Longitudinal Change in Apathy Following Deep Brain Stimulation for Parkinson's Disease

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INTRODUCTION

Apathy, a mood symptom common in Parkinson's disease, causes lack of initiative/productivity, loss of energy, and emotional indifference. Mixed findings suggest that Deep Brain Stimulation (DBS) may lead to a worsening in apathy. To date, five studies report an average worsening of chronic apathy post-DBS and two studies do not show a change.

A major limitation is the lack of longitudinal data, with most studies comparing apathy once pre- and once post-surgery. Also, studies have not examined site or laterality because they were all bilateral STN.

We used latent growth curve modeling with longitudinal data to examine pre- and post-DBS trajectory of apathy after unilateral Subthalamic Nucleus (STN) or Globus Pallidus interna (GPi) DBS. We modeled apathy at pre-surgery, 2, 4, and 6 mo. post-surgery. We then tested predictors to examine individual differences in apathy trajectory.

Two current theories propose that apathy after DBS is due to: a) stimulation of non-motor circuits surrounding the STN, or b) reduction in levodopa medications (LED) after successful surgery. We sought to examine both of these theories.

HYPOTHESES:

1.Apathy will increase significantly and linearly after DBS.
2.Older age, increased disease severity, increased depression pre-surgery will predict a higher pre-surgical level of apathy and a steeper incline in apathy after DBS.
3.STN (vs. GPi) implantation and greater reduction in LED after surgery will be related to a steeper incline in apathy after DBS.

SUBJECTS

48 patients with idiopathic Parkinson's Disease (PD)

Age (yrs)	60.3 yrs (9.0)
Gender	36 M, 12 W; 75% male
Education	14.4 (2.8)
Yrs Symptoms	10.7 (4.8)
Pre-DBS UPDRS-motor	21.6 (7.8) on meds
Pre-DBS BDI-II score	9.2 (6.9), range 1-31
Site of implantation	15 GPi, 33 STN
Laterality	31 left, 17 right
Pre/Post LED	1029 units/1017 units

Patients were recruited from Movement Disorders Center, University of Florida. PD patients completed the Apathy Scale (AS) prior to surgery, and during their DBS programming neurology appointments.

Copies of this poster can be found at www.phhp.ufl.edu/cogneuro

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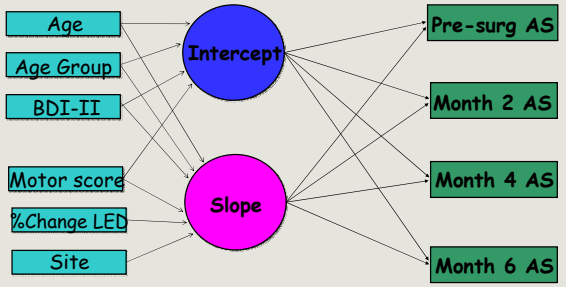
METHODS

NOTE:
Circles = factors
Boxes on left = predictors
Boxes on right = observed variables

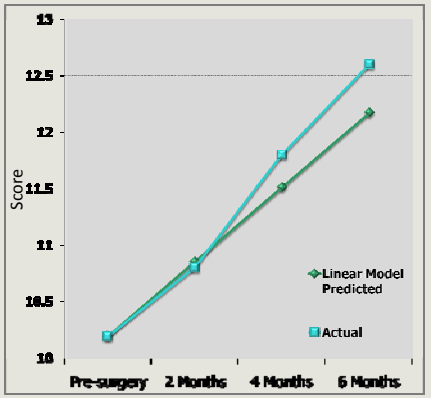
Path diagram: Intercept and Slope of Apathy after DBS



Latent growth curve modeling with AMOS 16 full maximum likelihood was used to describe the intercept and slope of apathy. Age Group ≥ 65 yrs and < 65, Motor score = pre-DBS UPDRS part III motor score, LED = Levodopa equivalent dosage, Site = STN or GPi.

RESULTS

Graph: Mean Apathy Scale Scores



Modeling Latent Growth:

Several unconditional models were tested. Linear growth best fit the data. Homogeneity of variance was relaxed. The unconditional linear model had a significant mean apathy intercept of 10.19 (p<.001) and significant mean apathy slope of rise of 0.66 points bimonthly (p = .014). See unconditional model fit indices below.

Predictors

There was significant variance in both intercept and slope factors; we added predictors to explain inter-individual differences. Age, older adult status (≥65 or not), pre-DBS BDI-II score, pre-DBS disease severity (UPDRS-motor) were added as predictors for intercept and slope. Site of implantation (STN vs. GPi) and percent change in l-dopa were predictors of slope. The conditional model fit the data well See conditional model fit indices below.

Fit Indices:	χ^2 (df)	NFI	RFI	IFI	TLI	CFI	RMSEA	AIC
Uncond. Model	6.42(6), p=.4	0.925	0.875	0.995	0.991	0.994	0.039	22.4
Cond. Model	13.82(18),p=.7	0.901	0.753	1.03	1.11	1	0	85.8

RESULTS Con't

Predictors of Pre-DBS Apathy:

- Significant positive relationship between BDI-II score and the intercept (b=.538, SE=.085, p <.001), indicating higher depression score pre-DBS is related to higher apathy score pre-DBS
- No relationship between pre-DBS apathy and age, disease severity, but trend for younger adults to have lower apathy pre-DBS than older adults (p = .077)

Predictors of Post-DBS Apathy Trajectory:

- Trend for relationship between being a younger adult (< 65 yrs) and faster rate of increase in apathy (b= -.987, SE = .527, p =.06)
- No relationship between pre-DBS depression, disease severity and rate of apathy change after DBS
- No relationship between site of implantation (STN vs. GPi) and apathy trajectory or percent reduction in LED and apathy trajectory

Laterality:

- Laterality was examined with a subset of patients (n = 29) seen both at 6 mo. and pre-DBS. We ran a mixed 2 x 2 ANOVA with IVs of time and side (right vs. left). We found a significant main effect of time, indicating that apathy increased from pre- to 6 mo., F(1,27)= 4.29, p= 048. There was no main effect for side or interaction between time and side

CONCLUSION

This study adds to the literature through its use of latent growth curve modeling to investigate apathy post-DBS. It is the first study to examine the relationship between apathy and implantation site and laterality.

Consistent with our hypotheses, we found that apathy (AS scores) increased linearly from pre-surgery to 6 months post-surgery. The average trajectory increased by .66 points every two months.

Next, we examined inter-individual differences in trajectories. Contrary to our hypotheses, we did not find that older age, increased depression, or increased disease severity were related to a steeper rise in apathy post-DBS. There was a trend for younger patients (< 65 yrs) to increase in apathy faster, however this appears related to their lower scores pre-DBS.

We did not find a relationship between apathy trajectory and site of implantation (i.e. STN vs. GPi), or percent reduction in LED. Thus, we did not find support for two of the main theories for why apathy increases post-DBS.

Overall, our results corroborate studies that report DBS may lead to a worsening of apathy after surgery. With treatments for apathy being developed, understanding post-DBS apathy progression will aid clinicians in treating this impairing mood symptom.