THE BACHMANN-STRAUSS
Dystonia & Parkinson Foundation, Inc.

Think Tank Focus: Interface Between Parkinson's Disease and Involuntary Movements

The ninth annual Think Tank on dystonia and Parkinson's disease brought together an international group of neurologists, geneticists, and pharmacologists to share their knowledge and clinical expertise during an intensive day in New York. The November 2010 event focused on the interface between dystonia and Parkinson's disease -- and how collaboration can help find effective treatments for both conditions.

Movement disorder specialists have long recognized that dystonia shares several features with Parkinson's disease. What is less clear is how lessons learned from one disorder can be applied to the other. One of The Bachmann-Strauss Foundation's focuses is on research projects that explore these overlaps. Think Tank participants discussed the commonalities and differences between the two disorders, and shared ideas on where future research should be directed.

Parkinson's disease and dystonia are disorders that can include motor and non-motor symptoms. Both conditions affect similar brain areas, with similarly disordered functions of the neurotransmitters dopamine and acetylcholine. Joel Perlmutter, MD, noted that about 40% of young onset Parkinsonism begins with dystonia. In addition, dystonia can be a side effect of Parkinson's disease treatments, specifically from levodopa, the gold standard drug for the condition. Conversely, some dystonia symptoms improve with levodopa, and levodopa can be used to treat certain subtypes of dystonia.

In addition to levodopa, other treatments have demonstrated benefits across both conditions. Botulinum Toxin, a drug specifically approved to treat certain forms of dystonia, has also been used off-label for Parkinson's symptoms. And the same drugs that act on dopaminergic receptors or block acetylcholine to treat Parkinson's disease are also used off-label in dystonia. Deep brain stimulation has also had great success.

The term "dystonia" refers to a number of disorders that affect different areas of the body and age groups, are linked to different genetic mutations, and produce different co-morbidities. For that reason, it may be unrealistic to expect a single drug treatment to work across the entire spectrum of the condition. "The management of people with dystonia has to be tailored to individual patients," said Kailash Bhatia, MD, DM, FRCP.

Dr. Kailash Bhatia, MD, DM, FRCP

Dopamine is part of the link that explains the overlap between Parkinson's disease and dystonia. Not only is it an effective treatment for individuals with dopa-responsive dystonia, but abnormal dopamine metabolism also plays a role in DYT-1 dystonia, the most common hereditary form of the condition.

While drugs that regulate dopamine and acetylcholine are a staple of dystonia treatment, large-scale, placebo-controlled, randomized clinical trials do not yet exist, Dr. Bhatia noted. Far more drug industry research has been focused on the field of Parkinson's disease, which has been perceived as a larger market with better-understood pharmaceutical targets. Jeffrey Conn, PhD, highlighted a number of drug candidates that are in development for Parkinson's disease and might also play a role in dystonia treatment. "As compounds such as these are developed for Parkinson's disease," Dr. Conn said, "the major question is whether they'll also work in dystonia. Once we have compounds in clinical development, it opens up the possibility of testing them."

In an open discussion, participants agreed that if drugs are developed that can reduce or prevent dyskinesia, they'll almost certainly be tested in dystonia. But questions remain: Are there certain patient populations that would benefit more than others? What criteria should be used to select a Parkinson's drug for further study in dystonia? And how should these agents ultimately be used alongside established treatments like Botulinum Toxin, which already shows good success in many patients?

Dr. Pisani, a co-chair of this event with Dr. Wichmann, challenged participants to consider a controversial statement: dystonia and dyskinesia are different and do not share common pathophysiologies. However, not every participant agreed. "Parkinson's and dystonia are two sides of a coin," said Mahlon DeLong, MD, who noted that the affected circuit is the same but the underlying mechanisms might not be.

Similarly, David Eidelberg, MD, noted that a treatment like deep brain stimulation provides "circuitry-specific modulation" and therefore has shown success across movement disorders. In the same way, drug compounds that address circuit-level dysfunction might work across Parkinson's disease and certain dystonia subtypes.

Participants acknowledged that it may take several more years for a truly targeted dystonia drug to emerge on the market – and highlighted areas for future research. There was consensus that more work is needed to better understand the steps that lead to dysfunction in dystonia as well as the exact role of dopamine. Animal models can then allow researchers to explore these targets to better piece together the biochemistry and genes involved, before these theories are tested in human trials. Participants also acknowledged that a number of pharmaceutical compounds might be needed to address all the different subtypes of dystonia. And, finally, once clinicians have a number of treatments at their disposal, comparative studies will help them choose the most appropriate therapies for their patients.

2010 THINK TANK PARTICIPANTS

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