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Unmet Needs in Rehabilitation Research for Multiple Sclerosis

**Announcer:**
You're listening to *NeuroFrontiers* on ReachMD. On this episode, we'll hear from Professor Robert Motl, who's a Professor in the Department of Kinesiology and Nutrition with a secondary appointment in the Department of Rehabilitation Sciences at the University of Illinois Chicago. Today, he'll be discussing unmet needs in rehabilitation clinical trials for multiple sclerosis, which was the topic of his session at the ACTRIMS 2024 Forum.

Let's hear from him now.

**Professor Motl:**
So to me, the largest barrier in having more high-quality randomized control trials of rehabilitation in multiple sclerosis is that most researchers don't follow a stage of different research approaches. That is, most individuals jump into doing trials that try to establish the efficacy of an intervention before they even know whether or not delivering an intervention is feasible. And so one of the things that we're trying to advocate for is adopting the National Institutes of Aging and stage model for research where you start with a very basic level of research just trying to understand the components of the intervention that you might put together. And then once you figure out what those components of the intervention should be, then you dive into stage 1, which is really feasible. What does it take to do the research? Can I do the research? How do I deliver the intervention? All of those things that help us understand whether or not it's even acceptable to utilize a specific rehabilitation intervention.

Once you've demonstrated that you can do the intervention—recruit participants, deliver the program, measure outcomes, keep people involved—then you can move on into what we call stage 2 and stage 3. Stage 2 is establishing the efficacy of the intervention for improving a specific outcome in people with multiple sclerosis and demonstrating that there is more signal with the intervention in improving an outcome than there is noise, and then once that's established in a very controlled environment, like a research laboratory, then we suggest that people move to really real world settings where they establish the efficacy in environments that people typically might go to for rehabilitation, such as a gymnasium or a community center or even their house. And then if you can pass stage 0, 1, 2 and 3, then you can move on into effectiveness, where you show that your intervention for rehabilitation is better than the other alternative approaches that currently exist in the world. If you can get through stage 4, which is really a very strident level of research, then you can move to stage 5, which is trying to implement and put your intervention into practice. And so the question really is how do we make our interventions more powerful for improving outcomes in people with multiple sclerosis? And there are a number of things that we can do. One of the most important things, I think, is we need to reconceptualize the starting point for designing our interventions, and we've really been advocating for this new discovery paradigm where you start with single bouts of exercise and find out which single bout of exercise or combination of single bouts of exercise looks like it has the best stimulus properties. And once you identify that and discern the best approach, then you move it into randomized controlled trials as a training stimulus.

Some of the other things that we need to do a better job on in the rehabilitation literature is we need to make sure that we're focusing on specific outcomes within populations that demonstrate impairments or dysfunction in those outcomes. So the standard approach is we'll study the effects of exercise on fatigue and ten other outcomes and people who don't have fatigue or problems on those ten other outcomes. And then our trials show really small effects, and oftentimes they don't show effects on the variable that was of most interest, and so we're left with this body of literature of small effects in nontargeted populations, and we don't know whether or not we can actually use our rehabilitation interventions to treat a focal problem in a population of individuals who have that problem.

The last major point that I would make is that we need to do things that help to enhance people's adherence and compliance with our interventions, and the simple idea is if you can't get people to do the intervention in the first place, how do you study whether the intervention is effective? And

that's really the realm of adherence. And then secondly, we need to understand compliance. That is what percentage of what we're prescribing to individuals in rehabilitation are they actually doing? Because that helps us understand how much of an intervention people need to do to reap the benefits of that specific intervention. So those are some of the main problems that I see that we can do a better job in moving past.

**Announcer:**
That was Professor Robert Motl discussing the current unmet needs in rehabilitation clinical trials for MS. To access this episode and others in our series, visit *NeuroFrontiers* on ReachMD dot com, where you can Be Part of the Knowledge. Thanks for listening!