Received: 6 April 2023 | Accepted: 14 December 2023

DOI: 10.1002/gps.6049

RESEARCH ARTICLE

International Journal of Geriatric Psychiatry WILEY

# Assessing patterns of delirium symptoms reveals a novel subtype among elective surgical patients with postoperative delirium

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**Funding information**

National Institutes of Health

## Abstract

**Objectives:** Prior studies reported incidence of hypoactive and hyperactive subtypes of postoperative delirium, but did not consider cognitive symptoms of delirium which are highlighted in the DSM-5 criteria for delirium. This study aims to address this gap in the literature by classifying cases of delirium according to their constellation of cognitive and motoric symptoms of delirium using a statistical technique called Latent Class Analysis (LCA).

**Methods:** Data were from five independent study cohorts ($N$ = 1968) of patients who underwent elective spine, knee/hip, or elective gastrointestinal and thoracic procedures, between 2001 and 2017. Assessments of delirium symptoms were conducted using the long form of the Confusion Assessment Method (CAM) pre- and post-surgery. Latent class analyses of CAM data from the first 2 days after surgery were conducted to determine subtypes of delirium based on patterns of cognitive and motoric symptoms of delirium. We also determined perioperative patient characteristics associated with each latent class of delirium and assessed whether the length of delirium for each of the patterns of delirium symptoms identified by the latent class analysis.

**Results:** The latent class model from postoperative day 1 revealed three distinct patterns of delirium symptoms. One pattern of symptoms, denoted as the Hyperalert class, included patients whose predominant symptoms were being hyperalert or overly sensitive to environmental stimuli and having a low level of motor activity. Another pattern of symptoms, denoted as the Hypoalert class, included patients whose predominant symptom was being hypoalert (lethargic or drowsy). A third pattern of symptoms, denoted as the Cognitive Changes class, included patients who experienced new onset of disorganized thinking, memory impairment, and disorientation. Among 352 patients who met CAM criteria for delirium on postoperative day 1, 34% had symptoms that fit within the Hyperalert latent class, 39% had symptoms that fit within the Hypoalert latent class, and 27% had symptoms that fit within the Cognitive Changes latent class. Similar findings were found when latent class analysis was applied to those who met CAM criteria for delirium on postoperative day 2. Multinomial regression analyses revealed that ASA class,

surgery type, and preoperative cognitive status as measured by the Telephone Interview for Cognitive Status (TICS) scores were associated with class membership. Length of delirium differed between the latent classes with the Cognitive Changes latent class having a longer duration compared to the other two classes.
**Conclusions:** Older elective surgery patients who did not have acute events or illnesses or a diagnosis of dementia prior to surgery displayed varying symptoms of delirium after surgery. Compared to prior studies that described hypoactive and hyperactive subtypes of delirium, we identified a novel subtype of delirium that reflects cognitive symptoms of delirium. The three subtypes of delirium reveal distinct patterns of delirium symptoms which provide insight into varying risks and care needs of patients with delirium, indicating the necessity of future research on reducing risk for cognitive symptoms of delirium.

**KEYWORDS**
aging, delirium subtypes, elective surgery, postoperative delirium

### Key Points

- Although hypoactive and hyperactive motoric subtypes of postoperative delirium have been identified in literature, prior studies have not considered cognitive symptoms of delirium which are highlighted by the DSM-5 criteria for delirium.
- Among elective surgery patients who did not have a diagnosis of dementia, and were not experiencing acute illnesses, events, or changes in mental status at hospital admission, we found that more than 40% of patients experienced cognitive symptoms of delirium using the long-form of the Confusion Assessment Method that comprehensively assesses cognitive and motoric symptoms of delirium and its range of symptoms.
- Latent class analysis revealed three patterns of symptoms: patients in the first latent class predominantly displayed a hyperalert level of consciousness; patients in the second latent class predominantly displayed a hypoalert level of consciousness; and patients in the third latent class predominately displayed acute onset of disorganized thinking, disorientation, and memory impairment.
- Compared to those in the Hypoalert latent class, those in the Hyperalert latent class were more likely to have general surgery and have lower preoperative mental status scores, and those in the acute onset of cognitive symptoms latent class (Cognitive Changes) were more likely to have lower preoperative mental status scores.

## 1 | INTRODUCTION

Delirium is characterized by acute changes in attention and cognitive functions that are not explained by preexisting medical conditions. Delirium is common among older hospitalized patients. Incidence rates of delirium among acutely ill patients range from 3% to 73%,[1] but rates are lower among hospitalized patients who are not acutely ill. For example, rates of delirium among older elective surgery patients range from 18% to 25%.[2–4] Delirium is associated with longer lengths of stay, discharge to nursing homes, and long-term declines in physical and cognitive functioning.[5–7]

The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria for delirium include acute change in mental status, inattention, and additional disturbances in cognition such as disorganized thinking, disorientation, or language, visuospatial, or perceptual disturbances. Compared to earlier DSM criteria that focused on level of consciousness, the (DSM-5) criteria place greater attention on global cognitive symptoms of delirium.[8] Cognitive symptoms of delirium are distressing to patients and can impact patients' care needs. Little is known about the incidence of cognitive symptoms of delirium or whether there is a distinct pattern of cognitive symptoms of delirium among older elective surgery patients who did not have acute events or illnesses or a diagnosis of dementia prior to surgery.

Evaluation of delirium is guided by standardized assessment tools. The Confusion Assessment Method (CAM) is the most common assessment tool for delirium.[9] The CAM includes assessment of all symptoms of delirium. Prior studies of delirium have not described which symptoms of delirium are most common among patients who meet CAM criteria for delirium. Recognizing common patterns of symptoms of delirium among patients with delirium offers the opportunity to determine whether different patterns of symptoms are associated with different risks. Further, recognition of patterns of symptoms would inform the development care plans that address the specific symptoms of delirium that patients are experiencing. To date, hospital-based strategies to reduce delirium have not considered whether interventions should be tailored according to the patients' patterns of delirium symptoms.

Prior studies have described motor subtypes of postoperative delirium,[10,11] but they did not consider a larger range of symptoms of delirium. Instead, they focused on whether the patient had a hyperactive motor state, a hypoactive motor state, or a mixed hyperactive/hypoactive motor state. For example, a study used the Richmond Agitation Sedation Score (RASS) to measure level of consciousness and did not include the cognitive symptoms of delirium[12] because the RASS does not include assessment of cognitive symptoms of delirium. To address the DSM-5's focus on cognitive symptoms of delirium rather than level of consciousness or agitation, we conducted assessments of delirium among patients who were not experiencing acute illness, events, or changes in mental status at hospital admission. The study examines whether patterns of delirium symptoms are discernible using an unbiased statistical technique called Latent Class Analysis. This approach will provide a novel insight into common patterns of symptoms of delirium. In addition, we will assess whether risks for delirium onset and total number of days of delirium differ for these distinct patterns of delirium symptoms.

## 2 | MATERIALS AND METHODS

### 2.1 | Participants

Five independent cohort studies conducted at the Department of Anesthesia and Perioperative Care at the University of California, San Francisco provided data from 1968 elective surgery patients for this study. All studies were focused on assessing the pathophysiology of postoperative delirium. Each study evaluated perioperative risk factors associated with incident delirium after elective surgery. Two clinical trials assessed the effects of nitrous oxide[13] and gabapentin[14] on postoperative delirium; another study evaluated whether an intervention to reduce time spent in burst suppression affected incident postoperative delirium.[2] None of the clinical trials showed a significant effect of the intervention on incidence of postoperative delirium. An observational study broadly assessed risks for developing delirium, including postoperative pain and patient-controlled analgesia device usage.[15] Another observational study assessed the impact of preoperative sleep disruption on postoperative delirium.[16] All studies used the same tool and criteria to measure postoperative delirium described below.

All subjects were aged 65 or older, fluent in English, and were scheduled for noncardiac elective surgery. Patients in these studies were expected to have a hospital length of stay of at least 2 days. Patients who were not able to provide informed consent preoperatively were excluded from the study. None of the patients from these studies met CAM criteria for delirium prior to surgery, nor did any patients in this study have a diagnosis of dementia. From these studies, only those patients who met CAM criteria for delirium after surgery were included in this study because it was not possible to determine patterns of delirium symptoms among patients who do not have delirium. The study was approved by the Institutional Committee on Human Research at both the University of California, San Francisco and Virginia Tech and written informed consent was obtained from all subjects.

## 3 | VARIABLES

### 3.1 | Assessment of delirium

The CAM was administered preoperatively. We considered delirium assessments up to 2 days after surgery because nearly all elective surgery patients are discharged on the second or third day after surgery. CAM is an evidence-based assessment instrument for delirium that can be administered by nonpsychiatric clinicians. It is one of the most commonly used methods for assessing delirium in clinical research studies.[17] The CAM includes nine symptoms of delirium: acute onset of mental status change, inattention, altered level of consciousness, disorganized thinking, disorientation, perceptual disturbances, memory impairment, psychomotor agitation, and psychomotor retardation. Note that the latent class analyses did not include acute change in mental status and inattention because these two items must be present for a diagnosis of delirium. The remaining seven CAM items were included in the latent class analysis. The CAM has high interrater reliability (kappa = 0.92). In addition, sensitivity ranged from 94% to 100% and specificity ranged from 90% to 95%.[9]

All CAM items were assessed in accordance with the CAM manual by a trained evaluator (e.g. clinician or research personnel).[18] The evaluator filled out the CAM form during a brief conversation with the patient. The conversation was typically focused on how the patient was feeling, their pain level, their current symptoms, and their postoperative inpatient medical care. Typically, the conversations took place during the middle of each postoperative day until the patient was discharged from the hospital. Using the CAM form, the evaluator determined presence or absence of each of the DSM criteria for delirium including the cognitive symptoms in accordance with the CAM training manual.

Altered level of consciousness was assessed as hyperactive, hypoactive, or normal. CAM symptoms of a hyperactive level of consciousness included being oversensitive to their environment (i.e., pulling on their IV lines) or being easily startled. Symptoms of hypoactive level of consciousness included drowsiness or difficulty being difficulty to arouse. Disorganized thinking was demonstrated by incoherent thinking including rambling conversations or unclear flow of ideas. Disorientation was assessed by asking the patient where they were and the time of day. Memory impairment was assessed by the patient's inability to recall hospital events or instructions. Perceptual disturbances were observed if the patient stated any visual or auditory hallucinations or illusions. Psychomotor agitation was observed through the patient's increased level of motor activity such as restlessness and frequent positional changes. Psychomotor retardation was observed through a patient's unusually decreased level of motor activity such as sluggishness and remaining in one unchanged position for a prolonged time.

## 3.2 | Patient characteristics

Patients' demographic characteristics and clinical characteristics were determined from their medical records and included age, sex, surgery type, and American Society of Anesthesiologists (ASA) classification of risk for post operative risk for complications or mortality.[19] In addition, baseline cognitive status was measured within the week prior to surgery using the Telephone Interview for Cognitive Status (TICS).[20] Prior to surgery, all patients were assessed for delirium using the CAM. Patients were assessed for delirium until discharge.

## 3.3 | Statistical methods

We used Latent Class Analysis (LCA) to determine common patterns of delirium symptoms. LCA is a statistical technique used to identify groups (a.k.a. latent classes) that share characteristics of interest. For this study, the characteristics of interest were the seven symptoms of delirium from the CAM that may be present but were not required for delirium diagnosis. Six out of seven symptoms were binary variables marking the presence of corresponding symptoms. Altered level of consciousness was a categorical variable with three categories: awake, hyperactive, and hypoactive.

Number of classes: Based on prior studies that classified delirium into two types: hyperactive and hypoactive,[21,22] we expected that the LCA model would include at least two latent classes. Determination of the optimal number of latent classes was based on the Bayesian Information Criterion (BIC) goodness of fit statistic. We kept increasing the number of latent classes up to six classes. Table 2 provides the BIC statistics of considered LCA models, showing that three latent classes is preferred over other latent class solutions. BIC is the most reported criterion for selecting the number of classes because it is the most reliable for model fit and rewards parsimony. Given that this study is focused on informing patterns of delirium in hospitalized patients, a parsimonious model is more appropriate for translation to clinical recommendations than a more complex model.[23–25]

Parameters for a LCA model included conditional probabilities of the presence of each of the seven symptoms for each class. Specifically, the conditional probability for a delirium symptom refers to the likelihood that a patient within a class would have that symptom. After determining the conditional probabilities of each of the seven symptoms for each class, we provided a label for each latent class. From this point, each patient with delirium in our dataset was categorized according to their predicted class membership.

Assessing Stability of the LCA findings across 2 days of delirium assessments: To determine whether latent classes associated with delirium were similar across different assessments days, we computed latent class models to determine whether findings were similar using data from postoperative day 2. We computed two additional LCA analyses to assess whether the results were similar to those obtained from using patient data only from postoperative day 1 (n = 352). First, we used all delirium assessments from day 2. This analysis included patients that had delirium on both postoperative day 1 and postoperative day 2 (n = 179), and patients who had delirium only on postoperative day 2 (n = 119), for a total of 298 patients. In another analysis, we included patients who only had postoperative delirium on day 2 (n = 119). For both scenarios, we obtained a LCA model with three latent classes. We found strong similarities in the conditional probabilities within each of the three latent classes. The findings suggest that the latent class solution was stable across patients who had delirium only on postoperative day 1, patients who had delirium on postoperative days 1 and 2, and patients who had delirium only on postoperative day 2.

Patient characteristics associated with class membership and the total number of days of delirium: We assessed the association between preoperative patient characteristics and class membership using multinomial regression analysis. We assessed the total number of days of delirium for each latent class of delirium symptoms by counting the number of days of patients who met CAM criteria for postoperative delirium. We compared the average number of days of delirium using ANOVA. Nearly all patients were discharged or transferred 3 days after surgery, so the length of delirium was only considered during the first 3 days after surgery. All analyses were done in R version 4.0.4 with LCA models constructed using poLCA package and further verification using Mplus software.

# 4 | RESULTS

## 4.1 | Analytic sample

Of 1968 patients from the five studies, 526 had a diagnosis of delirium. On the first postoperative day, 358 met CAM criteria for delirium, and 310 met CAM criteria for delirium on the second postoperative day (see Figure 1). Due to missing data for 6 cases, 352 patients were included in the postoperative day 1 Latent Class Analysis. Due to missing data for 12 cases, 298 were included in the postoperative day 2 Latent Class Analysis, and 119 were included in the postoperative day 2 analyses that included only those patients who developed delirium on day 2. Missing data occurred when one or more of the seven symptoms of delirium was missing. Specifically, among patients who met criteria for delirium (e.g. acute onset and fluctuating course, inattention, and disorganized thinking, or altered level of consciousness), they may have had one or more of the other CAM features of delirium missing. Only 96 patients were found to

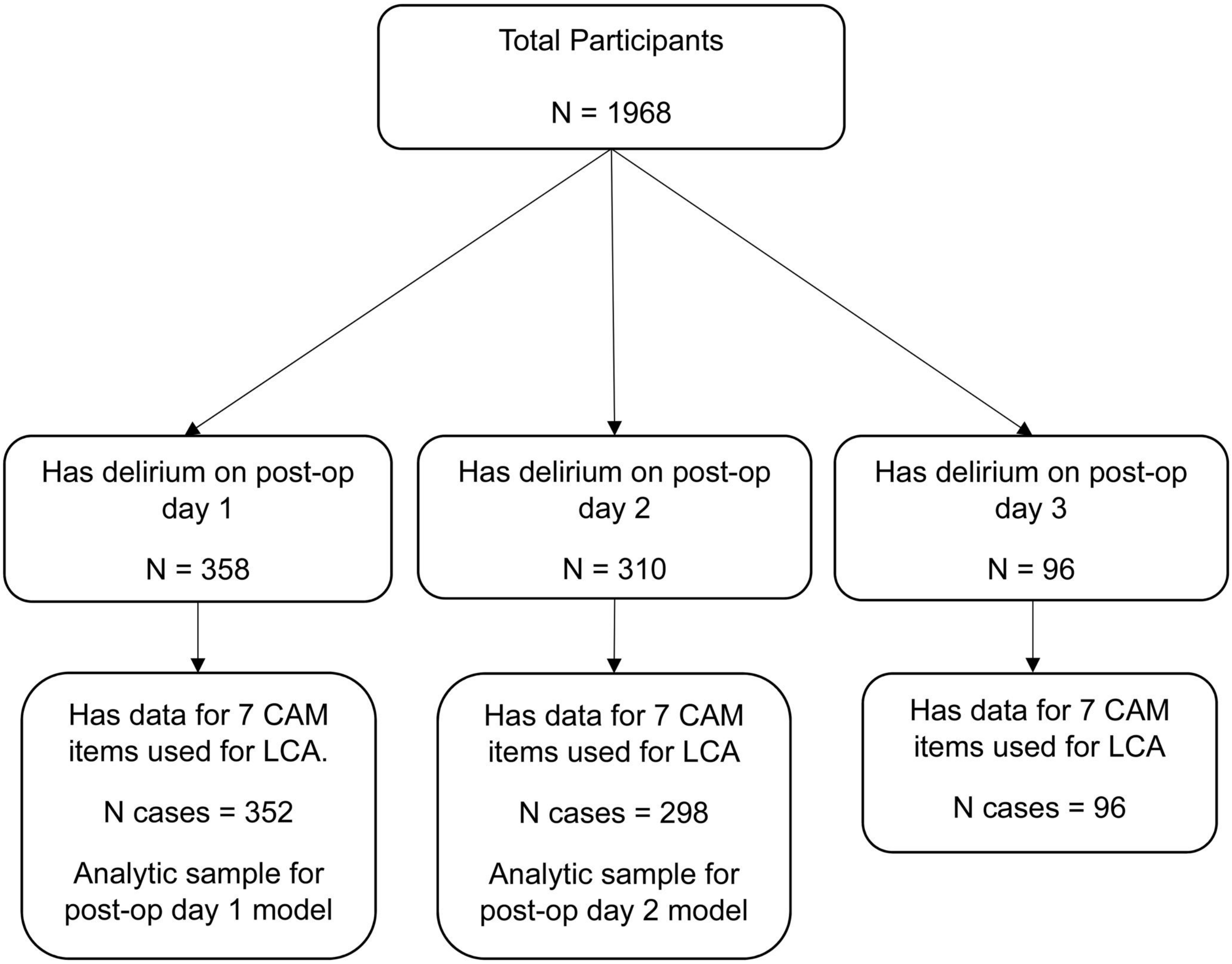


FIGURE 1 Derivation of analytic samples for LCA models.

have delirium on postoperative day 3, which was too few to conduct a latent class analysis because optimal solutions required at least 50 persons per class.[26]

### 4.2 | Symptoms of delirium

Table 1 provides descriptive statistics for each of the delirium symptoms included in the Latent Class analysis. More than half of the patients (57%) had a hyperalert level of consciousness, whereas 38% had a hypoalert level of consciousness, and 5% had a normal level of consciousness. Fifty-one percent had psychomotor retardation and 14% had psychomotor agitation. Disorganized thinking was present for 41% of patients and disorientation was present in 27%. Only 4% of patients had perceptual disturbances and 37% had memory impairment.

### 4.3 | Latent class analysis model

Table 2 provides model fit information for the Latent Class Model computed for postoperative day 1. The BIC is lowest for the Latent Class Model with three classes, indicating 3 classes provides the optimal model fit. Based on the conditional probabilities of each symptom of delirium within each latent class (Table 3), we labeled the three classes. The first class we labeled as Hyperalert because the predominant symptoms in the first class were being hyperalert or overly sensitive to environmental stimuli. The second class we labeled Hypoalert because their predominant symptoms were being lethargic or drowsy. The third class we labeled as Cognitive Changes with patients in this class experiencing new onset of disorganized thinking, memory impairment, disorientation and half had a low level of motor activity. We found that 34% of patients were in the Hyperalert latent class, 39% were in the Hypoalert latent class, and 27% were in the Cognitive Changes class.

For each class, Table 3 shows the probability of patients having each symptom of delirium. For patients whose symptoms situated them in the Hyperalert latent class, the probability that their level of consciousness was vigilant or overly sensitive to environmental stimuli was 100%, and their probability of having a low level of motor activity was 81%. Patients whose symptoms situated them in the Hypoalert latent class, had a 75% probability of displaying symptoms of being lethargic or drowsy, but had a low probability of displaying

TABLE 1 Descriptive statistics of 7 CAM symptoms used for LCA model for postoperative day 1.

| | (n) Percent |
|---|---|
| Altered level of consciousness | |
| Normal (awake) | 16 (4.55%) |
| Hyperalert | 202 (57.39%) |
| Hypoalert | 134 (38.07%) |
| Psychomotor retardation | |
| No | 173 (49.15%) |
| Yes | 179 (50.85%) |
| Psychomotor agitation | |
| No | 304 (86.36%) |
| Yes | 48 (13.64%) |
| Disorganized thinking | |
| No | 206 (58.52%) |
| Yes | 146 (41.48%) |
| Disorientation | |
| No | 257 (73.01%) |
| Yes | 95 (26.99%) |
| Perceptual disturbances | |
| No | 338 (96.02%) |
| Yes | 14 (3.98%) |
| Memory disturbances | |
| No | 223 (63.35%) |
| Yes | 129 (36.65%) |

TABLE 2 Model fit evaluation information for LCA model on delirium cases of postoperative day 1.

| Number of classes | Log-likelihood | Number of parameters | BIC |
|---|---|---|---|
| 1 | −1409.46 | 8 | 2865.826 |
| 2 | −1344.73 | 17 | 2789.136 |
| 3 | −1301.2 | 26 | **2754.849** |
| 4 | −1283.39 | 35 | 2772.009 |
| 5 | −1271.22 | 44 | 2800.43 |
| 6 | −1262.61 | 53 | 2835.987 |

other symptoms of delirium. Patients that fit within the Cognitive Changes latent class had a 90% probability of having symptoms reflecting disorganized thinking, a 59% probability that they displayed symptoms of disorientation, an 81% probability that they displayed symptoms of memory disturbances of events that occurred while they were in the hospital, and a 51% change of having a low level of motor activity.

To determine whether latent classes associated with delirium were similar across different assessments days, we computed two additional Latent Class models to determine whether findings were similar across days. Using data from postoperative day 2, we determined whether two additional LCA analyses provided similar results to those obtained from using patient data only from postoperative day 1. First, we used all delirium assessments from day 2. This analysis included patients that had delirium on both postoperative day 1 and postoperative day 2 (n = 179), and also included patients that had delirium only on postoperative day 2 (n = 119), for a total of 298 patients. In a second analysis, we included only those patients who had postoperative delirium only on day 2 (n = 119). For both scenarios, we obtained an LCA model with three latent classes. We found strong similarities in the conditional probabilities within each of the three latent classes. The findings suggest that the latent class solution was stable across patients that had delirium only on postoperative day 1, and patients that had delirium on postoperative days 1 and 2, and patients who had delirium only on postoperative day 2. Supplemental Table 1 reveals the LCA results from the postoperative day 2 assessments. The Latent Classes were very similar to those from postoperative day 1, revealing a Hyperalert class, a Hypoalert class, and a Cognitive Changes class. Furthermore, the conditional probabilities for each of the delirium symptoms were very similar for the latent classes from postoperative day 1 and postoperative day 2. Supplemental Table 2 shows that when a latent class analysis was conducted with those patients that had delirium only on day 2, the findings were similar.

### 4.4 | Patient characteristics associated with the latent classes

The multinomial regression analyses revealed that age and sex were not associated with class membership. However, ASA class, surgery type, and preoperative TICS were associated with class membership. Table 4 shows that compared to patients who were in the Hyperalert class, those in the Hypoalert class were significantly more likely to have ASA scores of three or higher, have spine surgery versus surgery on the hips or knees, and less likely to have general surgery rather than surgery on their hips or knees. Also, compared to the those in the Hyperalert class, those in the Hypoalert class were more likely to have higher preoperative TICS scores. Compared to patients in the Hyperalert class, those in the Cognitive Changes class were significantly more likely to have spine surgery. Across the three postoperative days, the average number of days of delirium significantly differed between the three classes (Table 5). The average number of days of delirium was 1.84 for those in the Cognitive Changes latent class compared to 1.55 for those in the Hyperalert class and 1.54 for those in the Hypoalert class ($F = 6.70$, df = 2349; $p = 0.001$).

## 5 | DISCUSSION

Delirium symptoms include acute changes in level of consciousness, psychomotor functioning, and cognitive functioning. Prior studies that assessed types of delirium have not considered the importance of

TABLE 3 Conditional probabilities of symptoms within latent classes for postoperative day 1 ($N = 352$).

| Model | Class | Altered level of consciousness | Disorganized thinking | Disorientation | Perceptual disturbances | Memory impairment | Psychomotor agitation | Psychomotor retardation |
|---|---|---|---|---|---|---|---|---|
| Post op day 1 model | Class 1 - hyperalert $N = 119$ (33.85%) | Hyper: 100.0 (0.0) | No: 63.9 (5.6) | No: 100.0 (0.0) | No: 99.2 (1.5) | No: 75.4 (5.2) | No: 81.0 (4.5) | No: 19.0 (6.2) |
| | | Hypo: 0.0 (0.0) | Yes: 36.1 (5.6) | Yes: 0.0 (0.0) | Yes: 0.8 (1.5) | Yes: 24.6 (5.2) | Yes: 19.0 (4.5) | Yes: 81.0 (6.2) |
| | | Awake 0.0 (0.0) | | | | | | |
| | Class 2 - hypoalert $N = 137$ (38.87%) | Hyper: 24.3 (6.5) | No: 87.7 (4.2) | No: 71.9 (4.5) | No: 98.3 (1.6) | No: 84.1 (4.3) | No: 98.3 (1.6) | No: 75.2 (4.4) |
| | | Hypo: 74.8 (6.5) | Yes: 12.3 (4.2) | Yes: 28.1 (4.5) | Yes: 1.7 (1.6) | Yes: 15.9 (4.3) | Yes: 1.7 (1.6) | Yes: 24.8 (4.4) |
| | | Awake: 0.9 (1.0) | | | | | | |
| | Class 3—Cognitive changes $N = 96$ (27.27%) | Hyper: 51.7 (6.8) | No: 10.3 (5.6) | No: 41.1 (7.6) | No: 88.9 (4.1) | No: 18.8 (6.1) | No: 76.0 (5.4) | No: 49.4 (6.6) |
| | | Alert: 32.9 (6.1) | Yes: 89.7 (5.6) | Yes: 58.9 (7.6) | Yes: 11.1 (4.1) | Yes: 81.2 (6.1) | Yes: 24.0 (5.4) | Yes: 50.6 (6.6) |
| | | Awake: 15.4 (4.3) | | | | | | |

*Note*: () among CAM features indicate standard deviation.

TABLE 4 Multinomial regression analysis of patient characteristics associated with latent classes.

| | Hyperalert referent group | Hypoalert | Cognitive changes | Hypoalert referent group | Hyperalert, | Cognitive changes |
|---|---|---|---|---|---|---|
| Age | - | −0.02 (0.02) | 0.02 (0.02) | - | 0.02 (0.02) | 0.04 (0.02) |
| Sex (male) | - | 0.13 (0.28) | −0.18 (0.30) | - | −0.13 (0.28) | −0.31 (0.30) |
| ASA class 3+ versus ≤ 2 | - | 0.78 (0.28)[a] | 0.38 (0.31) | - | −0.78 (0.28)[a] | −0.40 (0.31) |
| Surgery site: General versus Hips/Knee | - | −1.02 (0.36)[a] | −0.28 (0.37) | - | 1.02 (0.36)[a] | 0.74 (0.43) |
| Surgery site Spine versus Hips/Knees | - | 1.1 (0.31)[a] | 1.0 (0.35)[a] | - | −1.13 (0.31)[a] | −0.12 (0.33) |
| Pre-operative TICS | - | 0.14 (0.04)[a] | −0.02 (0.04) | - | −0.14 (0.04)[a] | −0.15 (0.04)[a] |

Abbreviation: TICS, Telephone Interview for Cognitive Status.

[a] $p$-value <0.05 when compared with the referent group; values in parentheses are the standard errors of the coefficients.

TABLE 5 Number of days of delirium.

| | Hyperalert | Hypoalert | Cognitive changes | |
|---|---|---|---|---|
| Days Mean (sd) | 1.55 (0.53) | 1.54 (0.66) | 1.84 (0.72) | $F = 6.70$, df = 2349; $p = 0.001$ |

Abbreviation: SD, standard deviation.

cognitive symptoms of delirium as advocated by DSM-5 criteria for delirium. By including cognitive symptoms of delirium, we found that 27% of elective surgery patients displayed symptoms of delirium that reflected postoperative cognitive changes. We also found that predominant symptoms for two of the latent classes reflected level of consciousness (hyperalert and overly stimulated by environmental stimuli vs. lethargic and drowsy), rather than purely motoric symptoms as was described in prior research. In fact, patients in the Hyperalert latent class had a high probability of having psychomotor retardation, providing novel evidence that level of consciousness is not associated with motoric symptoms. Our findings provide evidence that there are varying patterns of delirium, each requiring postoperative care that addresses patients' specific symptoms of delirium.

Patients in the Cognitive Changes class had a 50% probability of having psychomotor retardation which is defined as moving slowly, being sluggish, seemingly staring into space, and staying in one position for a long time. Membership in the Hyperalert class was also associated with a high probability of having symptoms of psychomotor retardation. The similarity in psychomotor symptoms between these two latent classes may be due to spine surgery being the most common surgery for both groups; 54% of those in the Hyperalert class and 44% of those in the Cognitive Changes class had spine surgery. In addition, results from the multinomial regression analysis reveal that the preoperative TICS scores were similar for the Hyperalert and Cognitive Changes groups. Future research is needed to determine whether perioperative procedures associated with spine surgery contribute to onset of psychomotor retardation. For example, spine surgeries typically require longer duration of general anesthesia and more extensive postoperative analgesia which may contribute to onset of these symptoms of delirium. It is also possible that perioperative opioid usage, other postoperative medications, or postoperative pain may have contributed to symptoms of psychomotor retardation. A study that examined preoperative risk factors among major noncardiac surgeries found increased rates of delirium among those who received opioids perioperatively.[27]

Patients in the Hyperalert and Cognitive Changes classes had higher probabilities of having disorganized thinking compared to patients in the Hypoalert latent class. It is possible that patients in the Hyperalert and Cognitive Changes classes would have benefited from hospital-based interventions to reduce incident delirium such as The Hospital Elder Life Program (HELP).[28] That program was designed to reduce cognitive disturbances by reducing common risks for delirium; it is considered among the most effective programs for reducing delirium, particularly the cognitive symptoms of delirium. Specifically, the intervention includes orienting the patient to time and place several times daily and having cognitively stimulating discussions with patients several times a day. In addition, the staff ensured that patients had access to essential items like hearing aids and glasses. They also minimized sleep disturbances by reducing ambient noise and strategically timing medications and procedures to promote sleep.

The advantage of assessing patients who were admitted for elective surgery is that the study's findings were not confounded by preoperative acute illnesses known to precipitate delirium (e.g., infection, organ failure, or acute severity of illness). Elective surgery patients have lower risk for delirium because they are not admitted with acute illnesses or acute events that increase risk for delirium.[29,30] This study provides evidence that the onset of delirium among the elective surgery patients is likely influenced by physiological changes that affected brain functioning. This suggests that onset of delirium in patients with chronic or acute illnesses may be complicated by physiological disturbances that are not explained by chronic or acute illnesses. Another advantage of our study is that we utilized the long form of the CAM, a highly reliable and valid instrument, that provides a more holistic assessment of delirium than assessment instruments that focus on level of consciousness or agitation. No prior studies used Latent Class Analysis to objectively detect patterns of delirium symptoms.

A limitation of this study is that patients were from a single academic center hospital. Also, the elective surgery patients included in this study were healthier than patients enrolled in most of the prior studies of delirium because they were not acutely ill and not requiring immediate surgery at admission. Thus, our findings may not be generalizable to patients who are admitted with acute illness (e.g. infections, stroke) or acute events (e.g. hip fractures). For example, we assessed characteristics associated with membership in each latent class. We found no significant differences in age or sex between the patients in the Hypoalert class and patients in the Hyperalert class. This is in contrast to a systematic review of 61 studies that described predisposing characteristics associated with the two motoric subtypes of delirium (hyperactive and hypoactive). They found that patients who had hypoactive delirium were older, had poorer cognitive functioning, and higher risks scores than those with hyperactive delirium. Those that developed hyperactive delirium were more likely to be younger, male, and have higher cognitive scores.[31] However, that review included studies that varied considerably in the reasons patients were hospitalized, including cancer, cardiac surgery, stroke, palliative care, urgent and elective surgeries, etc. In addition, prior studies used different methods for assessing delirium including the Richmond Agitation Sedation Scale and the Delirium Motor Subtype Scale which focus on symptoms of agitation and level of consciousness. In contrast, by using the CAM, we were able to examine a wider range of symptoms of delirium, including cognitive symptoms as discussed in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria for delirium. Consequently, the findings from this study should not be compared to prior studies with different patient populations whose symptoms of delirium were assessed using methods that did not include assessment of cognitive symptoms of delirium.

## 6 | CONCLUSION

Our study is the first to identify a novel delirium subtype based on delirium symptoms that reflected acute onset of cognitive disturbances after hospital admission. The cognitive changes that were observed included disorganized thinking, memory impairment, and disorientation. The findings provide evidence for the importance of assessing cognitive symptoms of delirium in addition to levels of consciousness, motoric symptoms, and agitation. Onset of cognitive disturbances can be distressing to patients and their families and require additional care from nursing staff. Before we can develop interventions to reduce cognitive symptoms of delirium, it is important to recognize that they exist and therefore should be assessed regularly. Future research is needed to determine perioperative risks for cognitive symptoms of delirium with the goal of developing interventions to reduce the incidence of these symptoms.

### ACKNOWLEDGEMENTS

We acknowledge the data collection efforts of the UCSF Perioperative Medicine Research Group.

### CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interests. Funding for this study was provided by R01 NR017622-02S1 and R01 NR017622-03.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in REDCap at https://www.project-redcap.org/.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

**How to cite this article:** Yang L, Do Q, Zhu X, Leung JM, Sands LP. Assessing patterns of delirium symptoms reveals a novel subtype among elective surgical patients with postoperative delirium. *Int J Geriatr Psychiatry*. 2024;e6049. https://doi.org/10.1002/gps.6049