



TSC AND AUTISM SPECTRUM DISORDERS

First described in 1943 as a syndrome impacting behavior, autism is typically diagnosed in early childhood. The new Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5), published in May 2013, lists the two diagnostic criteria for autism spectrum disorder (ASD):

1. An impairment in social communication and social interaction. Examples include:
 - a. difficulty in social-emotional reciprocity, such as failure to engage in back and forth conversation
 - b. lack of eye contact and disinterest in physical contact such as hugging or hand-holding;
 - c. problems in developing, maintaining and understanding relationships
2. A tendency to have narrow patterns of interests and activities coupled with repetitive and obsessive behaviors, and a lack of pretend or imaginative play; often children with autism find it necessary to have rigid and structured routines.

In the new diagnostic criteria, labels such as Asperger's syndrome and Pervasive Developmental Disorders-Not otherwise specified (PDD-NOS) are no longer included. Instead, the range of variants and associated behaviors now all fall under the umbrella of "autism spectrum disorder" or ASD. There is tremendous variability in severity in the autism spectrum. Symptoms must be present in early development and must cause significant impairment in functioning.

What Is the Link Between Autism Spectrum Disorder and Tuberous Sclerosis Complex?

Over the years, it has become recognized that between one-fourth and one-half of all children with tuberous sclerosis complex (TSC) develop ASD. The rate of ASD in the general population is substantially lower (around 1% of the total population), so there is clearly a very substantial increase in the rate of ASD in children with TSC. Although this is a relatively low rate it is still clearly much higher than the rate of TSC in the general population, which is somewhere between 1 in 6,000 individuals. Either way, the overlap between ASD and TSC is clear. Additionally, there is a very clear link between ASD and cognitive impairment in TSC.

ASD is usually diagnosed in young children between the ages of 2 and 4, but in individuals with TSC, the diagnosis of ASD may go unrecognized or be delayed due to other developmental disabilities. The importance of an accurate diagnosis of ASD for individuals with TSC is so that the individual can receive appropriate educational services and life-long support, as needed.

Why Do Individuals with TSC Frequently Develop ASD?

Current research does not definitely answer the questions related to the increase of ASD in individuals with TSC. However, some important leads are beginning to form the basis of an explanation for the link. In general, it is believed the abnormalities in brain development that occur in TSC sometimes interfere with the proper development of brain areas that are important for the development of social communication skills (the ability to appropriately interact with other individuals).

Early evidence suggested that cortical tubers (which develop in earlier stages of brain development), particularly in the temporal lobes, were associated with the development of ASD. The temporal lobes are important for processing auditory information, especially speech sounds as well as information about faces and facial expressions. Interference with the development of these key skills may then lead to the social communication difficulties that characterize ASD.

However, it is now clear that the presence of cortical tubers is not sufficient on its own to produce ASD. Instead, it appears that there are abnormalities in the way different parts of the brain connect to each other, not only in the temporal lobes but in many other parts of the brain as well. These abnormal connections, which occur independent of tubers, are associated with ASD in children and adults with TSC. Additionally, many studies have shown that seizures and, particularly, early onset of seizures, are associated with delayed development and ASD. Therefore, it is likely a combination of factors that leads to the much higher chance of ASD. Although the link with early onset epilepsy and infantile spasms raises the possibility that the seizures may play a role in interfering with normal development of brain systems important in social communication, it is possible that the link with early seizures instead reflects the presence of abnormalities in key locations in the brain. These abnormalities in connectivity may give rise to both the seizures as well as ASD. Further research to try to determine which of these two explanations is correct is required, especially as it has such important implications for treatment.

Is It Important to Diagnose ASD in Individuals with TSC?

Some people express the view that it is enough that an individual has TSC, so another diagnosis such as ASD is unnecessary. Although it makes sense to avoid adding diagnoses and labels, the diagnosis of an ASD is important for several reasons. A diagnosis can often help parents make sense of a range of rather unusual behaviors that otherwise seem extremely puzzling. Often, parents feel that somehow they have been doing something wrong in how they are parenting their child, and that the difficulties that the child is having in relating to others, communicating or playing is somehow the parents' fault. It can be quite helpful for parents to discover that some of the unusual behaviors their child may be demonstrating are part of the developmental delays a child may be experiencing related to the autistic process.

In addition, the diagnosis is important because children with ASD benefit from early intervention services that support improvement in speech, language and behaviors. Early intervention services are available for very young children and their families. These services include physical therapy, speech therapy and occupational therapy. Early intervention services work with not only the child with ASD, but also the parents and siblings. The goal of early services is to foster the development of children with ASD.

How Is the Diagnosis Made?

The diagnosis of an ASD is based on a report of the child's early development, detailing the way in which he or she acquired skills and the areas in which he or she has struggled, coupled with careful observations and assessments. These evaluations need to be performed by individuals who are experienced in evaluating individuals with complex developmental disabilities and ASD. The assessments are lengthy, and it may be necessary for the evaluator to see the child at home or in the playgroup or nursery setting, often referred to as a functional contextual assessment, before the diagnosis can be confirmed. The diagnosis of ASD is made through a team evaluation, including reports from therapists, pediatricians, teachers, parents and psychologists.

There are several assessments that are used to reach a diagnosis of ASD. In addition to the clinical gold standard, which is DSM-5, the most commonly used play-based measure is called the Autism Diagnostic Observation Schedule (ADOS). This assessment should be performed by someone familiar with ASD who is trained to utilize the ADOS.

When Is Diagnosis Possible?

To some extent the answer to this depends on the individual's overall level of ability. In individuals who have the most severe cognitive disabilities, it can sometimes be extremely difficult to make a definitive diagnosis. In general it is hard to make a confident diagnosis before the age of 18-months to 2-years. Research is continuing to identify the early markers of ASD so early treatments can be implemented.

What Treatment Is Suggested?

Treatment options vary based on the individual's age and ability. The focus of the treatment is often targeted at strengthening skills in individual areas of difficulty. Special education provisions and accommodations are incorporated in a child's individual education plan (IEP). This often includes the individual working with a multidisciplinary team of clinical professionals that provide several different services, including speech and language therapists, developmental and child psychologists and pediatricians.

Because of the great variability in the impairments, level of functioning and behaviors of children on the spectrum, there is no universal treatment for children with ASD.

According to the National Academy of Sciences (*Educating Children with Autism*, 2001), children with ASD should receive a minimum of 25 hours per week of educational services targeting their core deficits, with the specific educational plan tailored to the needs of the child. There are many possible types of educational interventions for children with ASD. Some of these include:

- Applied Behavioral Analysis (ABA) and Discrete Trial Training (DTT)
- Pivotal Response Treatment (PRT)
- Floortime therapy
- Treatment of Autistic and Related Communication Handicapped Children (TEACCH)
- Picture Exchange Communication System (PECS)

ABA and Discrete Trial Training (DTT) are often used interchangeably, even though DTT represents just one type of ABA. DTT includes intense repetitive, structured tasks in which good behavior is rewarded and undesirable behavior is ignored. It is time intensive and focuses on changing current behaviors and does not prepare individuals to respond in new situations. Some individuals with TSC who have ASD have significantly benefited from ABA programs.

Pivotal Response Treatment (PRT) is derived from ABA. It is play-based, and rather than target specific behaviors as in DTT, the therapist in PRT targets “pivotal” areas of a child’s development, such as motivation and initiation of social interaction.

Floortime therapy is a play-based treatment in which the therapist and parent engage with the child in activities that the child enjoys, and in the process target areas such as communication, self regulation, and emotional growth.

TEACCH (Treatment of Autistic and Related Communication Handicapped Children) was developed at the University of North Carolina. TEACCH focuses on adapting the environment to the individual with ASD instead of trying to make the individual adapt to the environment. This is achieved through high structure, organizational charts and schedules. While many favor this approach, some feel that it is too structured and makes the individual too dependent on charts and other organizational tools.

PECS (Picture Exchange Communication System) is used to encourage communication. By using pictures, an individual can point to or hand an object to someone to demonstrate what he or she wants.

Options vary and the treatment program needs to be tailored to the individual’s age and ability. Treatment is targeted at fostering skills in the three main areas of difficulty – social and communication skills and the development of imaginative play. In addition, treatment aims to ensure that the repetitive or obsessive behaviors do not become too marked or prominent and do not interfere with family life. Lastly, the treatment aims to help parents foster their child’s development and support them during the early, often very demanding, years.

There is growing evidence to suggest that early intervention programs may be one of the most effective current forms of treatment in individuals with ASD, but it is not yet known to what extent the intervention programs of this kind are helpful for children with TSC. Research is needed to evaluate effectiveness of these programs for individuals with TSC who have ASD. Current studies in the U.S. are exploring early intervention in infants with TSC, targeting behaviors that may predispose them to ASD.

Additionally, there are now two medications that are approved by the FDA for treating irritability in ASD. These are Risperidone and Aripiprazole (Abilify). No medications have been approved for treating the core symptoms of ASD.

What Will the Future Hold?

Detailed knowledge about the way individuals with TSC and ASD develop is currently being gained through studies in the U.S. and the U.K, so for now we can only be guided by the development of individuals with ASD who do not have TSC. The range of outcomes here is

very great. At one extreme, individuals can have persisting serious problems throughout childhood and into adult life. Some individuals with ASD are prone to self-injury, particularly if they get upset or frustrated when their routines or activities are interrupted, or if they get frustrated over their communication difficulties.

At the other extreme, individuals with high-functioning ASD can largely outgrow their difficulties and lead an independent or semi-independent life in adulthood. The outcome is to some extent related to the severity of the associated cognitive impairments or a demonstrated level of cognitive disabilities. Individuals who have severe or profound forms of cognitive ability are likely to have persisting difficulties. In addition, the amount of useful speech that the individual acquires indicates how they will fare in the future. Lastly, the severity of the social and communication difficulties and behavior problems is also helpful in determining what the outcome will be. The more severe the problems, the more persistent they tend to be.

Additional Resources

Autism Speaks

1 East 33rd Street, 4th Floor

New York, NY 10016

Phone: (212) 252-8584

Fax: (212) 252-8676

E-mail: contactus@autismspeaks.org

<http://www.autismspeaks.org/>

Autism Response Team

familyservices@autismspeaks.org

(888) AUTISM2 (288-4762)

En Español 888-772-9050

Autism Spectrum Disorders

Centers for Disease Control and Prevention (CDC)

Phone: 1-800-CDC-INFO

Email: cdcinfo@cdc.gov

www.cdc.gov/ncbddd/autism/

Autism PDD Resources

www.autism-pdd.net

Autism Resources

www.autism-resources.com

Autism Society of America

7910 Woodmont Avenue, Suite 300

Bethesda, MD 20814

Phone: 301-657-0881 or 1-800-328-8476

www.autism-society.org

Autism Today
www.autismtoday.com

Center for the Study of Autism
www.autism.com/
National Institutes of Health Autism Research Network
www.autismresearchnetwork.org/AN/

TEACCH Autism Program
University of North Carolina
Phone: 919-966-2174
E-mail: TEACCH@unc.edu
www.teacch.com

***This publication from the Tuberous Sclerosis Alliance is intended to provide basic information about tuberous sclerosis complex (TSC). It is not intended to, nor does it, constitute medical or other advice. Readers are warned not to take any action with regard to medical treatment without first consulting a health care provider. The TS Alliance does not promote or recommend any treatment, therapy, institution or health care plan.*

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