



Learning disability in Tuberous Sclerosis Complex (TSC)

Introduction

Vogt set forth the triad of learning disability, intractable epilepsy, and facial angiofibromas as the hallmarks of Tuberous Sclerosis Complex (TSC) in 1908. We now understand that only about 30-40% of affected individuals have all three of these features. While many people with TSC have normal intelligence, a large number do in fact suffer from cognitive impairment, or learning disability. Let's start by defining learning disability, which strictly speaking refers to a person whose intelligence quotient (IQ) is below the normal range, that is to say less than 70. A deficit in adaptive behaviour must also be present. This involves problems coping with new or different situations in a classroom or everyday life. When a person cannot cooperate with standardised IQ testing, such as is the case with young children and infants or the severely impaired, a psychologist can perform a standardised rating or estimate of cognitive ability based on their observations of the person. This can also serve as an index of learning disability. Examples of these kind of ratings include the Bayley scales of infant development, or the developmental quotient. After age 8 years, **and** in the absence of confounding factors, an IQ or other rating is generally felt to be stable over time. For example, a 5 year old with an IQ of 60 will probably have about the same IQ when he or she is 15 or 25 years old. Some things that can affect an IQ rating include medications, on-going seizure activity, whether a person is trying their best, or is anxious, frightened or tired. Whoever performs the test or evaluation must find out enough about the person being tested to determine if factors like these are affecting the result.

Diagnosis

It is critically important that the diagnosis of learning disability be based on objective criteria applied by qualified people, such as a psychologist or psychiatrist. Often care-givers, therapists, teachers, relatives, acquaintances, and even physicians may say that someone is "learning disabled" based only on their opinions or subjective impressions. While no harm may be intended, this kind of imputation can become a "label" that sticks with someone for many years, and is never questioned or re-evaluated. This is particularly true for children younger than 8 years of age, where assessments largely involve rating of intelligence by another person. The harm is that the person may not receive needed evaluations or services that could minimise their deficits and improve their function. For example, autism is often confused with learning disability. While the two conditions can co-exist in the same person, many times an autistic person in fact has normal intelligence. A child may be diagnosed with learning disability while on sedating drugs or experiencing frequent seizures. If these conditions improve or remit then significant increases in learning and cognition can occur over time.

Incidence

How common is learning disability in TSC? The answer is not clear. Doctors used to think that everyone with TSC had learning disability. Estimates range from 38% to 80% in different studies. Many factors make it difficult to determine this exactly. Assessment of learning disability is often based on inaccurate methods like telephone interviews, or someone's subjective impression, rather than standardised testing. People with TSC who do not have seizures or other problems may never receive the testing needed to make the diagnosis. Many physicians still do not recognise or diagnose TSC, particularly in milder forms or those that show up in adulthood. People who have a child with TSC may not wish to be tested or to know if they have the disease, for fear of the consequences that could follow. Currently the best data available suggests an overall incidence of

learning disability of approximately 40% in TSC. In this context consider also that the TSC 1 or 2 gene is estimated to be present in about 1 in every 8,000 to 10,000 people. Clearly, learning disability affects a large number of people with TSC and is a major problem.

A major finding in recent years has been the understanding that the more tubers a person has in their brain, the more likely they are to be learning disabled. While this is true as a statistical association, it does not allow prediction of a person's IQ based on the number of tubers they have. Neither is there a "threshold" or safe number of tubers to have, below which a child will not have learning disabilities. It makes sense that the more involvement there is in a person's brain the more likely they are to have problems. However, many, a few, or even one tuber can seriously disrupt brain function and development in a particular person. Whether or not someone has TSC, we cannot change the genetic "hand" we have been dealt. There are nonetheless many things that can minimise the burdens imposed by learning disability in this context.

Management

Interventions for learning disability ideally mean a pro-active approach. Pro-active strategies involve the early identification and treatment of learning disability, and whenever possible the prevention of factors known to aggravate it. Any child who is known to have TSC should be considered at developmental risk, even if they show no signs of abnormality at the present time. Early development centres on the acquisition of gross and fine motor skills, as well as the acquisition of language. For children diagnosed in infancy referral is made for evaluation and follow-up by the local child development centre. A paediatrician or neurologist should closely monitor the child's developmental status at periodic follow-up visits. From infancy to early childhood these should take place a minimum of every three to six months. In addition to physician assessment, performance of a developmental evaluation such as the Bayley scales of infant development is recommended between age 12 to 18 months, and again at 2 to 3 years of age. Less sensitive screening measures used by paediatricians for the general population, such as the Denver developmental screening test, can miss subtle deficits. Any suggestion of difficulty indicates the need for occupational,

physical, and/or speech therapy. Many physicians assume, incorrectly, that children cannot benefit from therapy before age three years or older. Early identification and treatment are critical to help avoid future problems. This is followed by a formal neuropsychological evaluation at or just prior to entering infant school.

Children who have no evidence of learning disability at this point will continue in mainstream schooling with standard assessments by their local school personnel. Children with identified cognitive or motor skill problems need an assessment for a Statement of Special Educational Needs to continue/supplement their special education whether in a mainstream or special school. Ideally an individualised educational plan (IEP) should be formulated with particular attention to the results of neuropsychological testing and close involvement of the educational psychologist. Follow-up neuropsychological testing with appropriate adjustments in the IEP should be undertaken every two to three years.

Seizures and Learning Disability

Epilepsy often begins in early childhood/infancy. This is the major treatable factor in TSC responsible for aggravation of cognitive and behavioural difficulties. People with TSC who have the onset of seizures after age five years are much less likely to have behavioural or cognitive problems than those in whom they start before this time. It is not known if people with worse TSC are more likely to have both earlier onset of epilepsy and learning disability, or if the early onset of epilepsy favours the development of learning disability. Seizures, as well as seizure activity recorded on an electroencephalogram (EEG), are associated with disruption of brain function, and can directly interfere with cognition, learning, and language development. These effects can be noticed in the short term, for example while the person is experiencing the seizures or seizure activity. It can also affect learning over the longer term, if seizures remain uncontrolled for months or years.

Epilepsy Treatment

It is important to provide the best seizure control possible for many reasons and avoiding aggravation of learning disability is one of the most important. At the same time, anticonvulsant drugs can often have sedating or "dulling" effects that can themselves hamper learning and

cognition. Some anticonvulsants can cause hyperactivity and attention problems. These side effects are more common when multiple anticonvulsants are used. Drugs that have sedative properties such as barbiturates (e.g. phenobarbitone) and benzodiazepines (e.g. diazepam) are especially likely to have this effect. Many times, any negative effect of medication is more than outweighed by the benefit on cognition of improved seizure control or seizure freedom.

The choice of an anticonvulsant depends on many factors and cannot be determined by a “cookbook” approach. Neither should the choice of medication be a matter of “trial and error”, despite appearances to the contrary. Each drug has particular advantages and disadvantages, and only a neurologist or physician thoroughly familiar both with the medications, and a particular patient, can select the best treatment. With this in mind, the following are generally agreed principles of anticonvulsant treatment among neurologists and epileptologists:

1. Multiple anticonvulsants (polytherapy) should be avoided whenever possible. Use of multiple drugs entails additional cost, side effects, and drug interactions. Only about 15 to 20% of epilepsy patients fare better on two or more drugs than they do on one.
2. The anticonvulsant most likely to be effective for a particular individual’s epilepsy is started, and the dose is then adjusted to maximal benefit.
3. Once a medicine has been shown not to be effective for a patient’s epilepsy, then it should be tapered and discontinued while another drug is added.
4. The cure should not be worse than the disease. That is, if a person’s seizures are controlled, but they are so sedated or impaired as to be non-functional, are they really better off?
5. “Rescue” medicines should be available for times of increased seizure activity, such as when the person is ill, has a fever, etc. This generally involves a fast acting drug such as diazepam or lorazepam, which can be given orally, rectally, or by injection.

Other Therapies

Finally, many people with learning disability have other behavioural issues (co-morbidity) that may be more disabling than their cognitive problems. Hyperactivity, inattention, aggressive behaviours, obsessions or compulsions can all cause major difficulties and secondarily inhibit a person’s ability to learn or participate in family/social activities. Behaviour modification techniques are very useful for these conditions and are employed first. This involves rewarding or encouraging desired behaviours, and discouraging undesirable ones. Consistent application between parents and other care-givers is very important. Guidance from an experienced psychologist or therapist is necessary to implement and monitor such a program. In selected cases specific medications may be useful as well. Stimulants such as methylphenidate (Ritalin) or dextroamphetamine (Dexedrine) can improve attention and a person’s ability to focus on assignments. Other drugs can help if learning is impaired by specific behaviours, such as obsessions, compulsions, outbursts of anger, etc. In each case the possible benefits of drug treatment must be carefully weighed against their side effects in a specific child or individual.

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