

On the treatment of Parkinson's disease—an interview with Prof. Nir Giladi

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Abstract

The article is an interview with Prof. Nir Giladi, Director of the Brain Department at Tel Aviv Sourasky Medical Center, conducted by Siyan Chen of the Department of Neurology, Shenzhen People's Hospital, on behalf of *Ag-ing Pathobiology and Therapeutics*.



Nir Giladi, PhD

Prof. Nir Giladi is the Yehezkel and Batya Sieratzki Chair in Neurology and Associate Dean at Tel Aviv Medical Center, Ichilov. He is a Professor of Neurology at the TAU Faculty of Medicine, Sagol School of Neuroscience, Tel Aviv University, Israel. His main areas of expertise are gait, parkinsonian gait, gait freezing, Parkinson's disease, genetics of Parkinson's disease, and precision medicine in Parkinson's disease. Nir Giladi is also the author or editor of more than 180 articles in medical journals. (<https://www.researchgate.net/profile/Nir-Giladi>)

Siyan Chen: Gait impairments are among the most common and disabling symptoms of Parkinson's disease, could

you please share some of your experiences in managing gait impairments?

Nir Giladi: Gait impairments in Parkinson can be separated to two basic types, the continuous and episodic ones. This is based on a paper I wrote several years ago. In that paper we described the difference between continuous, like walking slowly, short stride, stooped posture, balance problems. These are problems that are happening throughout the day and the work period. The other group is episodic. Phenomena that happen for a few seconds or sometimes even in a spite of a second, like freezing of gait, festination and dis-equilibrium. The continuous type of gait problems are easy to manage and patients are adjusting to the problem. The episodic ones happen all of a sudden and the patients cannot get prepared for them. As a result, they are very scary. And as you know, the most important complication of gait problems in Parkinson's disease is a fall.

Siyan Chen: Yes. Falling is the main problem, which leads the gait problem to one chief complaint of almost all Parkinson's patients. Most patients don't want to fall because of their fragile bones. However, current medication have limited efficacy in gait problem management. Can you share us some experiences in gait problem management? I also learned that neuromodulation may be effective in gait impairment treatment. Do you think this new neuromodulation therapy can be superior to the medication?

Nir Giladi: So when you compare neuromodulation to medications, you have to be more specific. First, there are many medications. Second, there are different types of neuromodulation. For example, medication includes levodopa or drugs that are affecting cognition, alertness, concentration, and split of attention. So these are different medications who have different purposes, and all of them may affect gait. In contrast, neuromodulation includes deep brain stimulation, tDCS, TMS, or even spinal cord stimulation. These are different modalities, some of which we have

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Received: 19 October 2023 / Accepted: 21 November 2023

Published: 26 December 2023

much experience and some of which we have little experience with. Some are commonly used in clinical practice and some are used only in research programs at the moment. So we have to be careful when we are comparing. I will refer patients to deep brain stimulation to improve gait only when their gait problems were responding to levodopa. For example, if one has response to freezing of gait, meaning that in spite of taking a good dose of levodopa, one freezes or even freezes more because of the levodopa. For this type of freezing gait, deep brain stimulation does not have any benefit. So deep brain stimulation is good for levodopa responsive gait features. The TMS and the tDCS have other features. In my opinion, this is still all very experimental and not really used in the clinical setting.

Siyon Chen: So you think the effect of TMS and the tDCS on PD is still not promising, right?

Nir Giladi: I didn't mean that their effects were not promising. What I said is that they haven't been proven by good clinical trials better than placebo.

Siyon Chen: But I noticed that you have conducted some clinical trials using both the drugs and the tDCS for PD, right? From your aspects, did you find out some good intervention strategies for PD gait management?

Nir Giladi: In the research setting, both tDCS and TMS have shown some beneficial effects, however it hasn't been implemented into long-term regular clinical practice, and I'm not sure if we have enough data to support it at the moment. So I am strongly in favor of having large scale clinical trials. But I'm not ready to promote tDCS and TMS as a treatment for purpose on patients in a regular clinical setting.

Siyon Chen: Okay, because I am also interested in TMS experiment. I was wondering when applying additional TMS or tDCS intervention with traditional medication on the PD patients, do multi-target stimulation be more beneficial than the single-target stimulation?

Nir Giladi: Absolutely.

Siyon Chen: We are exploring the therapeutic effects of neuroregulation and the corresponding stimulation targets,

but we are not sure whether single target stimulation or multi-target stimulation is better because we know that PD is actually a disease involving multiple neural circuits. So we think if we can target more than one neural network, the therapeutic effects might be better than just focusing on one. Do you have any experience with multi-target stimulation?

Nir Giladi: We have published several papers using multi-target approach and we have shown that it is better than single-target approach. We stimulated the prefrontal and primary motor cortex.

Siyon Chen: And another question is that we know that it is often difficult to distinguish late-stage Parkinson's disease from the Alzheimer's disease because they both present with the cognitive impairment and dyskinesia. So what's your opinion in detection of AD-related biomarkers in Parkinson's patients?

Nir Giladi: First of all, I think that this is your statement. I do not agree that it is difficult to distinguish advanced Parkinson's from advanced Alzheimer's. I think they are very different, but they are different in the way they have reached that point. If you see the patient at the end stage, the neural genetic process, when all the networks have already failed, it all looks very similar. They lie in bed, unable to function. But when you see how the disease is evolving, it's very different. And I think that the cognitive changes that we see in advanced Parkinson's are a mixture of the Alzheimer's changes and the Parkinson's components. But they are two different things. The similarities and the overlap are there, but clinically I think that it's quite easy to differentiate.

Siyon Chen: I know that in the early stage, Alzheimer's disease and Parkinson's disease are easy to distinguish. But in China, a developing country, many elderly people live alone far from their children in their ancestral homes, so they don't go to the hospital in the early stage of diseases. So when they come in the late stage, I find it difficult to differentiate. That's the reason why I raise this question. Thank you for your answer, Prof. Giladi. Thank you so much!

Nir Giladi: All right, thank you!