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Preoperative Cognitive Performance Dominates Risk for Delirium Among Older Adults

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Abstract

Background: Cognitive impairment is a well-recognized risk factor for delirium. Our goal was to determine whether the level of cognitive performance across the nondemented cognitive ability spectrum is correlated with delirium risk and to gauge the importance of cognition relative to other known risk factors for delirium. **Methods:** The Successful Aging after Elective Surgery study enrolled 566 adults aged $\geq$70 years scheduled for major surgery. Patients were assessed preoperatively and daily during hospitalization for the occurrence of delirium using the Confusion Assessment Method. Cognitive function was assessed preoperatively with an 11-test neuropsychological battery combined into a composite score for general cognitive performance (GCP). We examined the risk for delirium attributable to GCP, as well as demographic factors, vocabulary ability, and informant-rated cognitive decline, and compared the strength of association with risk factors identified in a previously published delirium prediction rule for delirium. **Results:** Delirium occurred in 135 (24%) patients. Lower GCP score was strongly and linearly predictive of delirium risk (relative risk = 2.0 per each half standard deviation difference in GCP score, 95% confidence interval, 1.5-2.5). This effect was not attenuated by statistical adjustment for demographics, vocabulary ability, and informant-rated cognitive decline. The effect was stronger than, and largely independent from, both standard delirium risk factors and comorbidity. **Conclusion:** Risk of delirium is linearly and strongly related to presurgical cognitive performance level even at levels above the population median, which would be considered unimpaired.

Keywords

delirium, cognitive impairment, epidemiology

Delirium affects up to half of older adults during surgery or hospitalization and results in more than $164 billion in US health-care costs per year.[1] Cognitive impairment is a recognized risk factor for delirium. In fact, in a recent systematic review of delirium prediction rules, cognitive impairment was second only to age as the most commonly replicated predictor of delirium, occurring in 10 of 37 published risk prediction models.[2] A limitation of risk modeling in delirium with regard to cognitive functioning is that the measurement of cognition is typically accomplished with short mental status instruments originally developed to screen for dementia. Such measures often demonstrate substantial ceiling effects and are insensitive to performance gradients at higher levels of ability.[3] Our goal was to overcome this limitation by examining the risk associated with postoperative delirium attributable to cognitive performance level across the full spectrum of cognitive ability. We also aimed to characterize the strength of this association relative to and controlling for demographics, vocabulary ability, informant ratings of cognitive decline, and risk factors identified in a previously published and validated delirium prediction rule.[4,5]

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Methods

The Successful Aging after Elective Surgery (SAGES) study is an ongoing prospective cohort study of older adults undergoing elective major noncardiac surgery. The study design and methods have been described previously.[6] Briefly, eligible participants were 70 years and older, English speaking, scheduled to undergo elective surgery at 1 of 2 Harvard-affiliated academic medical centers, and with an anticipated length of stay of at least 3 days. Eligible surgical procedures were total hip or knee replacement; lumbar, cervical, or sacral laminectomy; lower extremity arterial bypass surgery; open abdominal aortic aneurysm repair; and colectomy. Exclusion criteria were evidence of dementia, delirium, hospitalization within 3 months, terminal condition, legal blindness, severe deafness, history of schizophrenia or psychosis, and history of alcohol abuse. A total of 566 patients were enrolled between June 18, 2010, and August 8, 2013. Written informed consent was obtained from all participants according to the procedures approved by the institutional review boards of Beth Israel Deaconess Medical Center and Brigham and Women's Hospital, the 2 study hospitals, and Hebrew SeniorLife, the study coordinating center, all located in Boston, Massachusetts.

Participants and Assessments

Participants were interviewed in their own homes on average 2 weeks prior to surgery. During hospitalization, participants received a daily delirium assessment (described in the following section). Interviews were fully structured and conducted by lay research associates who received at least 4 weeks of intensive training and semiannual standardization. Chart reviews were performed by a trained research physician. All data collection staff were blinded to the study hypotheses and to the data collected in previous interviews.[7]

Delirium assessment. Delirium assessments, conducted daily in hospital beginning with postoperative day 1, involved brief mental status testing with tasks of attention, orientation, and memory.[6,8] Delirium symptoms were assessed with the Delirium Symptom Interview[9] and interviews with nurses and, if available, family members. Delirium case identification used the Confusion Assessment Method (CAM)[10] and a standardized chart review method for delirium.[11,12] If either was positive, the patient was considered delirious.

Cognitive performance assessment. At preoperative baseline, participants were assessed with a neuropsychological battery that included tests of attention, recall, memory, language, executive functioning, and visuospatial processing.[6,13,14] Performance on Trails A and B,[15] Digit Span Forwards and Backwards,[16] Semantic and phonemic fluency,[17] the Boston Naming Test,[18] Digit Symbol Substitution,[19] Hopkins Verbal Learning Test[20] immediate recall (sum of 3 learning trials) and delayed recall, and the Visual Search and Attention task[21] were combined into a single unidimensional composite using a graded item response theory model.[22] Details of the composite construction have been previously described.[13] The resulting composite—the general cognitive performance (GCP) score—is calibrated against data from the Aging, Demographics, and Memory Study, a substudy of the Health and Retirement Study. In a sample representative of the community-dwelling older adults (age 70+) living in the United States, the GCP has a mean of 50 and standard deviation of 10, and scores 45 and higher are consistent with unimpaired cognitive functioning (Mini-Mental State Examination [MMSE][23] scores of 24 and higher).[13]

An additional cognitive measure in our preoperative baseline battery, but not included in the GCP composite, was the Wechsler Test of Adult Reading (WTAR).[16] The WTAR includes 50 irregularly spelled words of increasing complexity that the participant is asked to read aloud. The total score is the number of words correctly pronounced (range: 0-50). The WTAR and similar tests such as the Wechsler Adult Intelligence Scale–Vocabulary subtest[24] and the National Adult Reading Test[25] are often used as indicators of premorbid intelligence.[26] We also conducted interviews using the Informant Questionnaire for Cognitive Decline in the Elderly[27] (IQCODE), an informant-rated (family member) measure that records potential cognitive decline observed over the previous 10 years.

Delirium Risk Factors

The measure of delirium risk we use was published and validated by Inouye and colleagues (1993).[4,5] This risk index was chosen since it has been validated in both medical[4,5] and surgical[4,5] patients. The risk index includes 4 risk factors: vision impairment, defined as best-corrected vision worse than 20/70 on both near and distant binocular tests; cognitive impairment, defined as performance of less than 24 of 30 on the MMSE; severe illness defined as an Acute Physiology and Chronic Health Evaluation II (APACHE II)[28] score above 16; and dehydration, defined as a blood urea nitrogen (BUN)/creatinine ratio 18 or more.[29] We optimally rescaled the additive sum of risk factors. The motivation for this rescaling was to obtain a linear predictor of delirium risk that could be used as a continuous predictor in regression models and meaningfully contrast effect estimates against other continuous predictors. To accomplish this, we regressed the risk for postoperative delirium on the count of risk factors as a categorical predictor. Then, we assigned values to the counts based on the log odds ratio (relative to the lowest count value) for delirium estimated for each count level. To minimize risks for a chance association, we repeated this process in 1001 bootstrap replications and used the mean log odds regression weights as the new scaling metric. The ascending values assigned were: 0 (no risk factors present), 0.20, 1.40, and 2.34 (all 4 risk factors present).

Additional Study Variables

The baseline interview assessed sex, race, ethnicity, education, and the Modified MMSE,[30] which was equated to the MMSE

and used in the delirium risk index. Age and Charlson comorbidity score[31] were determined from chart review.

Statistical Analysis

Logistic regression models were used to characterize the relationship between GCP scores and the risk of postoperative delirium. Covariates were mean centered, except for age, which was centered at 75 years, near the median of the baseline age distribution. Relative risk estimates were obtained as a nonlinear combination of estimated logistic regression parameter estimates, and interval estimates were derived from variance estimates of the nonlinear combinations using the delta method. Continuous predictors were standardized to 2 standard deviations following the suggestion of Gelman.[32] The 2 standard deviation standardization metric is useful because this scaling strategy places effect estimates associated with continuous predictors on approximately the same scale as those for binary predictors. Parameter estimates were obtained with Stata software version 14.1 (Stata Corp, College Station, Texas).

We estimated 3 models. In the first, we regressed the risk of delirium on GCP score. For descriptive purposes, we also investigated the bivariable association of demographic, vocabulary ability, delirium risk factors, and medical comorbidities. In the second, we add demographic predictors including age, sex, race (white, non-Hispanic participants vs all others), WTAR score, and IQCODE score to the model with GCP predicting delirium. The remaining coefficient for GCP score in this multivariable-adjusted model tells us about the remaining explanatory power of GCP after accounting for demographics and WTAR score. In the third, we add risk factors for delirium identified in a published clinical risk prediction rule for delirium, as well as medical comorbidity.

Finally, we evaluated the relative importance of predictors in the risk for delirium model using dominance analysis.[33-35] Dominance analysis decomposes the average R^2 statistic (in our regressions, McFadden R^2) across all risk factors. The relative importance of a variable in a multivariable regression is its contribution to the overall model R^2 including direct and indirect effects on an outcome. This is a strong approach when predictors are correlated: if we examined only the magnitude of the regression coefficient, we would only be using information regarding the direct effect of a predictor.

Sensitivity Analyses

To assess the possibility that our results were sensitive to the distribution of background delirium risk factors in our SAGES sample, we performed 2 sensitivity analyses. The first involved restricting the sample to SAGES participants with at least 1 of the Inouye et al (1993) delirium risk factors. The second involved reestimating our predictive models for delirium given GCP and other predictors, and the dominance analysis, within multiple (1001) bootstrap, draws from our original sample, where persons were selected with weights producing a distribution on the categorized sum of Inouye et al (1993) delirium risk factors that matches that of the validation sample studied in Inouye et al (1993). This represents an approximate Bayesian[36] poststratification approach to address potential selection bias.[37] We undersample from among patients with 0 and 1 to 2 of the 4 risk factors and oversample from the patients with 3 to 4 risk factors.

Table 1. Baseline Characteristics of the SAGES Study Cohort.[a]

Characteristic	Full Sample, N = 566	Delirium, n = 135	No Delirium, n = 431
Age, mean (SD), years	76.7 (5.2)	77.5 (5.0)	76.4 (5.3)
Female, n (%)	330 (58)	82 (61)	248 (58)
Nonwhite, n (%)	43 (8)	13 (10)	30 (7)
Education, mean (SD), years	15.0 (2.9)	14.7 (3.0)	15.0 (2.9)
Married, n (%)	335 (59)	79 (59)	256 (59)
Lives alone, n (%)	169 (30)	40 (30)	129 (30)
Charlson score, n (%)			
0	260 (46)	54 (40)	206 (48)
1	140 (25)	23 (17)	117 (27)
2+	166 (29)	58 (43)	108 (25)
IQCODE score, mean (SD)	3.12 (0.25)	3.20 (0.22)	3.18 (0.30)
GCP score, mean (SD)	57.5 (7.4)	54.6 (6.6)	58.4 (7.4)
WTAR score, mean (SD)	37.7 (10.0)	35.7 (9.8)	38.3 (9.9)
Inouye (1993) delirium risk score, mean (SD)	0.19 (0.15)	0.33 (0.55)	0.15 (0.28)
Vision impairment, yes, n (%)	3 (0.5)	2 (1.5)	1 (0.2)
Cognitive impairment, yes, n (%)	33 (6)	15 (11)	18 (4)
Severe illness, yes, n (%)	33 (6)	23 (17)	10 (2)
Dehydration, yes, n (%)	275 (49)	66 (49)	209 (49)

Abbreviations: GCP, General Cognitive Performance; IQCODE, Informant Questionnaire for Cognitive Decline in the Elderly; SAGES, Successful Aging after Elective Surgery; SD, standard deviation; WTAR, Wechsler Test of Adult Reading.

[a]The Charlson comorbidity score ranged from 0 to 35, with scores of 2 or more indicating higher comorbidity. The Inouye (1993) risk score ranges from 0 to 2.34 as explained in text and is the weighted sum of 4 markers: vision impairment, vision worse than 20/70 on both near and distant binocular tests; cognitive impairment, less than 24 of 30 on the Mini-Mental State Examination; severe illness, Acute Physiology and Chronic Health Evaluation II (APACHE II) above 16; dehydration, blood, urea, nitrogen/creatinine ratio 18 or more.

Results

Baseline characteristics of the patients overall and by the delirium group are shown in Table 1. The mean age (SD) of the sample was 76.7 (5.2) years, and 58% were women. Delirium occurred in 135 (24%) of the 566 patients. At baseline, the delirium group had greater levels of comorbidity and lower GCP scores. The baseline mean GCP values in both groups were above 50, the expected mean for a representative sample of US older adults.[23] It is also important to point out that, as expected, the delirium risk score was higher and most of the 4 indicators comprising the delirium risk score were more prevalent in the group that developed delirium, the notable exception being BUN/creatinine ratio.

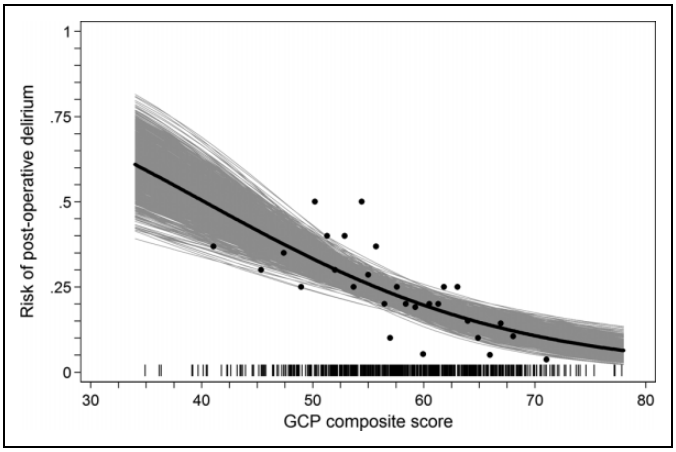

Figure 1. Risk for postoperative delirium as a function of general cognitive performance (GCP) score: Results from the Successful Aging after Elective Surgery (SAGES) study (N = 566). This demonstrates the relationship between the risk for postoperative delirium and preoperative GCP score. The heavy line demonstrates the observed relationship as derived from a logistic regression model. Dispersion is illustrated with fitted lines from 1001 bootstrap replications from the observed data. The points depict observed rates of postoperative delirium among groups of patients binned according to GCP score, allowing no fewer than 20 persons in each bin and plotted at the median GCP score within the bin. The rug marks at the bottom of the figure illustrate the distribution of persons according to their GCP score.

Table 2. Relative Risk of Postoperative Delirium in Bivariable and Multivariable Models: Results From the SAGES Study.[a]

	Relative Risk (95% CI)		
Predictor	Bivariable Models	Multivariable Model 1	Multivariable Model 2
Lower GCP score (per half SD)	2.0 (1.5-2.5)	2.0 (1.3-2.6)	1.9 (1.2-2.6)
Higher age (per half SD)	1.3 (1.0-1.7)	1.0 (0.6-1.3)	1.0 (0.6-1.3)
Female (vs male)	1.1 (0.8-1.4)	1.2 (0.8-1.5)	1.2 (0.8-1.7)
All other race and ethnicity groups (vs white, non-Hispanic)	1.0 (0.4-1.6)	0.5 (0.1-1.0)	0.7 (0.2-1.1)
Lower education (per half SD)	1.1 (0.9-1.2)	0.9 (0.7-1.1)	0.9 (0.7-1.1)
Lower WTAR score (per half SD)	1.4 (1.1-1.8)	1.3 (0.8-1.9)	1.2 (0.6-1.7)
Higher IQCODE score (per half SD)	1.6 (1.2-2.0)	1.5 (1.1-1.9)	1.5 (1.1-2.0)
Higher Inouye 1993 risk score, optimum scaling (per SD)	1.7 (1.3-2.1)	-	1.6 (1.2-2.0)
Higher Charlson comorbidity (per SD)	1.2 (1.0-1.4)	-	1.1 (1.0-1.3)

Abbreviations: CI, confidence interval; GCP, General Cognitive Performance; IQCODE, Informant Questionnaire for Cognitive Decline in the Elderly; SD, standard deviation; WTAR, Wechsler Test of Adult Reading.
[a]N = 566.

Delirium and Cognitive Performance: Bivariable Model

We examined the risk for postoperative delirium associated with GCP score (Figure 1 and Table 2). In Figure 1, the probability of developing postoperative delirium as a function of preoperative GCP score is illustrated. The relationship is plotted with a heavy black line and is derived from a logistic regression model using a linear function for GCP. The dispersion in this relationship is illustrated with 1001 separate predicted lines from as many bootstrap resamples drawn from the observed data. In the observed and bootstrap samples, we allowed for a competition between linear and quadratic functions for GCP, and in all cases, the linear model was judged to be superior by Bayesian information criteria. The rug illustrates the distribution of GCP scores in the observed sample and observed proportions of persons with delirium where sample participants have been binned according to ascending GCP score values. This plot demonstrates that the relationship between delirium risk and preoperative cognitive performance is strong and linear across the range of observed cognitive performance. This result implies that across all levels of cognitive function, even high function, persons with better cognitive function are expected to have a lower risk of delirium than persons with lower levels of cognitive function. In Table 2 (Bivariable Models column) for each half standard deviation lower GCP score, the relative risk of developing postoperative delirium is 2.0 (95% confidence interval [CI]: 1.5-2.5). This association is stronger than associations identified for age (relative risk per half standard deviation, $RR_{s/2} = 1.3$), education ($RR_{s/2} = 1.1$), WTAR score ($RR_{s/2} = 1.4$), proxy report of cognitive decline (IQCODE score, $RR_{s/2} = 1.6$), and the optimally scaled delirium risk rule of Inouye et al (1993; $RR_{s/2} = 1.7$).

Delirium and Cognitive Performance: Multivariable Model Including Demographics

We examined the risk for postoperative delirium associated with general GCP score and adjusted for demographics and vocabulary ability (Table 2, Multivariable Model 1). The association of GCP and delirium is unchanged ($RR_{s/2} = 2.0$, 95% CI: 1.3, 2.6), implying that the association of GCP and delirium risk is not confounded or mediated by other demographic, vocabulary ability, or proxy report of cognitive decline (IQCODE score). On the other hand, with the exception of proxy-reported cognitive decline, all sociodemographic risk factors significant in the bivariable case (95% CIs do not include 1.0) have attenuated associations that are not significantly different from what might be expected due to chance when GCP is controlled. Therefore, the association of age is fully mediated, and vocabulary ability is partially mediated, by GCP in explaining postoperative delirium risk.

Delirium and Cognitive Performance: Multivariable Model Including Delirium Risk Score

Table 2, Multivariable Model 2, shows the results of the multivariable model for delirium risk adjusted for demographics,

vocabulary ability, and published delirium risk factors. In this model, the association of lower GCP score is only slightly attenuated and probably reflects that cognitive impairment is included in the Inouye 1993 delirium risk score. The association of the delirium risk score is also slightly attenuated relative to the bivariate model, reinforcing this interpretation. Only GCP, IQCODE, and the Inouye 1993 delirium risk score were significant predictors of postoperative delirium as suggested by CIs not including 1.0.

Relative Importance (Dominance) Analysis

The results of the dominance analysis are reported in Table 3. The Relative Importance column indicates the proportion of the total model R^2 (McFadden[39] pseudo-R^2) that is attributable to the risk factor. The 95% CI is derived from 1001 bootstrap replications. The Dominant in Bootstrap Replication (%) column indicates the proportion of the 1001 replicates in which the risk factor dominates all other risk factors. Which "dominates" is based on the R^2 contribution—including direct and indirect effects—for the risk factor is greater than any other risk factors' total effect. In our observed data, the GCP score is the dominant risk factor. It accounts for 29% of the model R^2 (which was relatively small, $R^2 = .09$), and in half of all bootstrap replications was the dominant covariate. The second most important predictor was the Inouye 1993 risk index, which contributed 25% of the model R^2 and was the dominant risk factor in 35% of the 1001 bootstrap replications. The IQCODE score was occasionally (12% of the 1001 replications) the dominant risk factor. The remaining risk factors (WTAR score, age, sex, race/ethnicity, and education) were relatively unimportant risk factors for postoperative delirium in this analysis.

Table 3. Dominance Analysis of Multivariable Model for Postoperative Delirium Risk.[a]

Predictor	Relative Importance	95% Confidence Interval	Dominant in Bootstrap Replication (%)
Lower GCP score (per half SD)	0.29	(0.11-0.51)	0.50
Higher Inouye 1993 risk score, optimum scaling (per SD)	0.25	(0.05-0.49)	0.35
Higher IQCODE score (per half SD)	0.16	(0.02-0.37)	0.12
Higher Charlson comorbidity (per SD)	0.09	(0.00-0.27)	0.03
Lower WTAR score (per half SD)	0.07	(0.02-0.18)	0.00
Higher age (per half SD)	0.04	(0.01-0.13)	0.00
All other race and ethnicity groups (vs white, non-Hispanic)	0.03	(0.00-0.12)	0.00
Lower education (per half SD)	0.03	(0.01-0.10)	0.00
Female (vs male)	0.03	(0.00-0.13)	0.00

Abbreviations: GCP, General Cognitive Performance; IQCODE, Informant Questionnaire for Cognitive Decline in the Elderly; SAGES, Successful Aging after Elective Surgery; SD, standard deviation; WTAR, Wechsler Test of Adult Reading.

[a]The Relative Importance column indicated the proportion of the total model R^2(R^2= .09) that is attributable to the risk factor. The 95% confidence interval is derived from 1001 bootstrap replications of each model. The Dominant in Bootstrap Replication (%) column indicates the proportion of the 1001 replicates in which the risk factor dominates all other risk factors. Dominates means the R^2contribution including direct and indirect effects for the risk factor is greater than any other risk factors' total effect.

Sensitivity Analysis

Sensitivity analyses reveal that our inferences are sensitive to the distribution of delirium risk factors in the sample. In the restriction sensitivity analysis—omitting patients with none of the Inouye et al (1993) delirium risk factors—our pattern of results in terms of risk ratios was unchanged, with the GCP having the highest relative risk, followed by the Inouye et al (1993) risk score and IQCODE ($RR_{s/2}$ of 1.9, 1.7, and 1.6, respectively). However, the dominance analysis favored the Inouye et al (1993) risk score, followed by the GCP and then IQCODE. The poststratification sensitivity analysis revealed the Inouye et al (1993) risk factor score, WTAR, and GCP to have as approximately equivalent risk ratios ($RR_{s/2}$ of 1.8, 1.8, and 1.7, respectively), but the dominance analysis clearly favored the Inouye et al (1993) risk score. These sensitivity analyses demonstrate that GCP remains among the most powerful delirium risk factors, but dominance over other risk factors is sample dependent. Caution in interpreting the results of these sensitivity analyses is called for because the restriction sensitivity analysis might attenuate the effect of the Inouye et al (1993) delirium risk score due to restricted range, and the poststratification sensitivity analysis makes inordinate use of the 5 (1%) patients falling into the highest risk strata to represent 25% of the weighted sample of patients matching the Inouye et al (1993) validation sample.

Discussion

In this prospective cohort study of high functioning older persons undergoing major scheduled noncardiac surgery, we demonstrated that risk of delirium after surgery is strongly related to presurgical cognitive performance level, even at levels above the population median, which would be considered unimpaired. This risk gradient appears to be linear across the range of cognitive ability included in our sample and measured with a neuropsychological battery capable of measuring very low and very high levels of cognitive performance. Additionally, we show that GCP is more important than other risk factors from a previously described and validated delirium risk tool and appears to act directly on delirium risk in a manner robust to control for patient sociodemographic characteristics and additional clinical factors.

There are several plausible interpretations of our finding that the GCP is a strong predictor of delirium risk, even after adjusting for age, sex, race/ethnicity, vocabulary performance,

and informant report of long-term cognitive decline. One is that persons with GCP scores that fall below levels predicted by the covariates we included in our models, their demographic profiles, and markers of cognitive decline are at increased risk for postoperative delirium. Among likely explanations for having GCP levels lower than expected is the presence of preexisting cognitive decline. Such declines could be due to unmeasured individual difference factors and/or lifetime exposures that contribute to accumulating cognitive impairments (eg, lead exposure, repeated head trauma[39]) or might reflect the effect of accelerated brain aging or relative decrements in brain plasticity.[40] They might also reflect the presence of a preclinical neurodegenerative or dementing process, potentially predisposing factors for delirium.[41] These hypotheses would require confirmation in future studies. Studies measuring mechanisms of brain cortical plasticity using noninvasive brain stimulation methods[42,43] and determinations in the cerebrospinal fluid or neuroimaging studies to identify possible amyloid deposits and other biomarkers of preclinical dementia would be valuable to extend our findings.

Our findings do not amount to a test of the cognitive or brain reserve hypothesis in delirium.[44] Reserve is a concept used to explain the observation that some individuals function better than others in the presence of brain pathology.[45] This analysis does not include measures of brain pathology. Moreover, current (preoperative) cognitive level is not a commonly used indicator of cognitive reserve,[46] although the strategy has been proposed.[47]

Our study has some important strengths, including a relatively large prospective cohort and state-of-the-art delirium assessments and high-quality data collection with little missing data.[7] However, several limitations should also be mentioned. First, we only chose to use 1 predictive model for proof of principle. Several others might have been chosen. The model we chose has been widely used and validated in both medical and surgical samples. Another limitation is our cognitive battery, although being relatively extensive in the field of delirium research, would be considered overly brief in the field of developmental psychology and provides limited assessment of individual cognitive domains. Additionally, our study included only persons aged at least 70 years and excluded persons with evidence of dementia by chart review or self-report or severe cognitive impairment. It may be that if we had included younger adults, age would emerge as the dominant risk factor, or if we had included persons with dementia, the relationship of cognitive performance and delirium risk would be nonlinear.

In addition, our sample represents a highly educated population from a single geographic location. Although the internal validity is not threatened, generalizability may be limited and the findings will need to be replicated in more diverse populations and settings. We conducted 2 sensitivity analyses, both addressing the distribution of the Inouye et al (1993) delirium risk factors in our sample. In either restricting to patients with at least 1 risk factor or matching the distribution of delirium risk factors to Inouye et al's (1993) validation sample, we continue to see general preoperative cognitive performance as a strong risk factor, but dominance over the Inouye et al (1993) risk score is sample dependent.

Our study finds that preoperative cognitive level is strongly and linearly related to the risk of postoperative delirium. This effect is independent of—and more important than—other published and validated delirium risk factors, medical comorbidity, and sociodemographic factors. The cause of the association is not well understood. The importance of cognitive level as a risk factor for delirium may have been overlooked in previous research as a consequence of the use of mental status screening instruments with low measurement fidelity at average and higher levels of cognitive ability. Our findings may encourage greater efforts to identify subtle or mild degrees of cognitive impairment preoperatively, since these patients may benefit from institution of delirium prevention strategies.

Appendix A

Preoperative Cognitive Performance Is the Dominant Risk Factor for Delirium Among Older Adults

Richard N. Jones, et al.

SAGES Study Group: (Presented in alphabetical order; individuals listed may be part of multiple groups but are listed only once under major activity). Overall Principal Investigator: Sharon K. Inouye, MD, MPH (Overall principal investigator [PI], Administrative Core, Project 1; Hebrew SeniorLife [HSL], Beth Israel Deaconess Medical Center [BIDMC], Harvard School of Public Health [HMS]). Project and Core Leaders: David Alsop, PhD (Project 3; BIDMC, HMS); Richard Jones, ScD (Data Core, Project 4; Brown University); Thomas Travison, PhD (Data Core, HSL), Edward R. Marcantonio, MD, SM (Overall Co-PI, Epidemiology Core, Project 2; BIDMC, HMS).

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Authors' Note

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