Title

Corpus callosotomy versus vagus nerve stimulation for atonic seizures and drop attacks: A systematic review.

Authors

Rolston, John D
Englot, Dario J
Wang, Doris D
et al.

Publication Date

2015-10-01

DOI

10.1016/j.yebeh.2015.06.001

Peer reviewed

Published in final edited form as:

Epilepsy Behav. 2015 October ; 51: 13–17. doi:10.1016/j.yebeh.2015.06.001.

Corpus callosotomy versus vagus nerve stimulation for atonic seizures and drop attacks: A systematic review☆

John D. Rolston[a,*], **Dario J. Englot**[a], **Doris D. Wang**[a], **Paul A. Garcia**[b], and **Edward F. Chang**[a]

[a]Department of Neurological Surgery, University of CA, San Francisco, USA

[b]Department of Neurology, University of CA, San Francisco, USA

Abstract

Atonic seizures are debilitating and poorly controlled with antiepileptic medications. Two surgical options are primarily used to treat medically refractory atonic seizures: corpus callosotomy (CC) and vagus nerve stimulation (VNS). However, given the uncertainty regarding relative efficacy and surgical complications, the best approach for affected patients is unclear. The PubMed database was queried for all articles describing the treatment of atonic seizures and drop attacks with either corpus callosotomy or VNS. Rates of seizure freedom, >50% reduction in seizure frequency, and complications were compared across the two patient groups. Patients were significantly more likely to achieve a >50% reduction in seizure frequency with CC versus VNS (85.6% versus 57.6%; RR: 1.5; 95% CI: 1.1–2.1). Adverse events were more common with VNS, though typically mild (e.g., 22% hoarseness and voice changes), compared with CC, where the most common complication was the disconnection syndrome (13.2%). Both CC and VNS are well tolerated for the treatment of refractory atonic seizures. Existing studies suggest that CC is potentially more effective than VNS in reducing seizure frequency, though a direct study comparing these techniques is required before a definitive conclusion can be reached.

Keywords

Corpus callosotomy; Vagus nerve stimulation; Drop attacks; Atonic seizures

1. Introduction

Atonic seizures, often called “drop attacks” [1], are identified by frequent and sudden reductions in muscle tone, which can be partial (i.e., in single muscle groups, such as the head and neck or a single limb) or generalized across all muscle groups [2]. These latter generalized cases are more dangerous, in that unpredictable falls often lead to repeated and serious trauma. Patients may be required to wear helmets, and environmental modifications are regularly used to mitigate mechanical injury from ground-level falls. Atonic seizures

☆No part of this work has been published previously.

*Corresponding author at: Department of Neurological Surgery, University of California, San Francisco, 505 Parnassus Avenue, Box 0112, San Francisco, CA 94143-0112, USA. Tel.: + 1 415 353 7500. john.rolston@ucsf.edu (J.D. Rolston).

Disclosure

The authors have no conflict of interest to disclose.

carry a very poor prognosis, with almost all patients having seizures refractory to multiple antiepileptic medications [3]. Roughly half of patients exhibit concomitant developmental delays [3], and atonic seizures are frequently found in patients with devastating childhood syndromes like Lennox–Gastaut syndrome and myoclonic–astatic epilepsy of early childhood (Doose syndrome) [4].

Because atonic seizures are difficult to control medically and have such a severe impact on patients, surgical therapies are often proposed for their treatment. If patients have obvious focal lesions, they can undergo resective surgery, which is potentially curative. However, patients more often harbor either diffuse parenchymal changes or nonlocalizable seizure foci. For this latter group of nonlesional patients, two palliative surgical treatments are available: corpus callosotomy and vagus nerve stimulation.

Corpus callosotomy (CC) was first described by van Wagenen and Herren in 1940 as an attempt to stop epileptic discharges spreading from one cerebral hemisphere to the other, thereby preventing generalization [5]. Callosotomy has been in continuous use since, and is most often used to treat epileptic drop attacks, though CC can also be used for Lennox–Gastaut syndrome, recurrent status epilepticus, generalized tonic–clonic seizures, absence seizures, and complex partial seizures [6]. The procedure is typically done with a midline craniotomy overlying the sagittal sinus [7]. The interhemispheric fissure is carefully dissected, and the corpus callosum is divided at its midline. The extent of callosal resection has been frequently studied, with many practitioners first resecting the anterior corpus callosum and reserving further complete resection for recurrent seizures [6,8,9]. Complete callosotomy, as opposed to anterior callosotomy, confers an estimated additional 10% improvement in seizure control for all types over partial callosotomy but is believed to carry a higher morbidity, especially in regard to the disconnection syndrome [6].

Vagus nerve stimulation (VNS) is an ostensibly less invasive method of controlling seizures, with both US FDA (1997) and CE Mark (1994) approval [10]. The procedure entails wrapping a patient's vagus nerve in a spiral-shaped electrode, with a connected pulse generator implanted below the patient's clavicle in the anterior chest. The electrode then delivers intermittent electrical stimulation to the vagus nerve, with the ability to manually trigger additional stimulation using an external magnet. Stimulation of the vagus nerve activates fibers projecting to the nucleus tractus solitarius, which then projects widely to the brainstem and cerebral cortex. It is these widespread connections that presumably mediate the antiseizure effects of VNS, though the precise mechanisms are still unknown.

Multiple studies attest to the efficacy of VNS, including two successful randomized controlled trials, titled E03 [11] and E05 [12], both funded by Cyberonics, Inc., the manufacturer of the VNS system. E03 and E05 both showed significant reductions in seizure frequency (24.5% and 27.9%, respectively) after three months of treatment [10]. Importantly, though, both studies were limited to the study of partial seizures; neither addressed atonic seizures as a primary endpoint. Nevertheless, many patients with mixed seizure types (including atonic seizures) were subsequently implanted and treated with VNS, which has allowed us to estimate the efficacy of VNS in treating this particular seizure subtype. Moreover, because of the perceived noninvasiveness of VNS, many practitioners

have gone to VNS as a first-line treatment for atonic seizures in lieu of the irreversible corpus callosotomy. Below, we examine the evidence-based outcomes for both procedures, including their documented morbidities, and try to provide guidance for the treatment of this challenging seizure subtype.

2. Materials and methods

The PubMed database was queried on May 10, 2015, for English language articles using the following Boolean terms for CC: “callosotomy” AND (seizure OR seizures OR epilepsy) AND (atonic OR “drop attack”) and for VNS: (vagus OR vagal) AND (stimulation OR stimulator) AND (seizure OR seizures OR epilepsy) AND (atonic OR “drop attack”). Only those articles with outcome data specific for atonic seizures were included. That is, articles with grouped data (multiple seizure types grouped together for composite outcomes) were excluded. Although the Epilepsy Foundation defines atonic seizures and drop attacks as synonymous [1], there is a chance that some articles included drop attacks induced by seizures other than atonic seizures (e.g., tonic and generalized) that produced a drop attack phenomenon. We, therefore, also ran a separate analysis where we excluded drop attacks and only included seizures explicitly listed as atonic seizures.

Outcomes in the original studies were grouped inconsistently (e.g., >70% seizure reduction and >50% reduction). We, therefore, regrouped the atonic seizure outcomes into (1) complete seizure freedom, (2) >50% reduction in seizure frequency, and (3) <50% reduction in seizure frequency.

Statistics were computed using SPSS version 22 (IBM Corp., Armonk, NY). Risk ratios were calculated with the χ^2 statistic, with 95% confidence intervals indicated. Group means were compared using Student's *t*-statistic.

3. Results

Eighteen articles were identified for VNS and 62 for CC. Of these, 19 articles on CC [8, 13–30] and 7 on VNS [23,26,31–35] met the inclusion criteria (see the Materials and methods section), corresponding to 317 patients undergoing CC and 38 patients undergoing VNS (Table 1). Median follow-up was 2 years for CC patients and 1.5 years for VNS patients. When patients were pooled across studies, significantly more patients experienced a >50% reduction in seizures after undergoing CC (281 (88.6%) patients) than after undergoing VNS (20 (52.6%) patients), with a risk ratio (RR) of 1.7 (95% CI: 1.2–2.3).When looking at complete seizure freedom from atonic seizures, again, significantly more patients were seizure-free after undergoing CC (184 (58.0%) patients) than after undergoing VNS (8 (21.1%) patients), with a RR of 2.8 (95% CI: 1.5–5.1). Documented adverse events were far more common with VNS (e.g., 20.1% hoarseness and voice changes), compared with CC, where the most common complication was the disconnection syndrome (13.2%; see Tables 2 and 3). Severe complications were infrequent, mostly reflecting differing surgical risks (cortical disconnection and craniotomy for CC and vagus nerve manipulation for VNS) or the expected residual seizures for these palliative techniques (e.g., SUDEP; Tables 2 and 3).

Because there is concern that some authors might include under the name “drop attacks” events other than atonic seizures, we ran an additional analysis where we included only those studies that specifically analyzed atonic seizures and excluded those referencing drop attacks (Table 4). This analysis had similar results to those above, though with less power since fewer patients were analyzed. Again, significantly more patients experienced a >50% reduction in seizure frequency with CC than with VNS: 73 (88.0%) patients versus 17 (50.0%), respectively, (RR: 1.8; 95% CI: 1.2–2.5). Additionally, more patients achieved seizure freedom with CC (33.7%) than with VNS (23.5%), though this difference was not significant (RR: 1.4; 95% CI: 0.7–2.8).

4. Discussion

Atonic seizures are a severe manifestation of epilepsy, frequently refractory to antiepileptic medications. There are two predominant surgical treatments available: corpus callosotomy (CC) and vagus nerve stimulation (VNS). By examining the medical literature, we were able to evaluate the evidence supporting these methods with respect to comparative efficacy and morbidity.

Corpus callosotomy has been available as a treatment for far longer than VNS (1940s versus 1990s), which is likely responsible for the greater number of available case series available for CC patients with atonic seizures (19 studies for CC versus 7 studies for VNS). Many more studies exist for both methods in regard to general seizure control, but only the above-described subset specifically comments on atonic seizures, which is likely due to the relative rarity of this seizure subtype compared with generalized tonic–clonic and focal seizures.

While both surgical methods offer a degree of seizure control, CC appears possibly more successful than VNS, with 58.0% of patients being free of atonic seizures after CC compared with 21.1% of patients being free of atonic seizures after VNS (RR: 2.8; 95% CI: 1.5–5.1). These results also hold for seizure reduction rather than for complete seizure freedom: 88.6% of CC patients experienced a reduction in seizures of >50% versus 52.6% of VNS patients (RR: 1.7; 95% CI: 1.2–2.3).

While the above analysis offers insight into relative efficacy, there has never been a study evaluating the relative cost-effectiveness of each procedure and none concerning CC specifically. One study in 2000 reported an upward CC surgical cost of $3995 [36], while the cost of the VNS device alone was roughly £5500 (in 2006 prices) [37]. Multiple cost-effectiveness studies of VNS have been undertaken and are favorable [38,39]. However, again, there is no comparable study of CC and no comparison of the two modalities.

Surgical complications were more prevalent in patients treated with VNS than with CC, although the most prevalent complication of VNS was relatively mild: hoarseness in 20.1% of patients. The most frequent complication of CC was disconnection syndrome, reported in 13.2% of patients. Patients are often able to adapt to disconnection syndromes, but the studies did not provide clear descriptions as to the duration of this complication. Focusing on severe, potentially life-changing complications, we found that VNS was associated with SUDEP, status epilepticus, and vocal cord paralysis (Tables 2 and 3). Severe complications

of CC included epidural and subdural hematomas, ataxia, hemiparesis, and one surprising partial hand amputation (from an unexpected and severe arterial line complication). There were two reported deaths in the CC cohort, both from the earliest of the cited studies, Murro et al., from 1988; one due to an unrecognized bleeding diathesis; and the other due to disseminated intravascular coagulation (DIC) [13].

While these reported complication rates for VNS and CC are low, these findings should be interpreted cautiously. Primarily, these studies are heterogeneous and did not agree on a common lexicon for complications nor did they agree upon common reporting standards. For example, the low frequency of disconnection syndrome might be surprising to those without extensive experience with the technique. Although it might reflect underreporting, other meta-analyses, like that of Lancman et al. [40], have shown similar low estimates of disconnection. Events like SUDEP, which were only reported above in VNS, might reflect the timing of the CC studies, many of which predated the formal definition of SUDEP in 1996 by Nashef [41]. Both status epilepticus and SUDEP are expected outcomes in these patients who will continue having at least some type of seizures after surgery.

Another limitation is the increase in surgical safety, especially in anesthesia techniques, over the past several decades. For example, arterial line complications requiring amputation are almost unknown in contemporary surgical practice. Surgical improvements with intraoperative neuronavigation and operating microscopes are now commonplace, as well as innovations in the surgical technique itself [7]. In a direct comparative study done today, increases in the safety of both procedures might reduce complication rates, though it is unclear if one surgical treatment would benefit from these improvements in safety more than the other.

Lastly, the above analyses are based on aggregated literature, which is the only guidance we have in lieu of a direct randomized controlled study comparing CC with VNS for atonic seizures. However, because of this, the usual limitations of systematic reviews hold: the patient populations are different between each study, reporting standards are not uniform, follow-up varies, surgical techniques are heterogeneous, and so on. In particular, the technique of CC varies greatly depending on the extent of callosotomy — for example, only the anterior two-thirds, or a complete callosotomy [42]. Furthermore, even in “complete” callosotomies, there is often a lack of neurophysiologic [43] or imaging evidence of the true extent of disconnection (e.g., with diffusion tensor tractography) [44]. The result is a heterogeneous group of procedures all under the broad designation of callosotomy. The only remedy for these issues is a direct head-to-head prospective comparison of the two treatments. Based on the best available current data, both techniques are safe, but CC provides a much better chance for effectively treating this highly morbid seizure type.

5. Conclusions

Atonic seizures are debilitating, have a poor prognosis, and are incredibly difficult to control with antiepileptic medications. Two surgical treatments are primarily used to address atonic seizures: corpus callosotomy (CC) and vagus nerve stimulation (VNS). Examining available data, we found that CC appears to offer significantly better chances of seizure freedom

compared with VNS: 58.0% versus 21.1% (RR: 2.8; 95% CI: 1.5–5.1) and seizure control: 88.6% versus 52.6% of patients, respectively, (RR: 1.7; 95% CI: 1.2–2.3). Both techniques have low morbidity at least for severe, procedure-related complications. Acknowledging that there are clear limitations in using systematic reviews to guide clinical practice, these data suggest that CC might be more effective than VNS for atonic seizures. Nevertheless, more definitive studies are clearly needed to understand which procedure is more beneficial for these patients.

Acknowledgments

JDR was supported in part by a fellowship from the Congress of Neurological Surgeons.

References

1. Sirven JI, Sirven J, Devinsky O. Atonic seizures. [[accessed May 17, 2015]] http://www.epilepsy.com/learn/types-seizures/atonic-seizures.
2. Proposal for revised clinical and electroencephalographic classification of epileptic seizures. From the Commission on Classification and Terminology of the International League Against Epilepsy. Epilepsia. 1981; 22:489–501. [PubMed: 6790275]
3. Tinuper P, Cerullo A, Marini C, Avoni P, Rosati A, Riva R, et al. Epileptic drop attacks in partial epilepsy: clinical features, evolution, and prognosis. J Neurol Neurosurg Psychiatry. 1998; 64:231–237. [PubMed: 9489537]
4. Oguni H, Fukuyama Y, Imaizumi Y, Uehara T. Video-EEG analysis of drop seizures in myoclonic astatic epilepsy of early childhood (Doose syndrome). Epilepsia. 1992; 33:805–813. [PubMed: 1396420]
5. van Wagenen WP, Herren RY. Surgical division of commissural pathways in the corpus callosum: relation to spread of an epileptic attack. Arch NeurPsych. 1940; 44:740–759. http://dx.doi.org/10.1001/archneurpsyc.1940.02280100042004.
6. Asadi-Pooya AA, Sharan A, Nei M, Sperling MR. Corpus callosotomy. Epilepsy Behav. 2008; 13:271–278. http://dx.doi.org/10.1016/j.yebeh.2008.04.020. [PubMed: 18539083]
7. Chang, EF., Rowland, NC., Barbaro, NM. Corpus callosotomy: indications and techniques. In: Quiñones-Hinojosa, A., editor. Schmidek and Sweet: operative neurosurgical techniques. Elsevier Health Sciences; 2012. p. 1295-1299.
8. Kim D-S, Yang K-H, Kim T-G, Chang J-H, Chang J-W, Choi J-U, et al. The surgical effect of callosotomy in the treatment of intractable seizure. Yonsei Med J. 2004; 45:233–240. [PubMed: 15118994]
9. Oguni H, Olivier A, Andermann F, Comair J. Anterior callosotomy in the treatment of medically intractable epilepsies: a study of 43 patients with a mean follow-up of 39 months. Ann Neurol. 1991; 30:357–364. http://dx.doi.org/10.1002/ana.410300307. [PubMed: 1952824]
10. Rolston JD, Englot DJ, Wang DD, Shih T, Chang EF. Comparison of seizure control outcomes and the safety of vagus nerve, thalamic deep brain, and responsive neurostimulation: evidence from randomized controlled trials. Neurosurg Focus. 2012; 32:E14. http://dx.doi.org/10.3171/2012.1.FOCUS11335.
11. A randomized controlled trial of chronic vagus nerve stimulation for treatment of medically intractable seizures. The Vagus Nerve Stimulation Study Group. Neurology. 1995; 45:224–230. [PubMed: 7854516]
12. Handforth A, DeGiorgio CM, Schachter SC, Uthman BM, Naritoku DK, Tecoma ES, et al. Vagus nerve stimulation therapy for partial-onset seizures: a randomized active-control trial. Neurology. 1998; 51:48–55. [PubMed: 9674777]
13. Murro AM, Flanigin HF, Gallagher BB, King DW, Smith JR. Corpus callosotomy for the treatment of intractable epilepsy. Epilepsy Res. 1988; 2:44–50. [PubMed: 3197679]

14. Rappaport ZH, Lerman P. Corpus callosotomy in the treatment of secondary generalizing intractable epilepsy. Acta Neurochir. 1988; 94:10–14. [PubMed: 3177040]
15. Papo I, Quattrini A, Provinciali L, Rychlicki F, Paggi A, Del Pesce M, et al. Callosotomy for the management of intractable non-focal epilepsy: a preliminary personal assessment. Acta Neurochir. 1989; 96:46–53. [PubMed: 2929391]
16. Nordgren RE, Reeves AG, Viguera AC, Roberts DW. Corpus callosotomy for intractable seizures in the pediatric age group. Arch Neurol. 1991; 48:364–372. [PubMed: 2012509]
17. Fuiks KS, Wyler AR, Hermann BP, Somes G. Seizure outcome from anterior and complete corpus callosotomy. J Neurosurg. 1991; 74:573–578. http://dx.doi.org/10.3171/jns.1991.74.4.0573. [PubMed: 2002370]
18. Sakaki T, Nakase H, Morimoto T, Hoshida T, Tsunoda S. Partial corpus callosotomy beneficial for Lennox–Gastaut syndrome — report of two cases. Neurol Med Chir (Tokyo). 1991; 31:226–232. [PubMed: 1720213]
19. Nakatani S, Nii Y, Ikejiri Y, Tanabe H, Mogami H. Partial callosotomy for Lennox–Gastaut syndrome — first cases in Japan. Neurol Med Chir (Tokyo). 1990; 30:930–939. [PubMed: 1710321]
20. Cendes F, Ragazzo PC, da Costa V, Martins LF. Corpus callosotomy in treatment of medically resistant epilepsy: preliminary results in a pediatric population. Epilepsia. 1993; 34:910–917. [PubMed: 8404746]
21. Spencer SS, Spencer DD, Sass K, Westerveld M, Katz A, Mattson R. Anterior, total, and two-stage corpus callosum section: differential and incremental seizure responses. Epilepsia. 1993; 34:561–567. [PubMed: 8504787]
22. Kwan SY, Wong TT, Chang KP, Chi CS, Yang TF, Lee YC, et al. Seizure outcome after corpus callosotomy: the Taiwan experience. Childs Nerv Syst. 2000; 16:87–92. [PubMed: 10663813]
23. Cukiert A, Cukiert CM, Burattini JA, Lima AM, Forster CR, Baise C, et al. Long-term outcome after callosotomy or vagus nerve stimulation in consecutive prospective cohorts of children with Lennox–Gastaut or Lennox-like syndrome and nonspecific MRI findings. Seizure. 2013; 22:396–400. http://dx.doi.org/10.1016/j.seizure.2013.02.009. [PubMed: 23490456]
24. Hodaie M, Musharbash A, Otsubo H, Snead OC, Chitoku S, Ochi A, et al. Image-guided, frameless stereotactic sectioning of the corpus callosum in children with intractable epilepsy. Pediatr Neurosurg. 2001; 34:286–294. [PubMed: 11455228]
25. Maehara T, Shimizu H. Surgical outcome of corpus callosotomy in patients with drop attacks. Epilepsia. 2001; 42:67–71. [PubMed: 11207787]
26. You SJ, Kang H-C, Ko T-S, Kim HD, Yum M-S, Hwang YS, et al. Comparison of corpus callosotomy and vagus nerve stimulation in children with Lennox–Gastaut syndrome. Brain Dev. 2008; 30:195–199. http://dx.doi.org/10.1016/j.braindev.2007.07.013. [PubMed: 17825516]
27. Sunaga S, Shimizu H, Sugano H. Long-term follow-up of seizure outcomes after corpus callosotomy. Seizure. 2009; 18:124–128. http://dx.doi.org/10.1016/j.seizure.2008.08.001. [PubMed: 18799327]
28. Iwasaki M, Uematsu M, Sato Y, Nakayama T, Haginoya K, Osawa S-I, et al. Complete remission of seizures after corpus callosotomy. J Neurosurg Pediatr. 2012; 10:7–13. http://dx.doi.org/10.3171/2012.3.PEDS11544. [PubMed: 22681320]
29. Stigsdotter-Broman L, Olsson I, Flink R, Rydenhag B, Malmgren K. Long-term follow-up after callosotomy — a prospective, population based, observational study. Epilepsia. 2014; 55:316–321. http://dx.doi.org/10.1111/epi.12488. [PubMed: 24372273]
30. Yang P-F, Lin Q, Mei Z, Chen Z-Q, Zhang H-J, Pei J-S, et al. Outcome after anterior callosal section that spares the splenium in pediatric patients with drop attacks. Epilepsy Behav. 2014; 36:47–52. http://dx.doi.org/10.1016/j.yebeh.2014.04.019. [PubMed: 24857808]
31. Ben-Menachem E, Hellström K, Waldton C, Augustinsson LE. Evaluation of refractory epilepsy treated with vagus nerve stimulation for up to 5 years. Neurology. 1999; 52:1265–1267. [PubMed: 10214754]
32. Holmes MD, Silbergeld DL, Drouhard D, Wilensky AJ, Ojemann LM. Effect of vagus nerve stimulation on adults with pharmacoresistant generalized epilepsy syndromes. Seizure. 2004; 13:340–345. http://dx.doi.org/10.1016/j.seizure.2003.09.002. [PubMed: 15158706]

33. Buoni S, Mariottini A, Pieri S, Zalaffi A, Farnetani MA, Strambi M, et al. Vagus nerve stimulation for drug-resistant epilepsy in children and young adults. Brain Dev. 2004; 26:158–163. http://dx.doi.org/10.1016/S0387-7604(03)00120-7. [PubMed: 15030903]
34. Kostov K, Kostov H, Taubøll E. Long-term vagus nerve stimulation in the treatment of Lennox–Gastaut syndrome. Epilepsy Behav. 2009; 16:321–324. http://dx.doi.org/10.1016/j.yebeh.2009.07.038. [PubMed: 19699154]
35. Hajnsek S, Petelin Z, Poljaković Z, Mrak G, Paladino J, Desnica A. Vagus nerve stimulation in the treatment of patients with pharmacoresistant epilepsy: our experiences. Coll Antropol. 2011; 35:755–760. [PubMed: 22053552]
36. Fandiño-Franky J, Torres M, Nariño D, Fandiño J. Corpus callosotomy in Colombia and some reflections on care and research among the poor in developing countries. Epilepsia. 2000; 41(Suppl 4):S22–S27. [PubMed: 10963473]
37. Forbes R. Cost-utility of vagus nerve stimulation (VNS) therapy for medically refractory epilepsy — an update. Seizure. 2008; 17:387–388. [PubMed: 18584780]
38. Forbes RB, Macdonald S, Eljamel S, Roberts RC. Cost-utility analysis of vagus nerve stimulators for adults with medically refractory epilepsy. Seizure. 2003; 12:249–256. [PubMed: 12810336]
39. Boon P, Vonck K, D'Have M, O'Connor S, Vandekerckhove T, De Reuck J. Cost-benefit of vagus nerve stimulation for refractory epilepsy. Acta Neurol Belg. 1999; 99:275–280. [PubMed: 10674145]
40. Lancman G, Virk M, Shao H, Mazumdar M, Greenfield JP, Weinstein S, et al. Vagus nerve stimulation vs. corpus callosotomy in the treatment of Lennox–Gastaut syndrome: a meta-analysis. Seizure. 2013; 22:3–8. http://dx.doi.org/10.1016/j.seizure.2012.09.014. [PubMed: 23068970]
41. Nashef L. Sudden unexpected death in epilepsy: terminology and definitions. Epilepsia. 1997; 38:S6–S8. http://dx.doi.org/10.1111/j.1528-1157.1997.tb06130.x.
42. Kasasbeh AS, Smyth MD, Steger-May K, Jalilian L, Bertrand M, Limbrick DD. Outcomes after anterior or complete corpus callosotomy in children. Neurosurgery. 2014; 74:17–28. http://dx.doi.org/10.1227/NEU.0000000000000197 [discussion28]. [PubMed: 24089047]
43. Okumura E, Iwasaki M, Sakuraba R, Itabashi I, Osawa S-I, Jin K, et al. Time-varying inter-hemispheric coherence during corpus callosotomy. Clin Neurophysiol. 2013; 124:2091–2100. http://dx.doi.org/10.1016/j.clinph.2013.05.004. [PubMed: 23756060]
44. Choudhri AF, Whitehead MT, McGregor AL, Einhaus SL, Boop FA, Wheless JW. Diffusion tensor imaging to evaluate commissural disconnection after corpus callosotomy. Neuroradiology. 2013; 55:1397–1403. http://dx.doi.org/10.1007/s00234-013-1286-y. [PubMed: 24113714]

Table 1

Reported results for drop attacks and atonic seizures treated with corpus callosotomy and VNS.

Surgery type	Authors	Year	No. of patients (all seizure types)	No. of patients with atonic seizures and drop attacks	Seizure-free (%)[a]	>50% reduction (%)[a]	<50% reduction (%)[a]	Follow-up (years)
CC								
	Murro et al.	1988	25	1	1	0	0	2.5
	Rappaport et al.	1988	9	4	3	1	0	1
	Papo et al.	1989	12	10	5	5	0	1
	Nordgren et al.	1991	18	9	7	2	0	2
	Fuiks et al.	1991	78	6	1	4	1	0.75
	Sakaki et al.	1991	2	2	2	0	0	6
	Nakatani et al.	1991	4	3	3	0	0	1
	Cendes et al.	1993	34	18	0	16	2	3.5
	Spencer et al.	1993	50	9	0	6	3	NR
	Kwan et al.	2000	74	11	6	2	3	2
	Hodaie et al.	2001	80	17	5	8	4	3
	Maehara et al.	2001	52	52	42	6	4	2
	Kim et al.	2004	21	21	12	6	3	1
	You et al.	2008	14	13	4	4	5	1
	Sunaga et al.	2009	78	73	61	9	5	3
	Iwasaki et al.	2012	13	12	11	1	0	1
	Cuckiert et al.	2013	24	10	0	9	1	2
	Yang et al.	2014	29	29	15	11	3	5.2
	Stigsdotter-Broman et al.	2014	33	17	6	7	4	2
CC total			650	317	184 (58.0)	97 (30.6)	38 (12.0)	
VNS								
	Ben-Menachem et al.	1999	64	7	0	1	6	NR
	Holmes et al.	2004	13	5	0	2	3	1
	Buoni et al.	2004	16	3	1	2	0	1
	You et al.	2008	10	4	0	3	1	1
	Kostov et al.	2009	30	12	5	3	4	4
	Hajnsek et al.	2011	11	2	2	0	0	2

Surgery type	Authors	Year	No. of patients (all seizure types)	No. of patients with atonic seizures and drop attacks	Seizure-free (%)[a]	>50% reduction (%)[a]	<50% reduction (%)[a]	Follow-up (years)
	Cuckiert et al.	2013	20	5	0	1	4	2
VNS total			164	38	8 (21.1)	12 (31.6)	18 (47.4)	

NR: not reported.

[a]These numbers apply only to atonic seizures and drop attacks.

Epilepsy Behav. Author manuscript; available in PMC 2017 January 24.

Table 2

Documented complications with corpus callosotomy for all seizure types in the referenced studies. These complications are from all patients discussed in the above studies and are not limited to those with atonic seizures.

Complication	No. of patients (%)
Disconnection	86 (13.2)
Transient akinesia	14 (2.2)
Superficial surgical site infection	9 (1.4)
Aseptic ventriculitis	8 (1.2)
Epidural hematoma	5 (0.8)
Deep surgical site infection	4 (0.6)
Subdural hematoma	3 (0.5)
Status epilepticus	3 (0.5)
Death[a]	2 (0.3)
Intracranial hemorrhage	2 (0.3)
Pneumonia	2 (0.3)
Tracheostomy	2 (0.3)
Aphasia	1 (0.2)
Ataxia	1 (0.2)
Hemiparesis	1 (0.2)
Pulmonary edema	1 (0.2)
Hand amputation (from arterial line complication)	1 (0.2)

[a]These two deaths are both from the first study in 1988, Murro et al.

Table 3

Documented complications from VNS for all seizure types in the referenced studies (not limited to atonic seizures).

Complication	No. of patients (%)
Hoarseness	33 (20.1)
Drooling	7 (4.3)
Throat pain	6 (3.7)
Status epilepticus	3 (1.8)
SUDEP	2 (1.2)
Vocal cord paralysis	2 (1.2)
Dysphagia	2 (1.2)
Cough	2 (1.2)
Dyspnea	2 (1.2)
Transient asystole	1 (0.6)
Transient hypotension	1 (0.6)
Tachycardia	1 (0.6)
Enuresis	1 (0.6)
Photophobia	1 (0.6)
Fever	1 (0.6)
Headaches	1 (0.6)
Wound infection	1 (0.6)

Table 4

Reported results for atonic seizures (excluding drop attacks) treated with corpus callosotomy and VNS.

Surgery type	Authors	Year	No. of patients (all seizure types)	No. of patients with atonic seizures	Seizure-free (%)[a]	>50% reduction (%)[a]	<50% reduction (%)[a]	Follow-up (years)
CC								
	Murro et al.	1988	25	1	1	0	0	2.5
	Rappaport et al.	1988	9	4	3	1	0	1
	Papo et al.	1989	12	10	5	5	0	1
	Nordgren et al.	1991	18	9	7	2	0	2
	Fuiks et al.	1991	78	6	1	4	1	0.75
	Sakaki et al.	1991	2	2	2	0	0	6
	Nakatani et al.	1991	4	3	3	0	0	1
	Cendes et al.	1993	34	18	0	16	2	3.5
	Spencer et al.	1993	50	9	0	6	3	NR
	Kwan et al.	2000	74	11	6	2	3	2
	Cuckiert et al.	2013	24	10	0	9	1	2
CC totals			330	83	28 (33.7)	45 (54.2)	10 (12.0)	
VNS								
	Ben-Menachem et al.	1999	64	7	0	1	6	NR
	Holmes et al.	2004	13	5	0	2	3	1
	Buoni et al.	2004	16	3	1	2	0	1
	Kostov et al.	2009	30	12	5	3	4	4
	Hajnsek et al.	2011	11	2	2	0	0	2
	Cuckiert et al.	2013	20	5	0	1	4	2
VNS totals			154	34	8 (23.5)	9 (26.5)	17 (50.0)	

NR: not reported.

[a]These numbers apply only to atonic seizures and exclude drop attacks.