Complicated epilepsy surgery: the importance of balancing benefit and deficit

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Abstract

The risk–benefit ratio of epilepsy surgery needs careful consideration, is different for each individual and requires a careful, informed dialogue between the person concerned and their medical advisers. We illustrate this process with Virginia, who has had refractory focal epilepsy from age one year and a left hemiparesis. At age 45 years we discussed the possibility of epilepsy surgery and went through non-invasive investigations with structural and functional MRI, tractography, scalp video-EEG telemetry, neuropsychological and neuropsychiatric evaluations. This was followed by a decision to carry out intracranial EEG to define the area of seizure onset and its relation to an area of focal cortical dysplasia, eloquent cortex and tracts. We agreed to carry out a focal resection in the knowledge that this would result in a loss of left-hand function. One year later Virginia is seizure free on reduced medication. We describe the steps in the process with Virginia's views.

Key words: epilepsy surgery, focal cortical dysplasia, post-operative deficit

Introduction

Epilepsy surgery can bring seizure control for those with medically-refractory seizures who have not been controlled with antiseizure medication (1), with long-term remission of 60–70% in ideal situations. The epileptogenic zone is defined as that part of the brain removal of which results in seizure freedom. Epilepsy surgery has risks, depending on the location of the epileptogenic zone and the operation performed. There are both expected deficits and the risk of unanticipated complications (2). If the epileptogenic zone involves critical grey matter and white matter tracts, a new deficit is expected. The severity and impact of the new deficit depends on the site and extent of resection and whether the individual has a pre-existing deficit. In general, if there is a pre-existing deficit, the impact is expected to be less than if function is not impaired.

The maxim "not about me without me" is nowhere more apposite than when considering epilepsy surgery with a high risk of causing a deficit. The individual concerned must be at the centre of discussions about the chances of seizure remission, or improvement, and the likelihood of causing new deficits and their impact of these on daily life. A key role of the medical team is to put the facts and uncertainties before the individual in a clear manner, recognising uncertainties and, in the elective situation, not to rush decision-making.

Here, we illustrate these principles with Virginia Beech's story and her commentary on the process.

Clinical history

Virginia was first seen in 2016 in the epilepsy clinic at the National Hospital for Neurology and Neurosurgery, Queen Square, London UK. She was 45 years old and right handed. She worked as a local government youth worker and was married with two children. She had lost her third child who had spina bifida and hydrocephalus; she had been prescribed sodium valproate through that pregnancy.

When she was aged 1 year, Virginia's mother noticed shaking of her left leg and left arm. Epilepsy was diagnosed at age 2 years, and she started taking phenobarbital. Epileptic seizures continued without remission throughout life, despite trying many antiseizure medications including phenobarbital, phenytoin, valproate, carbamazepine, lacosamide, lamotrigine, topiramate, levetiracetam, zonisamide, perampanel, oxcarbazepine, pregabalin and cenobamate.

The current seizure pattern comprised episodes of tingling and burning sensation in left arm and leg, followed by tonic-clonic jerks of the left arm and leg. Variably the jerks of the left arm and leg were associated with tonic extension and elevation of right arm. There was no loss of awareness but she would be unable to communicate. Postictally there was increased weakness of left arm and leg. The Frequency was 5–20 times a day. Approximately monthly these focal aware seizures would evolve into focal-to-bilateral tonic-clonic seizures.

Comorbidities included a lifelong persistent left sided weakness, which had been getting more severe over many years. Virginia had depression and anxiety, for which she took venlafaxine, and was also troubled by irritable bowel syndrome and a lumbar disc herniation.

Neurological examination

On examination, there was a mild left facial weakness, evident in the lower half of her face. The left-sided limbs were slightly smaller than the right-sided limbs. Tone was reduced in the left arm. She could elevate her left arm at the shoulder and move the elbow. Shoulder abduction was grade 4+, elbow flexion and extension grade 4, wrist flexion and extension grade 3, small hand muscles grade 1–2. Left fine finger movements were very slow and clumsy.

Virginia dragged the left leg on walking. In the left leg: hip flexion was grade 4+, hip extension 4++, knee flexion 4++, knee extension 5–, extensor hallucis longus and ankle dorsiflexion 2, ankle inversion and eversion grade 1.

On sensory testing, pinprick, light touch, joint position and vibration sense were reduced on the left side. There was inaccuracy of joint position sense in the left fingers and toes.

Preliminary discussion

We discussed that with a fixed deficit, seizures continuing for 44 years despite trying over 10 antiseizure medications, and having a focal abnormality on the MRI that the chances of remission with further medical therapy was less than 3%; the worsening left limb function was likely to become more severe in future years and that there was a 1/1000 risk of fatality with each focal-to-bilateral tonic-clonic seizure. We noted that resective surgery could at best have a 60–70% chance of long-lasting remission and would be likely to cause impairment of left limb function. There was 1% risk of catastrophic consequences of neurosurgery.

Virginia's view at the time:

I wanted the chance of a life that was not destroyed daily by seizures and I was aware that this was not going to come without risk. I had tried nearly every route open to me and in all honesty, I was tired and I had lost so much to epilepsy, including my beautiful daughter. With regards to the odds, yes, I might still have a disability but I would know what each day would hold for me, and how to handle it and I would know what I could or couldn't do. My life currently was chaotic and I had a fear of sleeping. I was lucky in that my husband had had a traumatic brain injury and I understood where determination could take you in recovery.

Initial investigations

We agreed to proceed with non-invasive investigations.

MR scan of brain (Figure 1) showed a focal intrinsic lesion in right central region involving white matter. The appearances suggested focal cortical dysplasia 2B .

Motor functional MRI (fMRI). Movement of the left hand activated the right pre- and post-central gyri and right supplementary motor area. The area of activation over the right precentral gyrus projected over the lateral aspect of the region of cortical dysplasia. Movement of the left foot activated the right paracentral lobule and supplementary motor area, bilaterally. The area of activation in the paracentral lobule overlapped the superior margins of the cortical dysplasia.

Language fMRI. Verbal fluency and verb generation were associated with bilateral activation (Fig 2).

Scalp video-EEG telemetry. In a 5-day recording, without reduction of antiseizure medications, there was no definite interictal epileptiform abnormality. Seventeen habitual seizures were recorded. There was one tonic seizure affecting left arm and face, 14 tonic seizures affecting the left arm, face/ and leg; two seizures began as a left foot clonic seizure, evolving to a left arm, face and leg tonic seizure. Postictally there was left arm paresis. Ictal EEG changes were non-lateralising, midline and central, or maximal in the right paracentral region and vertex.

Neuropsychology and Psychiatry. Intellectually, Virginia was low average, slightly below estimated mid-average potential. Episodic memory was impaired, verbal fluency reduced and there was processing slowness. Language functions and working memory were satisfactory. Low mood and medication were thought to be adversely affecting her cognitive performance.

Epilepsy surgery multidisciplinary team meeting

The clinical history and results of the non-invasive (Phase 1) investigations were reviewed in the Epilepsy Surgery multidisciplinary team (MDT) meeting (3). Key features were that:

- Virginia was severely affected by refractory epilepsy, with a progressing fixed deficit.
- The chances of remission with medical therapy was remote.
- She was keen to pursue definitive treatment even if that was associated with a risk of an increased motor and sensory deficit.

Whilst response-mode stimulation, with an implanted closed loop stimulator (Neuropace RNS) had been associated with some good results in USA, this was not available in Europe and would not be so in the foreseeable future. Vagus nerve stimulation offered a 30% chance of a 50% or more reduction of seizure frequency, but without the expectation of remission, and without the risks of cranial neurosurgery. Other operative options included a lesionectomy of the MRI-visible lesion, which would offer a 50% chance of long-term seizure remission and loss of distal left arm function. With the lifelong hemiparesis and hemiatrophy, the MDT felt that whilst there would likely be increased weakness of the left leg post-operatively, this would return to baseline within weeks. There was also the likelihood of worsened joint position sense that would compromise any fine movement.

The third option was to try to better define the epileptogenic zone with intracranial EEG, and the relationship of this to critical tracts and cortex, in the hope of maximising the chance of seizure freedom and minimising the risk of causing an increased deficit. The options were then discussed with Virginia, with the MDT view that the third option was felt to be most appropriate.

Virginia's view at the time:

I was extremely happy that the multidisciplinary team were proceeding with my best interest at the centre of their considerations, especially with regard to their explanations all the way through.

Intracranial EEG Recording

The implantation comprised a subdural grid over the abnormality and the pre- and post-central gyri and paracentral lobule and with depth electrodes passed into the depth of the malformation (Fig 3). Seizure onset was over the area of dysplasia with early spread superiorly and posteriorly, involving pre- and post-central gyri, eloquent cortex.

Virginia's view at the time:

Having the grids implanted was a fairly easy process from my point of view. I was not, however, prepared for how I would feel when there was the electrical testing of each area, but I was well supported by the team and my family.

Discussion

The prediction was that there was a 50% chance that a lesionectomy would bring seizure-freedom but that there was likely to be a post-operative flaccid paralysis of the left arm and leg and that Virginia might also develop altered sensation down the left side. As the hemiparesis was lifelong, it was expected that her ability to walk independently would recover over weeks. It was expected that she would not achieve independent left finger function, and left finger function would be reduced, and the left arm was likely to be weaker, with uncertain prospects for its recovery.

These results were discussed with Virginia, who pointed out that she had had seizures every day with jerking of the left limbs that might propel her out of the bed, and that she was keen to proceed with resection.

Virginia's view at the time:

I had always understood that there were risks with this operation. If I didn't have it I was declining every day in strength and I was a at real risk of dying from a seizure, and if I did have surgery, there were multiple ways that it could go wrong. I strongly held trust in the team and my own resolve, so we decided to go ahead.

Surgery

Virginia was admitted for surgery in January 2023 using interventional MRI. We discussed if surgery should be carried out with Virginia awake and concluded that due to the nature and frequency of the seizures this was not safe. Navigation was used to identify the borders of the area of dysplasia and checked with operative photographs of grid insertion and surface veins. Asleep neurophysiological mapping of leg, foot, arm and hand was carried out, under anaesthesia. A subpial dissection of lesion was carried out anterior and posterior to large draining veins on the cortical surface. The resection, including the tail, extended inferiorly. The large cortical draining veins were patent at the end of the resection. The right primary motor and sensory areas for leg and arm were removed. Subcortical mapping of corticospinal tract at end of procedure showed that the tract was intact. Intraoperative MRI was performed to make sure that the lesion had been completely excised. Pathological analysis confirmed that the lesion histology was focal cortical dysplasia, type 2B.

Post-operative course

Initially, there was a flaccid left hemiparesis and slurred speech. Light touch and joint position sense were not different from pre-operatively. After one week, there was muscle tone returning in the left leg and her left facial weakness was improved. At two weeks, there was voluntary movement in left leg. At four weeks, Virginia was weight-bearing on her left leg. In her left arm, the wrist was flexed, there was a pyramidal increase in tone and no voluntary movement.

Three months after surgery, she could stand for 5 minutes, and was starting to take steps. Sensation had increased in the left hand. Virginia's Left arm had become stiff and painful, with some flickers of movement. Local botulinum toxin injections reduced the increased tone. Virginia was seizure free and was not troubled by depression or anxiety. MR scan of brain 3 months after surgery showed the resection (Fig 4).

Virginia's comment on how she was at 3 months after surgery: At month three I was starting to feel changes in my mood. This followed my move to a local rehabilitation centre, that seemed to assume my abilities were worse than they were, At a goal setting meeting I was advised that I probably should go home in a wheelchair as they did not expect much more recovery. It was my resolve that fought for what I could do. My feelings are that my local centre did not fully understand my operation, and what could be done by myself as they hadn't been involved in my care initially. I think that the local rehabilitation could have been better integrated with the epilepsy surgery MDT.

MR scan of brain 3 months after surgery showed the expected changes with the resection cavity and no adverse features (Fig 4).

One year following surgery, Virginia remains seizure free. She is walking around her house. Her left hand movements have improved and she now has some flexion and extension of fingers together, but not independently, and she can grip with her left hand. Her left shoulder has been partially subluxed, which has been painful. This has improved with physiotherapy and local injections. Antiseizure medication is being reduced, with tapering of perampanel. Oxcarbazepine and cenobamate are unchanged. If seizures are controlled following epilepsy surgery, we would generally start to reduce medication after one year, aiming for monotherapy at two years post-operatively.

Virginia's comment on how she is at 12 months after surgery:

Twelve months after surgery, I am a different person, learning who I am on daily basis. I am still very much continuing rehabilitation with a private physiotherapist who believed there was much more that I could gain. That extra physiotherapy pushed my confidence forward massively.

Discussion

Virginia had severe, medically refractory focal epilepsy throughout her life. A key facet is that epilepsy surgery that stood a reasonable chance of bringing seizure remission was anticipated to cause loss of function, particularly loss of any fine movements with the left hand. The process was multistep and prolonged, with informed decisions on choices and whether to proceed or not.

Individual factors clearly have a marked effect on decision making. An individual who did not have a fixed deficit would be less likely to feel that a deficit was a price that was worth paying, particularly if

that would involve their dominant hand, or if fine finger movements was essential, for example for a musician.

Virginia's view was that with seizures occurring many times every day and night, disturbing sleep, she already had a neurological deficit and an increased deficit was a price that was worth paying.

The general principle is to evaluate the options and the chances of each choice having a good result in terms of seizure outcome, and the impact of this on an individual's life, and weighed against the risks of adverse effects, and the impact of these on daily activities.

Virginia's view on her situation

Compared to the pre-operative situation, what have been the benefits for daily life, and for mood?

My situation has changed in a variety of ways. There are areas in which I need more support than I did, such as the worse use of my left hand, but this is predictable every day, instead of the frequent cancellations of plans because of seizures. I did go through a period of depression and anxiety in the weeks after surgery, which I had partially expected and it was more about adjustment for me. Before the surgery, the epilepsy depression I suffered was like a big black hole of sadness that was there on a daily basis.

I am now free of the black hole, the tiredness, the anxiety from continual seizures. I would even say my mobility is better. I am not scared to sleep as I was. We know what I need support with and it never changes, whereas epilepsy was unpredictable every day. I feel stable even, with my deficits. Yes, there are things I can't do that I am having to relearn but I'm confident that eventually I will get there.

What have been the downsides?

The main downsides have been that away from the National Hospital there has been little understanding and support for the rehabilitation journey. I think I possibly misunderstood what extensive rehabilitation meant in practice. I think I would have liked a post-operative support plan with goals and educational information relevant to my journey.

How was the decision-making process and time frame for you?

I think the decision-making process was just right for my case. At each stage I believe I was adequately informed as too much information could create overload. As I recovered to a good stage of health I needed information more on handling post-surgery defects such as the spasticity.

What was done well, what could have been done better?

The best part of this journey was the quality of my team around me. I was so well informed and encouraged to ask whatever I needed.

Key points

- Neurosurgical treatment can be curative for drug refractory focal epilepsy
- A detailed multidisciplinary work-up is needed
- The person concerned needs to be at the centre of decision-making
- If the epileptogenic zone includes eloquent cortex and white matter tracts, a new fixed deficit may be a price that is worth paying for seizure freedom, in selected people

Figure legends

Figure 1. MR scan of brain a focal intrinsic lesion in right central region involving white matter. This measured 24 mm (superior-inferior) x 40 mm (medial- lateral) x 35 mm (antero-posterior) in the paracentral lobule, extending into post-central, pre-central and superior frontal gyri. There was a conical transmantle extension to the ependymal surface, with mild thickening of overlying cortex, with increased T2 signal and an indistinct grey–white matter junction. The appearances suggested focal cortical dysplasia 2B. Top left: Coronal T1-weighted MRI. Top right: Coronal FLAIR MRI. Lower left: Coronal T1-weighted MRI. Lower right: Axial T1-weighted MRI.

Figure 2. Functional MRI and tractography. In the right hemisphere, the area of focal cortical dysplasia is coloured red. The tractographic representation of the corticospinal tract is blue. Left limb motor fMRI activation is shown in green.

Figure 3. Top left: Coronal T1-weighted MRI showing the subdural grid (GA) overlaying the malformation on the right hemisphere convexity and the pre- and post-central gyri. A depth electrode samples from the deeper parts of the anterior (aL) malformation. Lower left: Coronal T1-weighted MRI showing the subdural grid (GA) overlaying the malformation on the right hemisphere convexity and the pre- and post-central gyri. A depth electrode samples from the deeper parts of the posterior (pL) malformation. Right: Surface reconstruction of the right cerebral hemisphere, showing subdural grid (yellow), a posterior subdural strip (purple) and the area of malformation (red).

Figure 4. MR scan of brain 3 months following surgery showing the resection cavity. Left: Coronal T2-weighted MRI. Right: Axial T1-weighted MRI.

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Further reading

Duncan JS. Multidisciplinary team meetings: the epilepsy experience. Pract Neurol. 2022 May 9:practneurol-2022-003350. doi: 10.1136/practneurol-2022-003350.

References

1. De Tisi J, Bell GS, Peacock JL, McEvoy Aw, Harkness WFJ, Sander JW, Duncan JS. The long-term outcome of adult epilepsy surgery, patterns of seizure remission and relapse: a cohort study. Lancet. 2011 Oct 15;378(9800):1388-95.

2. Gooneratne IK, Mannan S, de Tisi J, Gonzalez JC, McEvoy AW, Miserocchi A, Diehl B, Wehner T, Bell GS, Sander JW, Duncan JS. Somatic complications of epilepsy surgery over 25 years at a single center. Epilepsy Res. 2017 Mar 1;132:70-77.

3. Duncan JS. Multidisciplinary team meetings: the epilepsy experience. Pract Neurol. 2022 May 9:practneurol-2022-003350. doi: 10.1136/practneurol-2022-003350.

DISCLOSURES

Contributorship statement

JS Duncan, V Beech, F Chowdhury, A McEvoy, A Miserocchi all made substantial contributions to the acquisition of data for the work.

And also all:

Drafted parts of this paper and revised the whole paper critically for important intellectual content.

Approved the final version to be published.

Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Competing interests

JS Duncan, V Beech, F Chowdhury, A McEvoy, A Miserocchi have no competing interests.

Ethical approval.

There was no relevant ethical approval required.