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An Interview with Dr. Kathryn Moore (MD) from the Duke Neurology Department on Clinical Neuroscience and Research

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1. Introduction

On Tuesday, April 1st, Dr. Kathyrn Moore (MD, Msc) from the Duke Neurology Department virtually spoke with three authors of the Morganton Scientific. Both Adrija Sarkar and Leyla Urmanova conducted original research to better understand therapies for Parkinson's Disease; their articles are included in the 2nd Edition of the Morganton Scientific. Additionally, Leyla Urmanova and Navya Bansal wrote literature reviews evaluating topics important to clinical psychology and neuroscience. Laira Lee, one of the chief editors of the Morganton Scientific, and Mrs. Jennifer Williams, the sponsor of the Morganton Scientific, assisted during the interview. A great thanks goes to Mr. Christopher Collins for helping set up the interview and reaching out to Dr. Moore.

Dr. Moore is a Movement Disorders Neurologist and works with patients with a variety of diseases, including Huntington's and Parkinson's. She is a graduate of NCSSM Durham in 2003. Since then, Dr. Moore has pursued an undergraduate degree at Duke University and medical training at UNC Chapel Hill and the University of Florida.

2. Interview

2.1. ***[Laira]: Since I think we have three budding clinicians on the call just like how do you feel about keeping an open mind to various specialties along your medical journey, or do you feel like you started out in college, knowing neuroscience was your thing? Can you speak on developing your interest into motor disorders, etc?***

[Dr. Moore]: I discovered the brain in about the sixth grade. And I just thought it was the coolest thing. And what makes you tick? What makes you as a person? And I think many students get into the neuroscience aspect of like what is the seat of me, right? Whereas the Greeks thought it was in the liver and now we're thankfully aware it's the brain.

And over time what I found is like what my scientific interests are and what my clinical interests are, like who do I like taking care of. What kind of space I want to be in as a clinician is very important.

So for instance, I really enjoy working with people long term and talking about heavy issues. I talk about hospice on a regular basis.

Like what does death look like? And spent a lot of time in that space. I have colleagues that do exactly what I do who don't enjoy talking about that. But none of us are going in and removing a tumor, closing it up, and waving goodbye.

So you have to think about, what is my approach to taking care of patients?

So really, my first clinical experience was as an undergraduate, I was doing glioblastoma research, brain tumor research. And had an opportunity to go to the clinic and meet people with brain tumors. And I thought, oh, this is great. This is a bad disease. It's messy,

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it's rough. There's ways that I can help these folks understand what's happening to their brain. There's treatments even though they were not great at the time. Survival was nine months.

And so that part was really interesting to me. And then I realized it was more oncology than neurology. And again, 12 year old me really loved the brain and what makes you move and tick and do.

And so neurology you know neuroscience as an undergraduate was more like what is dopamine? Very science based, not really clinical.

But as a medical student and thinking about this, I tried to keep an open mind, but I had a first love, you know, it was donezo for me.

And what I love about neurology really is that it's the bastion of clinical care. So everybody, not to beat on everybody else, but they ordered more tests than you would believe. Whereas I go in the room, I spend 45 minutes to an hour with a new patient. First of all, I know a lot about them at the end of that hour. That's a sacred space. But I can do some maneuvers with them and 95% of the time I can tell them what they have, what the rest of their life is going to look like. I mean, that's cool.
So inside of neurology, some of the subspecialties are more on that physical exam and versus um I'm ordering more MRIs or EEGs or what have you. And I really liked the magic of examining somebody, watching them move and figure out exactly how to describe that and figure out what's going on. There's an art to that.

And that was really cool for me. I could watch people walk all day. Don't sit me down in the food court at the mall because we'll never get up because we're watching everybody.

But the clinical care I'm doing, right? That's interesting. I'm teaching that. I'm really into teaching at the clinic but talking to somebody about things like what does it mean if you need end of life care and how do we work this out and you know your husband's getting chemo, how do we make sure that you need it while he's doing that.

And so that kind of dirty, messy space. And I'm very lucky. I have great social workers. We have a chaplain. Like I'm not doing this by myself. But I found a space where I love what I am doing.

I knew I could do it and I knew that not everybody could. And I think that's what a calling comes down to.

2.2. ***[Laira] : Do you feel medicine should be less focused on finding a cure-all and move more towards early detection of diseases? Or does this mindset even apply to something like movement disorders where there are not currently cures for diseases like Parkinson's and Huntington's?***

[Dr. Moore]: It's interesting that you ask that because they are very tightly entwined with one another. You can't do one without the other. So although we don't have cures for anything yet, yet being the operative word. I do think that by detecting disease earlier, we will be able to better intervene with what we call disease modifying treatments.

So I think, you know, if I had a crystal ball and said, what is the world going to look like in 10, 20, 30 years with these diseases, I think what'll happen is we will be more focused on detecting it early because if we start a medication early, we can make it more of a chronic disease like diabetes or high blood pressure than something that is terminal.

And so a lot of the research going on now parallel to treatment options, looking at disease modifying therapy is for accurate and reliable ways to detect it early.

And so instead of relying on me doing an exam when it takes six to nine months to get an appointment with me, maybe the family doctor in your local community can do a blood test or a skin biopsy or an MRI with AI that does special measurements to detect that early.

So I think it's both. It has to be both.

2.3. ***[Leyla]: I'm really interested in Parkinson's disease and was just wondering if there are any specific clinical trials or new research studies that you're excited about in that field.***

[Dr. Moore]: When you're talking to people about research in general, most people, like Laira was saying, are focused on cure and detection.

But I see a value in multiple areas of research. I'm excited for these disease modifying trials, but I gotta be honest, it's very hard to get really attached to them because so many do fail. That's the nature of research. My heart has been broken so many times. We're going to enroll people in these clinical trials, but I try not to get too attached to it.

As for some of the things that are really cool that are happening now in the treatment space. Just in the last year, we've had a new oral medication for Parkinson's, the approval of subcutaneous medication for Parkinson's, and something called adaptive DBS, which is where the deep brain stimulator responds to particular patterns in brain activity so that it's not constantly on, it adjusts to what the patients need. That was just approved within the last month.

So there's a lot of movement there in terms of treatment options.

I'm also very interested in how we best take care of patients and caregivers, right? And so that's something that has been part of why I chose medicine and why I chose some of these complicated diseases to take care of people when they're going through these really hard times.

There's really cool studies going on across the country about how we best support people in that journey. So to me, all of that is exciting. Even if you get the best early detection and the best disease modifying treatment, you're still going to have lessons that you learn from all of those things that are going to help people moving forward.

2.4. ***[Adrija]: I'm really interested in deep brain stimulation particularly. I think it's absolutely fascinating. So what would you say are some of the most significant limitations of current deep brain stimulation techniques and what innovations or potential therapeutics do you think could possibly enhance those treatments?***

[Dr. Moore]: So I think the biggest limitation to people doing well is the selection of the correct patient for the procedure, which is paramount. I think where most missteps happen is when you're not picking the right patient to move forward with that procedure. And so if you look at the data around success rates of DBS, it is not necessarily indicative of an individual group, an individual surgeon and how they work together to select patients and make sure that they do well. I think information around choosing patients and techniques of those procedures. It is a treatment that requires a lot of interdisciplinary collaboration. I think that's really a big barrier.

The other is our understanding of who is going to do well and who isn't at a microcosm kind of level. And so we do know a lot about Parkinson's, although that field is growing in terms of who's going to respond well and not from a genetic marker perspective.

But there's a real opportunity for the use of DBS in something called dystonia. So dystonia is not a single diagnosis, but a large group of diagnoses involving excess pulling or posturing of the muscles coming from the deep brain regions.

And it can happen with Parkinson's, it can happen with Huntington's, but there are also many diagnoses that are just dystonia in some form or another. And so we're really getting a handle on what of those patients will do well, who won't, and how to expand DBS to other indications.
So it is being explored for ticks and Tourette's syndrome. It's being explored for OCD, Alzheimer's disease, and a number of other things. So I think understanding the target, what to expect and who is the right kind of patient for this is really important.

What's coming very quickly at us now is something called closed loop DBS.

And so right now with this adaptive DBS, I'm still doing the programming. I'm still setting up the machine to do what it needs to do, but then we're able to use these advancements in DBS to say, okay, within these measurements that I'm giving you, you can bounce between those if you're asleep or walking or what have you.

The dream is to put this in, we press a button and it programs itself. It does everything it needs by itself. But we're getting there.

2.5. ***[Navya]: Okay, so my question is also about neurodegenerative diseases. So I know that although there aren't specific causes to a lot of neurodegenerative diseases, there have been correlations between neurotransmitter levels and certain hormone levels to neurodegenerative diseases. Have you seen any promising research or clinical trials that specifically target neurotransmitter regulations in order to treat both motor and cognitive symptoms for neurodegenerative diseases?***

[Dr. Moore]: Yeah, absolutely. The dysregulation of neurotransmitters really is fundamentally what the disease is rather than a cause of it. The causes of neurodegenerative disease by and large are genetic and environmental.

Huntington's is all genetic with some environmental spring in. Parkinson's is mostly environmental with some genetics resulting in low dopamine. And so most of the treatment is in that space downstream of everything else. So treatments for Parkinson's disease are mostly dopamine, to supplement. And in Huntington's disease where people have too much dopamine, we're blocking the dopamine.

There is some research into this space with acetylcholine, which would be more of a cognitive chemical. You think about antidepressants. They help you keep your serotonin around. So all this is a very well-established area of modulation of these neurodegenerative diseases or chronic brain diseases.

2.6. ***[Laira]: I had one follow up to the question Adrija asked you. You mentioned genetic markers for deciding whether or not to treat with DBS. I was wondering how does your role typically interact with genetic pathologists or even like how is your data set of biomarkers increasing for Parkinson's? At least when I've looked into specific genetic markers for disease, it's often very small subgroups of people being tested and it's very hard to get a breadth and diversity of people and their genetic markers. How has this kind of been a factor in Parkinson's research moving forward?***

[Dr. Moore]: Yeah, so there's a lot to unpack there. I would say that clinically speaking for Parkinson's disease, genetics has little clinical implication right now.

I think it's helpful for some patients to say, I have this gene, but really that is in the research space. And that comes in two ways. One is when you find a genetic cause of a disease, right? So we're talking about a phenomenon like a phenotype here, right? So Parkinson's is many, many diseases.

It really is because there's different genes involved, there's different chemical exposures involved. And so there are small groups of people where in a family, they all get it in their 30s. Everybody has it. It has a particular flavor to it and it's caused by a specific gene, right?

And so we can use that information, use that gene to say, well, what does that gene affect at the cellular level? And how can that help us explain how Parkinson's is caused in everybody with this phenotype?

So there's that stuff. And that's where you see PARK2, PRKN, and some of these other smaller families and scientists get really excited when they find a family and they build a career off these people.

The other side is for us to understand at a population level what's happening with Parkinson's disease. I'm going to use Parkinson's here because it is different from Huntington's, where you have the gene, you have the disease. If you don't have the gene, you don't have the disease.

These are variable levels of penetrance, right? Which means I can have the gene and never get Parkinson's. And certainly you could have Parkinson's and not have any of these genes.

And so at the translational research point now, what they're typically looking at is the two most common genes involved in Parkinson's, which is GBA and LRRK2. LRRK2 research has been the most successful so far. And so I can see at some point saying, hey, we're going to test you for these genes because you might be able to participate in this clinical trial or have this medication accessible to you that's not accessible to other people. And that's certainly the way it is in a number of diseases.

Right now, the way genetic testing occurs is I can certainly order you a very expensive panel or series of panels, but the Parkinson Foundation is currently conducting a trial called PD generation. It's either a blood test or a swab to test for the seven most common genes involved in Parkinson's disease. They have genetic counselors both in English and Spanish, I believe some other languages. Their goal is to try to get a better sense of what's the genetic profile of people with Parkinson's across the globe, mostly in the United States. But you're right, most of the studies have been in the Ashkenazi Jewish population and various groups within the country where there are researchers already in that space and a genetically isolated people group. And so that's already ongoing and that work is there and can expand in Parkinson's pretty easily.

But it's very hard to get a genetic counselor. Like maybe a health system will have one.

They're mostly like in the pediatric side and understanding if you're at risk for having a baby with Tay-Sachs. What does that mean? Right. And so in the Huntington's disease space, ideally you have a genetic counselor that's part of your team. But it's not always the case. And we sort of play one on TV and try to do what we can. Fortunately, with Huntington's disease, it's one gene, one disease. So it doesn't get too terribly complicated, but I am often testing patients with an HD-like disease for other things if their HD test is negative.

2.7. ***[Leyla]: Going off of what you believe contributes to the cause of Parkinson's is environmental factors. I recently got really interested in the gut microbiome and how that plays a role. And from speaking to Mrs. Cummings, she mentioned how many patients have come in complaining of GI issues and constipation. How many of them might have some leaky gut or something penetrating their intestinal barrier?***

[Dr. Moore]:
Right. So the evidence is longstanding and very strong for both prodromal gut symptoms in patients with PD and disruption of the biosphere there as well as very longstanding evidence about environmental exposures.

Relating to environmental exposures is Camp Lejeune and Agent Orange. And there's a lot of work that's gone on that shows that in specific populations with specific exposures, as well as in specific regions of the country that there are much higher rates of Parkinson's that's not otherwise able to be explained.

So like Michael J. Fox, who was like the sort of public spokesperson for Parkinson's says, and I don't love this analogy, but he says this, that the genes load the gun and the environment fires the gun when you're talking about Parkinson's. I don't love gun analogies, but there you go.

Again, not like Huntington's, one gene, one disease. This is a conglomerate of things. And we see this often in our patients. So we'll have a number of them that present with a certain flavor and others that present in a different way.

The gut association was described many, many years ago by Brock thinking about Parkinson's. And so many people come in with decades of constipation. The current research in this space says, yeah, there's clearly a difference between people who have Parkinson's and those who don't with their gut flora, and you may have heard of fecal transplants, which thankfully you don't take it by mouth. It goes all the way down to the stomach and someone else's fecal material is put in you to help balance out your flora.

But where the space is right now is at some point we're going to be saying, take this probiotic, that prebiotic, what have you, but it's not quite there yet. So if patients are saying, should I take this? Well, if it helps your constipation, yeah.

But in terms of managing your Parkinson's, we can't say that. The world experts in this space say, we're not to the point to tell you which bacteria can be helpful. And in fact, a probiotic may be harmful if it somehow increases the other bacteria.
And in fact, if you say, all right, in someone with Parkinson's, this bacteria is low, this bacteria is high.So I need a supplement that does this. Well, that's like saying, you know, we need less lions in the Sahara and more giraffes. You're messing with a bigger system than you realize. And so you have to be really careful with that.

We can't go off like trends and feelings. We're scientists.

2.8. ***[Adrija]: I had another question about deep brain stimulation again. You were talking about how you had to look for certain patients that you think that the treatment would work the best in or ideal candidates. How exactly is it that you go about determining who would benefit the most?***

[Dr. Moore]: Yeah, so this has been very well described in the literature in terms of thinking about who we implant. So number one, you have to have the right diagnosis, right?

Number two, the goals have to be aligned. So if the person says, my left toe hurts, I want DBS, we may do DBS for other reasons, but that's not going to align with what you're trying to get here.

Right. And so I was saying before about how interdisciplinary teamwork is so important because I do DBS all the time. This is the person's one and only time they're going to do it. It's very complicated and overwhelming. And so you have to make sure that what you're hearing, what they want. Is it possible and aligned?

The other thing is you have to think about what are the potential harms I'm going to cause this patient. And that's true for anything you do as a physician, right? And so the things that I'm particularly looking at is, is this patient, number one, a surgical candidate?

This isn't major surgery, but it sort of is too, right? And so making sure that they're going to tolerate that, they're not on blood thinners that they can't come off. They don't have a horrible lung disease. They are able to be awake and laying flat for multiple hours with their head kind of stuck to the board, those things.

And then the other part is if they have cognitive issues, implanting this device may accelerate that. Less important, but part of what we think about is swallowing problems and balance problems that can be worsened by it.

I think the other thing too, for me, is that there has to be ethical reasons for putting this device into somebody's brain. Do I think their specific symptoms are going to improve or not? And is this too early, too late? And that's sort of the art of medicine

And thinking about candidacy for surgeries. I will say I think DBS is under offered for women and people of color and that's something that is being worked on certainly at our institution and at the global level from the Parkinson's Foundation. I think I want to just take a minute to emphasize that. It's certainly not about race or gender. We want to make sure that those people are getting offered those procedures.

Certainly walking them through if they'd be a candidate, it's frightening for many people of any background, but that's a huge part of it.

2.9. ***[Navya]: I know that you've led an international lecture series on movement disorders, and I thought that that was very, very impressive. What are the biggest gaps in current training for future neurologists that you've seen when it comes to understanding the basics of movement and cognitive disorders?***

[Dr. Moore]: Yeah. So good question. I think two things. Speaking first to someone going through their neurology residency in the United States. This is changing, but most programs are very inpatient heavy. And we won't get into the medical, legal, financial aspects of that, but the residents are not really in the outpatient setting that much. And so it's been well recognized that the outpatient exposure that residents have is not as strong as we would like it.

And someone in the hospital with Parkinson's looks very different from someone in the outpatient setting with Parkinson's and their care is very different.

So that's something that we as a group of movement disorder doctors around the country and the world have really worked on. From a national perspective, let's talk about North America. There are about 50 Movement Disorders fellows trained in North America every year. This varies. It depends on how many people are interested. So it's somewhere between 30 and 80. And you think about

And in this country, there's about 1.2 million people with Parkinson's in the United States. That's not enough neurologists for Parkinson's, ticks, Huntington's, dystonia, tremors, everything, right? So training people and increasing the number is important.

But the fellowship training is not regulated. Residency is, fellowship is not. There are clear pros and cons to that, right? So I'm able to offer at my center for my fellows extensive training in the operating room for DBS and ultrasound procedure, et cetera. And not every place is going to have that. And so if I say, well, only people that have DBS can train people, that's going to limit the number of trainees.

But how do we regulate that? There's some sort of like, let's call it a code of honor. And we have sort of recommendations that come to us from the movement disorder society, but they're at this point in time with the field of movement disorders being about 50 years old. So it's a baby field.

Internationally. In the continent of Africa there is about one neurologist for 2 million people. I've spoken to my African colleagues about this, they're dealing with cultural things like, if you have Parkinson's, some believe you've done some evil deed, you know, like all of this stuff that goes on and not to mention the resources that they have. So I've had patients that have moved from the United States back to Kenya or the Ivory Coast. And they maybe can buy something called Sinemet, but is it Sinemet? And it's all out of pocket. So the care is very, very different.

So one of the goals of the series is to you know with the North American trainees, you're going to get top world experts in every little field, whereas in your home institution, you may have five people you're working with if you're lucky and they're not going to, A, have time to give lectures, B, be good at lectures, or C, they have sub expertise in all these areas.

But on a global scale to say to our friends and colleagues around the world, whether that be Malaysia, Australia, Africa, what have you, this is what we're doing here are some fundamental things to consider.

We're keenly aware of the disparities that are there. But if I've got a lecture series that's going out to 100 North Americans, why not give everybody else the Zoom link? I think that's where we are.

It's a very complicated issue.

2.10. ***[Leyla]: What do you think the greatest barrier within neurodegenerative care is?***

[Dr. Moore]: Yeah. Diagnosis. Diagnosis especially with atypical diseases takes years to get the diagnosis.

These are complex diseases, right? They can present in non-movement sort of ways, constipation, low blood pressure, sexual dysfunction, all different kinds of things. And so it takes number one, that somebody in the community goes, this is neurologic. You need to see a neurologist.

And then maybe you see a general neurologist who's like, this is in the movement family. We're going to treat it like Parkinson's. So then maybe I'm going to send you to a movement specialist.

The patient has been told eight different things by the time they come to see me and now this strange lady is telling him they have a terminal illness.

Two, and this is very fresh in my mind, we're trying to enroll patients in this progressive supernuclear palsy study. In order to enroll in the study, people have to be ambulatory. They have to be able to walk. Well, by the time they get to us, they're not walking.

Diagnosis, diagnosis. So this goes back to the whole early detection thing. If I can say, here's a blood test. Done, right? You get a brain scan and this program reads it and tells me if you should see a neurologist or not.

Done, right? So that would expedite things. And, you know, a lot of the referrals I get are not a movement disorder at all. And that's a space that could have been used by somebody else. So that access to care and getting the right diagnosis is a huge thing.

Because it affects not only that individual patient and family, but it has larger implications on research and how we move the field forward.

3. Discussion of Research Projects with Dr. Moore

[Laira]: Okay, so why don't we just kind of go in order and give a little synopsis of your research project and maybe Dr. Moore can ask you some questions or just have a conversation about your ideas.

[Leyla]: I wanted to see how introducing a probiotic treatment, a mixed probiotic treatment to be specific. I didn't isolate a strain or anything. How that would influence the motility, the lifespan, and the aggregation of alpha-synuclein within *C. elegans*. Which were my model organisms. It was a nice preliminary experiment because I could see how these aggregates diminished, if at all. And they were promising results in the sense that, yes, these probiotics did have some positive effect, although we can't make any definite conclusions with this research. We can say that it did overall have a more positive effect compared to the control whether that be reducing the alpha-synuclein aggregation, promoting vitality and reproduction, and also just increasing the thrashing behavior of the worms. My research ended up changing a lot because I did not want to go with the gut microbiome in the beginning but here I am, and I'm actually kind of glad because it shows that, you know, it's great to have accessible treatments as well for people who don't really have access to certain medications and surgeries.

[Dr. Moore]: Absolutely. How did you find it working with *C. elegans*? Did you enjoy it or was it gross or what?
What did you think?

[Leyla]: So Adrija and I both worked with them and we can say that they've been a hassle But there was definitely a learning curve working with them especially because you know, you have to work with so many, for the replicates in my experiment

But overall, I would definitely want to continue researching with *C. elegans* and then move on to mice because they actually have more complex digestive systems than *C. elegans*. *C. elegans* is just your intestine and then your anus. They don't even have stomachs.

[Dr. Moore]: And that brings up a great point about how we think about a model for disease.

Right. Versus a patient in the clinic with me. Like say you go home for the spring break and a cousin says, well, uncle so-and-so has Parkinson's.

Should he start a probiotic? What do you tell them?

[Leyla]: Honestly, I'd say that it wouldn't hurt but I was presenting my research at a science fair and one judge mentioned that one of their family members suffered from

Parkinson's. They were put on these probiotics as well as antibiotics. And then some infection ended up developing and they ended up potentially passing away from that infection, which was concerning but I guess it's just a matter of that balance because the antibiotics could have wiped out a bunch of good bacteria. And then it's a matter of whether probiotics actually contributed to actually helping restore that balance.

[Dr. Moore]: Yeah, I have to say that makes… That does not make clinical sense to me.

At all. But what I will tell you is… where I did my residency, we were not allowed to let patients continue their probiotics in the hospital. And I asked around to find out why. And this, I think, is very interesting, just a thought, you know, as we think about stuff that is not FDA regulated.

Supplements that we see in the store and how we counsel our patients about them, right?

So this is a bit of an extreme story, but there was a child getting a bone marrow transplant in this hospital. And so he had no immune system. He became septic. So he had bacteria in his blood. We couldn't figure out what it was. Unfortunately, the child passed and they were able to isolate the bacteria and discover that it's not something that's just roaming around in the world. That it was from one of these pills, one of these probiotics.

So natural, you know, cyanide and, um, arsenic are natural, so just be careful.

[Leyla]: That's good to know.

[Dr. Moore]: How do you think the research project and what you worked on is going to impact what you think about doing and are doing in the future? As you move forward to graduation.

[Leyla]: Yeah, so I was looking into some labs at Duke and there's this lab that has really interesting research with neuropsychology and gut microbiome I heard about on the Huberman Lab podcast.

I'm interested in looking into that and potentially deviating a bit from Parkinson's and looking into some of the other ways that our gut microbiome can influence our mental health and also behavior.

[Dr. Moore]: Yeah. And just the idea that there are more cells in your body that aren't you than cells that are you. That's weird. I'm sorry. That's just weird. Super. Well, I encourage you all as you think about moving to the next step, don't be afraid to cold call, cold email these labs.

They will have work for you to do, I promise, okay?
It's a tough time in research right now, as you may have seen on the news, but I think If you're waiting for somebody to call you, it's not going to happen. So call around. Don't be shy. The worst they can tell you is no. That's how I got my first lab job.

This is way off topic now, but I think you all are very well prepared just for being in the college environment. Everybody else is figuring out how to have a roommate and laundry and all that nonsense.

And so you can hit the ground running in a way that your classmates at college may not be able to.

Make sure you're doing okay in that environment and your grades before you start taking on a whole bunch of extra. That's just a pro tip.

[Laira]: Okay, Adrija, do you want to give your synopsis?

[Adrija]: Sure. So like Leyla said, I also worked with C. Elegans and I also researched Parkinson's disease specifically. I came across this article where some researchers took the structure of the alpha-synuclein protein and they did a computational study where they used an electric field to denature the protein. And so I wanted to know if this is a viable form of degradation of the protein in a model organism. So I used C. Elegans and I exposed them to an electric field and essentially tried to see if there was any decrease in the amount of protein in the worm. And also with that, in terms of motor dysfunction, seeing if there would be a benefit or I guess an increase in their neuromuscular function in terms of thrashing assays and velocity.

[Dr. Moore]: And you measure total protein or did you measure alpha-synuclein? Very good.

[Adrija]: Alpha-synuclein.

[Dr. Moore]: I'll be honest, I've not heard of that study, there are thousands of papers about Parkinson's released every day.

[Adrija]: Yeah, this is kind of why I kept asking questions about deep brain stimulation like. Right now, it's a relatively invasive technique. For potential applications of my research, some form of surgery I mean, obviously like *C. elegans* to humans is a huge jump that should not be made, but like in terms of, I guess the general idea of maybe more of like an outside exposure rather than like a direct, internal, invasive procedure.

[Dr. Moore]: Yeah. The questions that come to my mind, and I'm not expecting you to answer these, but the things that I think about hearing that is.

Well, how is it specific to alpha-synuclein is it? Is it specific to the different forms of alpha-synuclein versus its aggregated form, or phosphorylated form?

And… always thinking about down the road, and this is something that we in the last few have taken on, where patients and patient families are involved in research and research planning far earlier on rather than just like, here's this medicine we made. You may now take it.

And I think even if you said to me here's how this works. The branding around that would have to be really specific.

Because people are already spooked by EMF and all this other stuff. And there's no evidence that intense cell phone use makes you less likely to get Parkinson's.

One of the challenges in research is where you end up, right? Are you a basic researcher where I'm just learning how this process works? Versus translational, where my goal is to bring it from the basic lab, like this fact that we know about alpha-synucleins, and how do I bring it to patient care And so when you're in that translational space.

You have to be thinking about, is this something that is going to work? Like if you say, oh, I have a cure for left hand tremor is to take off your left hand. Great. It cures left hand tremor.

But no one, well nearly no one, is going to sign up for that.

So it's just something to think about as you're doing research. I think you shouldn't be afraid to try different things. But quite frankly, the funding agencies are going to help you with that by saying like, no, we don't think that's going to move anywhere. This is more where a whole bunch of brains in a room think and say, I think we need to move it in this direction.

Now, there are external procedures that are not medical. Are not pharmaceuticals. So there is high intensity focused ultrasound, it does cause a permanent change in the brain.

There's also TMS, right? And so there's been some, I think just this week, a release about a portable TMS device. And TMS is used for depression and all this. We're exploring it at our Center for Dystonia and a number of other things.

So it's not to discount external electromagnetic stuff, but I think we'd have to really think about how that works and what that does.

The other thing is when you're reading about Parkinson's, what you learn is alpha-synuclein, Lewy bodies, yada, yada. There's actually a really big argument going on for many years in space as to whether or not alpha-synuclein is the cause or the effect.

So we don't really know. They think it's the cause, but there are people with Parkinson's who have no alpha-synuclein.

And so it's really challenging to know where this is going to end up. And I think when you're thinking about research, whether it's basic, translational, pharmaceuticals, whatever, things happen in parallel and not everything pans out the way you hope it will.

But it's a really cool idea. I mean, I think there are plenty of my patients who would jump into a human-sized microwave to get rid of their Parkinson's for sure.

It sounds to me like Adrija, that you might be an engineer in the making.

What do you say?

[Adrija]: I think the interdisciplinariness of neuroscience is what really draws me to it. I don't necessarily think that I want to go the engineering route. That being said.

Especially this past year, doing research has made me really interested and more aware, I guess, of some of the relationships between biology and physics and the blend between the two of them. So I definitely want to study biophysics a lot more, but I think I'm also interested in more of the clinical side of medicine and applying some of the things that those engineers might end up making or doing.

[Dr. Moore]: Well, we definitely all work together, right? Some of these people overlap and so they have degrees in both and that's a very interesting place to be in. But I would at least make friends with some engineers. I certainly have over the years, more after college than during.

They're really cool people in helping us figure out how we do this adaptive DBS? How do we do a closed loop?

And then they come and teach us like, here are the buttons you press to make this happen. It's very collaborative in the neuromodulation space.

Very good. Well, when you get your Nobel Prize for microwaving Parkinson's, I will fly to Europe and wave my pom pom. I think it's a cool idea.

[Adrija]: Thank you.

[Nayva]: Okay, so my independent study isn't necessarily in the Parkinson's route, but it's about Alzheimer's. And what my group is doing is potato beetles produce a certain toxin called leptinotarsin and that toxin is associated with increasing your levels of acetylcholine in the body. So we're trying to see if we can take the leptinotarsin and turn off certain parts of the toxin so that we remove the toxic part of it.

Can we essentially mitigate the symptoms of Alzheimer's? And we're studying this using *C. elegans* with Alzheimer's. And my independent study is starting in the fall of this year, and I would really love your input on the direction I can go, the things I can keep in mind.

[Dr. Moore]: I will remind you all that I'm a clinician.

Let me see. So I definitely understand that you're talking about symptomatic management here and mitigating neurotransmitters after the fact.

And what I think about when I think about something like gene targeting or cellular targeting, and we're using a virus or a toxin or whatever, you have to be really careful about how am I taking out the toxin part?

And what am I adding in, you know. I think that's one of the big challenges with any of these gene therapies or what have you is making sure that you're targeting the right cell and the right and the right parts of the body. So I think that would be a big challenge which is way outside my scope of practice in terms of thinking about toxins.

But sometimes movement disorders share medicine with Alzheimer's. I'll say to my patients, look, here's the memory medicines that we borrow from Alzheimer's.

They don't really work all that great. So I think that would be an amazing space to be in.

Because unfortunately, like I was saying, everybody's goal is, how do we reverse this? How do we stop it?

But I think the reality is that if and when we can get disease modifying treatments for these there's still going to be some level of symptomatic management that's going to be needed.

[Navya]: That was very insightful. Thank you so much.

[Dr. Moore]: I'm happy you all are using *C. elegans*. When I was in school in Durham, my hall was sort of adjacent to the biology floor.

And you could always tell when it was like Drosophila season because they would escape. So I got really good at your age at killing fruit flies.

It's a special skill on my CV from Science and Math.

Killing fruit flies.

[Leyla]:
No, they still escape at our school. We find them everywhere.

[Laira]: Thank you. If anybody else has any lasting questions, feel free to.

[Leyla]: This is just one really quick question, but as an undergraduate student, like I know you mentioned earlier to get immersed in research early on, would you give any other advice for someone hoping to pursue that field of medicine?

[Dr. Moore]: I will tell you what I heard from a good friend of mine who's on the School of Medicine Admissions Committee.

And he's a lovely person. He lives on the freshman campus here. In his 60s with his wife, who's a geriatrician. It blows my mind, but there you go. He said you know your first year, put your head down, get the work done. It's those classes that are like, you just got to do basic bio, you got to do calculus, stuff that you have done for the past two years.

It's just in a different space. They may not be the most interested in your learning the way you're blessed to have right now. Right. And so that's it. It's challenging. It's not going to not be challenging, but focus on that.

Get your feet under you. Start to explore things in your sophomore year. By all means, call the lab in your freshman year, but like really getting into it and all of that in sophomore year, really exploring things.

Try new things. And then by the time you hit your junior year, it's really focusing on certain projects and the story that you're going to tell.
That can go on into senior year if you're going to take time apart from your education to do various things.

But the story that you're going to tell and a clear understanding of what career you want to pursue.

I know that this is changing in terms of shadowing, but I think now, this new show, The Pitt, is really good. But most doctor shows are not accurate. There's no real way of knowing what it's like without seeing it yourself. And if you were going to commit yourself to a lot of hard work. Cognitively, emotionally, physically hard work. I strongly encourage you to shadow in various areas. The undergraduates that come and shadow me, they're not there to learn medicine and science. They're there to see what Dr. Moore does on a Wednesday and what does that look like? So see that for yourself so that when you apply and they say, why do you want to be a doctor?

You have your reasons. And not just sort of, I think it's cool. I watched Grey's Anatomy. That's not going to work.

So anyway, those would be the things I would think about, but have fun, you know. Get out, get some sunshine. Play some pickleball, do something fun too.

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