INTRODUCTION
Despite the success of levodopa-based treatment for Parkinson’s disease (PD), over time many patients develop disabling motor side effects. One alternative for these patients is deep brain stimulation (DBS), which has been shown to be effective for treating the motor symptoms of PD. However, DBS is not without its own side effects profile. In particular, a high prevalence of neuropsychological effects has been observed in this patient population. Hence a significant problem for these patients is the titration of stimulation parameters to provide symptomatic relief without neuropsychological effects. And because these effects may take days or weeks to present, patients who experience these side effects must have their stimulation parameters revised many times. We are addressing this problem by combining patient-specific computational modeling with a data bank of neuropsychological outcomes in PD and essential tremor (ET) patients. Preliminary results from a recently completed prospective study of motor outcomes indicates that the stimulation targets of DBS vary on a per-symptom basis in the region of the subthalamic nucleus (STN). This was determined by constructing a probabilistic atlas of clinical outcomes that were correlated with model-predicted volumes of activation. In the present study, we are using a similar methodology to determine whether stimulation-induced activation of brain regions is correlated with changes in cognitive and neuropsychological outcomes. The central hypothesis of this work is that cognitive and psychological outcomes in PD (DBS target: subthalamic nucleus STN) and ET (DBS target: ventral intermediate nucleus (VIM)) patients are correlated with stimulation-induced activation of specific brain regions.

OBJECTIVES
1. Create a probabilistic atlas of neuropsychological outcomes from DBS
2. Use neuropsychological evaluation and patient-specific computational models to identify regions that, when activated during DBS, result in statistically significant changes in clinical outcomes

NEUROPSYCHOLOGICAL EVALUATION
We tested two groups as detailed in Table 1. Each patient had a battery of pre-operative and post-operative neuropsychological tests which were administered to measure a range of cognitive functions including intellectual capacity, complex problem solving skills, processing speed, verbal fluency, word finding, spatial skills, and learning/memory. The tests are summarized in Table 2. The primary outcome measure for this study is the difference between pre- and post-operative neuropsychological scores or subscores for each test. T-tests (p<.05) were used to identify significant differences in pre- versus post-operative scores after patients were grouped by disease and stimulation target.

PROBABILISTIC ATLAS
We used a previously published method to predict the volume of tissue activated (VTA) during DBS on an individual patient basis. Pre- and post-operative images were coregistered each other and with an atlas brain. Hence, the electrode locations and VTAs for all patients were expressed in a common anatomical framework. Clinical scores for each test were assigned to each VTA for each patient at best therapeutic stimulation settings. Statistical analysis was performed on a per-voxel and per-test basis to identify regions where stimulation-induced activation was correlated with differences between pre- and post-operative neuropsychological test scores.

RESULTS
Parkinson’s Disease Group Statistics
PD patients who received STN stimulation showed significant test score differences for:
- Wechsler Abbreviated Scale of Intelligence: Vocabulary
- Wechsler Memory Test - III: Learning/Memory II
- Controlled Oral Word Association

Essential Tremor Group Statistics
ET patients receiving VIM stimulation showed significant test score differences for:
- Symbol Digit Modality Test
- Wisconsin Card Sorting Test: Perseverative Errors
- Total Errors

Probabilistic Atlas: Regions With Significant Pre-Post Neuropsychological Score Differences
All results are for PD except as noted. Red volumes indicate statistically significant activation regions for each test.

CONCLUSION
The group statistics for the PD and ET samples used in this study are consistent with recently reported neuropsychological patient outcomes in DBS patients. Changes in neuropsychological scores from pre- to post-operative testing could be attributed to potential possible sources: DBS; aging; changes in medication subsequent to DBS; progression of the disease. In this study we have assumed that these changes were primarily attributable to DBS, and used computational methods to determine regions where activation was significantly correlated with changes in test scores on a per-voxel and per-test basis. Many of the regions that showed significance were in the posterior portion of the STN, as well as ZI/H2 and thalamus. In addition, many overlapped with target regions for therapeutic DBS.

We recently started a prospective movement disorders database which is designed to examine these findings in a larger patient sample. Our goal is to use this information for pre-operative surgical targeting and post-operative stimulation parameter selection to minimize adverse outcomes for DBS patients.

REFERENCES