Neuroimaging in Tuberous Sclerosis Complex: Implications for behaviour

Introduction

Neuroimaging is one of the most important considerations in the diagnosis and management of tuberous sclerosis complex (TSC). This involves performance of either computerized tomography (CT) or magnetic resonance imaging (MRI) scans of the brain. Over 90% of people with TSC will have seizures, and all of these will have some type of malformation of their brain/central nervous system. Some people may only have brain involvement from TSC. The most common findings include cortical tubers, subependymal nodules, and giant cell astrocytomas. Less frequently abnormalities of blood vessels such as aneurysms can occur. The cortical tuber is the feature of TSC that has given it its name. Tubers are zones of malformed brain tissue that are the hallmarks of TSC. Subependymal nodules are pieces of tissue that protrude into the fluid spaces or ventricles of the brain. They usually develop calcium deposits as a person grows older. This build-up is helpful in diagnosing TSC, but does not itself cause a problem. Sometimes they grow and obstruct the flow of the cerebrospinal fluid in the ventricles of the brain. This can cause worsening seizures, headaches, and/or changes in behaviour. When this occurs they are called giant cell astrocytomas and require surgery to remove them. Subependymal nodules are most likely to turn into an astrocytoma during childhood and adolescence.

After the diagnosis has been made, periodic follow-up scans may help identify areas of change or deterioration. In this fact sheet these techniques will be described, as well as their usefulness and limitations in persons with TSC. At the end the recommended technical factors for performance of CT and MRI in TSC patients are listed.

Computerized Tomography

CT scans produce a picture of the brain by directing a beam of X-rays through the body at many different angles. A detector measures how much of the beam comes out on the other side, just like a piece of film does when a regular X-ray picture is taken of a bone, etc. A computer than constructs a cross-sectional picture of the brain, based on many hundreds of readings from the detector. Contrast (X-ray dye) may be given by vein to help blood vessels or certain types of tumours show up better. CT scans take less time than MRI scans; in fact some machines can scan the brain in as little as 25 seconds. Nonetheless, it is important that a person hold as still as possible during the scan, so that the best possible pictures can be obtained.

CT scans show things well that tend to block a lot of the X-ray beam, like blood or calcium deposits. They can show tubers and growths (tumours), but usually not as clearly as a MRI. Build-up of fluid in or around the brain (hydrocephalus) can also be seen well on CT. Because they can be performed relatively quickly and are more easily available than MRI, CT can help to exclude a major abnormality or dramatic change. Examples would include a tumour or hydrocephalus when a person with TSC has a sudden change in behaviour, increase in seizures, or the abrupt onset of severe headaches. These are conditions that can require swift medical or surgical treatment. Disadvantages include the need for exposure to radiation, albeit at very small doses, need for sedation in patients who cannot hold still, and lower resolution than MRI. CT typically identifies only the largest tubers, and even then usually underestimates their size. In adults who are suspected of having TSC, a CT scan is generally an adequate evaluation. This is because adults and adolescents with TSC generally have subependymal nodules, which show up well on CT due to their high calcium content. Also, adults rarely need sedation for a CT scan.

Magnetic resonance imaging

MRI involves placing a person in a tube inside a very strong magnet. This causes the atoms inside the body to line up in a specific way. Once this is done radio waves (similar to those you hear everyday) are beamed at the part of the body being scanned. Some of the atoms absorb the radio waves and then release them back to the outside where they can be picked up by an antenna (coil) that is placed over the area being scanned. This information is then converted by a computer into a cross-sectional picture. MRI's provide a much more detailed picture of the brain. They can also be used to identify blood flow (perfusion imaging), chemical composition (spectroscopy), flow of spinal fluid (cinematography) and blood vessels (angiography) in various areas of the brain. They can identify tubers much better than CT scans; particularly using a technique called FLAIR (fluid attenuated inversion recovery). Contrast is usually given and can help determine if a subependymal nodule is beginning to grow into an astrocytoma. MRI is better able to assess any changes in tubers, tumours, or subependymal nodules that can occur over time. A MRI scan takes much longer than a CT, as long as 45 minutes to an hour, and some special scans may take even longer. It is also more expensive. The space in the magnet for the person being scanned is rather small, and many people get claustrophobic. So-called "open" MRI's have magnets that are open on the sides, and are less confining, however their image quality is poor, and they are not desirable for use in TSC. It is very important to hold perfectly still during a MRI, as the pictures are easily distorted by movement. Most children and many adults will require sedation. An advantage is that MRI does not require exposure to radiation. This can be important since many people with TSC need to have several brain scans over a lifetime. In fact, some centres do brain scans as often as every year until puberty to screen for complications.

Other techniques

Some brain scans involve injection of a radioactive dye into the bloodstream, which is then absorbed by the brain and measured by a special camera. The amount of radioactivity is very small and does not pose a significant risk. The types of scans that use these techniques are either positron emission tomography (PET) or single photon computed tomography (SPECT). They provide a picture of the brain based upon blood flow, or the brain's metabolism of certain chemicals. Sedation may be necessary if the patient cannot lie still for the scan. These scans are often helpful to identify an area of the brain from which seizures are coming. In certain cases these regions can be removed surgically in the hope of providing better seizure control. A PET or SPECT scan can be superimposed over corresponding MRI pictures of the brain. In this way the brain's structure or specific tubers can be identified in terms of metabolic activity. This aids the neurologist and surgeon in determining who might benefit from seizure surgery.

Sedation

Many people will need to be sedated for one of these techniques. It is critical that sedation be performed safely and by experienced personnel, but also that it be sufficient for the patient to remain asleep throughout the entire procedure. Taking mild sedatives prescribed by a family doctor are almost always inadequate. In fact many people become more anxious or agitated when they receive such a medicine. Since CT scans without contrast are so quick sedation is often not necessary. Scheduling a scan when a child is already sleepy or just after an infant has been fed ("milk sedation") can be very useful. For MRI scans infants and young children are often sedated with an oral medicine called chloral hydrate. Older children usually need intravenous sedation. Certain people may require an anesthesiologist to be safely and adequately sedated. Whatever technique is employed it is important to be sure that the staff at the scanning facility are thoroughly trained and able to handle any problems that may arise. This is particularly true for infants and children. Some children may have problems after being sedated for a scan or other procedure. Specifically, they may wake up and feel nauseated, sick, or be agitated or irritable. If not told this already, parents should ask what to do and whom to call in the event of a problem. If you had to travel a long distance from home to have the scan you may want to consider spending the night afterwards, rather than trying to drive home with a child who could have after effects of the sedation. Generally you should gently attempt to comfort the child if they are agitated, realizing that it may take several hours for this to pass. When the child is alert, small sips of clear liquids should be given and gradually increased. Contact your doctor if there should be any fever, prolonged vomiting, extreme behaviour changes, or prolonged somnolence. Remember, it is always best to call if you are concerned or unsure about something. Despite these cautionary statements, the overwhelming majority of children tolerate sedation without any serious problems and wake up afterwards with little or no problem.

Implications for behaviour

Neuroimaging is extremely useful in determining if an abrupt change in behaviour, or other symptoms such as seizures, are the result of a brain tumour, increase in pressure, or other deterioration. Some centres perform screening brain scans every few years through adolescence to screen for growth of tumours or other changes. The hope is to be able to treat these problems earlier and hopefully avoid problems. This practice is controversial. Many doctors feel a patient can be followed just as well by regular check-ups, with scans whenever there might be a change or worrisome symptom. There are concerns about treating people only on the basis of test, particularly if they are not having any symptoms. Even the brain tumours in TSC may sometimes stabilize and stop growing without treatment. It is not clear whether exposing someone to a brain surgery just to avoid problems that **might** occur is worthwhile.

The likelihood of learning disability in TSC has been shown to be greater in individuals that have higher numbers of tubers in their brains. Greater numbers of tubers are also more likely to be seen in people with difficult-to-control epilepsy. Autism does not seem to relate to the overall number of tubers, but may be more likely when certain areas of the brain are involved, such as the temporal lobes or cerebellum. However, the association of autism in TSC with certain types of brain involvement has not been conclusively proven. It is understandable that a parent or person with TSC would want to know the extent of their child's or their own brain involvement. Nonetheless, it is critically important not to view this information as foretelling future problems or an individual's mental outcome. These associations are statistically true for large groups of affected people, not necessarily for individuals. Some people with large tuber counts do very well cognitively and may have little trouble with seizures. Another concern is the difficulty actually counting the tubers or the amount of brain involvement. Sometimes tubers are very close to each other, making it hard to determine where they start and stop. Also, different radiologists may come up with different numbers, especially if they do not have experience with TSC. It is important that every child or person with TSC be treated as an individual with their own particular abilities and needs. No one should be "assigned" a certain future outcome based solely on a medical test.

Recommended technical factors for performance of CT/MRI in TSC

You may wish to share these with your doctor or radiologist.

CT

5 mm sections through the posterior fossa and 10 mm sections through the supratentorial brain pre- and post-contrast.

MRI

Field Strength	1.5 Tesla
Sequences:	Sagittal T1
	Axial T1 pre- and post-contrast
	Axial T2
	Axial FLAIR
	Coronal T1 post-contrast

***David Neal Franz**, MD, Associate Professor of Pediatrics and Neurology Director, Tuberous Sclerosis Clinic , John C Egelhoff, DO, Associate Professor of Radiology and Pediatrics, University of Cincinnati College of Medicine Children's Hospital Medical Center, Cincinnati, Ohio, USA*

References:

1. Evans JC, Curtis J, The radiological appearances of tuberous sclerosis *Br J Radiol 2000* Jan; 73(865): 91-8.
2. Roach ES, DiMario FJ, Kandt RS, Northrup H, Tuberous Sclerosis Consensus Conference: Recommendations for Diagnostic Evaluation. *J Child Neurol* 1999 June;14(6): 401-7.
3. Christophe C, Sekhara T, Rypens F, Ziereisen F, Christiaens F, Dan B, MRI spectrum of cortical malformations in tuberous sclerosis complex, *Brain & Development 2000* 22: 487-493

Further information on TS and the work of the TSA can be obtained from: Diane Sanson, Head of Administration,
P.O. Box 12979, Barnt Green, Birmingham, B45 5AN.
Tel/Fax: 0121 445 6970
Email: diane.sanson@tuberous-sclerosis.org
Web: www.tuberous-sclerosis.org

Tuberous Sclerosis Association