Episode 16: A noninvasive approach to improving motor function in people with SCI

HOST, SHARON PARMET:

Welcome to Inside the OUTcomes: A Rehabilitation Research Podcast from the Center for Rehabilitation Outcomes Research at Shirley Ryan AbilityLab.

Today my guest is Monica Perez, PT, PhD, the scientific chair of the Harris Family Foundation Arms + Hands Lab at Shirley Ryan AbilityLab and an internationally-recognized researcher in spinal cord injury.

Some of Dr. Perez’s research focuses on the use of neurostimulation together with physical therapy to provide lasting functional improvements in people with spinal cord injury.

Welcome to the podcast, Dr. Perez.

DR. MONICA PEREZ:

Thank you, Sharon. It is wonderful to be able to share our experience with you.

SHARON:

Tell us what happens to someone when they sustain a spinal cord injury. What happens to the nerves and what are some of the problems that arise from that?

DR. PEREZ:

Yes, the outcome from spinal cord injury really depends on the level of the injury and the severity of the injury. For example, spinal cord injury can be affecting the cervical spinal cord and depending on the severity of the injury, you can have more or less voluntary deficits in functions of your arms and also functions of your legs. So if you have a thoracic injury, depending on the level of the thoracic injury, also the deficit, meaning your upper limb function will not be affected by the injury but the lower limb muscles and your trunk control will be much more affected. So, there are two factors that are very important for spinal cord injury for the outcomes – the level of the injury and the severity of the injury.

So basically, what we try to do is to understand the connections that are still available after the injury in humans in the sub-acute phase soon after the injury, or more in the chronic phase after spinal cord injury.

SHARON:

So can you talk a little bit about your neurostimulation research, and how it’s changed over time and bring us up to speed?

DR. PEREZ:

Yes. So we started… this is a protocol we used for the first time in humans with spinal cord injury in 2012, when we were at the University of Pittsburgh. So it started as a proof of principle. We try to aim to get to the spinal cord by stimulating descending motor axons noninvasively, and also activating, or stimulating motor neurons noninvasively at the level of the peripheral nerve. So when we time action potentials properly, we can actually potentiate activation of spinal cord excitability. And we make those estimations based on electrophysiology. So we published a series of proof of principle studies where we demonstrate the mechanism of this plasticity and that it was possible to elicit upper limb muscles and lower limb muscles and then we moved to randomized placebo-controlled clinical trials. At the moment, we have published two placebo-controlled clinical trials in humans with chronic incomplete, but severe, spinal cord

injury where we use the neurostimulation. It depends on the protocol – we have used it for 30 minutes, or almost an hour, and then that is followed up by exercise rehabilitation conventional physical therapy.

We have published the effect of 10 sessions, 20 sessions, 40 sessions, and we have shown that the dose of the stimulation, in terms of the number of sessions is quite important for functional outcomes. SO we have been spending several years optimizing this neurostimulation protocol.

SHARON:

Can you talk a little bit more about the neurostimulation itself? What is the purpose of it? What is going on that you’re … is there a kind of a gap in the nerve that you’re trying to overcome?

DR. PEREZ:

Yes. So, after spinal cord injury, most spinal cord injuries in humans are anatomically incomplete, so we have residual axons that make synaptic connections with spinal motor neurons, directly or indirectly. And we aim with this protocol to strengthen that connection. We aim to strengthen synaptic activity. And we have a little bit of evidence, based on electrophysiological outcomes, that we can do this non-invasively in humans.

So we think that in many patients, those connections are there but they are weak. SO with our neurostimulation, we target those synaptic connections in the spinal cord and we try to make it stronger for functional restoration.

SHARON:

And with your protocol, the neurostimulation is delivered through a patch on the skin – is that correct?

DR. PEREZ:

Yes, that’s correct. So we select very specific places, so we are going to peripheral nerves, and we stimulate peripheral nerves on the surface of the skin, so we don’t go to the muscle, we go to a nerve. And with that, we try to activate more effectively, motor axons. And we also go to descending motor axons from the primary motor cortex on the surface electrically with currents that pass through the spine to get to descending motor axons.

SHARON:

So as patients are undergoing the neurostimulation, it goes on for different lengths of time. You’ve published on different time periods. What is the purpose of doing it over and over again? The connections are being strengthened as more neurostimulation is applied?

DR. PEREZ:

Yes, so when we conducted the proof of principal studies, we demonstrated that we use this neurostimulation for 20, 30 minutes, 40 minutes, actually that increases excitability in the spinal cord and that synaptic connection and that is very important because this is when patients complete the exercise rehabilitation. So we stimulate for a period of time that causes an aftereffect in the spina cord, and we use that aftereffect to facilitate the effect of physical therapy. So we hopefully can have a synergistic effect, stronger effect of physical therapy compared to when we do the same exercise but without the preceding neurostimulation.

SHARON:

What are some of the outcomes you’ve seen with this technique?

DR. PEREZ:

So our primary outcome measurement, we have functional measurements, so for example, the 10 Meter Walk Test. There is a new publication that we submitted very, very recently where we combine this neurostimulation protocol also with a medication to try to even further accelerate recovery. Ans so out outcome measures have focused on locomotor output, including the 10 Meter Walk Test, the 6 Meter Walk Test, also grasping behaviors, so the ability to complete precise actions with your fingers. And we also use a lot of electrophysiology to understand the excitability of descending motor pathways before and after the protocol.

SHARON:

Have you had participants who have participated in your studies who essentially couldn’t really take a step, and after participating, could actually take steps?

DR. PEREZ:

Yes. SO especially the last publication, it was published in Annals of Neurology at the end of last year, three of the participants enrolled in that trial were not able to initiate a single step before the stimulation. And think about that – these are people with chronic injuries with extensive rehabilitation before. So if we do the comparison, before and after the protocol, they were able to move the legs with body weight support, or with a walker, but without the need of a physical therapist. So that was remarkable.

If you think about non-invasive stimulation, it is very targeted and targets multiple muscles simultaneously, could actually result in this strong functional restoration. We still have a long way to go. We are still working on making this protocol more powerful to accelerate recovery, but it’s really remarkable that with 40 sessions, actually you can move your leg without the assistance of one or two therapists in many cases.

SHARON: 8:37

I know that some of your results have shown that the neurostimulation combined with physical therapy, that improvement in motor function, grasping, or walking or moving the legs, last quite a while. Going forward, do you see the protocol might be used on an ongoing basis to maintain improvements? Where would it fit in to a patient’s ongoing therapy?

DR. PEREZ:

Our view is that at some point there could be some Centers of Excellence where patients would go to receive this very specialized protocol. And in our experience, patients come back to Shirley Ryan every six months to eight months for another dose of the stimulation. We call it a booster, so they can maintain the gains, but there is still a need to come once a year for the stimulation protocol.

So the vision is that at some point we would create Centers of Excellence throughout the country where patients would be able to go and receive this type of therapy and go home. Or even have a device that patients can take home and deliver the stimulation guided by the Center of Excellence and deliver that treatment at home.

SHARON:

Your research shows the effects last several months?

DR. PEREZ:

So the effects are six, nine months, between six and nine months and even a year they last. It’s not happening in every subject, but we have a good group of individuals who have prolonged functional restoration and we’re trying to

understand if these are more structural changes. Do they last more permanently? But the system seems to need exercise or some kind of input in order for these changes to become more permanent.

SHARON:

With the Centers of Excellence it sounds like you go in for a tune up?

DR. PEREZ:

Yes! We refer to it a s a booster. We took that terminology from COVID times. And I think it really is a booster. We are happy that people feel a difference and they want to come back for more, but our goal, of course, is that they don’t have to come back anymore. But we’re not there yet. But the fact that they recover some function and they are asking to come back and ask for more neurostimulation from us is quite an achievement because as you know, we don’t have an FDA approved treatment for spinal cord injury now. SO we are all looking for approaches that have benefits that last longer and longer periods of time for our patients.

SHARON:

So what are some next steps in your research? What are you looking at next?

DR. PEREZ:

So we continue to work in protocol optimization, we are focusing on using pharmacological agents at the moment that have a synergistic effect with our protocol. One of those agents is NAME OF AGENT HERE and this is a potassium blocker that works in transmission of axons and also in strengthening synaptic connections so because our protocol is aiming to enhance synaptic strength, we have a little bit of evidence that they could have a synergistic effect.

So the idea, is if you think about, to try to have our protocol has been effective in proving to some extent, functional restoration in individuals who have some connections and some voluntary control, and next step is to go to individuals who have much more severe injuries and have an impact at that level. So we are combining therapies. In spinal cord injury, we have good evidence that combinatorial approaches that target different aspects of the pathophysiology of spinal cord injury are likely to be more beneficial for humans, for humans with spinal cord injury, so this is what we are doing. We are combining medications with the neurostimulation and exercise. And I think it’s important to think about these improvements in performance are quite similar to what has been observed with invasive approaches. SO it’s remarkable. I want to emphasize the need for noninvasive approaches and the need to optimize these noninvasive approaches and to understand the results mechanistically and how to make this protocol stronger for functional restoration. So you might not need to go to an invasive approach.

Another possibility is to combine these approaches with cell therapies, with new scaffolds, so proteins that are working on regeneration. So we have ideas on how to combine the neurostimulation protocol that we have with those approaches to continue to further rehabilitation and actually have a synergistic effect between therapies. It’s important to not combine therapies for the idea of conducting combinatorial approaches, but I think you have a strong mechanistic approach and a strong hypothesis of why these therapies can help each other, and that’s the key that is very critical for making this protocol stronger and faster and resulting in better functional restoration outcomes for our patients.

SHARON:

So it sounds like there’s still a long, long road ahead of therapies to investigate that might work well with your existing protocol. And you mentioned that your neurostimulation is noninvasive, so with your neurostimulation protocol, it is delivered just through the skin as opposed to having to go inside and stimulate muscles or nerves directly. That’s right?

DR. PEREZ:

Yes, yes. This is noninvasive and I think that is what makes this therapy more attractive. And at the same time, through optimization, we have been able to get to similar levels of functional restoration as you can get with more invasive approaches.

So I think our next goal is to go to people with much more severe injuries, individuals with AAS A or B, that means motor complete. Many of them have residual connections but no voluntary movement at all. Move these therapies to sub-acute patient sooner. Very soon after they get their injury to understand if we can have an impact in those patients. SO there’s a lot to do, the results look very promising but we continue to work to have these therapies available to the majority of people and then to make it faster and stronger.

SHARON:

Is there anything else you want to add?

DR. PEREZ:

Learn about the trials, and learn about how you can participate. I think for researchers, it’s quite important. We need your cooperation and we need your input. And participation in these trials so hopefully we can help each other. We can help to develop better treatments, and we can help you if there is any effect in functional restoration.

SHARON:

Thank you so much, Dr. Perez, This is very exciting research and it seems like it’s just going to get better and better and we’re really looking forward to hearing about your results on a future episode.

DR. PEREZ:

Thanks, Sharon. It was wonderful. Thanks so much for the opportunity and to everyone who has listened to the podcast and let’s be in touch.

SHARON:

If you’re interested in learning about Dr. Perez’s research or joining her clinical trial or another clinical trial at Shirley Ryan AbilityLab, you can go to the Shirley Ryan AbilityLab homepage at s r a lab dot org and if you scroll down a little bit, you’ll come to a section called Clinical Trials and that’s where you can register for a clinical trial at the hospital.

This has been Inside the OUTcomes: A Rehabilitation Research Podcast. This podcast is supported by the national Institute on Disability, Independent Living and Rehabilitation Research. I’m your host, Sharon Parmet, signing off.