

## Council briefed on Parkinson's premotor symptoms research

By Ernie Hood

At the Feb. 19-20 meeting of the NIEHS National Advisory Environmental Health Sciences Council, panel members were treated to a talk by [Honglei Chen, M.D., Ph.D.](#), head of the Aging and Neuroepidemiology Group.

Chen, who was recently awarded tenure (see [story](#)), updated the council on his group's research into the clinical implications of premotor symptoms in Parkinson's disease, and the potential for better understanding what causes the disease.

### Major disease, major unmet need

As Chen related, Parkinson's disease is the second most prevalent neurodegenerative disease after Alzheimer's, afflicting more than 1 percent of the U.S. elderly population at an annual cost of \$23 billion. Current therapies can help control symptoms, but there is no cure for Parkinson's, and no therapy to stop or even slow disease progression.

Parkinson's may develop over the course of decades, and by the time the motor symptoms appear allowing definitive diagnosis, it is too late for any effective intervention. Motor signs include slow physical movements, shaking, muscle stiffness, and impaired balance and coordination.

Thus, Chen focuses his research on the premotor, or prodromal, symptoms of Parkinson's, striving to answer the fundamental questions of when, where, and how Parkinson's disease starts.

"There is no dispute that the motor signs of Parkinson's are just the tip of the iceberg, and that patients suffer from a variety of very prominent nonmotor symptoms," Chen said. "These symptoms may precede the onset of Parkinson's motor signs by years. We call these the premotor symptoms of Parkinson's."

Identifying patients with premotor symptoms can give some indication of who will be at risk for Parkinson's and pinpoint a window of time when new interventions may work to prevent or delay full onset. This could also increase understanding of the early disease process of Parkinson's, which has been largely uncharted thus far. That is especially true for environmental risk factors, which are strongly suspected to combine with genetic risk factors to increase risk of Parkinson's and may be a point of therapeutic attack.

### Premotor symptoms appear much earlier

The most important premotor symptoms of Parkinson's may appear as early as 20 years prior to the onset of motor symptoms. They include loss of smell, rapid eye movement sleep behavior disorder, constipation, daytime sleepiness, depression, and anxiety. Chen emphasized that it is important to study the entire group of premotor symptoms, since individually they are often nonspecific.

"The key concept is not one single, particular symptom, but rather to look at multiple symptoms and future risk for Parkinson's," he said. In one unpublished case-control study Chen described, individuals with three of the six premotor symptoms were 31 times more likely to have Parkinson's than controls. That data also suggested a potential gender difference, with a stronger association in men than women.

According to Chen, in the past 10 years, substantial evidence has accumulated that premotor symptoms occur prior to diagnosis of Parkinson's. His work will continue and expand in the future.

"My overall approach will be to study the disease from the beginning to the end, trying to identify an intermediate phenotype that can help us identify high-risk populations," he said. "We particularly want to study what environmental factors can modify this process, from the high-risk population to final Parkinson's disease, and try to understand what environmental factors can give rise to these symptoms."



*"We've made a lot of progress in understanding the etiology of Parkinson's. We've learned of many genetic risk factors from recent GWAS studies, and we've also identified a number of nongenetic or environmental risk factors for Parkinson's," Chen noted in his remarks to the council. (Photo courtesy of Steve McCaw)*



*One of Chen's research methods is the Sniffin' Sticks smell test, in which participants are asked to smell and identify twelve common odors such as banana, coffee, rose, and fish. A score of 6 or less indicates anosmia, or loss of sense of smell, one of the premotor symptoms of Parkinson's disease. (Photo courtesy of Honglei Chen)*

(Ernie Hood is a contract writer with the NIEHS Office of Communications and Public Liaison.)

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