Gene therapy and Subsequent Deep Brain Stimulation for Parkinson's Disease

Parkinson's disease (PD) is the second most common neurodegenerative disorder, projected to afflict 700,000 individuals by 2040 (Rossi et al., 2018). Several advanced therapies for PD directly target brain function via electrical stimulation or gene infusion. In this study, we conducted a retrospective analysis of PD patients that participated in a gene therapy trial using stereotactic injection of adeno associated viral (AAV)-mediated delivery of GAD (glutamic acid dehydrogenase). We focus on the subset of patients who did not benefit adequately from GAD gene therapy and subsequently underwent DBS (deep brain stimulation). The purpose of this study is to determine the outcomes of patients who initially had GAD treatment and subsequently underwent DBS.

Methods

In total, 11 patients from the GAD gene therapy study were included in our study. Five patients who received GAD treatment later underwent DBS, while 6 did not. Data from 3-, 6-, and 12-months post GAD and DBS surgery were collected. We measure the following outcomes: Motor scores (MDS-Unified Parkinson's Disease Rating Scale) and LEDD statistics (levodopa equivalent daily dose).

Results

Preliminary data analysis presents LEDD dose values and UPDRS scores for patients receiving GAD+DBS and patients who received GAD treatment only. Results show that mean patient LEDD dose values were significantly lower ($p<.05$) at 3- and 6-months post DBS, and UPDRS motor scores were significantly lower at 6 months post DBS. GAD-only patients did not show statistically significant decreases in LEDD dose values.

Conclusion

DBS is a highly effective treatment for the motor symptoms of PD but does not address disease progression. GAD gene therapy aims to address disease progression. As DBS and GAD gene therapy have individual benefits, positive outcomes in patients who received both treatment modalities suggest the treatments are compatible.

References

Rossi, A., Berger, K., Chen, H., Leslie, D., Mailman, R. B., & Huang, X. (2018). Projection of the prevalence of Parkinson's disease in the coming decades: Revisited. Movement Disorders, 33(1), 156-159. doi:10.1002/mds.27063