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

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Objective: The purpose of this study is to determine the outcomes of patients who received GAD gene therapy treatment and subsequently underwent DBS for Parkinson's Disease.

Background: Several therapies for Parkinson's disease (PD) target brain function via electrical stimulation or gene infusion. We conducted a retrospective analysis of PD patients that participated in a gene therapy trial via stereotactic injection of adeno associated viral (AAV)-mediated delivery of GAD (glutamic acid decarboxylase). We studied the outcomes of a subset of patients who did not benefit adequately from GAD gene therapy and subsequently underwent subthalamic nucleus (STN) deep brain stimulation (DBS).

Method: This study focuses on 4 patients from the gene therapy study who received GAD gene therapy and later underwent DBS. Data at baseline and at 3-, 6-, and 12-months post GAD and DBS were collected from this subset of patients. Analysis was performed in three conditions: pre surgical treatment (pretreatment), upon receiving GAD (post GAD), and upon subsequent DBS (post GAD+DBS). Potential effects were assessed via the MDS-Unified Parkinson's Disease Rating Scale Part III and levodopa equivalent daily dose (LEDD).

Results: ANOVA analysis of compressed time points for Pre-GAD and Post GAD+DBS of LEDD and UPDRS patient data were performed. Results yield significant differences between Pre-GAD and Post GAD+DBS for LEDD (p=.027) and UPDRS off medication (p=.079), but not UPDRS on medication (p=.414) scores. LEDD Dunn's post-hoc analysis found significant differences between Pre-GAD vs. Post GAD+DBS at 3- (p=.041), 6- (p=.06), and 12-month time points (p=.018). LEDD Dunn's post hoc analysis also revealed significant differences between Post GAD vs. Post GAD+DBS at the 12-month timepoint (p=.006). UPDRS on medication score Dunn's post hoc analysis found that there were significant differences between Post GAD 12 month vs. Post GAD+DBS at 6 (p=.041) and 12-month timepoints (p=.036).

Conclusion: The clinical effects of combining GAD gene therapy and DBS have not been fully assessed. In this subset of patients treated with GAD gene therapy and subsequent STN-DBS, UPDRS scores and LEDD scores show improvements after combined treatment compared to pretreatment baseline and to post GAD treatment measures. Positive outcomes in patients receiving both therapies suggest the treatments are compatible.

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