



Non-cardiac Surgery, Cognitive Decline, and PD: A “Proof of Principle” Study

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INTRODUCTION

Studies have shown that after non-cardiac surgery, ~15% of cognitively well (MMSE > 27; screened for illnesses) older adults continue to experience a two standard deviation decline in cognitive function at three-months after major non-cardiac surgery [1].

Some individuals experience changes only in memory functions, while others experience change in executive functioning, or a combination of both memory and executive functions [2].

These findings in combination with theories of cognitive and brain reserve, led us to hypothesize that patients with pre-surgical cognitive impairments may be at particular risk for accelerated cognitive change after elective major non-cardiac surgery. In particular, we are concerned about participants with Parkinson's disease because of subcortical structure vulnerability to surgery variables and known relationships between subcortical and executive functions. We hypothesize surgical vulnerability for accelerated executive dysfunction relative to non-surgery PD peers.

We chose to examine cognitive function after hip and knee replacement surgery, because they are:

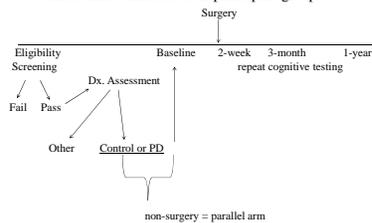
- 1) associated with cognitive change
- 2) typically elective, use a standard protocol, and involve general anesthesia. This allows us to test participants well before surgery to achieve a good baseline.

Here, we provide preliminary reliable change and group mean data for our ongoing “proof of principle” pilot study examining if:

- 1) Individuals with PD who elect major non-cardiac surgery experience greater executive function decline relative to non-surgery peers.
- 2) Individuals with PD who elect major non-cardiac surgery experience more cognitive decline relative to non-disease (“no-PD”) surgery peers.

METHODS

Design – Prospective longitudinal study with parallel control arms. There are four participant groups.



METHODS

Participants Groups:

- 1) Non-demented idiopathic PD ‘on’ medication undergoing total knee arthroplasty
- 2) Non-demented idiopathic PD ‘on’ medication not electing surgery
- 3) Non-demented ‘non-PD’ age matched adults having total knee arthroplasty
- 4) Non-demented ‘non-PD’ age matched adults not electing surgery.

Recruitment and Screening of Participants –

Recruitment – Participants were recruited from the UF Movement Disorder Center, the UF Orthopedic Surgery and Rehabilitation Center, local newspaper and radio advertisements, and television specials.

Eligibility Screening – We have screened 152 total hip, knee, or shoulder elective surgery candidates for exclusion and inclusion diagnostic criteria.

Exclusion Criteria – Planned cardiac or neurosurgical procedures, central nervous system disorders, drug abuse, severe depression, stroke, learning disorders that would preclude cognitive testing, or English as a second language.

Inclusion Criteria – Age 55 or greater, elective knee, hip, or shoulder surgery involving general anesthesia.

Diagnosis Assessment – Individuals with PD are largely referred to us from the UF MDC, but also outside clinicians. After initial eligibility screening, we conducted a brief neuropsychological assessment for cognitive inclusion.

“Normal” cognitive criteria:

- MMSE score > 27
- Intact cognitive function on formal testing
- Instrumental IADL function intact

Non-demented idiopathic PD ‘on’ medication

- United Kingdom PD Society Brain Research Center criteria
- Hoehn and Yahr scale range 1-3
- No dementia; same as control info above

Moderators to Control/Watch for:

Baseline IQ – Wechsler Abbreviated Intelligence Scale
Anesthesia – General anesthesia in OR. Nerve catheters and PCA for pain relief after surgery. See authors for more details.

Comorbidity - Charlson Comorbidity Index [3]; score range of 0-30; 30=severe; assessed at baseline

Delirium: Confusion Assessment Measure; assessed acutely post-operatively and again at each time point.

Post-Operative Pain – visual analog scale at all time points

Neuropsychological Outcome – Standardized test scores were created into composites of:

- Memory** – Hopkins Verbal Learning Test Delay and Discrimination subtests
- Executive Functions** – Trail Making Test, Part B
Stroop Color Word Test C-Word Score
- Verbal Fluency** – Controlled Oral Word Association, Animal Fluency
- Motor** – Finger Tapping Dominant, Non-Dominant

RESULTS

Basic Participant Characteristics – Study Still Ongoing

		Age in yrs	Education Yrs	*Co-morbidity	IQ
Surgery	‘Control’ (n=13)	72.15 ± 5.64	15.54 ± 3.53	.62 ± .87	116.62 ± 8.34
	PD (n=5)	63.80 ± 6.76	16.20 ± 2.48	.00 ± .00	124.67 ± 12.98
No-Surgery	‘Control’ (n=13)	72.92 ± 6.28	16.54 ± 3.15	.15 ± .38	112.80 ± 14.69
	PD (n=3)	78.00 ± 5.00	16.00 ± 2.00	.00 ± .00	122.00 ± 15.13

**Charlson Comorbidity Index 0 to 30; 30=severe
 Respective surgery and non-surgery groups currently differ by age [p=.02], with the PD surgery currently younger in age.

Individual Frequency of Decline

We used Reliable Change Statistics to identify how many PD surgery participants experienced statistically significant and reliable decline over and above that of comparison groups (Nonsurgery PD peers, No-PD surgery peers).

Using the equation,

$$\frac{\text{Surgery Mean } \Delta \text{ Score} - \text{Control Mean } \Delta \text{ Score}}{\text{S.D. of Control } \Delta \text{ Score}}$$

cognitive domain composite z-scores were created from patient pre-post change scores and matched peer group means (i.e., PD surgery compared to PD non-surgery; control ‘non-PD’ surgery compared to control ‘non-PD’ non-surgery)³.

Change identified as significant if RCI z-score > 1.50 decline

How many PD surgery patients experienced decline greater than their PD non-surgery peers?

2-week post-op **3-month post-op**

Memory	1/5; 20%	0/5; 0%
Exec Fx	1/5; 20%	2/5; 40%
Fluency	0/5; 0%	0/5; 0%
Motor	0/5; 0%	0/5; 0%

How many PD surgery patients experienced a decline greater than non-PD ‘healthy’ surgery peers?

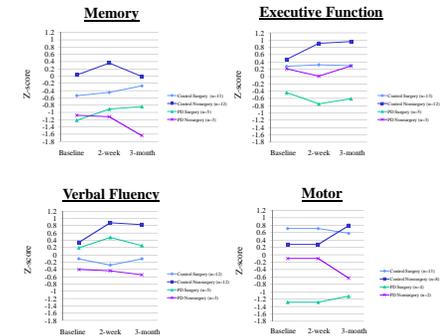
	2-week post-op	3-month post-op
Memory	0/5; 0%	1/5; 20%
Exec Fx	2/5; 40%	2/5; 40%
Fluency	0/5; 0%	0/5; 0%
Motor	0/5; 0%	0/5; 0%

*No patient experienced delirium; there were no differences in pain.

RESULTS cont.

Group Cognitive Domain Means by Time Period
 The figures below show mean cognitive domain composite z-scores for each participant group by time period. Sample size restricts formal analyses.

NOTE: Group means hide frequency of individual change (hence our use of RCI analyses shown in the third column).



CONCLUSIONS

Reliable change analyses indicate that two of five PD patients electing surgery experienced significant declines in executive dysfunction at three months after surgery. These changes were significantly greater those of PD non surgery peers and healthy surgery peers.

Group mean comparisons also suggest changes in executive function for the PD surgery group relative to other groups. Group mean comparisons cannot be completed at this stage, however, due to our small sample size.

We are continuing to follow all patients and are actively recruiting new participants. We are attempting to improve group matching with regard to age and baseline functioning.

Overall, these preliminary data support the need for continued study of PD and vulnerability to cognitive change after elective surgery. Multicenter studies are encouraged.

REFERENCES

1. *Anesthesiology* 2008; 108: 18-30
2. *Anesthesiology* 2008; 108: 8-17
3. *Archives of Neurology*, 1999; 56, 303-308.