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Type and Severity of Cognitive Decline in Older Adults after Noncardiac Surgery

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Background: **The authors investigated type and severity of cognitive decline in older adults immediately and 3 months after noncardiac surgery. Changes in instrumental activities of daily living were examined relative to type of cognitive decline.**

Methods: **Of the initial 417 older adults enrolled in the study, 337 surgery patients and 60 controls completed baseline, discharge, and/or 3-month postoperative cognitive and instrumental activities of daily living measures. Reliable change methods were used to examine three types of cognitive decline: memory, executive function, and combined executive function/memory. SD cutoffs were used to grade severity of change as mild, moderate or severe.**

Results: **At discharge, 186 (56%) patients experienced cognitive decline, with an equal distribution in type and severity. At 3 months after surgery, 231 patients (75.1%) experienced no cognitive decline, 42 (13.6%) showed only memory decline, 26 (8.4%) showed only executive function decline, and 9 (2.9%) showed decline in both executive and memory domains. Of those with cognitive decline, 36 (46.8%) had mild, 25 (32.5%) had moderate, and 16 (20.8%) had severe decline. The combined group had more severe impairment. Executive function or combined (memory and executive) deficits involved greater levels of functional (*i.e.*, instrumental activities of daily living) impairment. The combined group was less educated than the unimpaired and memory groups.**

Conclusion: **Postsurgical cognitive presentation varies with time of testing. At 3 months after surgery, more older adults experienced memory decline, but only those with executive or combined cognitive decline had functional limitations. The findings have relevance for patients and caregivers. Future research should examine how perioperative factors influence neuronal systems.**

A COMPANION article by Monk *et al.* and other studies on postoperative cognitive dysfunction (POCD)[1,2] demonstrate that individuals 60 yr or older are at increased risk for developing cognitive impairment after major, noncardiac surgery. To date, however, little is known about the *type* of cognitive change experienced by this population group. Within the disciplines of behavioral neurology and neuropsychology, brain function is typically subdivided into domains or systems.[3] For example, our capacity for learning and remembering is an essential brain function (*i.e.*, represents the memory domain). Another critical function is our ability to efficiently process information, concentrate, and self-monitor (*i.e.*, executive function domain).[4] Cognitive functions are localized or associated with specific brain regions (*e.g.*, medial temporal lobe for memory; frontal lobe and subcortical network systems for executive function) and differentially change with age or with aberrant brain processes, such as dementia or stroke. With regard to understanding POCD, examining the type of cognitive change may give us information as to which brain systems are most vulnerable to perioperative and operative events. It may also have implications for postsurgical rehabilitation approaches.

We report on a subgroup analysis of older adults enrolled in a larger investigation on POCD.[2] We hypothesized that older adults would present with different types of cognitive impairment at 3 months after noncardiac surgery. We analyzed the data from the study by Monk *et al.*[2] to determine whether there were varying types of cognitive impairment after surgery. Because of the selective nature of the tests in this study, we focused our examination of the incidence of decline on measures predominantly assessing memory or executive function. The severity of cognitive decline within each of these domains was labeled as mild, moderate, or severe depending on the SD change score from baseline (1, 1.5, or 2 SDs, respectively). Type of cognitive function was also examined for different outcomes in instrumental activities of daily living (IADLs).

Materials and Methods

The current study is a subanalysis of a larger investigation completed by Monk *et al.*[2] as reported in a companion article. Informed written consent was obtained according to University of Florida Institutional Review Board (Gainesville, Florida) guidelines and the Declaration of Helsinki. From 1,064 participants in this larger study, the data from 417 participants aged 60 yr or older were assessed. Of these older adult participants, 355

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underwent major noncardiac surgeries that required a minimum of a 2-day inpatient stay (50 minimally invasive, 167 intraabdominal/thoracic, 138 orthopedic). The remaining 62 participants served as nonsurgical controls. As part of the larger investigation, all participants were asked to participate in a prospective longitudinal study evaluating the frequency of cognitive change after major, noncardiac surgery.[2] Participants were excluded from the study if they were undergoing cardiac, carotid, or neurologic surgery or presented with significant cognitive impairment as suggested by a score of less than 24 on a preoperative Mini-Mental State Examination.[5] Other exclusionary criteria included a diagnosis of central nervous system disorders, a current or past history of a psychiatric illness, taking antidepressant or antianxiety medications, or a history of drug or alcohol abuse. To be included, participants were required to have English as their first language and be able to speak and read fluently in English. All surgery was performed with general anesthesia, and there were no restrictions on the type of anesthesia or postoperative analgesia.

Procedure and Materials

Each participant underwent neuropsychological testing at three time points: up to 14 days before surgery, upon hospital discharge (or at 1 week after surgery if still hospitalized), and at 3 months after surgery. All patients completed baseline assessments of general cognitive functioning as assessed by the Mini-Mental State Examination,[5] depression as assessed by the Beck Depression Inventory,[6] current and general anxiety as assessed by the State Trait Anxiety Inventory,[7] and pain as measured by a numerical pain rating scale (0 = no pain; 10 = severe pain). Health status at the time of enrollment was calculated using a measure of comorbidity.[8] IADLs were assessed[9] at baseline and again at 3 months after surgery with a questionnaire that contained seven questions related to the use of the telephone, commuting, shopping, preparation of meals, housework, medication taking, and finances. This questionnaire was completed by both the patient and an informant (a member of the patient's immediate family). If a patient could do the activity without assistance, the score was 0; if some assistance from other people was needed to do the activity, the score was 1; and if the patient could not do the activity, the score was 2 (scores ranged from 0 to 14). Higher scores indicate increasing difficulty in engaging in daily activities.

Neuropsychological Assessment

The procedures for the neuropsychological assessment protocol are described elsewhere.[2] The protocol included the tests used to evaluate patients for POCD in the International Study of Postoperative Cognitive Dysfunction 1 and 2 (ISPOCD1 and ISPOCD2).[1,2,10–12] Three parallel forms of the tests were used in a sequence using a full Latin square design for tests other than the Stroop Color Word Test. Patient assignment to one of six possible sequences was random. For the current study, only dependent variables that have been routinely shown to be either associated with executive function (involving the concepts of concentration/set-shifting/processing speed) or learning/memory functions were analyzed. The Concept Shifting Task and the Stroop Color Word Test provide two dependent variables: time to completion (seconds) and number of errors. Only time to completion was analyzed because it is more commonly used within the neuropsychological literature and allows for more robust statistical analysis.

Executive Function: Concentration/Processing Speed/Self-Monitoring.

Concept Shifting Task, part C: A version of the Trail Making Test[13] that is used to assess mental processing speed, visual scanning, and the ability to ignore distracting stimuli. Part C of the Concept Shifting Task is analogous to Trail Making Test part B in that it requires rapid alternation between letters and digits. For the current study, the dependent variable was the number of seconds required to complete the task.

Stroop Color Word Test, part 3: A version of the Stroop Color Word Test[14,15] used to assess concentration and the ability to ignore distracting stimuli. In part 3 of the Stroop Color Word Test, the participant views words that spell out a color but are printed in contrasting ink colors (*e.g.*, *red* is printed with blue ink). The participant is instructed to tell the color of the ink in which the words are printed rather than read the actual word. For the current study, the dependent variable was the number of seconds required to complete the task.

Letter–Digit Coding: A European version of the Digit Symbol subtest from the Wechsler Adult Intelligence Scale[16] that is used to assess concentration, processing speed, and visual scanning abilities. For this test, participants are required to quickly match nine letters with nine different symbols within a 1-min time period. For the current study, the dependent variable included the total number of symbols correctly matched within the allotted 1-min time period.

Learning and Memory.

Visual Verbal Learning: This is a visual version of the Rey Auditory Verbal Learning Test.[17,18] In this test, 15 words are individually presented in a visual format over a series of three learning trials. Each word is visually shown at a rate of one word per 2 s. At the completion of each trial, participants are asked to immediately recall as many words as possible. This test contains two separate recall indices that uniquely assess learning and memory abilities.

Immediate recall: An index of the Visual Verbal Learning Test used to assess immediate learning ability of the 15 words presented in three separate trials. The dependent variable of interest includes total number of correct words recalled across all three learning trials.

Delayed recall: An index of the Visual Verbal Learning Test used to assess retention of the learned words after a 15- to 25-min delay. The dependent variable of interest included total number of correct words recalled on this index.

Statistical Analysis. Of the initial 417 older adults enrolled in the study, 60 controls and 337 surgery patients completed baseline, discharge, and/or 3-month postoperative measures. Data were processed by checking for item nonresponse, distributional forms (*e.g.*, normality of continuous data elements), and creating derived variables (*e.g.*, measure of comorbidity, IADL change scores). SAS version 9.1 (SAS Institute Inc., Cary, NC) statistical software was used for all statistical analyses. Frequencies and percents were calculated for categorical data, and means and SDs were calculated for numerical data. Chi-square and Fisher exact tests were used to test relations between bivariate categorical data; Wilcoxon rank sum and Kruskal-Wallis tests were used to test relations between categorical data (*e.g.*, groups) and numerical measures. A chi-square goodness-of-fit test was used to test for equality of proportions.

Factor analysis was used to confirm our conceptual grouping of the neuropsychological variables and to reduce the number of neuropsychological variables, thereby decreasing the number of statistical analyses and improving cognitive domain reliability.[3] Factor analysis was performed using a variable clustering approach implemented with the variable cluster analysis (VARCLUS) procedure in SAS. This approach combines traditional factor analysis with hierarchical clustering to produce scales that are simple and easy to interpret. The variable cluster analysis procedure uses iterative splitting and factor analysis methods to divide a group of variables into discrete (nonoverlapping) subgroups that are relatively highly correlated. Splitting continues until a stopping criterion (a mathematical optimization based on eigenvalues) is reached. Data were available for 345 patients undergoing surgery on the five baseline neuropsychological assessments considered in this study. Factor analysis yielded two clusters: an executive function/set-shifting/processing speed cluster (minimum proportion of variation explained by cluster was 0.56) consisting of Concept Shifting Task part C, Stroop Color Word Test part 3, Letter–Digit Coding, and a learning/memory cluster (minimum proportion of variation explained by cluster was 0.68) consisting of Visual Verbal Learning immediate and delayed recall. Proportion of variation explained by both clusters was 0.89. For simplicity, we termed the executive function/set-shifting/processing speed cluster as an "executive function" index and the learning/memory cluster as the "memory" index.

Reliable change scores were used to assess cognitive change from baseline to discharge and then from baseline to 3 months for each patient undergoing surgery. Reliable change methods have been routinely used to assess changes in cognition after neurologic surgeries.[19,20] The reliable change score for each neuropsychological assessment was calculated by (1) computing the change score (difference of baseline to the postsurgery time point) for each subject, (2) finding the mean and SD of change scores for the control group, and (3) standardizing the change score for surgery patients by subtracting the mean of the control group then dividing by the SD of the control group. The formula for the reliable change score is $\text{Reliable Change Score} = [(\text{Change Score}\ )\ (\text{Mean Change Score}_{\text{control group}})]/(\text{SD}_{\text{control group}})]$.

We next formed composite scores for the executive function and memory indices. The executive function composite change score was created by averaging the reliable change scores for the executive function neuropsychological measures (*i.e.*, Concept Shifting Task part C, Stroop Color Word Test part 3, Letter–Digit Coding). The reliable change scores for the memory neuropsychological measures (*i.e.*, Visual Verbal Learning immediate recall, Visual Verbal Learning delay recall) were averaged to create a memory composite change score.

The severity of cognitive change on each of the executive function and memory indices was graded as mild, moderate, or severe based on the SDs of the composite scores. Mild decline is defined as a change of 1 SD, moderate as a change of 1.5 SDs, and severe as 2 SDs or greater. Patients were then classified into one of the following four mutually exclusive types: (1) no impairment, (2) executive function (no decline on the memory index), (3) memory (no decline on the executive function index), and (4) combined (decline in both executive function and memory domains).

Results

As shown in table 1, the control and surgery patients matched on all demographics, baseline mood, pain, and general cognitive functioning abilities (Mini-Mental State Examination).[5] Table 2 provides a summary of the raw, standardized neuropsychological variables and reliable change scores by group (control, surgery).

Discharge Results: Type and Severity of Cognitive Impairment

Of 334 surgery patients who completed discharge testing, 148 (44.3%) did not experience a change in cognitive function equal to or greater than 1 SD from baseline performance, 75 (22.5%) experienced a decline on the executive function index, 61 (18.3%) experienced a de-

Table 1. Control and Surgery Baseline Demographics

	Control Participants* (n = 60)	Surgery Participants* (n = 337)	*P* Value
Age, yr	68.3 ± 5.2	69.7 ± 6.8	0.2075
Sex, %			
Male	43	43	0.9648
Female	57	57	
Years of education	13.7 ± 2.7	13.4 ± 2.8	0.4034
Beck Depression Inventory score	6.1 ± 5.4	5.8 ± 5.1	0.6850
State Trait Anxiety Index			
Trait anxiety	31.6 ± 8.2	29.9 ± 8.3	0.0866
State anxiety	36.4 ± 12.8	33.2 ± 11.1	0.0934
Mini-Mental State Examination	29.1 ± 1.3	28.8 ± 1.4	0.0775

Data are mean ± SD or percent.

* Had discharge and/or 3-month neuropsychological data.

cline on the memory index, and 50 (14.9%) experienced a decline on both the executive function and memory indices (*i.e.*, a combined impairment). Among those with cognitive decline at discharge, there was no difference between frequency of cognitive type ($\chi^2 = 5.06$, $df = 2$, $P = 0.0794$).

In addition, among those with cognitive impairment, there was an equal distribution for severity of decline from baseline to discharge (mild [n = 67, 35.8%], moderate [n = 60, 32.1%], or severe [n = 60, n = 32.1%] decline; $\chi^2 = 0.52$, $df = 2$, $P = 0.7695$).

3 Months after Surgery: Type and Severity of Cognitive Impairment

Of the 308 surgery patients completing cognitive testing at 3 months after surgery (tables 3 and 4), 231 (75.1%) did not experience a change in cognitive function equal to or greater than a 1 SD decline from baseline performance, 26 (8.4%) experienced decline on the executive function index, 42 (13.6%) experienced decline on the memory index, and 9 (2.9%) experienced decline on both the executive function and memory indices (*i.e.*, combined group). Among those with cognitive impairment, there was a significant difference in the frequency of type of cognitive decline ($\chi^2 = 21.22$, $df = 2$, $P < 0.0001$), with more patients declining on the memory index relative to the executive function index ($P = 0.0523$) and more patients declining on the executive function index relative to combined index ($P < 0.0041$).

Among those with cognitive decline, there was a significant difference in the proportion of patients demonstrating mild (n = 36, 46.8%), moderate (n = 25, 32.4%), or severe (n = 16, n = 20.8%) decline from baseline to 3 months after surgery ($\chi^2 = 7.82$, $df = 2$, $P = 0.0201$). Pairwise comparisons identified that there were many more mildly impaired relative to severely impaired pa-

Table 2. Neuropsychological Test Raw (Baseline, Discharge, 3-Month) and Standardized Reliable Change Index Scores for the Control (n = 60) and Surgery (n = 337) Groups

	Baseline	Discharge	3 Months	Discharge Reliable Change Score	3-Month Reliable Change Score
Controls	n = 60	n = 59	n = 56		
Verbal Learning Test, learning trials	26.4 ± 6.4	27.2 ± 6.3	28.9 ± 8.7	NA	NA
Verbal Learning Test, delay	9.2 ± 3.2	8.8 ± 3.4	9.8 ± 3.7	NA	NA
Concept Shifting Task, part C, number/letter task, time in seconds	35.6 ± 10.3	35.2 ± 11.1	34.2 ± 11.4	NA	NA
Letter–Digit Coding	32.6 ± 6.4	33.0 ± 8.4	33.0 ± 6.3	NA	NA
Stroop Color Word Test, part 3, interference task, time in seconds	51.4 ± 13.4	46.6 ± 13.2	47.5 ± 13.4	NA	NA
Surgery patients	n = 337	n = 334*	n = 308	n = 334	n = 308
Verbal Learning Test, immediate, total correct across three learning trials	25.6 ± 6.0	23.7 ± 6.6	26.5 ± 6.1	−0.5 ± 1.2	−0.3 ± 0.9
Verbal Learning Test, delay, total words correct after filled time delay	8.3 ± 3.1	6.7 ± 3.2	8.4 ± 3.2	−0.5 ± 1.3	−0.2 ± 1.0
Concept Shifting Task, part C, number/letter task, time in seconds	40.9 ± 15.7	48.1 ± 22.9	40.0 ± 17.4	−0.9 ± 2.3	0.0 ± 1.8
Letter–Digit Coding, total correct in 60 s	29.0 ± 7.4	25.4 ± 7.4	30.3 ± 7.2	−0.6 ± 0.9	0.1 ± 1.2
Stroop Color Word Test, part 3 (interference task), time in seconds	56.3 ± 15.8	61.1 ± 22.2	53.4 ± 16.9	−1.1 ± 2.0	−0.1 ± 1.7

Data are mean ± SD.

* 333 completed all seven indices as reported in Monk *et al.*[2]

NA = not applicable.

Table 3. Summary Statistics of Reliable Change Index by 3-Month Cognitive Type

	Standardized Composite Change Score			
	No Decline (n = 231)	Executive Decline (n = 26)	Memory Decline (n = 42)	Combined Decline (n = 9)
Verbal Learning Test, learning trials	−0.1 ± 0.8	−0.0 ± 0.8	−1.5 ± 0.6	−1.3 ± 0.2
Verbal Learning Test, delay total	0.1 ± 0.8	0.2 ± 0.8	−1.7 ± 0.8	−1.8 ± 0.9
Concept Shifting Task, part C (number/letter task), s	0.3 ± 1.5	−2.2 ± 2.2	−0.0 ± 0.9	−2.5 ± 3.9
Letter–Digit Coding, total	0.3 ± 1.2	−0.6 ± 0.9	0.2 ± 1.0	−1.8 ± 2.1
Stroop Color Word Test, part 3 (interference task), s	0.1 ± 1.3	−1.9 ± 2.5	0.2 ± 1.7	−2.6 ± 3.4

Data are mean ± SD, calculated using a reliable change score formula: Reliable Change Score = [(Change Score) − (Mean Change Score$_{control\ group}$)]/(SD$_{control\ group}$)].

tients (P = 0.0055), with all other comparisons statistically equal.

There was a significant cognitive type by severity type interaction (χ^2 = 23.16, df = 4, P = 0.0001; table 4). Groups differed by classification of impairment, with executive function and memory groups having more patients classified as mildly impaired rather than severely impaired and the combined group having more patients classified as severely impaired rather than mildly impaired (Fisher exact test, P = 0.0202).

Cognitive Type and Failure to Complete 3-Month Testing

A set of 29 patients who completed discharge testing did not complete testing at 3 months after surgery. Of these 29 patients, 14 (48.3%) had not exhibited any cognitive decline at discharge, 10 (34.5%) had declined on the executive function index, 3 (10.3%) had declined on the memory decline, and 2 (6.9%) had a combined executive function and memory decline at discharge. No difference was found between groups on the number of patients who had died, were unable to complete testing, or refused further participation (table 5).

Change in Cognitive Type from Discharge to 3-Month Testing

Of the 75 patients demonstrating primary executive function decline at discharge, 10 (13.3%) did not complete follow-up testing, 45 (60.0%) no longer exhibited any decline at follow-up, 13 (17.3%) remained classified as executive function, 6 (8.0%) changed classification to memory, and 1 (1.3%) changed to combined. Of the 61 patients demonstrating primary memory decline at discharge, 3 (4.9%) did not complete follow-up testing, 42 (68.9%) no longer exhibited any decline at follow-up, 3 (4.9%) changed to executive function, 12 (19.7%) remained memory, and 1 (1.6%) changed to combined. Of the 50 patients demonstrating a combined decline at discharge, 2 (4.0%) did not complete follow-up testing, 29 (58.0%) no longer exhibited any decline at follow-up, 2 (4.0%) changed to executive function, 11 (22.0%) changed to memory, and 6 (12.0%) remained combined (table 5).

3-Month Cognitive Type and Demographic, Mood, Pain, and Surgery Variables

Three-month cognitive types (no impairment, executive function, memory, combined) were compared on baseline demographics, mood, pain, surgery, and anesthesia variables (tables 6 and 7). Of the demographic variables, the individuals with a decline on the combined index had lower levels of education than the no impairment group (P value = 0.0039) and the memory group (P = 0.0160). Baseline Mini-Mental State Examination scores were statistically different among the groups; however, these differences were minimal and not likely to be clinically significant. There were no significant differences in baseline mood, general cognitive, pain, or general surgery variables among the groups.

Living Placement at 3 Months

Of the 308 patients who completed 3-month testing, 2 of 42 individuals (4.8%) with a memory decline and 2 of 9 individuals (22.2%) with a combined executive func-

Table 4. Raw Number (%)* Distribution of Executive Function, Memory, or Combined Cognitive Types by Severity of Cognitive Change from Baseline to 3 Months after Surgery

	No Decline	Executive Decline (Memory Not Impaired)	Memory Decline (Executive Not Impaired)	Combined (Memory and Executive Decline)	Total
Mild†		13 (4.2)	22 (7.1)	1 (0.3)	36 (11.7)
Moderate‡		9 (2.9)	13 (4.2)	3 (1.0)	25 (8.1)
Severe§		4 (1.3)	7 (2.3)	5 (1.6)	16 (5.2)
Total	231 (75.1)	26 (8.4)	42 (13.6)	9 (2.9)	308

* Percentages reflect frequency relative to the entire sample of 308 surgery patients. † Mild impairment = decline of 1–1.5 SDs from baseline performance. ‡ Moderate impairment = decline of 1.5–2 SDs from baseline performance. § Severe impairment = decline of 2 SDs or more from baseline performance.

Table 5. Raw Number (%)* Distribution of Executive, Memory, or Combined Cognitive Types by Discharge and 3 Months after Surgery

	Status 3 Months after Surgery				
Status after Discharge	Data Missing at Time Point	No Impairment	Executive Impairment (Memory Not Impaired) (n = 26)	Memory Impairment (Executive Not Impaired) (n = 42)	Combined (Memory and Executive Impaired) (n = 9)
Data missing	0 (0)	3 (0.9)	0 (0)	0 (0)	0 (0)
No impairment	14 (4)	112 (33)	8 (2)	13 (4)	1 (0.3)
Executive impairment (memory not impaired) (n = 75)	10 (3)	45 (13)	13 (4)	6 (2)	1 (0.3)
Memory impairment (executive not impaired) (n = 61)	3 (0.9)	42 (12)	3 (0.9)	12 (4)	1 (0.3)
Combined (memory and executive impaired) (n = 50)	2 (0.6)	29 (9)	2 (0.6)	11 (3)	6 (2)

* Percentages reflect frequency relative to the entire sample of 337 surgery patients.

tion–memory decline had been moved to a residential living center. All other patients and nonsurgical controls continued living at home (no statistics were completed because of small cell sizes).

Type of Cognitive Decline and Instrumental Activities of Daily Living

Regarding patient reports, cognitive types differed significantly on IADL function after controlling for baseline IADL ability ($F_{3,299} = 5.84$, $P = 0.0007$). Follow-up Tukey *post hoc* analyses identified that executive and combined groups experienced greater postsurgery IADL dysfunction relative to the memory group ($P = 0.0032$ and $P = 0.0096$, respectively; table 8). IADL item analysis suggests that the executive function group, followed by the combined group, required more postoperative assistance with six of the seven IADL items (all $P < 0.01$; table 9).

After controlling for baseline IADL reports, there were significant differences in caregiver/informant observations of postsurgery IADL function based on patient cognitive type ($F_{3,264} = 5.37$, $P = 0.0013$). Follow-up Tukey *post hoc* analyses identified that the informants of the combined type identified significantly more postoperative IADL dysfunction relative to the executive function ($P = 0.0195$), memory ($P = 0.0005$), and intact groups ($P = 0.0048$). This difficulty was significant among six of the seven IADL items (all $P < 0.01$). Of these groups, informants for the memory group reported the least amount of problems at this time point.

Discussion

As an extension to the study conducted by Monk *et al.*,[2] we examined type and severity of noncardiac post-

Table 6. Demographic, Mood, General Cognitive, Pain, and Surgery Variables by Cognitive Type (No Impairment, Attention, Memory, Combined)

	No Impairment (n = 231)	Executive Impairment (n = 26)	Memory Impairment (n = 42)	Combined Impairment (n = 9)	*P* Value
Age, yr	69.3 ± 6.4	71.7 ± 7.4	68.8 ± 6.3	71.8 ± 7.3	0.2281
Sex, %					0.8772
Male	76.7	7.5	13.5	2.3	
Female	73.7	9.1	13.7	3.4	
Years of education	13.7 ± 2.9	12.7 ± 2.3	13.5 ± 2.4	11.0 ± 2.5	0.0078
Beck Depression Inventory score	5.5 ± 4.8	6.8 ± 5.4	5.1 ± 5.1	7.8 ± 5.7	0.2846
State Trait Anxiety Index					
Trait anxiety	29.5 ± 8.1	33.3 ± 8.5	28.3 ± 6.9	32.6 ± 7.9	0.0540
State anxiety	32.8 ± 10.7	36.0 ± 14.3	30.7 ± 8.8	33.4 ± 8.7	0.6117
Mini-Mental State Examination score	28.9 ± 1.4	28.3 ± 1.6	28.8 ± 1.3	29.7 ± 0.7	0.0452
Visual analog pain score	2.5 ± 3.1	2.7 ± 3.3	2.1 ± 2.7	2.8 ± 3.1	0.9005
ASA physical status, %					0.1059
I	76.5	0.0	23.5	0.0	
II	79.1	4.6	13.7	2.6	
III	68.5	14.6	13.1	3.9	
IV	100.0	0.0	0.0	0.0	
Charlson Comorbidity Index	1.9 ± 2.1	2.4 ± 2.2	2.1 ± 2.1	1.5 ± 1.0	0.6168

Data are mean ± SD or percent.

ASA = American Society of Anesthesiologists.

Table 7. Surgical Procedure and Hospital Stay by 3-Month Cognitive Type

	No Impairment (n = 231)	Executive Impairment (n = 26)	Memory Impairment (n = 42)	Combined Impairment (n = 9)	*P* Value
Type of surgery					0.6965
Minimally invasive*	81.0	4.8	9.5	4.8	
Intraabdominal/thoracic	72.4	8.0	16.7	2.9	
Orthopedic	75.8	10.2	11.7	2.3	
Duration of anesthesia, min	214.1 ± 112.1	195.1 ± 89.4	207.9 ± 88.2	177.7 ± 48.1	0.6736
ICU stay					0.2835
No ICU stay	74.0	9.5	13.0	3.5	
Yes ICU stay	79.6	3.7	16.7	0.0	
Duration of hospital stay, days	5.3 ± 5.4	5.0 ± 2.7	4.6 ± 3.1	4.4 ± 1.1	0.9461

Data are mean ± SD or percent.

* Minimally invasive surgery included laparoscopic surgery and superficial reconstructive surgery.

ICU = intensive care unit.

operative cognitive difficulty among adults aged 60 yr or older with three neuropsychological composite indices labeled as executive function, memory, and combined (representing a decline on both executive function and memory indices). Our findings indicate that postoperative cognitive presentation and severity varies with time of testing and has functional relevance.

Type and Severity of Cognitive Presentation by Time Point

At hospital discharge, there was an equal distribution of cognitive impairment in executive function, memory, and combined groups, with the severity of cognitive decline also evenly distributed among mild, moderate, or severe impairment. In contrast, at 3 months after surgery, many more patients were impaired on the memory index (54%) relative to the executive function (34%) or combined (12%) indices. In the majority of patients with memory or executive decline, the impairment was mild in severity, whereas patients with a combined executive function–memory disturbance at 3 months were more likely to experience a severe cognitive impairment.

Dropout and changes in cognitive classification from discharge to 3 months seem to explain the dominance of memory impairment at 3 months after surgery. Of the 29 people who dropped out after discharge testing, three times as many executive function patients (35%) did not complete the 3-month follow-up relative to that of the memory (10%) or combined (7%) groups. In addition, a small set of executive function (8%) and a large set of combined patients (22%) converted to memory impairment at 3 months. Very few patients (5% from the memory, 4% from the combined) converted into the executive function or combined group. These findings indicate that, of the three cognitive groups, individuals diagnosed with memory impairment at discharge were more likely to remain in the investigation and continued to experience this primary memory impairment at 3 months after surgery. Individuals with executive dysfunction at discharge, by contrast, were more likely to drop out from further testing. Executive function impairment results in a fundamental problem with planning and organizational skills, both of which are important in making sure a subject returns for a follow-up appointment.[21] This may explain the higher dropout rate among patients with executive function impairment. For those with more global "combined" cognitive impairment, difficulties with executive dysfunction seemed to resolve, leaving behind only memory dysfunction at 3 months.

Dropout from discharge to 3 months was not completely dependent, however, on whether a person had cognitive impairment at discharge. Of the 29 patients who did not complete follow-up 3-month testing, 48% included patients who were cognitively intact at discharge. Among those who dropped out between discharge and 3 months, just as many cognitively intact patients experienced death between discharge and 3 months or declined further participation at 3 months.

Table 8. Total Instrumental Activity of Daily Living* Score by Cognitive Type for Baseline and 3-Month Time Points

	No Impairment	Executive Impairment	Memory Impairment	Combined Impairment
Patient				
Baseline	0.53 ± 1.27	1.20 ± 1.68	0.36 ± 0.91	0.78 ± 0.83
3 months	1.18 ± 1.82	2.44 ± 2.31	0.44 ± 0.78	3.11 ± 4.07
Informant				
Baseline	0.82 ± 1.90	1.08 ± 1.56	0.44 ± 0.94	0.78 ± 0.83
3 months	1.38 ± 2.12	1.81 ± 2.77	0.54 ± 0.90	4.63 ± 4.47

Data are mean ± SD.

* Possible score range: 0–14.

Table 9. Number (%) Requiring Assistance* in Activities of Daily Living by Cognitive Type at 3 Months

Activity of Daily Living	No Impairment	Executive Impairment	Memory Impairment	Combined Impairment	*P* Value†
Telephone	2 (1)	0 (0)	0 (0)	0 (0)	—
Commute/travel	47 (20)	9 (36)	3 (7)	3 (33)	0.0049
Shopping	33 (19)	11 (44)	1 (2)	3 (33)	<0.0001
Meal preparation	36 (16)	8 (32)	2 (5)	2 (22)	0.0017
Housework	90 (39)	18 (72)	11 (27)	7 (78)	<0.0001
Medicine	6 (3)	3 (12)	0 (0)	1 (11)	0.0410
Finances	14 (6)	4 (16)	0 (0)	2 (22)	0.0035

* By patient report. † Comparison of impaired groups only.

This suggests that while executive function impairment initially seems to be a more risky diagnosis for dropout relative to the other two groups in our sample, postdischarge difficulties still occurred even when there was no evidence of acute cognitive impairment.

Instrumental Activities of Daily Living

Our study demonstrates that the type of cognitive decline at 3 months after surgery has functional significance for older adults. In our cognitively impaired sample, memory impairment was most common, but these individuals had the least amount of functional impairment on IADLs according to both patients and their informants. The executive function and combined groups, in contrast, had the most severe decline in IADL function and reported needing minimal to complete assistance for six of the seven IADL abilities (*i.e.*, commuting, shopping, meal preparation, housework, medicine, finances). The caregivers of patients with combined impairment (both executive function and memory difficulties) corroborated the increased IADL difficulties.

These findings support the current knowledge about IADLs and cognitive function in normal aging and the dementia population. Many investigators have identified that greater executive dysfunction, not memory dysfunction, has been independently associated with IADL decline among intact and moderately demented adults.[22–25] The presence of combined executive decline and memory decline has been associated with declines on more basic activities of daily living (*e.g.*, grooming).[26] This may explain why, within our investigation, change in IADL status was most noted among the caregivers of patients with combined impairments (both memory and executive function disturbances). Therefore, impairments on combined memory and executive function domains not only implicate a more severe cognitive disturbance but also poorer functional status at home.

Our findings may help to clarify conflicts in the literature regarding the relation between IADL and POCD. The ISPOCD1 study identified a significant correlation between declines in IADL scores and cognitive dysfunction at 3 months after surgery.[1] The companion article by Monk *et al.*,[2] however, did not find a relation between the occurrence of POCD and declines on IADLs at 3 months after surgery. Based on our study results, we believe that the findings of Monk *et al.* may partially reflect the distribution of cognitive type within their patient sample (*i.e.*, more memory impairment than other forms). We do not know the pattern of cognitive impairment in the ISPOCD1 study. Therefore, we can only speculate that the cognitive distribution in the ISPOCD1 study may largely reflect a decline that includes executive function or combined disturbances, because executive function disturbance is more synonymous with IADL dysfunction.

Three-month cognitive types were also examined for differences in demographic, mood, baseline general cognitive status (*i.e.*, Mini-Mental State Examination), pain level, and surgery variables. We identified group differences in education; individuals with combined executive–memory impairment were significantly less educated than the other two cognitive impairment types. Monk *et al.* report that lower educational level predicted the incidence of POCD at 3 months after noncardiac surgery. Our further analysis of the elderly patients in the study of Monk *et al.* indicates that lower educational level seems to be not only a risk factor for developing POCD but also a possible risk factor for developing more global cognitive impairment when measured by neuropsychological measures. Although reasons for the protective effect of education are not fully known, possible explanations include the concept of cognitive reserve[27,28] and associated factors of better test-taking ability, social support, and better postoperative medical care. Our comparison of baseline cognitive variables between groups did reveal a statistical difference on a general cognitive status examination (Mini-Mental State Examination), but the findings have little clinical significance because all groups performed well within what is considered to be the normal range.[3]

Future Clinical and Research Implications

The collective findings have clinical and research implications. Older adult communities continue to grow in number throughout the country. As life expectancy increases, it is projected that "quality-of-life" surgeries (*i.e.*, joint replacement surgery) in addition to health urgency surgeries will increase. Given that older adults have been shown to have longer-lasting cognitive impairment after major surgeries and potentially that postsurgical cognitive impairment may herald greater mortality,[2] it is paramount that we continue pursuing more in-depth examinations into the treatment and mechanisms that result in postoperative cognitive impairment. Understanding the etiology of cognitive types may help to develop strategies for preventing POCD. It is known from traumatic brain injury and stroke research that the type of cognitive impairment influences inpatient and rehabilitation strategies.[29,30] The same may hold true for different types of postoperative cognitive impairment. Furthermore, research on types of cognitive impairment may inform us about which brain systems are more vulnerable to perioperative events.

Some may question our differentiation of executive function from that of memory. Although we agree that executive function and memory systems are intimately related (*i.e.*, aspects of executive function are required for a person to effectively learn and retrieve information), there is substantial literature supporting dissociations between the two cognitive functions from a neuroanatomical perspective. Executive function, although multifactorial (as exemplified by the overlapping terms such as concentration, selective attention, set-shifting, self-monitoring, processing speed), is most commonly associated with the frontal cortex,[31,32] subcortical nuclei, and white matter fibers.[33,34] Memory functions, in contrast, have been classically associated with three neuroanatomic regions within the brain (and the pathways that interconnect them). These include the medial temporal lobe (hippocampus, entorhinal cortex),[35–37] the thalamus (dorsomedial, anterior nuclei),[38] and the basal forebrain, which innervates the hippocampus with essential cholinergic neurons.[39,40] Disruption to any of these brain systems can occur during perioperative events. Future studies investigating postoperative cognitive types should explore specific perioperative events beyond that of surgery type alone or duration of anesthesia (two factors we did not find to be influential on our cognitive subtypes). In addition, future studies should address the contribution of preexisting anatomical abnormalities (*e.g.*, hippocampal atrophy), which may result in specific cognitive subtypes.

A limitation of our findings may be the European-based measures used to assess cognitive domains in a US sample. These measures, however, were designed to imitate commonly used neuropsychological measures in the United States which have been shown to be reliable and valid.[12] In addition, our results with these neuropsychological measures support the current findings in the literature about postoperative cognitive change. We identified that there were larger and equivalent numbers of cognitive type and severity at the 2-week time point. This finding reflects the accepted view that the acute discharge time point associates with a higher rate of cognitive dysfunction and more cognitive variability due to associated factors (*e.g.*, fatigue, pain, medications).[12] As the time after surgery increases, these external variables should resolve, providing a more accurate picture of cognitive function. This seems to be true for our current sample. By 3 months we clearly identified two important patterns: Memory disturbance was prominent, and individuals with executive function disturbance had the more severe functional limitations. A limitation, we acknowledge, is that we classified memory impairment with the composite measure of the immediate and delayed indices from one test. To increase the robustness of a memory assessment and the reliability of a composite, we urge future investigators to attempt to replicate our findings with two or more tests of memory.

To our knowledge, this is the first study to specifically examine cognitive subtypes of postoperative cognitive complications. Our findings indicate that postoperative cognitive presentation varies with the time of testing and has functional relevance for the patient and caregiver. These findings require replication. Future examinations within larger samples should be conducted to determine which neuronal systems are most influenced by perioperative factors.

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