

# Motor Subtypes of Postoperative Delirium in Older Adults

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**Hypothesis:** Increased knowledge about motor subtypes of delirium may aid clinicians in the management of postoperative geriatric patients.

**Design:** Prospective cohort study defining preoperative risk factors, outcomes, and adverse events related to motor subtypes of postoperative delirium.

**Setting:** Referral medical center.

**Patients:** Persons 50 years and older with planned postoperative intensive care unit (ICU) admission following an elective operation were recruited.

**Main Outcome Measures:** Before surgery, a standardized frailty assessment was performed. After surgery, delirium and its motor subtypes were measured using the validated tools of the Confusion Assessment Method-ICU and the Richmond Agitation-Sedation Scale. Statistical analysis included the univariate *t* and  $\chi^2$  tests and analysis of variance with post hoc analysis.

**Results:** Delirium occurred in 43.0% (74 of 172) of patients, representing 67.6% (50 of 74) hypoactive, 31.1%

(23 of 74) mixed, and 1.4% (1 of 74) hyperactive motor subtypes. Compared with those having mixed delirium, patients having hypoactive delirium were older (mean [SD] age, 71 [9] vs 65 [9] years) and more anemic (mean [SD] hematocrit, 36% [8%] vs 41% [6%]) ( $P = .002$  for both). Patients with hypoactive delirium had higher 6-month mortality (32.0% [16 of 50] vs 8.7% [2 of 23],  $P = .04$ ). Delirium-related adverse events occurred in 24.3% (18 of 74) of patients with delirium; inadvertent tube or line removals occurred more frequently in the mixed group ( $P = .006$ ), and sacral skin breakdown was more common in the hypoactive group ( $P = .002$ ).

**Conclusions:** Motor subtypes of delirium alert clinicians to differing prognosis and adverse event profiles in postoperative geriatric patients. Hypoactive delirium is the most common motor subtype and is associated with worse prognosis (6-month mortality, 1 in 3 patients). Knowledge of differing adverse event profiles can modify clinicians' management of older patients with postoperative delirium.

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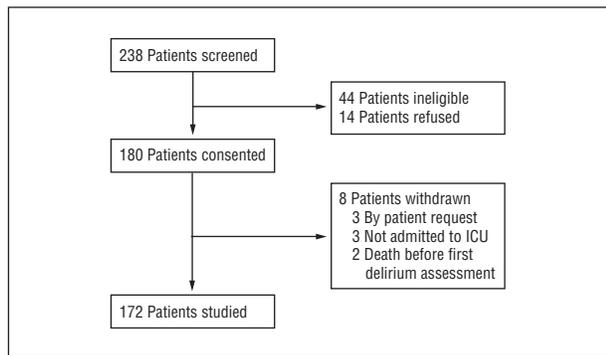
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**P**OSTOPERATIVE DELIRIUM IS the most common complication among older surgical patients.<sup>1</sup> More than half of all operations in the United States are performed on patients older than 65 years.<sup>2</sup> Risk factors for postoperative delirium include older age, cognitive dysfunction, functional impairment, multiple comorbidities, and malnutrition.<sup>3,4</sup> Postoperative delirium is associated with worse outcomes, including prolonged length of stay, increased incidence of discharge to another institutional facility, and higher mortality.<sup>3</sup> With an aging population, greater understanding of the clinical presentation and outcomes of postoperative delirium will become more relevant.

A potential means of increasing knowledge about postoperative delirium is rec-

ognition of motor subtypes of delirium that include hyperactive (pure agitation), hypoactive (pure lethargy), and mixed (fluctuation between lethargy and agitation).<sup>5</sup> Although a close relationship between delirium in hospitalized patients and poor outcomes is well established, outcomes following development of individual motor subtypes of delirium are less well defined. There is conflicting evidence about improved outcomes in hyperactive delirium<sup>6</sup> vs hypoactive delirium.<sup>7</sup> Adverse event profiles have also been shown to differ for delirium manifesting as agitation (hyperactive or mixed delirium) vs lethargy (hypoactive delirium).

Increased knowledge about motor subtypes of delirium may aid clinicians in the management of postoperative geriatric patients. The specific objectives of this study



**Figure 1.** Study enrollment summary. Forty-four ineligible patients included 39 undergoing brain operations, 3 with hearing impairment, and 2 with vision impairment. ICU indicates intensive care unit.

were the following: (1) to determine the incidence and natural history of motor subtypes of postoperative delirium, (2) to evaluate preoperative risk factors for developing motor subtypes of postoperative delirium, (3) to assess outcomes related to motor subtypes of delirium, and (4) to describe adverse events related to development of different motor subtypes of delirium.

## METHODS

The study was performed at the Denver Veteran Affairs Medical Center. Regulatory approval was obtained through the Colorado Multiple Institutional Review Board (COMIRB 05-0281) before initiating the study. Written informed consent was obtained from all participants. Risk factors for and outcomes of postoperative delirium were previously reported in 144 of 172 patients included in this study.<sup>3</sup>

Inclusion criteria were persons 50 years and older undergoing an operation with a planned postoperative intensive care unit (ICU) admission. Exclusion criteria were the following: (1) patients undergoing intracranial surgery, (2) patients with vision or hearing impairment (making the delirium assessment tool unreliable), (3) patients who could not speak English (making the delirium assessment tool unreliable), and (4) patients who could not provide informed consent.

Delirium was measured using the Confusion Assessment Method-ICU (CAM-ICU), which was administered daily at 7 AM to all participants throughout their ICU stay. The CAM-ICU has established reliability and validity in the diagnosis of delirium.<sup>8</sup> The CAM-ICU defines delirium by assessing the following 4 features: (1) fluctuation in mental status, (2) inattention, (3) disorganized thinking, and (4) altered levels of consciousness.<sup>8</sup> Delirium is diagnosed in the presence of features 1 and 2 and either feature 3 or 4. The CAM-ICU uses the Richmond Agitation-Sedation Scale (RASS) to determine the level of consciousness.<sup>9</sup> RASS is a 10-point scale ranging from unarousable (-5 points) or calm (0 points) to combative (4 points).<sup>9</sup> RASS has established reliability and validity in rating the level of consciousness of ICU patients.<sup>9</sup> If RASS scores of -4 or -5 were obtained (denoting deep sedation or unarousable), the CAM-ICU was not completed because delirium cannot be assessed in patients with this level of sedation (eg, delirium cannot be evaluated in a patient who is unarousable due to paralysis).<sup>10</sup> Because delirium is transient and fluctuates over time, delirium researchers have validated a medical record review process assessing the presence or absence of delirium that occurs at times other than during administration of the CAM-ICU.<sup>11</sup> Based on their methods, delirium is identified by searching the medical record for keywords related to delirium, with

the abstractor considering the following question: "Is there any evidence from the chart of acute confusional state (for example, delirium, mental status change, inattention, disorientation, hallucinations, agitation, inappropriate behavior, or other)?"<sup>11(pR123)</sup> The importance of including the medical record review is that it provides a validated reproducible dynamic picture of delirium (a process that is transitory and fluctuates throughout a 24-hour day) over an entire day, which is impossible by only performing the CAM-ICU assessment. In this study, delirium was defined as present if the CAM-ICU or the validated medical record review was positive for the diagnosis. Methods for detecting delirium have been described previously.<sup>3,12</sup>

Motor subtypes of delirium were defined using daily RASS scores as previously described.<sup>13,14</sup> Hyperactive delirium was defined as present in patients with all positive daily RASS scores (range, 1-4 points) associated with every positive CAM-ICU assessment. Hypoactive delirium was defined as present in patients with all neutral or negative daily RASS scores (range, 0 to -3 points) associated with every positive CAM-ICU assessment. Mixed delirium was defined as present in patients with daily RASS scores that included both positive values (range, 1-4 points) and neutral or negative values (range, 0 to -3 points) associated with every positive CAM-ICU assessment. The validated medical record review was not used to define which motor subtype was present because this method is not validated for this purpose.<sup>11</sup> Only daily RASS scores were used to define which motor subtype was present.

Before starting the main study, a pilot study of 100 daily encounters was completed to assess interrater reliability for delirium assessment using the CAM-ICU. Two of us (T.N.R. and C.D.R.) evaluating for the presence of delirium had high interrater reliability, with 98% concordance and a  $\kappa$  statistic of 0.96 (95% confidence interval, 0.91-1.00).

Routine preoperative clinical variables were recorded. In addition, preoperative assessment was performed of the following: (1) burden of comorbidities (Charlson Comorbidity Index, a sum of comorbidities that assigns weighted values to comorbidities based on 1-year risk of mortality),<sup>15</sup> (2) cognitive function (Mini-Cog test, a combination of 3-item recall with a clock-drawing task that accurately predicts cognitive dysfunction in older persons),<sup>16</sup> and (3) functional status (Barthel Index, which evaluates independence in activities of daily living).<sup>17</sup> Routine postoperative outcome measures were recorded. Mortality at 30 days and at 6 months was determined by both medical record review and telephone contact. Institutionalization was defined as discharge to another facility (rehabilitation, nursing home, or long-term care facility). A patient was not considered to be newly institutionalized after discharge if he or she resided in a care facility immediately before surgery.

Statistical analysis included univariate *t* and  $\chi^2$  tests and analysis of variance (ANOVA). Post hoc multiple comparisons of the ANOVA results were performed using Tukey honestly significant difference test.<sup>18</sup> Results were reported as the mean (SD), and statistical significance was set at  $P < .05$ .

## RESULTS

Between September 28, 2006, and October 26, 2007, a total of 172 patients were studied. Study enrollment is shown in **Figure 1**. Delirium occurred in 43.0% (74 of 172) of patients, representing 67.6% (50 of 74) hypoactive, 31.1% (23 of 74) mixed, and 1.4% (1 of 74) hyperactive motor subtypes (**Figure 2**). The one patient in whom purely hyperactive delirium occurred was ex-

cluded from statistical comparisons because of the small group size (n=1). The mean age of study patients was 64 (8) years; 96.5% (166 of 172) were male. The mean time to initial presentation of delirium in patients was 2.3 (1.8) days. The time to initial onset of delirium did not differ between the hypoactive (2.4 [1.7] days) vs mixed (2.2 [1.8] days) groups ( $P = .66$ ). The mean duration of delirium among patients in the hypoactive and mixed groups was 3.5 (4.5) days. The mean duration of delirium did not differ between the hypoactive (2.8 [1.4] days) vs mixed (3.9 [5.4] days) groups ( $P = .34$ ).

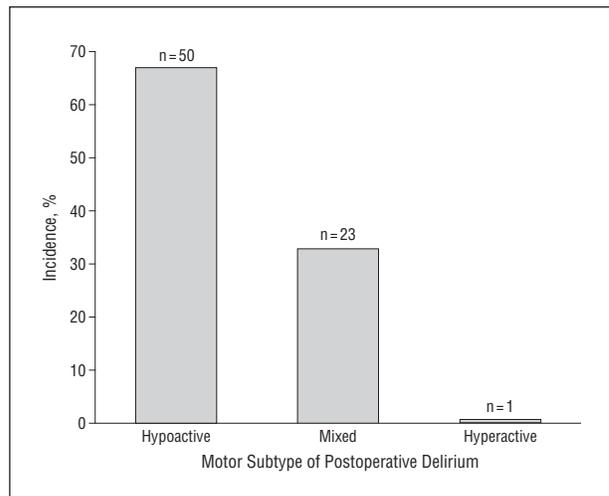
An overview of operations performed included 44.8% (77 of 172) abdominal, 37.2% (65 of 172) cardiac, 9.3% (16 of 172) noncardiac thoracic, and 8.1% (14 of 172) vascular. Among patients with delirium, the operations performed did not differ between the hypoactive vs mixed groups (**Table 1**).

Preoperative variables were compared among patients in the hypoactive vs mixed groups (Table 1). Compared with those having mixed delirium, patients having hypoactive delirium were older (mean age, 71 [9] vs 65 [9] years) and more anemic (mean hematocrit, 36% [8%] vs 41% [6%]) ( $P = .002$  for both) (to convert hematocrit to a proportion of 1.0, multiply by 0.01).

Intraoperative variables of blood transfusion, operating room time, and type of anesthesia were compared between the hypoactive (n=50) vs mixed (n=23) groups. Type of anesthesia is described as the percentage of patients who received general endotracheal anesthesia (all other patients received general endotracheal anesthesia with an epidural). The 2 groups showed similar mean variables, including blood transfusion quantity (3.0 [3.2] U in the hypoactive group vs 3.6 [3.8] U in the mixed group,  $P = .64$ ), operating room time (268 [117] minutes in the hypoactive group vs 325 [155] minutes in the mixed group,  $P = .12$ ), and the use of general endotracheal anesthesia (80.4% in the hypoactive group vs 69.2% in the mixed group,  $P = .35$ ).

Outcomes were compared between the hypoactive vs mixed groups. Six-month mortality was higher in the hypoactive group (32.0% [16 of 50] vs 8.7% [2 of 23],  $P = .04$ ) (Table 1). Outcomes were compared between 98 patients who did not develop delirium vs 74 patients who developed delirium of any motor subtype. Patients who developed delirium of any motor subtype had longer ICU stays (mean, 9.1 [7.7] vs 4.6 [2.6] days;  $P < .001$ ), longer hospital stays (mean, 14.6 [10.7] vs 8.0 [4.6] days;  $P < .001$ ), higher incidence of discharge to another institutional facility (mean, 39.1% vs 3.1%;  $P < .001$ ), higher 30-day mortality (mean, 10.9% vs 1.0%;  $P = .005$ ), and higher 6-month mortality (mean, 24.2% vs 2.1%;  $P < .001$ ).

Among 73 patients with hypoactive or mixed postoperative delirium, 23.3% (n=17) had at least 1 delirium-related adverse events (**Table 2**). Two patients had 2 adverse events each. Therefore, 19 adverse events occurred during the study among patients in the hypoactive and mixed groups. Adverse events included inadvertent tube or line removals (57.9% [11 of 19]), sacral skin breakdown (31.6% [6 of 19]), and falls (10.5% [2 of 19]). Among patients with delirium-related adverse events, sacral skin breakdown occurred in 66.7% (6 of



**Figure 2.** Incidence of motor subtypes of postoperative delirium among 74 patients.

9) of patients in the hypoactive group vs 0 of 10 patients in the mixed group ( $P = .002$ ), and inadvertent tube or line removals occurred in 90.0% (9 of 10) of patients in the mixed group vs 22.2% (2 of 9) of patients in the hypoactive group ( $P = .006$ ). The one patient who developed purely hyperactive postoperative delirium had 3 delirium-related adverse events (2 peripheral intravenous pulls and 1 self-extubation).

#### COMMENT

Hypoactive delirium occurred in two-thirds and mixed delirium in one-third of the older patients who developed postoperative delirium in the surgical ICU. Purely hyperactive delirium rarely occurred. Patients with hypoactive delirium were older and more frequently had preoperative anemia. Patients with hypoactive delirium had higher 6-month mortality vs patients with mixed delirium. Delirium-related adverse event profiles differed for the mixed vs hypoactive groups. Inadvertent tube or line removals occurred more frequently in the mixed group, and sacral skin breakdown occurred more frequently in the hypoactive group. A major limitation of this study is that most patients were male, prohibiting generalizability of our results to both men and women because sex differences in motor subtypes of delirium were unable to be detected.

The reported incidence of motor subtypes of delirium has varied based on the patient population studied. Two previous studies<sup>7,14</sup> evaluated motor subtypes of delirium in postoperative patients. Among patients (mean age, 55 years) who required mechanical ventilatory assistance in a surgical ICU, the overall incidence of postoperative delirium was 73%, hypoactive delirium occurred in 88% of all cases of delirium, mixed delirium occurred in 12% of all cases of delirium, and no patient developed purely hyperactive delirium.<sup>14</sup> In patients (mean age, 79 years) following hip fracture repair, 71% of all cases of delirium were purely hypoactive.<sup>7</sup> Older patients in the ICU, whether surgical or medical, rarely develop purely hyperactive delirium.<sup>13,14</sup> The results of our

**Table 1. Motor Subtypes of Postoperative Delirium Among the Study Sample**

Variable	No Delirium (n = 98)	Postoperative Delirium		P Value
		Hypoactive Group (n = 50)	Mixed Group (n = 23)	
<b>Preoperative Variables</b>				
Clinical factor, mean (SD)				
Age, y	61 (6)	71 (9)	65 (9)	.002
Charlson Comorbidity Index <sup>a</sup>	1.9 (1.5)	4.2 (2.3)	5.0 (2.1)	.15
Mini-Cog test <sup>b</sup>	4.6 (0.7)	2.7 (1.6)	2.7 (1.5)	.97
Barthel Index <sup>c</sup>	99 (3)	90 (11)	93 (11)	.17
Laboratory value, mean (SD)				
Albumin, g/dL	3.9 (0.5)	3.3 (0.7)	3.4 (0.7)	.75
Hematocrit, %	44 (4)	36 (8)	41 (6)	.002
Sodium, mEq/L	139 (3)	137 (3)	139 (3)	.42
Potassium, mEq/L	4.3 (0.5)	4.1 (0.5)	4.2 (0.5)	.58
Creatinine, mg/dL	1.1 (0.5)	1.2 (0.7)	1.2 (0.7)	>.99
Glucose, mg/dL	115 (41)	119 (44)	112 (34)	.76
<b>Operations</b>				
Abdominal	37/98 (38)	29/50 (58)	11/23 (48)	.46
Cardiac	45/98 (46)	13/50 (26)	6/23 (26)	>.99
Noncardiac thoracic	8/98 (8)	5/50 (10)	3/23 (13)	.70
Vascular	8/98 (8)	3/50 (6)	3/23 (13)	.37
<b>Outcome Measures</b>				
Stay, mean (SD), d				
Intensive care unit	4.6 (2.6)	8.8 (8.7)	9.2 (5.5)	.97
Hospital	8.0 (4.6)	14.4 (11.2)	14.5 (9.6)	>.99
Discharge to institutional facility, No. (%)	3/98 (3.1)	21/48 (43.8) <sup>d</sup>	6/22 (27.3) <sup>d</sup>	.30
Mortality, No. (%)				
30 d	1/98 (1.0)	7/50 (14.0)	1/23 (4.3)	.42
6 mo	2/96 (2.1) <sup>e</sup>	16/50 (32.0)	2/23 (8.7)	.04

SI conversion factors: To convert albumin to grams per liter, multiply by 10; hematocrit to a proportion of 1.0, multiply by 0.01; sodium and potassium to millimoles per liter, multiply by 1.0; creatinine to micromoles per liter, multiply by 88.4; and glucose to millimoles per liter, multiply by 0.0555.

<sup>a</sup>Measures comorbidities on a scale ranging from 0 (no comorbidities) to 19 (severe comorbidities).

<sup>b</sup>Assesses cognitive function on a scale ranging from 5 (no cognitive dysfunction) to 0 (severe cognitive dysfunction).

<sup>c</sup>Measures independence in performing activities of daily living on a scale ranging from 100 (no functional impairment) to 0 (severe functional dependence).

<sup>d</sup>Two patients with hypoactive delirium and 1 patient with mixed delirium entered another institutional facility before their operation and were not considered to be newly institutionalized after discharge.

<sup>e</sup>Two patients were lost to 6-month follow-up.

study confirm previous findings that hypoactive delirium is the most common motor subtype following an operation in geriatric patients.

The incidences of motor subtypes of delirium vary among different patient populations. Younger patient populations are more likely to demonstrate purely hyperactive delirium.<sup>12,19</sup> Our research group in a previous study<sup>12</sup> showed that 15% of all delirium cases were hyperactive among trauma ICU patients (mean age, 44 years) for whom substance withdrawal was a significant issue. Thirty percent of all delirium cases among a group of psychiatric inpatients were purely hyperactive.<sup>19</sup> The prevalences of motor subtypes of delirium were not previously found to differ between male vs female patients.<sup>6,7,13,19-21</sup>

In our study, preoperative risk factors for developing hypoactive delirium were older age and more severe anemia. Older age as a risk factor for hypoactive delirium has been reported in medical ICU patients.<sup>13</sup> Anemia has not previously been associated with the occurrence of hypoactive delirium to our knowledge. Why are older age and anemia associated with development of hypoactive delirium? The answer is likely that older age and ane-

mia are both markers of frailty, which is defined as a state of reduced physiological reserve that increases susceptibility to disability and creates limited reserve to withstand stressors.<sup>22,23</sup> Previous work linked the accumulation of 4 or more markers of frailty in older individuals to higher 6-month postoperative mortality.<sup>24</sup> Given that frail patients and patients who develop hypoactive delirium have high 6-month mortality, it seems reasonable that preoperative markers of frailty would be associated with the occurrence of hypoactive postoperative delirium. However, frailty is not the only possible explanation for the relationship between older age and greater anemia and development of hypoactive delirium; increased burden of chronic disease may result from advanced age and cause anemia.

Defining the long-term prognosis associated with different motor subtypes of delirium is the first important finding of our study. Higher 6-month mortality was found in patients who developed hypoactive delirium vs mixed delirium. In fact, one-third of all patients who developed hypoactive delirium died within 6 months of their operation. These findings are in line with previous work that recognized a worse prognosis among medically hos-

**Table 2. Adverse Events and Motor Subtypes Among 73 Patients With Postoperative Delirium**

Variable	No./Total No. (%)		P Value
	Hypoactive Group (n = 8) <sup>a</sup>	Mixed Group (n = 9) <sup>b</sup>	
Incidence of adverse events	8/50 (16.0)	9/23 (39.1)	
Adverse event			
Inadvertent tube or line removal	2/9 (22.2)	9/10 (90.0)	.006
Peripheral intravenous line	1	3	
Nasogastric tube	1	3	
Central venous catheter		2	
Urinary catheter		1	
Sacral skin breakdown	6/9 (66.7)	0/10	.002
Fall	1/9 (11.1)	1/10 (10.0)	>.99

<sup>a</sup>Nine adverse events.<sup>b</sup>Ten adverse events.

pitalized patients who develop hypoactive delirium.<sup>6,20</sup> However, contradictory findings indicate improved outcomes following development of hypoactive delirium after surgery for hip fracture,<sup>7</sup> which might reflect different study patient populations or our incomplete understanding about the etiology of motor subtypes of delirium. The clinician should not make false assumptions that delirium equates to mortality. Causes of mortality are likely multifactorial. Baseline frailty in older individuals predisposes to delirium and to mortality. There is no evidence that eliminating delirium, pharmacologically or otherwise, will improve outcomes. Recognizing the poor prognosis associated with hypoactive delirium may provide a better understanding of the prognosis among older postoperative patients.

The second important finding of our study is a description of the distinct inpatient adverse event profiles of different motor subtypes of delirium. Individuals with hypoactive delirium had more frequent sacral skin breakdown. Similar findings have been previously described in medically hospitalized patients.<sup>20</sup> Those with delirium who clinically manifested agitation, either mixed or purely hyperactive, more often inadvertently removed tube or lines. This seems unique to postoperative patients and has not been previously recognized by delirium studies evaluating medically hospitalized patients. In such work, agitation was associated with falls<sup>20</sup> and with urinary incontinence.<sup>25</sup>

Limitations of this study include the following: (1) The small sample of patients with purely hyperactive delirium did not allow for statistical comparison of this motor subtype of delirium with the other groups. The fact that our study found only 1 patient with hyperactive postoperative delirium likely reflects the older population studied and not all postoperative patients. (2) Most of our patients were male. As a result, this study was unable to detect potential sex differences in motor subtypes of delirium. The sex distribution of our study population reflects the patient population at the Denver Veterans Affairs Medical Center and not a selection bias. (3) The fact that delirium is fluctuating and transient in nature makes delirium research methods challenging. The delirium research community has developed validated tools that

quantitatively define the presence or absence of delirium (ie, the CAM-ICU<sup>8</sup> and the validated medical record review<sup>11</sup>). No single method is universally accepted to detect delirium.<sup>10</sup> Changes in research methods will alter the incidence of delirium detected, a fact that partially accounts for wide variability of delirium incidences reported in the literature. Our method of daily CAM-ICU and medical record review assessments has been validated as reasonable for detecting delirium.<sup>11</sup> (4) The association of delirium and postoperative complications with narcotic or sedative use was not accounted for in our study design. Benzodiazepines have been found to promote the transition to delirium,<sup>26</sup> and future work might focus on examining the relationship between postoperative factors and development of motor subtypes of delirium.

Our study found that hypoactive delirium occurred in two-thirds of older patients with postoperative delirium. Those with hypoactive delirium were older and had higher 6-month mortality. Future research is warranted to understand the underlying pathogenesis of motor subtypes of delirium and the possibility that differing treatment regimens may be tailored to optimally manage individual motor subtypes of postoperative delirium.

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