Reinventing the corpus callosotomy

Surgical section of the corpus callosum is an old operation. It was first performed to treat epilepsy more than 75 years ago. Early procedures often consisted of a “total commissurotomy,” performed through a right frontoparietal craniotomy, with division of the entire corpus callosum, the ipsilateral fornix, the anterior commissure, and even the massa intermedia of the thalamus. Subsequently, surgery has been limited to the corpus callosum, typically with sectioning of the anterior two-thirds (figure), sometimes followed by a second completion stage with a posterior transection if the first operation was ineffective.

Eventually, it was evident that corpus callosotomy was most effective for treatment of atonic and tonic seizures, although there is evidence that it may be helpful for generalized tonic-clonic seizures, and occasionally focal seizure types. This early work, and subsequent larger series, led to acceptance of the staged corpus callosotomy for palliation of drug-resistant seizures that cause falling (“drop attacks”), especially in patients with the Lennox-Gastaut syndrome.

Although it may benefit seizure control, cognitive and neurologic deficits can occur after total or partial callosotomy. One mechanism may be loss of interhemispheric compensation of function. Patients with left-handedness or atypical language dominance may experience a decline in language function. Some unilateral loss of motor dexterity may be seen when there is preexisting mild to moderate motor or memory dysfunction in the contralateral hemisphere.

An underlying assumption, long-held, is that corpus callosotomy controls seizures by preventing bilateral synchronicity of epileptiform discharges, particularly generalized fast electrodecremental ictal discharges. Support for this idea comes from postoperative EEG studies that typically show transformation of previously generalized epileptiform patterns into independent lateralized discharges.

The report by Paglioli et al.8 in this issue of Neurology® challenges the standard surgical approach to callosotomy. The authors hypothesized that successful control of drop attacks depends on sectioning of motor fibers in the corpus callosum, and that these fibers might be somewhat more posterior than previously believed, accounting for the cases in which the anterior two-thirds callosotomy fails to achieve seizure palliation. The implication of this hypothesis would be that the effect of callosotomy on seizures might not be directly due to loss of ictal electrical synchronization but to interference with the bilateral motor activity that causes the patient to fall during the seizure. The authors also expressed hope that a posterior callosotomy might carry less risk of cognitive decline.

This operative approach is feasible, and there is evidence that it is effective. In this work, 36 patients with refractory drop attacks and an IQ less than 85 had the posterior 50% to 60% of the corpus callosum sectioned and had drop attacks (but not other seizure types) tracked by seizure diaries with a median follow-up period of 5.75 years. Only 5 of the patients met criteria for the Lennox-Gastaut syndrome. Drop attacks decreased dramatically from a mean of 150 per month during a 3-month preoperative baseline to 0.5 per month afterward. A functional behavioral score was determined from information provided by caregivers, and was improved postoperatively.

This study was not a controlled clinical trial and only provides Class III evidence of efficacy. Other limitations include the absence of any EEG monitoring to assess postoperative seizure control, the omission of detailed structured neuropsychological assessments to screen for postoperative cognitive decline, and the lack of information on effects on other seizure types. It would be particularly important to know whether this procedure has benefit for generalized tonic-clonic seizures, similar to what is seen with a standard callosotomy. Finally, this work does not optimally test the authors’ hypothesis, since the sectioning was not confined to motor fibers, but also included the posterior half of the corpus callosum.

New methods are now available that could more directly test this report’s hypothesis, potentially leading to an even better surgical approach for controlling drop attacks. Callosal motor fibers could be precisely localized in individuals by functional MRI tractography, and this region then targeted for selective stereotactic laser thermal ablation under MRI guidance. Introduction of this less
invasive approach into practice would be expected to result in lower surgical morbidity and shorter hospitalizations, with greatly reduced risk of adverse effects on cognition—that is, if it proves to be effective for reducing seizures!

Sometimes progress in medical therapy can be impeded by unchallenged and seemingly universally accepted assumptions—established “known truths” that have never been sufficiently tested. For decades, there has been a wide consensus on the role of the corpus callosotomy in clinical practice, how it should be performed, and how it works. Paglioli et al. should be commended for questioning this conventional wisdom. If their hypothesis is confirmed by additional studies, it might eventually lead to a superior surgical procedure and perhaps a greater role for callosal surgery in epilepsy treatment.

REFERENCES