Dystonia Network of Australia
Zoom talk by Dr Julian Rodriguez 11 September 2020

I'm a neurologist. I'm 48 and been a neurologist for 16 years in Perth. In Perth there's very few sub specialist neurologists so movement disorder specialists do a bunch of things, but dystonia is definitely one of them. So, I'm frequently seeing new patients probably one or two every month, I guess. It's not that common but once you have dystonia sadly it doesn't go away. So, you tend to build up a bunch of people with dystonia that you see regularly.

I wanted to just do a bit of background on exactly what is dystonia. So sorry to burst your bubble but we don't know what dystonia is caused by. We have many, many scientists and clinicians, including myself who have studied it and can describe it and therefore hopefully improve the therapy for dystonia. I'm just thinking about when new patients turn up and how do we explain it to them. It's a very hard condition to wrap your head around, for doctors let alone patients. I like the name Dystonia Network of Australia because dystonia is a brain network disorder, like many other brain disorders. I only discovered DNA a couple of years ago and the handouts are now regularly given to patients before treatment or even my existing patients for many years have discovered the website and the informative handouts and it's very helpful.

So, what do I mean by a network disorder? The brain is not a single entity. It's a bunch of systems layered upon each other. I explain that the commonest form of dystonia would be cervical dystonia. There's a problem with the motor brain and the sensory brain and somehow the messages between them get distorted. So I sometimes explain it that if it's a primary dystonia, i.e., your brain looks normal on a scan and there's no reason, i.e., idiopathic, there's a problem with communication between multiple brain networks including sensory areas which need to know where your head is, for example, and the motor network to move your head around. People who come in with torticollis with their head off to the left, I explain that your brain has just decided that this is the new normal. You have a centre for control of head and neck movement, as we do for every limb and eye movement, they're complex networks. But in this situation the brain has decided that this is the new normal and if you try to turn to the other side, it tries to drive it back. People often point out large muscles that seem to be causing the condition and I explain that it's the brain that's hijacking these muscles and causing the movement and they're usually initially referred for Botox and I explain that no, we're not trying to unravel the brain disorder, we're trying to reduce the activators of the movement, be it a tremor or a pulling movement.

And underlying that, so if you actually map out the sensory and motor areas of the brain using scientific methods, in dystonia you'll see instead of a very one to one map of the sensory and motor network, that is distorted slightly. So when the signal goes out to move in this direction or in this body part, it doesn't happen, there's overlap and you get something called overflow and excessive movement and if there are two muscles that are actually the opposite normally, you'll actually get the opposite movements and that's what causes things like tremor.

I try and explain it mechanistically. It's hard to explain but anyway we work from the bottom up, as in the muscles back to the brain. There're all sorts of classifications, simple and more and more complex. But broadly speaking there's primary, where for no obvious reason dystonia starts. Then there's secondary where there's been insult or some kind of injury to the brain. That could be a metabolic disorder or a stroke or medications – psychotropic medications used for schizophrenia for example can cause dystonia. We call that tardive dystonia. There's an overlap between dystonia and other movement disorders so you can have Parkinson's and have a dystonic foot. You can have a disorder called myoclonus where there's twitching and dystonia is part of it. That's why it's hard to explain what dystonia is and therefore get the message out. It's a disease but it's not one disease, it can be a symptom of other diseases and then neurologists use it to describe a symptom like a dystonic tremor and such terminology.

I have a lot of patients and the range is extremely wide so I have patients who are high functioning and they come in for their blepharospasm once every four months or so, ranging to patients in wheelchairs with generalised dystonia, so it's hard to lump everyone with dystonia in the same category in terms of disability. And it can affect the whole body or specific body areas so if it's a focal dystonia you would say someone with writer's cramp where it's an extremely specific form of dystonia that only activates when you try and activate the writing program and their hand spasms up or trembles. So that's the focal dystonias. And they can be extremely focal. So, musician's dystonia is another form. It can be in a body area, so cervical, larynx, eyelids. I have patients where just one foot starts becoming dystonic and spasms when they walk. Segmental means more than one body area so speech and eyes and upper limbs, or head and speech. And then generalised is affecting the whole body and in general is more disabling. And the impact is not only on movement and mobility. Even with seemingly minor conditions that someone might think are minor such as a torticollis if you think about it. Take blepharospasm, excessive blinking and inability to open the eyes. Really if it's bad it can be disabling. We call it functional blindness. My worst patient, despite having Botox every eight weeks, still has difficulty keeping their eyes open when driving. That's why I find it difficult to describe what dystonia is.

With that in mind, I'm going to launch straight into only one aspect of treatment which is deep brain stimulation.

Dr Rodriguez activates screenshare so power point slides can be viewed.

Slide - Deep Brain Stimulation
Deep brain stimulation, or DBS for short from hereon in, is performed at multiple centres worldwide. In Perth I exclusively do DBS at Hollywood Private Hospital and the other two doctors are listed there (on the slide). And the picture you're seeing is actually from a patient from their planning software and I'll show you more of that to come.

Slide – Hollywood DBS
It's not called Hollywood DBS, but we work at Hollywood. We do have the occasional star pop in. The chap in the middle is the excellent surgeon I have the pleasure of working with, Dr Steve Lewis. And the German person on the left is Dr Jens Volkmann who is a world leader and is one of the reasons I went to Germany to gain additional expertise. There are

various things that will pop up over time. It's probably overhyped at times, like in the Women's Weekly but it is a real, effective treatment.

Slide – Talk Outline
I'm going to try and demystify it in three parts. What is deep brain stimulation and how do we do it, who should we be discussing DBS with and what happens after DBS?

Slide – What is DBS?
It's a surgical procedure. A lot of people come along for referral for deep brain stimulation and think that I'm a neurosurgeon and I have to explain that I'm not. There's a neurosurgeon involved to implant the system. Looking at the right side of the screen there's a cartoon of the cranial electrode with basically an extension cord that links it to a device which is implanted under the pectoral muscle. That's the pacemaker/battery or computer, whichever you like. There's about a couple of hundred thousand people that have had been treated with DBS. It's underused. That's all I'll say.

Slide – Is there good Evidence for DBS?
It's not (underused) because there's no evidence for DBS. And whether you look at the three main conditions where DBS is used (Parkinson's, Dystonia and Essential Tremor). Level 1 means that there's been a randomised controlled trial of some kind. I don't know why there hasn't been a level 1 trial in essential tremor because it's a condition where it's highly effective. Suffice to say these are good journals like the New England journal that these (trial) publications are in and there's many, many more, there's thousands of publications.

Slide - Tech Timeline: Late 1980's
As far as the tech goes, you might think it's all the latest high tech, but this started in the 1950's when surgeons were referred patients where physicians like myself could not help. Like with severe tremor or even Parkinson's. Dystonia in the 1950's wasn't really understood. That all came later. Thalamotomy is a lesion in the Thalamus. The thalamus is one of the targets for tremor. What you're seeing on the left is very, very early imaging, even before CT, where the surgeon would drill a hole in the head, squirt dye in so you're looking at the white line which is a cannula inserted into the ventricle, which are actually fluid filled cavities within the brain. The surgeon squirts in some dye and the radiographer takes a picture and then you get x, y and z coordinates based on the ventricles and then you can target areas of the brain moving off those midline x marks the spot coordinates. This medieval looking contraption we still actually use. It's very similar to what they used in the 1950's. It's a stereotactic frame or arc. You'll see from the bit at the top hence the arc name and that is fixed to the patient's head with these four pins and that allows the surgeon to make passes through the brain, very specific passes and aiming at targets deep within the brain and doing it safely. So, there's landmarks and there's a probe inserted. Up until the 80's and early 90s they actually passed a little probe through and that delivered heat and that's called a thalamotomy, or pallidotomy in the case of dystonia. It's essentially a very targeted, small hole in the brain. It doesn't sound great, but it'll make sense down the track. There's a network of badness that goes on in these disorders and that the lesion interrupts that network and it improves symptoms. So that's the background to stimulators. If you look on the right of the screen you can see on an MRI which they didn't have back then, that these procedures create a small, very targeted hole in the brain. The problem was that after

a few years, three to five years later, the symptoms would come back because the network would spread and it is possible to go in and do another small, conservative lesion but the problem is the bigger the lesion the more likely you are to damage nearby structures that cause slurred speech or balance issues. And you generally can't do both sides, so people with bilateral symptoms, tremor in both arms or widespread dystonia you can't do bilateral lesions because they get irreversible side effects.

Slide – 1987
So, the next phase was in the late 80's, one of the people doing surgery on the brain for movement disorders. I forgot to mention that as part of the whole procedure you insert a probe, electrically stimulated to find the target. Remember this is in awake patients with tremor. Surgery back then, time was 12 hours, and they would map out areas of the brain, very draining. Nowadays it's three to four hours, mostly asleep surgery for dystonia patients. But Professor Benaim in Grenoble France was the first person to rig up a system and it was literally Macgyvered up where they had an external pacemaker type device made by cardiac pacemaker company Medtronic and they discovered that for the first time that you could continually stimulate the area that was being lesioned and achieve the same effects as a single point in time lesion. And it's worth noting that in terms of computer technology in the 80's on the bottom right that was a portable computer, a 20kg device, so pretty groundbreaking.

Slide - Tech Timeline: 1990's - 2000's
There's been benefits of miniaturization, battery life and other things and suffice to say it's much more useable and user friendly. I started being involved in the early 2000's in Perth. The Globus Pallidus which is the name for the target we use in dystonia. That's also a target for Parkinson's so I've published on that with a lot of patients over the early 2000's.

Slide – My Practice
Fast forward to what I do now. I have fifty percent of my practice as movement disorders. It's mainly Parkinson's but it will be 10% dystonia and the other half is migraine for some reason. I won't expand on that. DBS is only one part of looking after the 100 or so dystonia patients. There's a big Botox clinic. Cervical dystonia is the most common form probably, followed by blepharospasm and then a grab bag of other forms.

Slide – The DBS team: Multidisciplinary
DBS is not performed in isolation. There are patients that I have, that I'm seeing regularly that are put up as candidates and I get referrals from other neurologists. There's a process that you work through I will explain. Basically as a neurologist my job is to select patients and make sure that everything has been done other than surgery, and that the patient's appropriate. A neuropsychiatrist is necessary to treat people's associated psychiatric problems. A lot of people with dystonia get social anxiety or just have depression and that's not a good state of mind to go into deep brain stimulation surgery. And obviously the surgeon and there's a whole cast of people that do other things.

Slides – DBS Surgery and Current DBS Targets for Movement Disorders
This part is focussing on how we actually target brain structures. In terms of what targets there are, the acronym at the top Subthalamic Nucleus, Globus Pallidus etc. his has been

worked out by scientists studying animals like rats and monkeys and then taking that into patients. I showed you the data before with respect to controlled trials so it's not experimentation. Just to give you an idea, you can actually implant into a few different targets for dystonia. That's the STN and the GPi. And I've even seen patients with predominantly dystonic tremor where the ViM, which is the Thalamic target has been effective.

Slide – DBS Targets and Effects
Pretty much if someone has dystonia GPi is the preferred target. Some sensors target the STN, although that is a more typical Parkinson's target. And pretty much everything I'll talk on from now on is to do with the GPi area.

Slide – Thorough Pre-Op Assessment
It doesn't take a long time to work out if someone needs DBS. There are a number of things to check off. You can get people ready within a month if necessary. But it's preferable not to rush things because you need to get your head around it. You can see here there's things like hardware education. If you're living with the device, we offer everyone the ability to talk to someone who's had surgery. And we don't pick people with perfect outcomes. It's better to just talk to people with real life experiences just to get the one on one story. And they often meet up and have coffee and things like that. It's necessary to have backup, whether that's family or a friend, so I want people to turn up with someone else to go over the whole process at least once, if not through the whole procedure and everything else. Expectations are important and medication is not so important for people with dystonia, more for Parkinson's.

Slide – Hollywood DBS Workflow
This is a collage of what happens in theatre. The take home message is that for dystonia is we don't need the patient awake. Unless it's someone with a prominent tremor and we want to assess the effects of stimulation on the table. You can't really assess them by bodily or neck posture during surgery. It's not necessary. What you're seeing there (on the left) is the anaesthetised patient having an intraoperative CT. The top right is the birds-eye view of the surgeon's approach to the scalp preoperatively and the bottom right is us doing microelectrode or brain cell recording. So, you can actually hear your brain cells up on screen if you're awake.

Slide – Microelectrode Recording
We did a dystonia patient recently with a quite bad tremor and we woke him up to assess the tremor during surgery. You can hear what neurons sound like, static basically. And you can hear a firing of the neurons and depending on what area you're in you can activate that set of neurons by moving the limb. So that's part of the process……

Slide – Awake Clinical Assessment (if needed)
People can wake up in the middle of surgery, talk to me, and we give them a sip of water because they can have a dry mouth and we can test their speech and vision and hand movements and other things. So, what you're looking at there is Simon our trusty anaesthetist, who is a genius at keeping people happy while they're bolted to a table. And through the plastic there, on that side is the surgical side, no touching. This side, we can

attend to the patient and test them. So that's Dr Lewis there, he has the patient in the frame, awake. On the right there, we had a patient who recently, with tremor, she couldn't draw that spiral at all beforehand, it was just a mess. And I thought I'd ask her to draw a little smiley face. So that was a nice little touch that she did that. Lovely lady.

Slide – New DBS Technology
The technology, that's kind of my thing so I've chosen the devices that we implant based on flexibility and programmability. Programming the brain is not like a computer hacker, we basically set specific parameters on how much amplitude and pulse width, and frequency. Very importantly, stimulation location. So, location, like in real estate, is critical in the brain. And the technology we use is something called directional leads whereby you can actually activate ….

Slide – DBS is not Fixed in One Location
Look at this graphic here, this is an electrode with eight contacts. You generally use four. You can activate each contact individually or separately. So, it's not a fixed therapy, you can actually optimise symptom control based on moving within a 1cm space in the brain.

Slide – Accuracy is Everything
There is an inherent variability in implanting electrodes in a soft structure like the brain. It might not sound like a lot but if you get more than about 1.5mm off target you are not able to control symptoms. Mainly because you're out of the sweet spot and also because you're in the area where you're causing side effects. We often get zero millimetres from the target, but generally less than 1 mm or 1.5mm is fine.

Slide – Frequency & Stimulation Location
Because of this whole ability ….. If you think of it as sculpting. The blue blob is the old-fashioned electrode where you can increase the stimulation and people's dystonia would improve and then they start getting slurred speech for example. And then we'd have to turn it down so they could speak properly. The slurred speech by the way is because the current is spreading into pathways to facial control that we don't want to stimulate. But we would just have to turn it down and live with a bit more dystonia or tremor or whatever the symptom is. On the right, the green blob you can see is sort of sculpted, away from areas where side effects can be caused. That's the programmer's job. More of a sculptor than a programmer.

Slide – What are the Possible Complications of DBS?
We are all obligated to give the bad news with the good news. There's a long list of side effects and I'm not going to go through all of them. But upfront we tell people, "Would you be prepared to have a hip replacement?" The overall risk of really bad things happening is about the same as having a hip replaced. Yes, there's specific things to do with DBS.

Slide – Is DBS Safe?
The biggest complication is bleeding deep in the brain causing a stroke. Fortunately, that's extremely rare. We've not had a case at Hollywood where that's happened. And this is from some friends of mine in the east. In 15 years of surgery there's been no deaths and no strokes. There's been things like seizures which are generally as you can see pretty rare and

people don't go on to have epilepsy. The main thing is surface bleeding on the top of the brain can happen, but it doesn't impair people. It can cause temporary confusion and things like that but surprisingly it can be completely asymptomatic. So that doesn't bother the patient long term. The long-term issues of a surgical nature are mainly things like keeping your hardware happy. Particularly in dystonia patients where there can be strong or violent twisting movements, the extension cord in the neck can get stretched and if people are thin the actual battery can erode through skin and need replacement. And then infection is occasionally a problem. And the downside of infection is you have to take the system out, usually the battery or extension leads, wait three months and then implant them back in. It's not from the fact that …. reimplant the cranial electrode in one patient. We've reimplanted and he's fine.

Part 2

Slide – Patient Selection – Who can DBS help?
In terms of who we select and who we think we can help with DBS.

Slide - DBS Treats Movement Disorders
Obviously, it's for movement disorders. All DBS centres, the majority of our patients are Parkinson's patients. Dystonia, like I said, it's underdone either because patients or the doctors don't know about it. Or they think it's some experimental or dangerous procedure. …. this is the numbers of patients we've implanted at Hollywood. 70 Parkinson's, 6 dystonia. And if you think about dystonia as a software disorder, it's the perfect condition where something like an electrical stimulator could possibly assist.

Slide – Who can DBS help?
There are no real Australian guidelines for DBS for dystonia. There are Parkinson's guidelines. To summarise, if you have disabling symptoms from dystonia then you should definitely consider it. Cervical dystonia, there's patients where you just cannot get symptom control up front. You'll inject them and they get side effects, or it doesn't improve their primary symptom. Their head's still stuck to their shoulder and nothing changes it. I usually want another injector's opinion so if a patient has come from another good injector or often two injectors, I'm happy. But if I've diagnosed and treated them, I always want to try and have a go with another injector in case their style is better than mine. Segmental, rarer but let's not go into that.

Slide – Can DBS help? What I tell patients
I tell people it's not a cure. It can be an amazing treatment, or it can be equivalent to what you were having before with our three-monthly visits for Botox injections. And there are some people that are still having Botox but that's like I said with both treatments. But I don't see having to do Botox in a DBS patient as a treatment failure. It's whatever improves the patient to their maximum capability. You might not actually be suitable for DBS but just get an opinion either way. And if you're not suitable you may at least get a second opinion on what alternatives there are. Sadly, there are no new oral medications for dystonia. We can talk about that later. And not everyone does as well as they would have liked to have done with DBS. And then I go back to well what can we add on. And I've had some patients that are doing really well, and they just forget to come back. So, one chap, he was implanted

three years ago, and he essentially has no symptoms, came back and his speech is slightly slow. And I said, “Do you know that was a stimulator effect?” And he said, “No.” So I’m trying to reprogram him to give him normal speech. He’s happy otherwise.

Slide – When should you not have DBS?
You shouldn’t have DBS when it’s not worth the risk or when the effect of alternative medical treatment is really, really good. I’ve had patients who’ve been having Botox for 15 or 20 years and they ask me should they have Botox or have DBS and I say, “Probably not.” If you don’t mind turning up every three or four months, within reason but that’s a negotiable thing. Active dementia is not negotiable. People with pathological anxiety, depression, you have to have that sorted out. I haven’t been involved with anyone with secondary dystonia but would be happy to consider them. So, there have been trials in dystonic cerebral palsy and post stroke dystonia. Tardive dystonia is another one. I haven’t implanted in anyone with that. Age-wise, if there’s an age-related illness that makes life more difficult than the dystonia, it’s debatable whether you should do it. We do implant patients with mild cognitive impairment safely. And if your overall general health is not sufficient then we wouldn’t put you through the whole process of surgery, you know, whether it was a replacement or DBS.

Part 3

Slide – Life after DBS – How does it work and what are the outcomes?
So, the all-important outcomes. What I don’t have here is quality of life outcomes. Quality of life is arguably the most important thing. There’s not a unifying measure for doing well in dystonia. There is in Parkinson’s. So, I do use motor outcomes for cervical dystonia. If someone’s not happy I try and work out why. That’s basic medicine.

Slide – How does DBS Work?
In this bit I just want to go through what we think about how DBS works. There are people actively working on this. You can actually implant an electrode now that records brain activity as well as delivering stimulus. I’ve seen patients where you do the microelectrode recording and there’s this four-cycles per second buzzing rhythm in the brain. We don’t know what it means but it does appear to be one of the signatures of dystonia in some people. And that’s as far as I can take it at this point. But obviously if you can measure something abnormal in the brain electrically and come up with a way of supressing it, either by a drug, or an electrode in the brain, that would be helpful. We don’t actually have a biomarker, as such, for dystonia. And when you implant someone with dystonia, you tell them this is not a quick fix, and we’re essentially trying to re-wire your mal-wired brain and that takes time.

Slide – Neural elements in a nucleus
This is a cartoon of, the thing with the red end is the electrode. The sun-like blob is the volume of the area that receives the electrical stimulation. It’s obviously stronger in the middle and drops off as it goes to the edges. And the VTA, the terminology, people agonise over what we’re actually activating and it’s so complex. There are the primary neurons in the target, that’s the Soma and the Axon is the wire that comes out of that cell body to distal brain areas. The Dendrites are the receiving antennae on the neurons. So, all those

are being stimulated, there's also fibres to and from other brain areas that are passing by, the Fibres of passage, and they're also going to be stimulated. When people say how does it work and I say I don't know, then this explains why.

Slide – Intranuclear effects of GPi-HFS
Then if you dig down into an animal brain, as these people do, and the model on the left is the wiring for various nuclei showing what happens when you stimulate these areas. The text says that microstimulation can inhibit some neurons and then other high frequencies can activate other parts. So, this is the background for that previous slide.

Slide – DBS works on short & long range timescales
If you want to get all bogged down, neuroplasticity just means the brain conducts things. Dystonia is an example of abnormal plasticity and DBS is somehow undoing those abnormal patterns. That all takes time.

Slide – Correlates with Timescale of improvement
I don't go into that much detail when I'm seeing someone. There's a process and afterwards where I say you get some improvement in certain things. Like if you have a jerky tremor or head or hands that can actually improve early on. If you have a longstanding abnormal posture of the neck or limbs, that's going to take some time. Generally, a few months. The good news is that people think that they might have not got as good as they're going to get and suddenly the second year they improve further. So, someone might improve their tremor and twisting movements and in the second year they're actually walking better.

Slide – Generalised Dystonia: Motor Outcomes
In terms of do we have a motor outcome, yes we do. For whole body dystonia BFM movement scale preop is on the left and shows patients in early studies from Steve Tisch, a neurologist at St Vincent's in Sydney. Some of these may be patients of Steve's. He's probably the national go to genius clever guy for dystonia. He published this is over ten years ago showing that it doesn't matter whether you have a genetic diagnosis because most patients don't. DYT1 is short for dystonia one, which was the first proven genetic cause of dystonia. This is just showing that everyone improved and it's debatable whether that slight, the bar is higher in DYT negative patients. but I don't think that's clinically significant.

Slide – Cervical Dystonia Rating Scale
For cervical dystonia, the inventive Toronto Western Spasmodic Torticollis Rating Scale AKA TWSTRS so lots of marketing done on that one.

Slide – Cervical Dystonia Rating Scale
This is the scale used for cervical dystonia components of where the head's going and what's happening, and component of what can you do, can you watch tv and drive and what's the associated disability?

Slide – Pallidal neurostimulation trial
So that's all collapsed into a global score and this is the data from the biggest trial in cervical dystonia with DBS. Having said that it was only 62 patients so that highlights that it is a fairly

uncommon condition and that there's scant data out there and that people like Jens Volkmann have done really good work showing that it definitely works. All of us have seen patients that have improved but funding bodies and other medical bodies were poo-p0ooing it and need proof. So, you need these kinds of studies to get over the line and get Medicare funding and all that sort of stuff. What they did was implant everyone with cervical dystonia with the same target and then for three months there was a group who were activated and a group that weren't activated and three months on everyone was activated. So on the left of the screen is the before and after using TWSTRS and on the right of the screen you can see with the switching on at three months, the line keeps going down for some patients, not all. So that just highlights the time factor is important. This study did not go out to two years but I'm sure if it did, you'd see improvement in some of these people, not everyone. But you would see definite improvement in the second year.

Slide – Cognitive Testing Post DBS
The neuropsychiatrist always tests cognition before and after. In dystonia we don't really use it as much as a Parkinson's cohort, but the GPi does not have cognitive functions for the most part. It's safe in respect to memory etc. And the subthalamic nucleus in Parkinson's patients can impact on mood and motivation and other things.

Slide – DBS: Initial Goals
After surgery once you've got someone through the first month of the implant, people actually recover really well. We put patients in ICU. A patient we did on Monday was standing up beside his bed on Tuesday. They're not all like that but some of these people can recover really well. So, people come in on the Monday and pretty much go home on the Wednesday or Thursday. If they're still in on Friday, because they're frail or for whatever reason of I'm still adjusting their medication, if it's Parkinson's then I'll refer them to rehab. 90% of patients have gone home by Friday. You achieve the initial goals of implanting and getting effective stimulation, reducing all the symptoms. With dystonia, there's a waiting game.

Slide – After Successful DBS: The Goalposts Move
If they have unrealistic expectations, we try and moderate those. If you're not better at 3 months, it doesn't mean you're not going to be better at 12. One of our cervical dystonia patients at 18 months had had 50% improvement and no matter what I did, we didn't get beyond 50. But this was the chap that had had pretty much no benefit from Botox. And I've been working on ultrasound guided Botox and I got him a bit better than the last time and I actually discovered that he has scar tissue in one of the neck muscles so he's one of the very few patients that I'm actually going to refer for surgical incision to lengthen the muscle and in general that's not a treatment for dystonia. If you cut the muscle in dystonia that's causing the problem, the brain just remaps to another muscle that causes the same movement. To be honest, when it goes well, it goes well, and we don't have to manage anything.

Body image is that slim people now have a device in their chest and wires and other things. You don't see the wires but some people, the device in their chest, they don't like. These are things that are in the long-term minor. Then I have to get on people's back about if you improved your dystonia and you used to be in a wheelchair and now you're walking, you

really need to go off and see a physio because you still have some issues with your ankle or knee. And people just want to get on with life and I and I have to remind them that, no, there's a bit more to dystonia than that.

Hardware troubles are things that include things like having a battery change every three or four years. We usually put a long-term rechargeable device that lasts twenty years in a dystonia patient and I've already mentioned we can have problems with wires breaking or eroding. Slurred speech is a reversible side effect. Generally telling patients to turn it down or I'm turning it down saying you're not going to get any better at a higher voltage. And then obviously the life role changes are dependent on how bad your dystonia was. For really disabled people, suddenly having to deal with life and kids and jobs.

Slide – Life after DBS
And then I tell them about the computers and don't forget to get your battery checked in case your battery shuts down suddenly you need a battery check because if your battery shuts down suddenly you can have a severe return of dystonia. If it's generalised dystonia that can be life threatening. And you should probably pop back in because you never know, there could be an upgrade available there.

Slide – DBS for Dystonia: Personal Experience
I'm just going to go over my personal experience and a few case studies and then I'll take questions. I've seen a bunch of patients that are in East and in Germany. Now these are the patients I'm currently managing. Not all of them were implanted at Hollywood. Some of them were from other centres. They are generalised, cervical and Meige's patients. You can see here one of the generalised patients, it was quite sad, she had no response and she lost function in her more useable upper limb. I wasn't involved in the implantation to know whether that was due to some kind of surgical issue but in general you don't see that. If there was a loss of function then it would be generally due to a deep bleed. Of the three patients I'm currently managing, one was implanted at Hollywood and he's doing fine, he's walking, speaking and moving better and his tremor in his upper limbs has improved. And most of the patients for cervical dystonia are not on Botox. They have such good control that I have to drag them back for follow up. I've only got the one patient where we're still plugging away trying to get him better. And the cranio-cervical patients, these are patients with really disabling blepharospasm and cervical dystonia. You would never promise anyone complete symptom relief. Two patients are quite happy, but one patient unfortunately still has such severe blepharospasm that he can barely walk around the house and we're probably going to implant him in another target.

Slide – Case Studies
This patient I inherited from another implant centre. He's a patient that is like the poster boy. In fact, he was the poster boy for Medtronic. Luke, he's quite happy for me to talk about him. So, he has DYT1 dystonia which came on at age 6. It rapidly disabled him. He was in a wheelchair. I remember seeing him with another neurologist and he had whole body Botox essentially. And one of my senior colleagues that I was working with at the time implanted him with DBS and he broke this rule of needing months to get better. Within days he was up and walking and kicking a football and everything else and now he's a guy who's working four days a week and a wife and kid and I just had to refer him to a physiotherapist.

Video - Luke walking
This is him probably about a year after surgery. So, he still has a dystonic gait. He's much better than this now. Because all his muscles hadn't been used for a long time, having been in a wheelchair. But I remember seeing him, as he wasn't my patient at the time, sort of walking by and it just blew me away that this guy was now just standing up talking to me. I wish everyone had that kind of outcome but sadly they don't.

Slide – Cervical Dystonia (not rare)
We have a cervical dystonia patient, a couple here. At the top of the screen is a chap that two of us had had a go at giving him Botox, huge doses, four or five goes, but he could not shift his left rotation. Literally his chin was stuck to his shoulder. And as I was saying the patients you have to get them back because they just disappear. I hadn't seen him for ages because he just got on with it and didn't have any issues. In this video I'm about to play, on the video the stimulator is off and immediately the symptoms return. He can't turn his head to the right. This is one of those patients where you know the stimulator is supressing that abnormal, mysterious rhythm. We turned the stimulator on and immediately it blocks that dystonia.

The patient down the bottom really worried me. She was a young patient from the UK. She'd been injected for a couple of years. She developed the rare blocking antibodies for Botox and it just stopped working. So, she didn't have a choice. She was implanted and on the right she's about 12 months. And you can see it's better, but it still wasn't a small tremor. She was still having big jerks but heaps better. Doctors and patients want perfection. Anyway, I don't have a photo of her because I bumped into her in the street and she's perfectly normal. She has no tremor at all. And that was at 18 months. She's still seeing the other centre.

Slide and video – Essential Tremor
I put this patient in, not because he has dystonic tremor, but a lot of patients with this so-called essential tremor or a tremble in both hands doing things or holding hands up. If you have dystonic posturing, then you call it dystonic tremor. Some people with a head tremor also have a hand tremor and we don't know really what to call it. But either way if there's significant disabling hand tremor you do DBS. This chap has lifelong severe essential tremor and it is a good example of a guy that probably should have had surgery a bit earlier. This guy is just getting on with it and he's still like this six years later.

There were a couple of tech things I was going to talk about if there's time but there probably isn't, so I'll pause for questions.

Laraine
Some of the questions Dr Rodriguez you've probably answered, but the first one, no. How successful is DBS for tardive dystonia?

Dr Rodriguez
Literature says it's less effective, but I haven't had any personal experience. But if you go from zero benefit from either oral medications or Botox, even at the lower end of

improvement we see it's about 30% but it's hard to work out what that 30% is. If it means that person can move their head a little bit or the pain is significantly reduced, then it's obviously an important 30%. No personal experience so I'm trying not to comment but it's not useless, put it that way. The party line is it's less effective than primary dystonia.

Laraine
Now there's another question. Is it likely that multifocal dystonia would respond to DBS and I think they've asked too; would you need multiple probes in the brain?

Dr Rodriguez
I think they're referring to either segmental or generalised dystonia and no, the target appears to be the same which is the GPi. All of those patients you saw they were all exactly the same anatomical targets whether it was the body or the head.

Laraine
So the person with the multifocal would have the same target?

Dr Rodriguez
Yes

Laraine
And do they respond well?

Dr Rodriguez
Yes, the same thing applies to everything I've said. When I was referring to generalised, multifocal I think would be generalised.

Laraine
How is the decision made about the best stage for a child with generalised dystonia to have DBS?

Dr Rodriguez
I've also never done any kids but would be happy to. But everyone says that you should implant earlier before you get all the joint deformities and other things. And just for people to obviously get their life back. So, colleagues who have implanted lots and lots of patients have operated on children and any children that need DBS go to Perth Children's Hospital where I don't work. But yes, the sooner the better.

Laraine
There's no age limit is there? Can they be too young?

Dr Rodriguez
That's probably more of a neurosurgeon question. A six-year-old, you can implant a six-year-old. The problem is the electrodes start here and then when their skull grows, we'd have to reimplant them when they got older. I failed to mention there's a reimplant rate of about one in fifty electrodes for various reasons and this would be a good one. If someone got six

years out of their electrodes and they grew tall and needed reimplantation, it's not a big deal.

Laraine
I think you've already spoken about this. The question was, does the child have to have a dystonia gene to be considered for surgery, but I remembered a slide where there were some with the gene and some without.

Dr Rodriguez
There are a few publications on different types of dystonia DYT1 and 6 and this, that and the other, but it hasn't really been proven. So, we've implanted one patient with secondary dystonia. That craniocervical patient actually has basal ganglia calcification and he's had definite benefit on the Parkinson's like symptoms, because he has an overlap, but not the Blepharospasm. His Parkinson's symptoms and cervical dystonia improved but he still can't see, or the blepharospasm is 50% better so we have to maybe implant another target, we're talking about that now. Does that answer the question?

Laraine
Yes. And you also answered this one. Do dystonia patients have to be awake during DBS, but you've already spoken about that.

Dr Rodriguez
It's not that big a deal actually. I've worked with three different surgeons, the first surgeon will do the whole operation awake including pinning the thing (to the head) under local anaesthetic and drilling the holes and chatting to the person lying there for three to four hours and giving them some sips of water. It's not preferable. What we do at Hollywood is we gently wake the person so they're breathing the whole time for themselves under Propofol which is a form of intravenous anaesthesia. You can lighten people; you can go up and down and you can give them enough so that they do need a breathing tube. The anaesthetist is really good at keeping people breathing for themselves and then we'll stop the infusion and people will gently wake up. It takes about 30 to 45 minutes to do the recording, test stimulating, implant that electrode then flip to the other side and do the same thing. We've not had anyone wake up stressed. We've had some people wake up who are fidgeting with their movement disorder which pops up and we put them back to sleep and then we just do the recordings and they wake up fine. It's just one added bit of assurance for someone with a visible symptom like a tremor, someone with stiffness, if it goes away with really low voltage, it's all nice and reassuring. And the other thing is we test their speech. So, everyone will get slurred speech from the stimulator when we turn it up after surgery. If that happens at a really low voltage then it's not a useable electrode and we have to reimplant and you may only find that out after you've implanted the target, that someone's sensitive for whatever reason.

Laraine
This one is which genetic variants do well with DBS?

Dr Rodriguez

I can't answer that. I wouldn't rule out anyone just because they have or have not got a genetic diagnosis. It's just basically what is necessary for their symptoms and syndrome.

Laraine
You may well have answered some of this too. What's the success rate of the various types of focal dystonias?

Dr Rodriguez
For people who've put themselves up for focal dystonia…. The problem is that someone with really, really bad writer's cramp for example, you can get away without writing for the most part. You know, at the meetings people will bring videos of musicians and guitarists playing the guitar while having the surgery but I don't know if I'd do that. I would consider it but that's why we have a neuropsychiatrist and other people, if a professional musician came along and said, I'm 25, I can't play violin, I have no other hopes and dreams and this is all I wanted to do, we'd absolutely consider it.

Laraine
It's patient by patient evaluation.

Dr Rodriguez
Yes. Of the small number of patients that we've implanted at Hollywood, no one has had zero benefit. If someone who gets 50% was hoping for more, they're going to be disappointed. It's almost like the people who do too well, don't take this to heart, but people who do really well kind of ruin it for the other patients. They have invisible dystonia, but you would never say that you're going have zero symptoms because there are patients that are like that. I just say, you're going to be somewhat better.

Laraine
Someone was asking how many Botox attempts would you think is reasonable before you would consider DBS?

Dr Rodriguez
Four. If someone else has injected the person and then I've had four goes, that's a year gone by. When I get a new patient, I ask them to give me three or four attempts to improve their dystonia. That's why I'm saying four. In some cases, after a year I want them to be better but they're quite happy, so I don't bring it up. The thing about DBS for convenience, like, if they have cervical dystonia do you say to the person, we're joined, medically speaking, for the next couple of decades or do you say there's this convenient option. I also don't do that, if the patient says, I've had enough of Botox, what else could be done, I would then consider the referral. I wouldn't say no but I'd just say if you're having 90 or 100% improvement in your TWSTRs or whatever score we're using, from Botox, maybe you should be happy with that. But I can't really dictate who should come for the next 20 years every three or four months and who should have surgery, so I would put them through the process.

Laraine
There's another one here. Is fatigue common after DBS?

Dr Rodriguez
Yes. The first, say, few weeks to couple of months, because of the whole draining process of having brain surgery and a general anaesthetic, probably a couple of weeks is normal. People want to bounce back and get back into everything, and some people do, but we don't like people driving for a month just to be safe, there's no strict drivers licence authority guidelines. Take six weeks off work, take a month off driving, most people are actually doing things way before six weeks. And the programming sessions in dystonia are fortnightly for the first couple of months, and then every month or so and then when you're stable, every three months. And when I say programming, in the second year I might not be doing anything.

Laraine
I'm just trying to find somebody to tell them, they wanted to ask you something directly. That will be our last question.

CB
I just wanted to touch base on something in relation to the question about the age of the children having it done. Being the mum of a child that had it done at such a young age. So, she was 6 when she had hers done the first time. She's now 12. Unfortunately, after the first DBS, her lead did dislodge 5 months post-surgery. We weren't aware of it until 15 months after the fact. Her symptoms were really bad again. The medications, we obviously had to increase. After the second device being implanted, we had a completely different response in terms of movement. So, the first time, she went from not being able to eat to eating, purposeful movement. It was just absolutely mind blowing. The second time we were really disappointed because it was such a different outcome. But in saying that, you say about 50% is better, then we're still in a better place. And that's what I've really had to come to terms with. That, yes, I don't have the same child after the first one but we're still in a better place. And then 18 months later her leads actually broke from all the movement and that sort of thing and while we were waiting for replacement, she actually developed an infection. So, the third placement again, we've had different results, we're on a lot more oral medication. But we've noticed since the last DBS setting, which was done 9 months ago, she has become extremely fatigued and has lost a lot of her movement. So, we've almost taken away all her movement where she is physically unable to have that purposeful movement. Is there a possibility that the setting could be impacting that quality of life for her now where she sleeps pretty much the majority of the time and we've lost so much of that movement that she's unable to lift an arm and unable to lift her leg. Is there something that I should be bringing up with our programmer?

Dr Rodriguez
That's probably enough info. My disclaimer is that I've never treated a child and they're obviously way more difficult. The second thing is the primary diagnosis, which we won't go into now, is obviously very important. I don't know what the diagnosis is and whether it's a progressive condition and whether that's relevant or not. For implanting, the DBS team can absolutely answer things like is the target the same, which areas are being stimulated. That should be an answerable question. That's all I'll say because without knowing points one and two. What you can do now is analyse lead location really accurately but it then depends on the system and software but my software, you grab a CT and you map it onto the

patient's MRI, if there's a recent MRI, or if the brain's growing and you can see exactly where you're stimulating and maybe answer some of those questions if they're anatomical. The side effects, if it's the GPi it can slow voluntary movement down. If you think of dystonia as a too much movement disease, find a brain target that, where it's stimulated it reduces excessive movement, but if you keep going you can actually slow down movement. So, the generalised dystonia patient you saw earlier in the video, Luke, he actually walks slower now, and I don't know whether it's the dystonia or this slow down effect. But what I do know is that whenever I try and reduce the stimulation to see, the dystonia immediately comes back. So sometimes it's a you've got to live with it type side effect. But I can't answer what you're asking about your daughter, I'm sorry.

CB
That's fine. I appreciate that. Thank you so much.

Laraine
I think that we'll have to call it a halt now.