Cognitive Reserve and Postoperative Delirium in Older Adults

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OBJECTIVES: To examine the role of cognitive reserve in reducing delirium incidence and severity in older adults undergoing surgery.

DESIGN: Prospective cohort study.

SETTING: Hospital.

PARTICIPANTS: Older adults (mean age 71.2, 65% women) undergoing elective orthopedic surgery (N = 142).

MEASUREMENTS: Incidence (Confusion Assessment Method) and severity (Memorial Delirium Assessment Scale) of postoperative delirium were the primary outcomes. Predictors included early- (literacy) and late-life (cognitive activities) proxies for cognitive reserve.

RESULTS: Forty-five participants (32%) developed delirium. Greater participation in cognitive activity was associated with lower incidence (odds ratio = 0.92 corresponding to increase of 1 activity per week, 95% confidence interval (CI) = 0.86–0.98, $P = .006$) and severity ($B = -0.06$, 95% CI = −0.11 to −0.01, $P = .02$) of delirium after adjustment for age, sex, medical illnesses, and baseline cognition. Greater literacy was not associated with lower delirium incidence or severity. Of individual leisure activities, reading books, using electronic mail, singing, and computer games were associated with lower dementia incidence and severity.

CONCLUSION: Greater late-life cognitive reserve was associated with lower delirium incidence and severity in older adults undergoing surgery. Interventions to enhance cognitive reserve by initiating or increasing participation in cognitive activities may be explored as a delirium prophylaxis strategy. **J Am Geriatr Soc 64:1341–1346, 2016.**

Key words: delirium; cognitive reserve; epidemiology

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Delirium is a major health problem. Older adults who experience delirium are at greater risk of functional decline, dementia, and mortality.[1–3] The severity of delirium also affects outcomes; individuals with more-severe delirium are at greater risk of institutionalization and death.[4] The concept of cognitive reserve postulates that some individual characteristics help maintain cognitive function in the face of accumulating brain pathology[5] and lower the risk of dementia.[6,7] Because dementia predisposes an individual to delirium, greater cognitive reserve may reduce the risk of developing delirium.[8]

Although improving cognitive reserve may be a potential delirium preventive strategy,[9] the link between cognitive reserve and delirium needs to be clarified. Findings from previous studies are mixed; some show an inverse relationship between education and delirium incidence,[10–12] whereas others reported negative results.[8,13–16] The limited studies have focused mainly on early-life cognitive reserve proxies such as literacy and years of education. Few have prospectively examined the role of later-life cognitive reserve proxies (e.g., cognitive activities) in reducing risk of delirium.

To address these gaps in knowledge regarding the role of cognitive reserve in delirium, a prospective cohort study was conducted in 142 older adults undergoing elective orthopedic surgery. Older adults undergoing surgery are at high risk of developing delirium,[1] with postoperative delirium incidence ranging from 12% to 51%.[3] Literacy was examined as a measure of cognitive reserve built up earlier in life and participation in cognitive activities as a late-life cognitive reserve measure. It was hypothesized that older adults with greater cognitive reserve (measured using literacy or cognitive activities as proxies) would have lower incidence and severity of postoperative delirium. Based on cognitive reserve studies in dementia,[17] it was predicted that the late-life cognitive reserve measure would be more strongly associated with delirium incidence and severity than the early-life measure. Unlike early-life cognitive reserve activities, activities that influence late-life cognitive reserve can be enhanced and encouraged. Establishing the effect of late-life cognitive activities on incidence and severity of delirium can help not only to improve delirium risk assessments, but also to guide development of new preventive strategies.

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METHODS

Study Population

This was a prospective cohort study to examine the role of cognitive reserve in delirium. Potential participants were recruited from patients of three surgeons attending the Montefiore Medical Center Orthopedics outpatient clinics (Bronx, NY) for preoperative evaluations for elective hip, knee, or spine surgeries from October 2011 to August 2014. This elective surgery population was selected because preoperative and postoperative schedules and management and postoperative mobilization procedures were standardized for the individual surgeries, and these schedules and procedures were not based on preoperative cognitive reserve status. Inclusion criteria were aged 60 and older and English speaking. Exclusion criteria were delirium at baseline, severe auditory or visual deficits, physician diagnosis of dementia, and Mini-Mental State Examination (MMSE) score of less than 24. The local institutional review board approved the study design and waived written consent because the study was deemed to be of no to minimal risk. Oral informed consent was obtained from participants.

Cognitive Reserve

Research assistants obtained information on baseline measures of cognitive reserve[5,17] and other covariates at the preoperative clinic visit. They also administered the Confusion Assessment Method (CAM), described below, to confirm absence of delirium at enrollment.

Literacy

Literacy was assessed using the American National Adult Reading Test—a 45-word reading test. Because of variability in quality of education, literacy may be a better measure than years of schooling.[17]

Cognitive Activities

Greater participation in cognitive activities is associated with lower risk of dementia[18] and was measured using a previously validated Cognitive Activity Scale.[6,7,17,19] Briefly, the Cognitive Activity Scale measured frequency of participation in 20 cognitive activities over the previous week. One point on the Cognitive Activity Scale corresponds to participating in one activity per day per week. Eight activities done by less than 5% of the sample were excluded to improve reliability and increase generalizability. The remaining 12 activities were reading newspapers, reading books, knitting, playing cards, playing board games, playing computer games, doing crossword puzzles, playing bingo, using electronic mail (e-mail), singing, writing, and attending group meetings. Participation frequency in the 12 activities was summed to generate an overall score (range 0–84 activity-days per week).

Covariates

Cognition was evaluated using the MMSE.[3] Mood was assessed using the 15-item Geriatric Depression Scale (GDS).[11,15,20] The Charlson Comorbidity Index was used to quantify medical comorbidity.[3] Preoperative functional status was assessed using a validated activity of daily living scale (range 0–14).[21] Other covariates with an inconsistent relationship with delirium in prior studies were not significantly associated with delirium incidence in this sample in the preliminary analyses and are not reported: head size, alcohol intake, medication count and class, visual loss, current or past smoking, and preoperative and postoperative levels of pain.[3,22,23]

Outcome Assessment

Primary outcomes were delirium incidence according to the CAM and delirium severity according to the Memorial Delirium Assessment Scale. A single investigator (AT) trained in delirium assessment and blinded to baseline assessments examined all participants after surgery. As in other hospital-based delirium studies,[24] participants were not evaluated in the first postoperative day to avoid confounding by any residual effects of anesthesia or pain medications on cognition. The initial examination was conducted in all participants at a median of 22 hours (interquartile range (IQR) 19–26 hours) after surgery, and the second assessment at a median of 32 hours (IQR 29–34 hours) after surgery. In individuals who did not meet delirium criteria at either in-person assessment, the investigator conducted a chart review of medical and nursing records for features consistent with confusion, altered mental status, or agitation.[16] All information was reviewed with a senior neurologist (JV), and no additional cases of delirium were identified beyond the cases identified during the two in-person assessments or chart review.

The CAM is the most widely used method of detecting delirium and is based on acute and fluctuating change in ability to maintain attention plus disordered thinking or altered level of consciousness.[25] A senior neurologist (JV) reviewed CAM interviews in 20 participants, and there was excellent agreement on delirium diagnosis (interrater reliability κ statistic = 1.00).

The Memorial Delirium Assessment Scale is a highly reliable scale that rates delirium severity on a 4-point scale on 10 items assessing disturbances in arousal and level of consciousness, attention, memory, cognition, and psychomotor activity (range 0–30).[26]

Data Analysis

All analyses were conducted using Stata version 11.2 (Stata Corp., College Station, TX). Descriptive statistics were used to compare baseline characteristics of participants who did and did not develop delirium. For delirium incidence, logistic regression was performed using cognitive reserve measures as predictors and reported as odds ratio (ORs) with 95% confidence intervals (CIs). The two predictors were examined individually and entered together in a single model adjusted for all covariates to assess their independent effects on delirium incidence. All models were adjusted for age, sex, comorbidities, and MMSE score. Covariates were chosen based on significant associations with delirium in univariate analyses and previous literature. The association between individual cognitive activities and delirium incidence was also explored. The final sample size (n = 142) and observed delirium incidence (32%) provided greater than 90% power to test the main hypotheses. Linear regression analysis was performed to assess the association between cognitive reserve measures and postoperative delirium severity and reported as estimates (B) with 95% CIs. The predictors were modeled individually and together in the fully adjusted models. The association between individual cognitive activities and delirium severity was examined as an exploratory analysis. Model assumptions were tested statistically and graphically and were adequately met.

Although individuals with dementia were excluded using the MMSE and clinical information, variability in cognitive status in this sample (including mild dementia cases) is expected. Baseline cognitive status was accounted for by adding MMSE scores to main models. Based on published norms,[27] subgroup analyses were conducted by stratifying participants into those with MMSE scores of 24–27 (mild cognitive impairment (MCI)) and those with scores of 28–30 (cognitively normal). Additional sensitivity analyses to account for effects of sex, surgery type, and influence of individual cognitive activities on delirium risk and severity were also performed.

RESULTS

Study Population

Of 178 individuals screened, 155 were enrolled, 15 declined, and eight were excluded. All were living at home before surgery. Reasons for exclusion were previous dementia diagnosis (n = 2), non-English speaking (n = 2), younger than 60 (n = 3), and failed medical clearance (n = 1). Of the 155 enrolled, eight dropped out before their surgery, two had surgery cancelled, and three were lost to follow-up, leaving 142 eligible participants (mean age 71.2, 65% women). Surgeries were performed 18 ± 15 days after baseline visit; there were 98 knee, 42 hip, and two spine surgeries. Seventy-seven participants received spinal, 60 general, and 52 epidural anesthesia. Delirium rates did not differ according to surgery or anesthesia type (Table 1).

None of the participants were taking cholinesterase inhibitors, anxiolytics, or antipsychotics preoperatively or were started on these medications during their hospital stay. No participant was taking a narcotic preoperatively. None were comatose, developed strokes or seizures, or required intensive care during or after surgery.

Forty-five participants (32%) developed postoperative delirium: 31 detected on the first assessment and 14 more on the second assessment. Mean hospital stay was 3 days; 82% were discharged by Postoperative Day 4 and 90% by Postoperative Day 5. Age, sex, comorbidity, depression scores, functional status, preoperative pain scores, and postoperative pain scores did not differ according to final delirium outcome status (Table 1). Those who developed delirium had lower literacy and less participation in cognitive activities (Table 1).

Delirium Incidence

The Cognitive Activity Scale but not literacy scores predicted delirium incidence when examined individually (Table 2). In a model with both cognitive reserve measures entered simultaneously, higher levels of cognitive activities (for each additional activity per week, OR = 0.92, 95% CI = 0.86–0.98) but not literacy (for each 1 point increase in literacy score, OR = 0.99, 95% CI = 0.95–1.04) predicted delirium incidence. Figure 1 illustrates incidence of delirium based on cognitive reserve levels; those with lower cognitive activity and literacy levels had higher incidence rates of delirium.

Of the 12 activities, reading books (OR = 0.85, 95% CI = 0.72–0.99), using e-mail (OR = 0.81, 95% CI = 0.68–0.96), and playing computer games (OR = 0.60, 95% CI = 0.39–0.95) were associated with lower risk of delirium incidence in the full models.

Table 1. Baseline Characteristics of Study Population

Characteristic	Overall	No Delirium, n = 97	Delirium, n = 45	*P*-Value
Age, mean ± SD	71.2 ± 7.5	70.9 ± 7.8	71.8 ± 7.0	.37
Female, n (%)	92 (65)	64 (66)	28 (62)	.71
High school–level education, n (%)	106 (75)	78 (81)	28 (62)	.02
General anesthesia, n (%)	60 (38)	40 (41)	18 (40)	.89
Regional anesthesia, n (%)	92 (65)	65 (67)	27 (60)	.42
Hip replacement surgery, n (%)	41 (29)	31 (32)	10 (23)	.25
Surgery length, minutes, mean ± SD	96.2 (27.9)	95.9 (27.0)	96.8 (31.2)	.87
Perioperative opiate use, n (%)	26 (18)	18 (19)	8 (18)	.92
Activity of daily living scale score, median (IQR) (range 0–14)	1 (0–2)	1 (0–2)	1 (0–2)	.48
Geriatric Depression Scale score, median (IQR) (range 0–15)	2 (1–4)	2. (1–4)	2 (1–4)	.45
Charlson Comorbidity Index >0, n (%)	73 (57)	50 (56)	23 (59)	.72
Body mass index, kg/m^2, mean ± SD	32.5 ± 6.5	32.8 ± 6.9	31.9 ± 5.8	.44
Preoperative pain score at rest, mean ± SD (range 0–10)	4.3 ± 3.0	4.3 ± 3.0	4.2 ± 3.2	.78
Postoperative pain score at 24 hours, mean ± SD (range 0–10)	8.3 ± 2.1	8.3 ± 2.1	8.5 ± 2.1	.48
Mini-Mental State Examination score, median (IQR) (range 0–30)	29.0 (26.0–30.0)	29.0 (27.5–30.0)	27.0 (25.0–29.0)	<.001
Cognitive reserve proxy scores, mean ± SD				
Number of American National Adult Reading Test errors (range 0–45)	21.2 ± 12.3	18.4 ± 10.9	27.0 ± 13.0	<.001
Cognitive Activity Scale score (range 0–84)	13.9 ± 9.7	16.5 ± 9.7	8.5 ± 7.2	<.001

SD = standard deviation; IQR = interquartile range.

Table 2. Incident Delirium Risk Associated with Cognitive Reserve Measures at Baseline: Logistic Regression Model

	Odds Ratio (95% Confidence Interval) *P*-Value	
Variable	Model 1	Model 2
Literacy, American National Adult Reading Test corrected	0.98 (0.94 to 1.02) .25	[a]
Cognitive activities, days per week[b]	[a]	0.92 (0.86 to −0.98) .006
Age	0.97 (0.91–1.04) .36	0.95 (0.88 to −1.02) .13
Sex	1.16 (0.46 to −2.96) .75	1.01 (0.38 to −2.71) .98
Charlson Comorbidity Index	0.96 (0.39 to −2.38) .94	1.04 (0.40 to −2.69) .94
Mini-Mental State Examination	0.67 (0.52–0.86) .002	0.67 (0.52–0.85) .001

Literacy (Model 1) and cognitive (Model 2) activities were examined individually (see Methods).

[a] Variable not included in model. Literacy or cognitive activities was included in each model. Results including both variables in one model are presented in the Results section.

[b] Reading newspapers, reading books, knitting, playing cards, playing board games, playing computer games, doing crossword puzzles, playing bingo, electronic mail, singing, writing, and participating in group meetings (range 0–84).

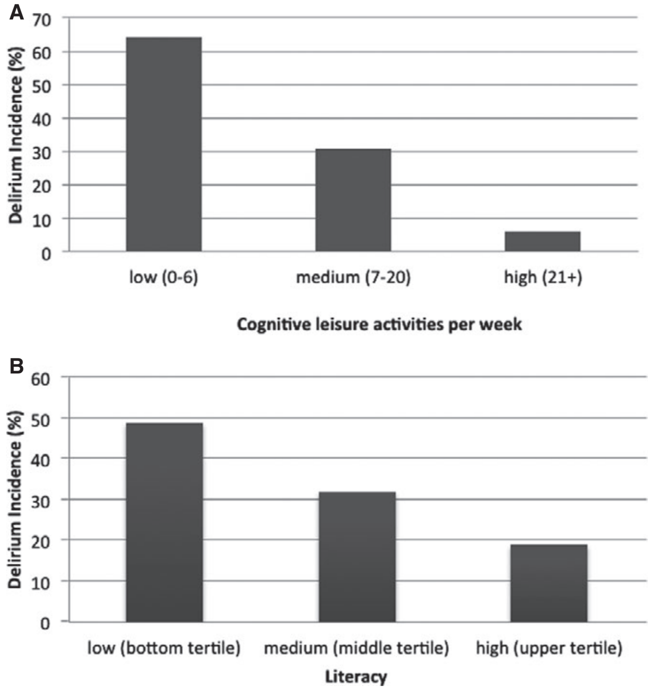

Figure 1. Postsurgical delirium incidence according to (A) tertile of cognitive leisure activity and (B) tertile of literacy.

Delirium Severity

Overall mean delirium severity on the Memorial Delirium Assessment Scale was 5.4 ± 2.8 points. Cognitive Activity Scale score but not literacy predicted delirium severity when examined individually (Table 3). Cognitive activities (B = −0.06, 95% CI = −0.11 to −0.01) but not literacy (B = −0.01, 95% CI = −0.06–0.04) predicted delirium severity when examined together.

Only computer games (B = 0.20, 95% CI = −0.39 to −0.02) and singing (B = −0.43, 95% CI = −0.80 to −0.07) predicted lower delirium severity.

Sensitivity Analyses

There were 93 (65.5%) participants with MMSE scores of 28–30 (cognitively normal) and 49 (34.5%) with scores of 24–27 (MCI). Cognitive activities predicted delirium incidence in cognitively normal participants (adjusted for age, sex, Charlson Comorbidity Index, OR = 0.90, 95% CI = 0.82–0.98) and in participants with MCI (OR = 0.89, 95% CI = 0.79 to 0.99). Literacy did not predict delirium incidence in participants with MCI (OR = 0.99, 95% CI = 0.93–1.05) or those who were cognitively normal (OR = 0.94, 95% CI = 0.88–1.00).

Sensitivity analyses comparing the association between the cognitive reserve measures and delirium incidence according to sex (men vs women), surgery type (hip vs knee replacement surgery) or anesthesia received (general vs spinal versus epidural) were not different and are not presented.

DISCUSSION

In this prospective cohort study, greater participation in cognitive activities was associated with lower delirium incidence and severity in older adults undergoing surgery, but greater literacy was not. Each additional day of participation in cognitive activities reported at baseline was associated with an 8% lower risk of postoperative delirium even after accounting for potential confounders. The sensitivity analysis suggests that this finding applied for cognitively normal participants and those with MCI. Delirium severity was mild, reflecting the healthy nature of the participants, who were undergoing elective, not emergency, surgery. Because delirium severity is linked with negative outcomes,[4] reducing severity is a worthwhile endpoint even if delirium incidence cannot be prevented.

Literacy was not a significant predictor of delirium incidence or severity. Literacy serves as a proxy for early-life cognitive reserve, whereas the Cognitive Activity Scale reflects reserve built up and maintained in later life.[17] A caveat is that literacy scores might also reflect later-life engagement in vocabulary-enhancing activities such as reading books. The findings suggest that, although early-life learning is important, it may be even more important to participate in later-life cognitive activities to reduce delirium risk.

A previous study[28] found that participation in leisure activities was associated with lower delirium incidence in hospitalized individuals and mediated the relationship between education and delirium. Unlike the current prospective study, that retrospective study[28] found that physical activity had a stronger effect on delirium

Table 3. Delirium Severity from Associated with Cognitive Reserve Measures at Baseline: Linear Regression Model

Variable	Beta Coefficient (95% Confidence Interval) *P*-Value	
	Model 1	Model 2
Literacy, American National Adult Reading Test corrected	−0.02 (−0.07–0.03) .39	a
Cognitive leisure activities, days per week	a	−0.06 (−0.11 to −0.01) .02
Age	−0.02 (−0.08–0.05) .60	−0.03 (−0.09–0.04) .37
Sex	0.24 (−0.75–1.22) .63	0.02 (−0.97–1.01) .97
Charlson Comorbidity Index	0.14 (−0.81–1.09) .78	0.23 (−0.71–1.17) .62
Mini-Mental State Examination	−0.39 (−0.66 to −0.13) .003	−0.34 (−0.57 to −0.10) .005

[a] Variable not included in model. Literacy (Model 1) or cognitive (Model 2) activities were included in each model. Results including both variables in one model are presented in the Results section.

incidence than cognitive or social activities. Greater literacy was associated with lower risk of delirium in adults undergoing surgery in the Successful Aging after Elective Surgery (SAGES) study.[16] Physical and cognitive activities in SAGES did not predict delirium incidence. The investigators suggested that cognitive and physical activities might be risk factors for dementia and not delirium because individuals with dementia were excluded based on interviews or modified MMSE cut score.[16] The current study also excluded individuals with dementia based on physician diagnosis and MMSE cut score. Unlike SAGES, cognitive activities predicted delirium incidence in the current study's cognitively normal group. Current level of cognitive activity participation was assessed, whereas SAGES assessed lifetime cognitive activity of participants (mean age 76.7) at four points starting at age 12, which may be prone to recall bias. SAGES assessed six cognitive activities (visiting the library, reading newspapers, reading magazines, reading books, writing letters, playing board or card games).[16] The current study did not assess visiting the library. Of the other five common activities, only reading books was significant in the current analysis, although three (computer games, e-mail, singing) of four cognitive activities associated with delirium incidence or severity in the current study were not assessed in SAGES. The association between specific cognitive activities and delirium should be further examined.

Playing computer games protected against incidence and severity of delirium. Computer-based cognitive remediation approaches have been reported to improve cognitive function and demonstrate neuroplasticity.[29] The 2013 American Community Survey reported that 71.0% of Americans aged 65 and older reported computer or Internet usage.[30] Given the ubiquity of computers in U.S. homes (65.1% of homes with a householder aged ≥65[30]), computer games should be further tested as a preoperative delirium preventive strategy.

Study strengths include its prospective nature, blinding of assessors, and use of validated and reliable measures to assess cognitive status.

Limitations

Although clinical, neuroimaging and pathological correlates of cognitive reserve have been described, a direct cognitive reserve measure has not been established. Hence, cognitive reserve proxies were used, as in prior studies.[5,8,18,31] Further research on the biology of cognitive reserve and delirium is needed to establish etiological factors. Although participants were not included or excluded based on education, future studies should include more educationally diverse groups. Only two individuals had surgeries cancelled after their baseline assessment. It was logistically challenging to conduct the assessments on the day of surgery. Individuals who developed and resolved delirium in the first postoperative day might have been missed. Less participation in cognitive activities might occur during the early stages of dementia, although the association between cognitive activities and delirium risk remained in the cognitively normal subgroup, suggesting that reverse causation may not account for the findings. The observational nature of the study does not establish causality, which needs to be tested in future clinical trials. Although formal diagnostic procedures for MCI and dementia were not used, the cognitively normal participants would have been unlikely to have met objective cognitive impairment criterion for MCI or dementia. Hence, it is expected that the prevalence of MCI in this sample was low and was not a major influence on findings. The cut score of 28 on MMSE is more stringent than cut scores used to define cognitive normalcy in many aging studies.

Unlike previous hospital-based delirium studies that combined unrelated surgery types,[16] the current study was restricted to orthopedic patients with hip and knee surgeries (2 additional participants had spine surgery). For instance, SAGES included individuals undergoing total hip or knee replacement, cervical or lumbar laminectomy, lower extremity arterial bypass, open abdominal aortic aneurysm repair, and colectomy.[16] Nonetheless, perioperative features of knee and hip surgeries are expected to be different, as are their postoperative management, but it is unlikely that type of surgery or anesthesia affected results because delirium incidence rates were similar in these different surgical and anesthesia subgroups. The association between cognitive reserve measures and delirium incidence was not different when analyzed according to type of surgery or anesthesia, although power for this subgroup analysis was lower. Postsurgical mobilization procedures for each surgery were also not different and not based on baseline cognitive reserve status. Furthermore, the same rehabilitation team in the same hospital performed the mobilization, reducing postoperative variability. The role of cognitive reserve in preventing delirium in other surgeries should be examined.

Greater cognitive reserve, as measured according to literacy and cognitive activity participation, is associated with lower incidence and severity of delirium in older adults undergoing surgery. Later-life cognitive reserve seems to be more important in preventing delirium, even after adjustment for baseline cognitive status, education, and literacy. These results will apply to older adults undergoing surgery, a group that is at high risk of delirium. These findings suggest that individuals with normal and poorer cognitive function can benefit from participation in leisure activities. If other groups validate the findings, randomized control studies should be conducted to see whether increasing preoperative participation in activities that enhance cognitive reserve can reduce postoperative delirium incidence and severity.

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