

## **Vagotomy: a clue to the pathogenesis of PD?**

**M. Lew, A Jocsos**

*Department of Neurology, Division of Movement Disorders, Keck/University of Southern California (USC) School of Medicine, USA*

Gastrointestinal dysfunction is a common prodromal non-motor symptom of Parkinson's disease. Studies reveal pathologic aggregates of GI tract  $\alpha$ -synuclein may exist many years prior to clinically evident PD. The Braack hypothesis entails that  $\alpha$ -synuclein pathology arises in the enteric nervous system and progresses retrograde to the CNS.  $\alpha$ -Synuclein fibrils have the capacity for antero- and retrograde transport along the vagus nerve, and aggregates have been detected in the dorsal motor nucleus of the vagus (DMV) in rats injected in the duodenum with  $\alpha$ -synuclein. Mice models with gastric exposure to rotenone showed  $\alpha$ -synuclein aggregation with secondary spread to the CNS. Hemivagotomy not only prevented abnormal protein accumulation in the DMV of these animals, but also prevented neuronal death in the ipsilateral SNpc. These models suggest that vagotomy may diminish a pathway of introduction for peripheral  $\alpha$ -synuclein transport and modify the risk/pathogenesis of PD. In Danish and Swedish cohorts, PD risk in truncal vagotomy patients versus the general population was lower compared to matched controls. Neither study, however, met statistical significance. The Swedish study reported a decrease in risk 20 years from vagotomy. The PD index rate for truncal vagotomy patients was statistically significantly lower after 20 years in the Danish study. Interestingly, for both studies, there was a higher risk for PD in selective vagotomy patients. Conflicting data clearly exist. This will fuel a lively debate regarding whether vagotomy modifies the pathogenesis and subsequent risk of developing PD.