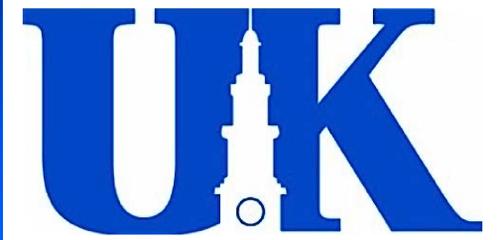


Effect of Combined Subthalamic and Nigral Stimulation on Gait and Postural stability in Parkinson's disease

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ABSTRACT

Objective: To objectively determine effects of combined STN and SNr stimulation on postural stability and gait in PD patients.

Study design: 8 PD patients, appropriately selected for DBS will be recruited. They will have significant gait and posture difficulties according to Unified Parkinsons disease rating scale (UPDRS). DBS electrodes will be placed in routine fashion with distal contact in SNr. Patients will be tested with stimulation off and STN on-stimulation at base line and then STN will be programmed to best results during first 4 months. At 4 months, testing will be done with on- STN and combined STN /SNr (via interleaving). Combined stimulation will be tried to best results for next 4 months. From 8-12 months, programming will be done using best setting. Standardized clinical testing for PD and gait including UPDRS, Timed sit, stand and walk test, Freezing of gait questionnaire, and Tinetti Performance oriented mobility assessment will be done during testing sessions to determine effect of different stimulation parameters.

Conclusion: We hypothesize that significant improvement in gait dysfunction and postural stability will be observed with combined STN and SNr stimulation as compared to STN stimulation alone.

BACKGROUND & HYPOTHESIS

•In addition to tremor, rigidity and bradykinesia, Parkinson's disease (PD) is frequently associated with gait difficulties and postural instability. Gait disorders include festination, reduced step length, start hesitation, and freezing, and postural instability leads to balance difficulties. Combined, these symptoms are responsible for the majority of falls in patients with PD.

•Levodopa therapy is effective for controlling the motor effects of PD, the therapeutic impact is sup-optimal for gait and postural difficulties. Deep brain stimulation (DBS) of subthalamic nucleus (STN) or Globus pallidus internus (GPI) in advanced forms of PD is similar to levodopa treatment in that it results in improvements in the segmental motor symptoms but does not have a significant effect on gait and posture problems.

• Stimulation of additional targets have shown promising results but most approaches require multiple electrodes and separate pulse generators which become impractical and expensive.

• One additional target, the SNr, is located just beneath STN and can be accessed during STN lead implantation by placing the most distal contact in SNr and still maintaining the more proximal contacts in STN.

•We aim to target SNr while placing STN leads and hypothesize that significant improvement will be observed with sombined nigral and STN stimulation.

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METHODS

• Eight PD Patients with gait and postural difficulties will be recruited from our UK Movement Disorders Clinic. These patients will be appropriate candidates for DBS as determined by a Movement Disorders neurologist and our DBS neurosurgeon.

•DBS electrodes will be placed in a routine fashion with the distal contact in the SNr.

• Routine STN stimulation will be achieved to best clinical effect in the initial post-operative period.

• Four months after surgery, patients will be tested with two different stimulation settings: (1) stimulation off and (2) on STN stimulation. At this point, interleaving stimulation delivery will be employed to stimulate the STN and SNr to best clinical benefit.

• At 8 months post surgery, participants will then be tested under 3 conditions. (1) stimulation off, (2) on STN stimulation only, and (3) interleaved STN and SNr stimulation.

• From 8 months to 12 months, participants will be programmed to best clinical outcome using best appropriate setting for individual.

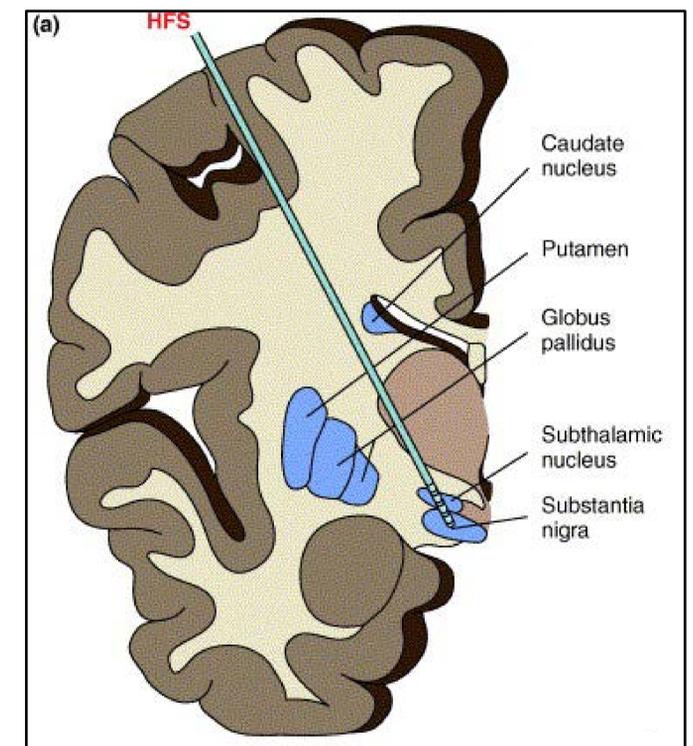
• At the end of 12 months, participants will then be evaluated again in the off setting as well as their best clinical stimulation parameter.

• Each setting will be made for 30 minutes before test administration. Patient will be advised to discontinue dopaminergic medications 12 hours before testing time.

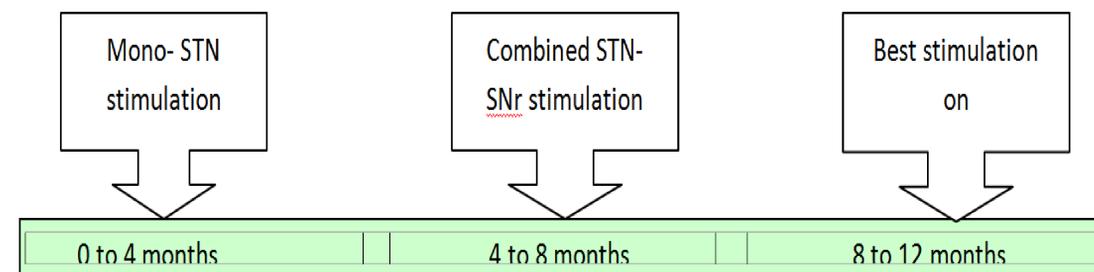
•Both patient and examining physician will be blinded to stimulation settings.

• Tests administered will include Unified Parkinsons Disease Rating Scale (UPDRS) part 3 (motor exam), axial subscales on UPDRS part 2 (items 13-15), Timed sit, stand and walk test, Freezing of gait questionnaire, and Tinetti Performance Oriented Mobility Assessment. Follow up examinations will be done after 2 weeks of constant stimulation of both STN alone and STN plus SNr during separate clinic visits.

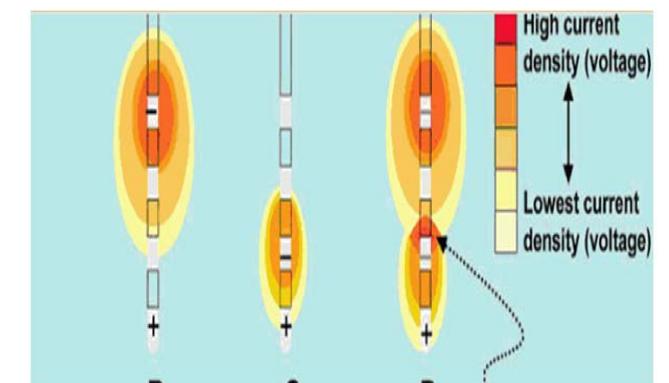
PROPOSED LEAD PLACEMENT



Timeline:



INTERLEAVED PULSES



CONCLUSION

Interleaved pulse delivery will allow to stimulation of both STN and SNr with different stimulation parameters. Our main objectives are to determine if stimulation of both targets can be accomplished safely and whether or not combined stimulation leads to greater improvement in gait compared to stimulation of the STN alone.