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Post-ICU consequences of patient wakefulness and sedative exposure during mechanical ventilation

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Abstract *Objective:* To determine the relationship between measures of critical illness (sedative/analgesic administration, wakefulness and organ dysfunction), intensive care unit (ICU) recall and symptoms of posttraumatic stress disorder. *Design:* Prospective, observational study with post-ICU follow-up. *Setting:* Medical and surgical ICUs at a teaching hospital. *Patients:* Two hundred seventy-seven subjects requiring $>$ 36 h of mechanical ventilation were enrolled; 149 completed follow-up interviews 2 months later and 80 at 6 months. *Interventions:* None. *Results:* ICU recall was greater for events occurring at the end of critical illness; however, 18% of subjects had amnesia for the entire ICU course. Factual ICU recall was weakly associated with increased wakefulness during mechanical ventilation ($r^2 = 0.03$–0.11, $p < 0.05$). Posttraumatic stress disorder prevalence was 17% at 2 months and 15% at 6 months. The avoidance-numbing cluster had the highest specificity (91%) for a formal diagnosis and the re-experiencing cluster had the lowest (69%). Recall of a delirious memory during critical illness was associated with more severe posttraumatic stress symptoms, but there was no association between posttraumatic stress symptoms and factual recall of ICU events. Neither ICU recall nor posttraumatic stress symptoms were associated with the intensity of sedative administration during mechanical ventilation. Posttraumatic stress symptoms were lowest in patients either the most awake during mechanical ventilation or the least awake. *Conclusion:* Wakefulness during mechanical ventilation has a greater influence on post-ICU recall and posttraumatic stress symptoms than sedative drug exposure or severity of illness. It is difficult to predict the future psychological consequences of an individual patient's critical illness.

Keywords Sedation · Amnesia · Stress disorders, post-traumatic · Intensive care units · Critical illness · Acute respiratory failure

Introduction

Many patients surviving critical illness have decreased recall of factual events during mechanical ventilation yet report delusional memories. In 13 studies with 1882 patients, the frequency-weighted proportion of patients amnestic for the intensive care unit (ICU) was 29.6% (95% CI 27.5–31.7%) [1–13]. Memories of unreal situations were associated with worse post-ICU psychological adjustment than recall of factual memories [5]. In 10 studies comprising 1435 patients, the frequency-weighted proportion of patients with delirious memories was 26.7% (95% CI 24.4–29.1%) [3–5, 7–10, 12–14]. Few studies have identified factors that predict post-ICU amnesia or psychological symptoms such as posttraumatic stress symptoms [15–17].

Table 1 Recall of the ICU experience by 146 subjects

Descriptor of patient's global recall of their time in the ICU[a]	*N* (%)
Remember all of the time	3 (2)
Remember most of the time	11 (8)
Remember some of the time	55 (38)
Remember a little of the time	49 (34)
Remember none of the time	28 (19)
Recall of specific ICU event or symptom[a]	*N* (%)
"Breathing tube in my throat"	72 (49)
"First got put on the respirator"	12 (8)
"People suctioning from breathing tube"	43 (29)
"When my breathing tube was taken out"[b]	74 (52)
"When I was moved out of the ICU"	102 (69)
"Able to track days and hours in the ICU"	21 (14)
"Recall being in pain"	41 (28)
"Recall being short-of-breath while on the respirator"	29 (20)
"Recall being terrified about my situation while in the ICU"	56 (38)
"Had hallucinations or nightmares when in ICU"[c]	75 (51)
"Think that some memories from the ICU were from situations that never really happened"[c]	72 (49)

Three subjects were unable to complete these items.
[a] Recall defined as choosing either "agree slightly, moderately or very much".
[b] $n = 141$ for this question as five patients still had tracheostomies at the time of the interview.
[c] For subsequent analyses, the 88 (59%) subjects with a positive response to one or both of these two items were defined as having a delirious memory.

Our study objectives were to (1) model the relationship between patient, medication or illness-related factors and post-ICU amnesia; (2) determine the relationship between ICU amnesia and posttraumatic stress symptoms; and (3) examine the domain structure of the posttraumatic stress disorder (PTSD) diagnosis for ICU patients. A version of this research was presented in an abstract [18].

Methods

We conducted a prospective study (approved by the Institutional Review Board for human subjects research) of adult patients mechanically ventilated for > 36 h in the medical and surgical intensive care units at the University of Minnesota Medical Center. Initial consent for enrollment was obtained by proxies (close family members in almost all cases) and a second consent to continue in the study was obtained from cognitively intact subjects before starting the follow-up interview. During the study period (2001–2003), the ICUs used sedation and analgesia guidelines including daily dose reduction for propofol [19]. However, there was not a protocol that recommended drug titration to a specific sedation level or mandated daily dose reduction for all sedatives. Nurses assessed patients' level of consciousness, spontaneous motor activity and overall sedation quality every 4 h using the Minnesota Sedation Assessment Tool (MSAT; see ESM) [20, 21].

Data were analyzed by 4-h time blocks during mechanical ventilation. Summed doses of midazolam, lorazepam, fentanyl, morphine, hydromorphone, and haloperidol dosages given during a 4-h time block were converted to mg/kg/4 h based on ICU admission weight. We considered 10 mg of intravenous morphine to be equivalent to 1.5 mg of hydromorphone and 0.1 mg of fentanyl [22]. Three milligrams of midazolam was equivalent to 1 mg of lorazepam [23]. Propofol and dexmedetomidine doses (μg/kg/min or μg/kg/h) were converted to μg/kg/4 h. There were 7750 4-h intervals for 149 subjects with follow-up data. Patients received at least one dose of a sedative medication in 6750 intervals (87%) and an arousal assessment was recorded during 5273 intervals (68%). 6/149 (4%) subjects received > 4 h of neuromuscular blockade during mechanical ventilation. Eleven other subjects received only a single dose for intubation or a procedure. Neuromuscular blockers prior to the ICU were not recorded.

We created and validated a sedation intensity score (SIS) to address the problem of aggregating sedative exposure across drug classes [21]. We first calculated the weight-adjusted dose of each medication administered during a time block. The dose was then categorized as 1–4 based on the quartile within the distribution of that drug for one time block in the sample ($n = 277$). For instance, if 0.1 mg/kg of lorazepam and 0.2 mg/kg of morphine were given during a 4-h interval and 0.1 mg/kg fell into the second quartile of the distribution of all 4-h lorazepam doses in the entire cohort and 0.2 mg/kg of morphine was in the third quartile, then the SIS for that time block was $2 + 3 = 5$. A subject's mean SIS score (quotient of sum of subject's SIS values and number of 4-h intervals on mechanical ventilation) represents the average sedative exposure per hour relative to all other subjects.

Eighty-seven percent of the 2-month interviews were conducted in the home or facility where the subject was residing. All 6-month interviews were by telephone.

The study's "memory" tests focused on episodic or explicit memories which are subject to patients' ability to consciously recollect internal or external experiences. The initial 11 items of the questionnaire (item phrasing in Table 1) had a six-level Likert-type response format of "disagree very much" to "agree very much." Questions 1–5 asked about events likely to occur in almost all patients (e.g., presence of endotracheal tube, suctioning, transfer out of ICU) so that a "disagree" response suggests amnesia for episodic memory. We summed responses from questions 1–5 to create the "ICU amnesia score", a scale ranging from 5 ("disagree very much" on all items suggesting complete amnesia) to 30 ("agree very much" on all items suggesting complete recall).

Posttraumatic stress disorder (PTSD) symptoms and diagnoses were made with the Posttraumatic Stress Diagnostic Scale [24]. This scale closely follows the Diagnostic and Statistical Manual of Mental Disorders, version 4 [25] criteria for PTSD, which require $\geq$1 positive response in the five-item "re-experiencing" B domain; $\geq$3 positive responses in the seven-item "avoidance-emotional numbing" C domain; and $\geq$2 positive responses in the five-item "arousal" D domain. Domain-specific and global PTSD symptom severity scores were calculated by multiplying the number of positive symptoms by frequency severity (1 = once a week or less; 2 = two to four times per week; and 3 = five or more times per week) and summing within

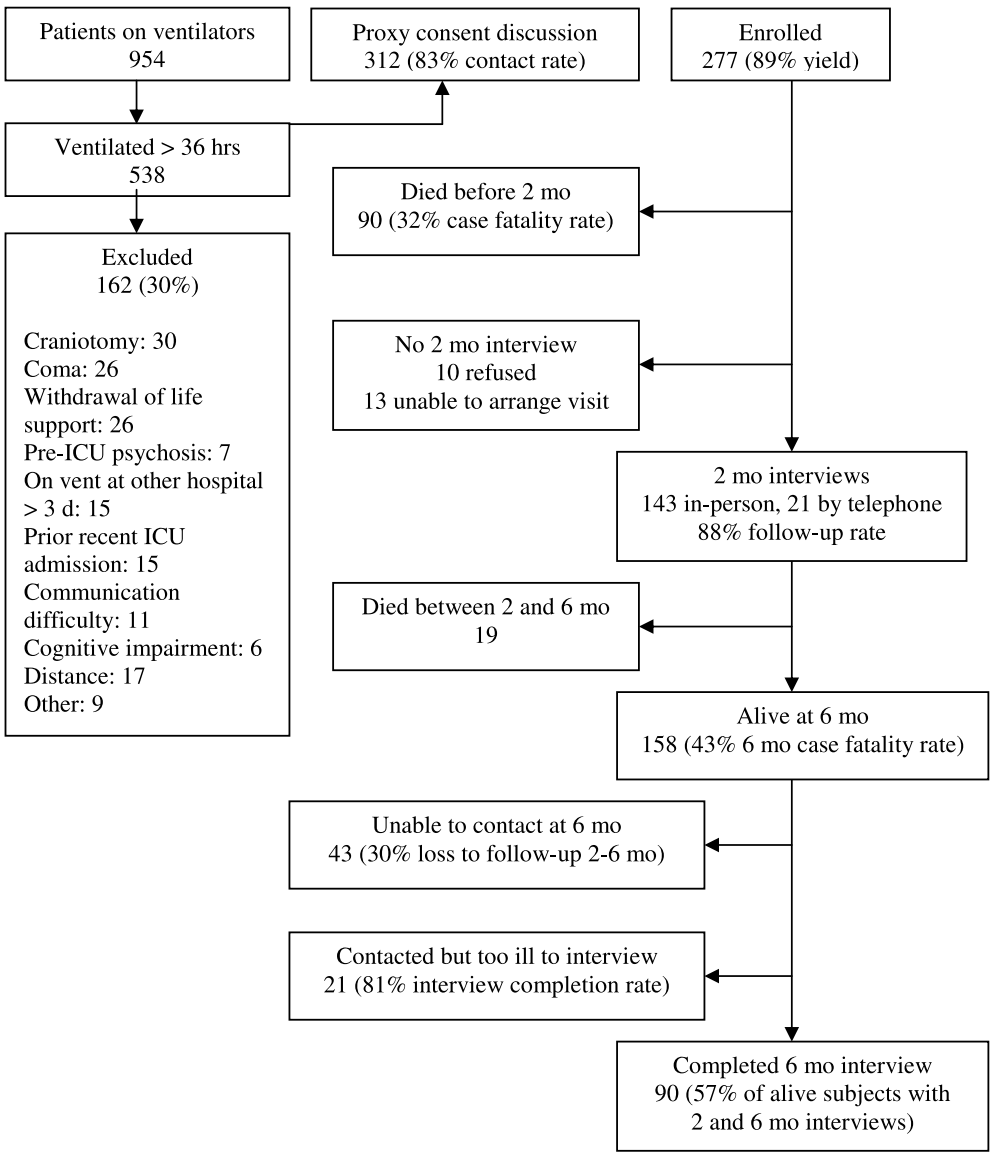

Fig. 1 Flow of subjects through the study

each domain (or over all three domains for a global score). Because a PTSD symptom severity score can be calculated for all subjects even if they do not have a PTSD diagnosis, to avoid misunderstanding, we renamed the global severity score the "PTSD-like severity score."

Statistical methods

Group means were tested for differences by *t*-tests or ANOVA or nonparametric tests, depending on the distribution. If global F tests were significant ($\alpha < 0.05$), post-hoc comparisons were tested with the Tukey HSD statistic.

Results

Figure 1 shows the enrollment and follow-up rates. Subjects had a broad range of indications for mechanical ventilation, with a median duration of mechanical ventilation of 6.8 days and a 32% 2-month case-fatality rate (Table 2). Compared to all enrollees ($n = 277$), those surviving and able to complete the PTSD assessment at 2-month follow-up ($n = 149$) were: (1) more likely to be treated in the SICU and have post-operative respiratory failure; (2) had shorter duration of mechanical ventilation; and (3) had better mental status prior to intubation.

Recall of the ICU experience

The median ICU amnesia score was 14 (IQR 8, 20) and 18% of patients had a minimum score of 5, suggesting complete amnesia for the time in the ICU. The validity of the ICU amnesia score was supported by a moderate correlation ($r = -0.69$, $p < 0.001$) between the ICU amnesia score and a separate single ICU recall item (item 1 in Table 1). Also, in asking patients which part of their ICU time they recalled most clearly, the group choosing "can't recall anything" ($n = 37$) had significantly lower mean ICU amnesia scores than those choosing a specific period ($n = 109$) [7.5 (SD 3.7) vs. 16.8 (SD 6.2), $p < 0.001$].

The prevalence of individual ICU recall events or symptoms is shown in Table 1 and shows less recall of early ICU events than of later events. When asked to choose a time they recalled "most clearly", only 4% chose "the beginning" and 71% chose "the end." Similar findings in the opposite direction were found for the time recalled "least clearly". About half the subjects reported memories of terror, hallucinations or unreal situations during their ICU stay.

Predictors of ICU amnesia

We found no relationship between the ICU amnesia score and three hypothesized predictors: SIS, duration of mech-

Table 2 Characteristics of study subjects at enrollment and at 2-month follow-up

	At initial enrollment ($n = 277$)	At 2-month follow-up ($n = 149$)[a]
Age, mean, median (interquartile range)	55, 55 (47, 65)	54, 53 (45, 63)
Male, *n* (%)	143 (52%)	78 (52%)
Treated in the surgical/cardiovascular ICU, *n* (%)	155 (56%)	95 (64%)
Treated in the medical ICU, *n* (%)	122 (44%)	54 (36%)
Primary reason for mechanical ventilation, *n* (%)		
Post-operative respiratory failure	97 (35%)	65 (44%)
Pneumonia, aspiration or acute lung injury	64 (23%)	33 (22%)
CHF, pulmonary edema or coronary ischemia	36 (13%)	18 (12%)
Sepsis/shock	27 (10%)	8 (5%)
Other[b]	53 (20%)	25 (17%)
Duration of mechanical ventilation (mean ± SD; median, interquartile range), days[c]	13.2 ± 17; 6.8, 3.6–16.7	9.9 ± 10.6; 5.6, 3.1–11.0
Mental status prior to intubation[d], *n* (%)	($n = 253$)	($n = 141$)
Alert and attentive	180 (71%)	113 (80%)
Inattentive or confused	51 (20%)	18 (13%)
Unresponsive or unable to verbally communicate	22 (9%)	10 (7%)

[a] Follow-up at 2 months defined as subjects completing the PTSD questionnaire by telephone or in person.
[b] Includes acute exacerbation of chronic respiratory disease, decreased level of consciousness, neuromuscular disease and cardiopulmonary arrest of unclear etiology.
[c] Days on ventilator while in ICU. Discontinuous episodes were summed for up to 2 months after enrollment. Days were not counted after ventilated patients were discharged to another facility.
[d] We reviewed subjects' charts for documentation of mental status. Elective surgical cases were assumed to be alert and attentive prior to surgery unless there was documentation otherwise. For all enrollees, 5% of charts were not available for review and 4% could not be classified after review. For those with 2-month follow-up, 1% of charts were not available for review and 5% could not be classified after review.

anical ventilation, or cumulative severity of illness by MODS. However, Fig. 2 shows a positive relationship between patient wakefulness during mechanical ventilation and the ICU amnesia score. This relationship was consistent across four separate analyses that had different thresholds for defining wakefulness. Although the correlation between the proportions of time spent at each level of wakefulness and the ICU amnesia score was statistically significant, the r^2-values were low (0.03–0.11), suggesting that other factors strongly affect ICU recall. For instance, subjects who were alert and awake prior to mechanical ventilation had a mean amnesia score of 15.3 (SD 6.9, $n = 114$); inattentive or confused, 12.1 (SD 6.7, $n = 17$); unresponsive or non-verbal, 12.5 (SD 7.0, $n = 8$) and unknown, 9.1 (SD 5.8, $n = 8$); global F = 3.1, $p = 0.03$.

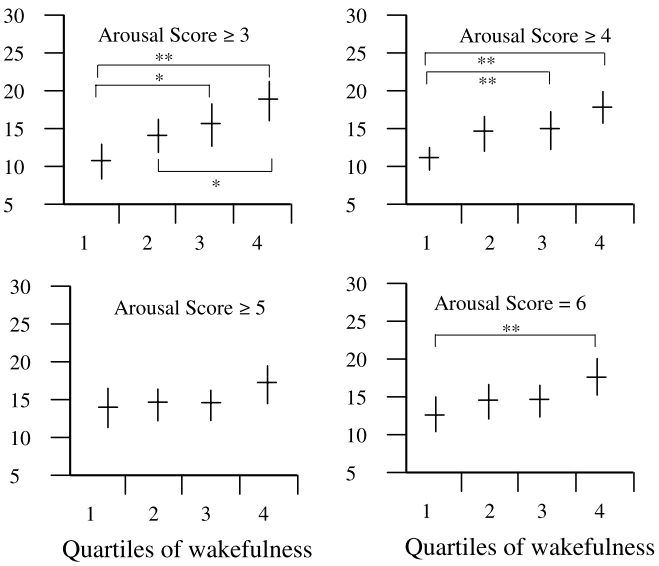

Fig. 2 Relationship between observed wakefulness during mechanical ventilation and ICU amnesia score. The *ordinate* is ICU amnesia score (5–30), with higher scores representing greater recall of factual ICU memories. The *abscissa* is quartiles of wakefulness, with quartile 4 representing cases with the greatest proportion of "awake" intervals during mechanical ventilation. Each plot uses a different Minnesota Sedation Assessment Tool Arousal threshold for defining the "awake" proportion: For each case we counted the number of 4-h time blocks which reached the threshold value divided by the total number of time blocks during mechanical ventilation. The mean ICU amnesia scores within each quartile group are compared with one-way ANOVA. A *single asterisk* indicates pair-wise comparisons are statistically different at a p-value of 0.01 to 0.05 and a *double asterisk* indicates a p-value of < 0.01. The *upper-left plot* defines "awake" as an arousal score of 3 or greater (global F = 8.2, $p < 0.001$. Pearson correlation before grouping by quartile was $r = 0.34$, $p < 0.001$). The *upper-right plot* raises the "awake" threshold to arousal score of 4 or greater (global F = 6.3, $p < 0.001$. Pearson correlation before grouping by quartile was $r = 0.32$, $p < 0.001$). The *lower-left plot* raises the arousal score to 5 or greater (global F = 1.7, $p = 0.17$. Pearson correlation, $r = 0.18$, $p = 0.04$). The *lower-right plot* defines "awake" as a score of 6 (global F = 3.8, $p = 0.01$. Pearson correlation, $r = 0.25$, $p = 0.003$). *Horizontal bars* are means, and *ends of each vertical line* are 95% confidence intervals

Diagnosis of posttraumatic stress disorder and specific symptom domains

Some 16.8% (25/149) of subjects at 2 months and 15% (12/80) at 6 months had a research diagnosis of PTSD (i.e., positive criteria for B, C and D domains). Women had more than twice the odds of having a PTSD diagnosis (OR 2.2, 95% CI 0.9–5.2), but this difference did not reach statistical significance.

More subjects met frequency criteria for individual symptom clusters than met diagnostic criteria for PTSD (see Table 3). The prevalence of subjects positive for the "re-experiencing" domain was greater than the other two domains, but the prevalence declined at 6 months, whereas symptoms in the "avoidance-numbing" and "arousal" domains were more persistent.

The "avoidance-numbing" cluster had the highest specificity (91.1%, 95% CI 86.1–96.6 %) for the PTSD diagnosis at 2 months. This means that 91% of all the subjects positive for the "C" domain met severity criteria for all three symptom domains. The "arousal" cluster had a lower specificity (78.2%, 95% CI 71.0–85.4%) and the "re-experiencing" cluster had the lowest specificity (68.6%, 95% CI 60.4–76.7%).

The 2-month PTSD-like severity score in the group with delirious memories was greater than subjects with no delirious memories [mean score 7.5 (SD 8.1) vs. 4.7 (SD 5.7), $p = 0.018$] but the proportion that had a formal PTSD diagnosis was not statistically different: 19.3% vs. 13.8%. We found no relationship between the extent of episodic memory (ICU amnesia score) and either the PTSD-like severity score or having recall of a delirious memory.

The presence of delirious memories was associated with higher (worse) scores in the "re-experiencing" [1.5 (SD 2.3) vs. 0.4 (SD 0.75), $p = 0.001$] and "avoidance-numbing" domains [3.3 (SD 3.9) vs. 2.1 (SD 3.2) $p = 0.05$] but not in the "arousal" domain [2.8 (SD 3.2) vs. 2.2 (SD 2.7), $p = 0.23$] than in subjects without a delirious memory. None of these relationships remained at 6 months.

Consequences of sedative exposure and wakefulness during mechanical ventilation

The sedation intensity score (sedative exposure averaged over the interval of mechanical ventilation) was not associated with three hypothesized post-ICU outcomes: PTSD diagnosis, PTSD domain scores or PTSD-like severity score. There was a linear positive relationship between SIS and having delirious memories: 42% of subjects in the lowest quartile of SIS (i.e., lowest sedative exposure) had a delirious memory compared to 66%, 58% and 71%

Table 3 Posttraumatic stress disorder symptom domains at 2 and 6 months after onset of respiratory failure

PTSD domain	Number (proportion) meeting threshold at 2 months ($n = 149$)	Number (proportion) meeting threshold at 6 months ($n = 80$)
"B" Re-experiencing	64 (43%)	23 (29%)
"C" Avoidance/numbing	36 (24%)	24 (30%)
"D" Hyperarousal	52 (35%)	27 (34%)
Global severity rating of "moderate" or worse[a]	32 (21%)	18 (23%)

[a] PTSD-like severity score value of ≥ 11 without regard to the presence of symptoms in all three domains

in quartiles 2, 3 and 4, respectively (test for linear trend, $p = 0.05$).

The association between wakefulness during mechanical ventilation and post-ICU PTSD-like severity score was non-linear (Fig. 3). Increasing wakefulness was associated with increasing PTSD-like symptom scores until the highest quartile of wakefulness, in which the mean score fell to below that in the first quartile. The same pattern was also observed if the data were analyzed by individual domain scores (data not shown).

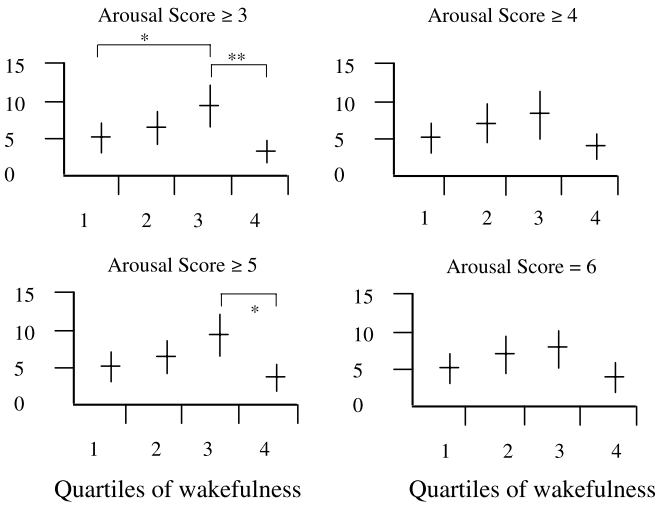

Fig. 3 Relationship between observed wakefulness during mechanical ventilation and PTSD-like severity score. The *ordinate* is the PTSD-like severity score, with higher scores representing more frequent re-experiencing, avoidance and arousal symptoms. The *abscissa* is quartiles of wakefulness, with quartile 4 representing cases with the greatest proportion of "awake" intervals during mechanical ventilation. Each plot uses a different Minnesota Sedation Assessment Tool Arousal threshold for defining the "awake" proportion: For each case we counted the number of 4-h time blocks which reached the threshold value divided by the total number of time blocks during mechanical ventilation. The mean PTSD-like severity scores within each quartile group are compared with one-way ANOVA. A *single asterisk* indicates pair-wise comparisons are statistically different at a p-value of 0.01–0.05 and a *double asterisk* indicates a p-value of < 0.01. The *upper-left plot* defines "awake" as an MSAT assessment with an arousal score of 3 or greater (global $F = 6.3$, $p < 0.001$). The *upper-right plot* raises the "awake" threshold to arousal score of 4 or greater (global $F = 2.3$, $p = 0.09$). The *lower-left plot* raises the arousal score to 5 or greater (global $F = 3.9$, $p = 0.01$). The *lower-right plot* defines "awake" as a score of 6 (global $F = 1.9$, $p = 0.13$). Linear correlation analysis was not performed because of the appearance of non-linearity. *Horizontal bars* are means, and *ends of each vertical line* are 95% confidence intervals

Discussion

Our main findings on ICU recall were that: (1) greater wakefulness during mechanical ventilation was associated with increased factual recall for the ICU experience, although the relationship was not strong; (2) episodic recall was greater for events that occurred near the end of an episode of respiratory failure; (3) complete amnesia for the ICU experience occurred in 18%.

We propose three explanations for the lack of association between sedative exposure and recall. First, we used an aggregate measure of sedative exposure averaged over the course of mechanical ventilation. However, we have previously reported that sedation intensity increases soon after intubation, peaks around the mid-point of the intubation interval and then slowly declines [21]. Therefore, it is possible that peaks and troughs in sedation administration that could affect recall were averaged out over the course of critical illness. Second, patients with metabolic encephalopathy may have amnesia in the absence of sedatives. Third, sedatives and their metabolites may persist for many hours, and changes in serum levels of benzodiazepines may influence explicit memory more than level of consciousness [26]. Our data suggest that the behavioral state of the patient (e.g., overall objective level of consciousness) is more predictive of factual ICU recall than the amount of sedatives they received. However, the relationship is not strong, suggesting that ICU clinicians cannot reliably predict the amount and content of an individual patient's post-ICU recall.

Our main findings on post-ICU PTSD symptoms were as follows: (1) The prevalence of a formal PTSD diagnosis was similar at 2 and 6 months although the 15–17% rate does not represent the same individuals. (2) PTSD prevalence was higher and more likely to persist if PTSD was defined by a global score that disregarded whether symptoms were distributed across three PTSD domains. This suggests caution in interpreting prevalence studies of "medical" PTSD because results may be strongly influ-

enced by case definition [27]. (3) Similar to community studies of PTSD, we found that women were more likely than men to develop PTSD [28].

The relationship between events during mechanical ventilation and PTSD was complex: Although the mean level of sedative exposure was associated with an increased risk of having a delirious memory; the intensity of sedative exposure, by itself, was not predictive of PTSD or PTSD-like symptom severity. Patients that were either the most awake or the most unresponsive during mechanical ventilation experienced the least amount of PTSD-like symptoms.

Results from this study are most readily comparable to eight prior studies [2, 5, 6, 8, 10, 14–16] although comparisons are limited by varied definitions of delirium, recall, PTSD and study design. Rotondi et al. [8] reported that amnestic subjects had greater day 1 APACHE III scores, whereas we did not find that severity of illness was associated with amnesia when we used a MODS score summed over the entire ICU stay. As in our study, Capuzzo et al. concluded that sedation did not affect recall of factual memories during ICU care [2]. We did not confirm Capuzzo's subsequent report that impairment in episodic memory was associated with delusional memories [14]. Kress et al. showed that patients treated with daily sedation interruption had lower Revised Impact of Events scores and PTSD prevalence than control patients even though the prevalence of ICU amnesia was equivalent (~31%) [6]. The study by Samuelson et al. had a prevalence of complete amnesia (18%) comparable to our study and we confirmed their observation that greater patient wakefulness was associated with increased ICU recall [16]. Girard demonstrated that duration of delirium (prospectively measured during mechanical ventilation) was not associated with PTSD symptom severity at 6-month follow-up although the aggregate amount of lorazepam administered was weakly associated with subjects' PTSD symptoms [17].

Our results are in partial agreement with Jones et al. [5] in that patients with delirious memories had more PTSD-like symptoms, but we did not confirm that factual recall had a protective effect against developing PTSD. Patients examined by Schelling et al. (a median of 4 years after ICU care) [10] had a PTSD rate slightly higher than ours (28%), and those authors concluded that greater recall of "adverse experiences" during mechanical ventilation led to higher PTSD symptom scores years later [10]. Similar results were reported by Deja et al. [29].

Schelling and Jones' results lead to opposing theoretical approaches to sedation as an intervention to improve post-ICU psychological outcome. Schelling's findings suggest that higher doses of sedatives would more reliably create amnesia for "adverse experiences" and thereby decrease PTSD. Jones' data suggest that sedation can lead to delirious memories and blunt factual recall, which, albeit unpleasant, is protective against persistent PTSD-like symptoms. Our data support both interpretations: we found that having delirious memories was associated with more PTSD-like symptoms but patients that were the most awake during mechanical ventilation also had the lowest levels of PTSD-like symptoms. Whether the lower prevalence of PTSD symptoms is a direct consequence of alertness or indicates milder illness or brain dysfunction cannot be established with this study design. Similarly, it has never been proven that delirium, as measured by an objective instrument during ICU care, is associated with patients' post-ICU report of delirious memories. There are many valid reasons for administering sedatives to patients with respiratory failure, and adverse events may occur if patients are not sedated adequately [30].

An issue that has been under-appreciated in medical PTSD studies is that a formal diagnosis requires sufficient symptoms in three clusters. Breslau et al. showed in a community-based sample that symptoms in the "avoidance-numbing" cluster were more predictive of a "pervasive disturbance" than symptoms in the B and D domains [31]. Our results, derived from a completely different type of stressor, also show that the C cluster had the highest specificity for a formal PTSD diagnosis. While this may be partially explained by the higher number of symptoms needed to achieve a "positive" result for the C domain, our results also suggest that the oft-mentioned "ICU flashback" symptom is only a weak predictor of a "full-blown" PTSD diagnosis.

We acknowledge several study design limitations. Subjects were not randomly assigned to different sedative regimens or level of wakefulness, so a cause-and-effect relationship between ICU conditions and post-ICU outcomes cannot be established. We had limited data on subjects' pre-ICU psychiatric symptoms, did not measure delirium during mechanical ventilation and did not assess the extent to which patients were functionally impaired by PTSD symptoms. In contradistinction to studies of memory function in patients given a few hours of general anesthesia, we did not expose subjects to standardized stimuli and then test for conscious and non-conscious learning [32, 33]. The 6-month follow-up assessment had significant attrition and therefore our conclusions about symptom persistence are more subject to bias.

Conclusion

Post-ICU amnesia and PTSD symptoms are likely caused by a complex interaction of pre-existing psychological and cognitive function, gender, level of consciousness before and during critical illness, type of sedative drug exposure and severity and class of organ failure. Because many of these factors are not routinely measured in general practice, it is unlikely that a clinician can predict the recall content and psychological consequences of critical illness for a specific patient.

Future research in PTSD associated with ICU care could benefit by evaluating the preventive and therapeutic interventions already tested in non-medical PTSD populations.

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