Transcript of When Seizures Return After Hemispherectomy: Reliability of Post-Operative EEGs
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Good morning everybody. Thank you for inviting me to be here and talk to you today. So I was asked a very simple question. Basically, how EEG works in a post hemispherectomy situation and how it could be helpful and how it may not be helpful in some situations.

So as a parent and as a doctor we had this fear before the hemispherectomy decision. So for parents maybe there are 2 or 3 fears: Number One: What if my child becomes more disabled or gets worse functionally after surgery. The second question: What if seizures come back? And thirdly, will their personality change? The third question is actually one of the most common questions I'm asked before surgery. For doctors, I've practiced in this field for decades and I still sometimes lose sleep before the final surgery because we have the same concerns as a physician, what if seizures come back?

And there are reasons, it could be from incomplete disconnection which is technical failure, which is the simplest way a way of explaining it. The second is what if seizures come from the other hemisphere, the relatively good hemisphere? And obviously as a physician we don't want to do any harm during the treatment process so what if the child gets an unexpected complications? Infection, bleeding and hydrocephalus. So these are real legitimate questions and in all this the common denominator seems to be what if seizures come back after hemispherectomy?

So seizures after hemispherectomy in some children if not all and there are three main reasons: The first one is seizures from the bad hemisphere which is the already operated side travel to the rest of the brain which is basically saying there's an incomplete disconnection. There are many different ways: The easiest one is corpus callosum, you can still see a little thread of corpus callosum connecting between hemispheres. Insular cortex could be a hidden focus, it is very difficult to detect, the insular cortex is buried under the front lobe and temporal lobe. (I'll show you the picture). Sometimes the basal frontal cortex and your hypothalamus - this area is very, very difficult to access because it is behind the very important cerebral vasculature called the anterior cerebral so a lot of neurosurgeons have a fear of getting too close to the hypothalamus area and that's why it is left and it could be the source of continuous seizures. When you find this, obviously you need a re-operation.

The second is probably the worst nightmare situation when you suspect that the seizure comes from the good hemisphere. This is probably most commonly found in hemimegalocephaly situations as you may have learned Hemimegalencephaly is now considered a genetic disease. It did not come from the parents but happens during development of the brain so we call it a somatic mutation and this could happen in mostly one hemisphere but it could also happen to the other hemisphere. So what you may see is only the bad hemisphere initially but once you do the disconnection to the bad hemisphere what happens is the relatively good hemisphere kind of takes over. The other situation is kindling and this is again really, really bad because kindling doesn't happen in one day or one year it happens after decades of seizures coming from the bad hemisphere to good hemisphere. So initially, the good hemisphere had no problem but because of delay in surgical intervention because of late decisions sometimes seizures cause seizures in the other hemispheres. Once that happens, unfortunately there's nothing you can do about it because you cannot really operate on the good hemisphere. So kindling you have to keep in mind and that's why we always emphasize that we've got to make a decision as early as possible.

Occasionally rarely hydrocephalus could be the cause of breakthrough seizures. We're not talking about a really obvious cause, sometimes it could be a very subtle change in ventricle size or when you put a shunt to relieve the pressure, a very minimum release of pressure sometimes seizures go away. So hydrocephalus could be one of the reasons. So in this case when seizures come from the other hemispheres re-operation is not necessarily indicated and we recommend no surgery except VP shunt when hydrocephalus is suspected.

Now finally if we don't really suspect this we could miss this – non-epileptic seizures. This is not uncommon. So you may have heard Psychogenic Non-Epileptic Seizures (PNES) or non-epileptic episodes. These not epileptic seizures, it has nothing to do with brain electrical activity, it is psychological or we call it depression or anxiety related. So this happens, there is a [---06:12] called forced normalization. They've been living with these seizures all their life and this happens typically to adolescent patients who had surgery a little late. So when things change dramatically from daily seizures to no seizures in one day they feel they have lost something. Even though it was a bad thing, it's a good thing to lose seizures, but it's not always felt that way by the child. That could be potentially primary or secondary gain: Primary gain meaning that you had a very tangible expected gain. For example, I don't want to go to school; suddenly I had to go to school because there's no excuse. So that is a primary gain, to have some episodes looking like seizures. Secondary gain is not really visual, not something you can really guess it could be from deep inside psychological processes. So sometimes you need ta psychiatrist to help you understand and the treatment for this is not surgery, not medication, it's really counseling and treatment of underlying mental health issues.

So what do we do when seizures come back? These are the steps that I take, not necessarily re-operation right away. First of all we like to know whether the child is compliant with the medication. If we confirm that then we try to ask the parents, 'are those episodes looking similar or the same as before'? So seizure similarity and then frequency and duration. The context of seizures: When does it happen? Does it happen when the child gets upset? And sometimes I ask them to take a video because tells a lot about what's going on, if not a 100% accurate answer.

So once we do this, the next step is we'll ask for long term video EEG monitoring and we try to capture more than 2 suspected seizure episodes. The primary reason is to really rule out non-epileptic episodes, something mimicking seizures but not necessarily epileptic. So once we confirm this is epileptic seizures then we have to do the work and that's when we have to spend a lot of time. So, for example the first job we do is look at the video and EEG and compare the ones that we have now with the previous pre-operative before surgery and the next step is to determine if this is from the bad hemisphere or the good hemisphere. Sometimes it is not easy with the EEG that is why I am getting asked this question because we can answer the questions that we have with video EEG that would be a lot easier. So sometimes we have to go back to look at the brain MRI, we use an MRI sequence called DTI which is Diffusion Tensor Imaging, just to look at the track connection and sometimes we do an impulse spec, other times we use a [---09:38] polygraphic.

So, let's say we confirm that seizures are there, it is coming from the bad hemisphere or the good hemisphere. What do we do? We, generally speaking, like to try medication first because if you could really spare another surgery with medication we will take that option anytime. So we try to at least maximize seizure medication. I don't go to like 11 more drugs; I usually stop at 2 first line drugs. So if that doesn't help then the next step is that if the seizures are definitely or clearly coming from the bad hemisphere I would suggest reoperation and this would be more like a functional hemispherectomy, so going back again, go after possible incomplete disconnection or a source of remaining seizure focus.

The sort of situation we are not 100% sure, there is unclear onset or the seizure activity seems to happen from both hemispheres and the evidence of incomplete disconnection is not really clear cut but the seizures look the same, exactly as before. Then that's when we generally speaking recommend anatomical hemispherectomy. So in other words just remove everything on the bad hemisphere so there is no room, no residual tissue there.

So shifting gear, I know you are already expert in the EEG and brain surgery, but let me tell you from a neurologist's point of view why it is sometimes very challenging to use EEG as a diagnostic tool. This is a simple diagram: As you can see, EEG, our brain is really like a computer, electrical circuits. So there's an electrical circuit here inside and electrodes are outside and there are multiple barriers in between. You can see spinal fluid, the dura mater, the covering of the brain, skull tissue, skull tissue, so much of a barrier so what we are seeing is little and a very artificially modified signal not the real signal. So compared to intracranial EEG, again intracranial EEG could be modified a little bit depending on the depth of the source and so on but scalp EEG is not really very clean or accurate technology, just to let you know. Then we place electrodes all over the scalp. So for example, we have electrodes on the front, in the back and at the top and at the bottom. So you may think that if you know where the seizure activity is coming from for example, from F3 that means frontal lobe. Well that's not always the case and there are many, many different reasons why EEG activity on the one channel may not necessarily mean that there's a small tissue that is causing seizure activity.

So this is an example to just kind of give you an orientation for you guys here: This is one channel, this is electrical activity coming from the frontal lobe and if you read the label it says FP1 F3 it's a channel that is composed of 2 electrodes in the left frontal lobe. Odd number is left side; even number is right side. If you read the label you can see frontal and central, parietal, occipital, that's how we read it. It is very simple and we can compare. Typically we lay out left side first and right side next so we compare side by side. Now this is EEG with spike. Patient is not seizing and you can see this is normal activity and suddenly there is a blip up and down, up and down. This is called spikes and reading the label it says FP1 F3 – left side frontal lobe. It's just approximate, it's not accurate. This is EEG during a seizure, this is a very simple example you can see suddenly there is very rhythmic activity up and down becoming faster, bigger. So this is called Evolving Pattern or we call it what you call ictal EEG or seizure EEG. We just read the label here, it looks like seizure activity is coming from the left side but it is not only one channel it involves at least 2 or 3 channels. So this is an easy one.

However, it is not always that simple. So despite the problems with the EEG the reason why we depend on scalp EEGs so much is because it is available in most hospitals and it's not expensive so if you want to do it we can repeat multiple times. Sometimes it can confirm or rule out epileptic seizure. This is a very important function actually: EEG can rule out epileptic or non-epileptic seizures. These 2 are pros as well as cons, meaning that sometimes it can give you accurate information other times you may give you false information. A very important point.

And finally you may miss the beginning of the seizure EEG from deep areas and you can only see once the EEG travels to the visual areas which are on the surface of the brain so you could totally miss the beginning portion of the seizure which is the most important areas that we talk about.

So just give you an example, the slides are all made from my own patients, this is an 18 month old who came in with daily seizures and history wise he had a congenital stroke, so there was a big stroke here, you can see that. This is the axial view, this is the coronal view. No question when you look at this MRI the seizures should start

from the right hemisphere, correct? This is what you see on the EEG. Now you look at this spike activity, I am reading the label that says F3 C3, it is the left side. The stroke is on the right side, the bad hemisphere on the right, abnormal activity is coming from the left. This is during the seizure, this is at the onset of seizure, clearly there seems to be seizure activity more pronounced on the left hemisphere. So what did we do? We did a hemispherectomy on the right side, despite all of this, based on MRI, based on the video we were convinced the seizure is coming from the right side even though it looks like the left side on EEG. Patient became seizure free, doing extremely well, no complications whatsoever.

Now this is another patient. This patient has actually [---17:17] complex and you can see has multiple tumors. And if you scan through this is the largest tumor and that is usually the candidate so we're hoping to see activity from here. This is the EEG during the seizure, what do you see? This is the beginning of seizure, it's all over. So this is how brain functions. Brain is all connected together especially if there are ongoing seizures daily. Between hemispheres they establish a superhighway for seizure activity, so even though it clearly starts from one hemisphere it goes to the other side.

This is the same patient. We look at the MEG, the MEG shows deep inside the structure called insular cortex. So this is a situation where EEG clearly doesn't give you any information but when you run the MEG you can see it is coming from deep under, buried under the frontal lobe and temporal lobe. This is when we placed electrodes using ROSA which is a robotic system and you can see it is different from scalp EEG. Scalp EEG looks all over but when you put electrodes inside the brain this is what you see. You have very limited electrodes and can confirm that this was from the insular cortex.

So this is generally speaking, a caveat of scalp EEG, now you are adding another layer of difficulty when you do hemispherectomy. First, seizures may arise from a very small focus, very deeply located like the insular cortex, basal forebrain, that doesn't get picked up on scalp EEG initially. So it only shows on healthy hemispheres, so you start from that hemisphere, small areas that don't have a lot of neuronal tissue there. Instead of showing EEG activity it goes to the other hemisphere and looks on the other hemisphere.

Now after him hemispherectomy seizures could change, maybe become very subtle and different from previous preoperative seizures. And finally EEG abnormality maybe more accentuated on the healthy hemisphere. Like I said there is nothing to really fire on the bad hemisphere after hemispherectomy. So there are all kinds of troubles thrown at us.

So when we run EEG, I am going to tell you my recommendation for post hemispherectomy EEG. My recommendation is don't do it unless you have questions because once you open the Pandora's box you will have all kinds of questions. So these are different patterns of scalp EEG post hemispherectomy. Ideally, you don't want to see any spikes or daily raised spikes or seizure activity – electro rapid seizure from the bad hemisphere or the good atmosphere. This is ideal but this is a very small population - less than 5%. The other 95% cent you will find some activity in one of the other. I am not going to go into detail but you will see electro rapid seizure spikes and so on because we stopped doing anatomical hemispherectomy a long time ago meaning there are some remaining issues inside in the bad hemisphere and it will show up on EEG.

So I will give you 3 examples of how thing challenge us. So this is a 3 year old boy who started seizures at birth, was having 20 to 30 clusters of infantile spasm daily and was diagnosed a right hemimegalencephaly at 1 month of age. This is a typical history. He had a functional hemispherectomy at 11 months of age at another children's

hospital out of State. Had seizures freedom for 9 days: Right after surgery he became seizure free and then started having seizures. It was exactly the same type of seizures, about 50% reduction in frequency though. So, from 20 clusters to 10 clusters. Does it make any difference? No way, it doesn't.

So, about 2 months later he had a reoperation in the same institution following an evaluation because they felt it was an incomplete disconnection. So after that unfortunately it didn't change; the seizures stayed the same way and in addition to ongoing seizures obviously there was developmental delay and did not improve. So this was in ictal EEG still coming from the right side and this is an EEG showing literally nothing. There is no clear onset, we couldn't tell whether it was coming from the right or left. This is MRI, we did MRI and DTI and there's no clue except there's a little remaining tissue here in the insular cortex and this was the case, we confirmed that with specs scan called Siscom and you can see clearly activity is coming from the temporal lobe maybe starting from the insular cortex. So in this case we had to go back and we did remove the insular cortex and the child became seizure free and started developing much better.

Briefly, this is the exact opposite. A 10 year old had surgery at the age of 2 and did very well, his family visited from out of State when they were visiting Disney World. This year, this Spring, the mom was calling us with a very distressed voice. He started having some recurrence of nominal pain, cramp so we went through a huge evaluation including EEG and one of the neurologists locally diagnosed him as having epileptic seizure based on the EEG. So they come back. This was the EEG, you can see this is the bad brain, you can see the activity all over especially at night. So if you just look at this without considering what happened in the past or MRI you will say, 'wow, this is horrendous, we've got a treat but this'. But again this was a case of typical post hemispherectomy EEG there was no clinical event that matches behavior and EEG so we said, 'don't worry, no seizure medication necessary', so it was a happy ending. So that's that.

This is the final case and one of our actual parents allowed me to use this video. Another very, very similar situation hemimegalocephaly or diffused cortical dysplasia, having daily seizures and came to us. He basically had a right hemispherectomy at 10 months of age. This is before surgery – this is the left and this is the right, you can see the seizures come from the right side and the EEG was clearly coming from the right side. So we did surgery – this is the MRI before, you can see that diffused cortical dysplasia which will call a Hemimegalencephaly and post-operatively no seizures but parents reporting some night time events; crying and stiffness. Also there was concern that the child was not showing the developmental progress they were expecting at the surgery so we brought him back and surprisingly there was an electrographic seizure coming from the right side here and then spread to the left right there. We felt that there was a little bit of clinical correlation, also there was a consequence which was developmental delay not improving so we did another reoperation, we went back and disconnected everywhere, basal frontal lobe, insular cortex and corpus callosum. After that we looked at the EEG again a few weeks ago, EEG showed no spread anymore and I hear that there's some improvement in development after that.

So this is part of the last slide: My recommendation post hemispherectomy EEG number one – don't do it. Number two – if you are going to do it make sure the neurologist is fully aware of the medical and surgical history of the child. And also the neurologist needs to be trained in post hemispherectomy EEG because if they haven't seen that they are going to be really panicking. And if you still have trouble, get a second opinion. I always recommend to my patients to get a second opinion because I like to have trust from the families. And do not rely on scalp EEG alone for re-operation decisions, this is very, very important, it could be misleading half of the time.

Thank you so much for your attention.

[Applause]

Questions from the audience:

Audience: Hi. So I have some questions, I do educational advocacy for the brain recovery project and I have a client who has got temporal lobe epilepsy and we think it's recurring but it also may be PNES which you mentioned. So how do you know if it's not epilepsy? She's seeing it as a push button event and it is not showing on imaging is that enough, or is further testing needed because the mom is convinced that it is actually epilepsy and that there's still events? You talk about the history: She had status seizures and she was 6 when she had her temporal lobe surgery so she did have 6 years of pretty intense seizures.

It is a very tough situation when a child says so and the parents are convinced that's a seizure. So, first time its video EEG. It's very rare that we risk the PNES vs epileptic seizure with scalp EEG. A scalp EEG is very, very sensitive and specific to that situation. Occasionally we have a situation where we did an anatomical hemispherectomy and there is no EEG from that hemisphere and still the patient seems to be having something clinically. So in that case we have to use spec scan. And spec scan could be very helpful if there is an increased activity at the time of episodes that could be supporting the evidence that there may be real epileptic seizures but generally speaking with scalp EEG we should be able to say this is psychogenic vs truly epileptic seizures.

Audience: This is a question a lot of people talk about in the group, if seizures recur after surgery are they generally the same types of seizure that occur before or different? Because sometimes parents are saying I think the child is having seizures again but they don't look the same as they used to. Is there a likelihood or one of the other generally or is it variable?

So, I think I have explained a little bit. If you see the same seizure exactly as preoperatively we generally assume that it is coming from the same hemisphere; the bad hemisphere, we just missed a small area. This is a very common situation in Hemimegalencephaly patients because when you have Hemimegalencephaly every single tissue is abnormal. So that if you leave just small amount of tissue that is still connected to the rest of the brain - I'm talking about the insular cortex, basal forebrain, those areas are very, very difficult to remove surgically unless you do an anatomical hemispherectomy. So if you are dealing with the same seizure, we generally recommend anatomical hemispherectomy if the first operation failed. If you are seeing different seizure type then that is a whole different story. Then you need to be really making sure that the other hemisphere is not involved. Sometimes you can still see the seizure coming from the same original bad hemisphere it just spreads so quickly to the other side. Remember that corpus callosum is not the only the connection between hemispheres there are other areas that sometimes surgeons cannot remove or disconnect completely. For example, there is an [---31:28] that a lot of time after hemispherectomy we see [---31:32] still connected, so there is still the possibility. That's a very challenging situation.

Audience: Thank you, so we did it, we had an EEG post hemispherectomy. The reason why was because my son is 3 years old and he was developing pretty normally after his hemispherectomy and we were thinking about starting to wean him off the last medication and the neurologist wanted a base line. What we saw was – he had a left hemi – and we saw some spiking on the right side spreading from the left. No clinical seizures, he is starting

to speak although his hemispherectomy was on the left side so I have my first question: Do you treat an EEG?

It is a very challenging question because first of all you need to really interpret a scalp EEG correctly. For example, let's say the seizure is coming from the bad hemisphere still and spread to the healthy hemisphere that is your question. You have to really look at it carefully. Sometimes there are 2 different ways of looking at the EEG: One way is called bipolar and the other way is referential montage. By changing the montage you can see that actually it is not spread it is all big activity from bad hemisphere a kind of showing the shadow on the other hemisphere so that was actually one of the examples I was going to show you. It looks like spreading but it is essentially the EEG electrode is picking up activity from the bad hemisphere so that's one thing. Secondly do we treat the EEG? No, we don't. Generally speaking we do not recommend starting medication unless there is a definite clinical correlation or there seems to be some developmental regression or arrest as a result of the [----33:52] activity.

For more information on seizures returning after hemispherectomy and post-operative EEGs, go to www.brainrecoveryproject.org