention
3. Develop specific therapeutic program for a child's developmental needs (preschool, 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 for adults
10. Provide support for parents and/or care givers

TSC behaviour consensus panel members

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