Epilepsy is a common manifestation of tuberous sclerosis complex (TSC). More than 80% of individuals with TSC will have seizures, most often beginning in childhood. Several new anticonvulsant medications have become available in recent years, and these drugs along with older medications control the seizures for many individuals. Unfortunately, for some individuals with TSC, the seizure activity proves intractable or refractory, which means that despite appropriate use of appropriate medications, the individual continues to have seizures. In these cases, other therapeutic options should be considered. Currently, these options include: the ketogenic diet, the vagal nerve stimulator (VNS), and epilepsy surgery.

Brain surgery can be quite successful in reducing seizures in individuals with TSC in the appropriately selected surgical candidate. Different procedures can be effective depending on the type of seizure an individual with TSC is exhibiting. Corpus Callosotomy (CC) is a procedure that “splits the brain” by dividing the corpus callosum, a structure that connects the right and left hemispheres, or halves, of the brain. This operation is considered when a localized seizure focus cannot be identified by the presurgical testing, yet the patient is suffering from disabling “drop” seizures. The more typical type of epilepsy surgery, however, is called resective surgery, which involves resection (removal) of the area(s) of the brain that is/are causing seizures.

The Ideal Surgical Candidate
Several reports in the medical literature suggest that epilepsy surgery can be a successful treatment for individuals with TSC. This has been and still is debated, primarily because individuals with TSC typically have more than one area of abnormal brain area, or tuber, and sometimes more than one seizure focus (area of the brain causing the seizures). The “ideal” candidate for resective surgery is a person with one seizure type and a clear correlation with one specific seizure focus (identified by EEG and brain MRI) in an area of the brain that can be safely removed without causing a significant loss of function. When a person has multiple seizure types (particularly “drop seizures”) that cannot be clearly localized (that is identified as coming from a single tuber or from a specific region of the brain), then a CC may be the more appropriate surgical procedure. Of course, epilepsy varies among individuals with TSC, so careful evaluations and planning by an experienced group of health care providers are critical to the process.

Often, individuals with TSC who have multiple tubers and multiple seizure types are not considered “ideal” surgical candidates. However, if the seizures are significantly impacting the individual’s quality of life, the possibility of surgery should be considered. Recent experience suggests that some individuals with difficult-to-localize seizures or with multiple seizure foci may still benefit from removal of one or more of the seizure-producing areas. Often, an extensive workup is needed to help determine which, if any, surgical procedure is appropriate.
Phase I (Presurgical Evaluation)

If surgery is to be considered, individuals should be evaluated at a center with a well-established comprehensive epilepsy program that includes epilepsy surgery. A pre-surgical or Phase 1 evaluation is performed to determine if an individual with TSC is a surgical candidate. This consists of a hospitalization on an epilepsy-monitoring unit (EMU) to record the seizure(s) with continuous video EEG monitoring. It is during this initial phase that the seizures are identified and the specific area where the seizures are starting is tentatively localized, if possible.

In addition to the video EEG to define the seizures, other evaluations may also be performed. Neuropsychological or developmental assessments are used to help establish a person’s functional strengths and weaknesses. These may also help localize the seizure focus because specific areas of the brain, along with their associated functions, may be impaired by uncontrolled seizure activity. Imaging studies, particularly MRI scanning, defines the structural abnormalities, or tubers. Depending on the institution, other structural as well as functional imaging studies may include positron emission tomography (PET), single photon emission tomography (SPECT), magnetoencephalography (MEG), Diffusion Tensor Imaging (DTI), and functional MRI (fMRI). All of these tests are done to clarify further the location of the seizure focus that can be removed surgically. Finally, a “Wada test” may also be performed. This is a cerebral angiogram, performed by a neuroradiologist who injects a medication (sodium amobarbital) that puts each hemisphere of the brain “to sleep” one at a time. The neuropsychologist then does behavioral testing to identify in which hemisphere language and memory function are located.

All study results are used to determine which individuals may proceed to the next phase. Once again, the individuals that may be the best candidates for resective surgery will be those who have a clear focal onset of their seizure from an area with a tuber that is not in an important functional area of the brain. However, even when someone may not be an “ideal” candidate, the information from the Phase I evaluation may still suggest that a surgical option is possible and that they may proceed to Phase II.

In some cases it may be decided after the Phase I evaluation that a resection is not possible. This may be because a single, dominant focus cannot be identified or that it could not be safely removed based on its location or proximity to important brain function. However, recent data suggests that, in select cases, tubers or seizure foci may be resected from “eloquent” regions of the brain, like the motor cortex, without long-term permanent neurologic deficits. If there is a concern that a resective surgery would result in significant impact on important brain function, other options may be considered, including a CC. This is an option in very specific situations, in particular if the person has Lennox-Gastaut Syndrome with drop seizures or has frequent episodes of prolonged seizures (status epilepticus). On rare occasions, following a CC, the seizures may change and suggest a focal onset so that it becomes feasible to consider a resection and proceed to Phase II.

Phase II (Resective Surgery)

Following the Phase I evaluation, the epilepsy surgery team, which includes the epileptologist, neurosurgeon, neuroradiologists and neuropsychologists, reviews all the collected data and decides if epilepsy surgery would likely lead to a significant reduction in seizures without causing a loss of important function, such as speech, use of a hand, etc.
This evaluation frequently identifies the tuber or tubers thought to be involved in the individual’s epilepsy that could be safely removed.

In many cases, particularly for individuals with TSC and multiple tubers, further monitoring is necessary to better delineate the epileptogenic region(s). This involves invasive monitoring with subdural electrodes, rather than a scalp EEG. This means the individual has an initial stage of surgery to place special electrodes on the surface of the brain, or directly into the tubers, for another session of video EEG monitoring. This recording produces a “map” of the seizure focus. These same electrodes are also used for making a “functional map.” This is done by using a small electrical current to directly stimulate the surface of the brain to identify the functional area monitored by the electrodes (i.e., speech, hand movement, etc.). The map of the seizure focus and the functional map are then combined into a single map. In some cases, mapping can be done in the first part of the same surgical session in which resection will be done, if possible.

If the seizure focus does not overlap with any important function, it may then be removed, which will hopefully result in good seizure control. If the seizure focus overlaps with an area of important function, complete removal of the tuber may not be possible.

There may also be situations when it is necessary and safe to record and map the seizure focus and function in both hemispheres to remove seizure foci (and tubers) on both sides of the brain. This approach is even more complicated than a resection in one hemisphere and, therefore, is extremely rare.

The time needed to complete Phase II (the mapping and resection) varies depending on how long it takes to record enough seizures and finish the functional map.

Conclusion
Seizures are extremely common in individuals with TSC. They may be frequent and severe enough in spite of treatment with multiple medications to consider other therapeutic options, including epilepsy surgery. This is a complex process intended to achieve the desired outcome of seizure control, with or without the continued need for anticonvulsant medications. Safety is always the top consideration in the risk-benefit assessment of each patient. Therefore, it is best to go to a comprehensive epilepsy center to obtain a complete evaluation from health care providers who have performed this type of evaluation and surgery on individuals with TSC.

The goal of any treatment for seizures is complete seizure control with minimal or no side effects to the treatment and with improved quality of life for the patient and his or her family. It is appropriate to pursue all reasonable means to achieve this goal, including epilepsy surgery.

References


Resources
Epilepsy Therapy Development Project: www.epilepsy.com/

National Institute of Neurological Disorders and Stroke, National Institutes of Health: www.ninds.nih.gov/disorders/epilepsy/detail_epilepsy.htm#48923109

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**This publication from the Tuberous Sclerosis 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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