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Research Article

RESEARCH ARTICLES

Intraoperative electroencephalogram suppression at lower volatile anaesthetic concentrations predicts postoperative delirium occurring in the intensive care unit

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Abstract

Background: Postoperative delirium is a common complication associated with increased morbidity and mortality. A recently-reported association between intraoperative electroencephalogram suppression and postoperative delirium might be mediated in some patients by a heightened sensitivity to volatile anaesthetics.
Methods: This retrospective cohort study included 618 elective surgery patients with planned intensive care unit admission, who also received intraoperative electroencephalogram monitoring and had delirium assessments documented in the medical record. Sensitivity to volatile anaesthetics was assessed using a mixed effects model predicting the likelihood of electroencephalogram suppression at each time point based on the current end-tidal anaesthetic concentration. Patients with a random intercept above the population median (electroencephalogram suppression at lower anaesthetic concentrations) were classified as having heightened sensitivity to volatile anaesthetics. Delirium was defined as a positive Confusion Assessment Method for the Intensive Care Unit assessment anytime in the first five postoperative days.
Results: Postoperative delirium was observed in 162 of 618 patients (26%). Patients who experienced electroencephalogram suppression at lower volatile anaesthetic concentrations had a higher incidence of postoperative delirium [109/309 (35%)] than other patients [53/309 (17%)] [unadjusted odds ratio 2.63; 95% confidence interval (CI), 1.81–3.84, $P<0.001$]. This association remained significant after adjusting for patient characteristics, surgical variables, and duration of electroencephalogram suppression (adjusted odds ratio 2.13; 95% CI 1.24–3.65, $P=0.006$).
Conclusions: These data support the hypothesis that patients with electroencephalogram suppression at lower volatile anaesthetic concentrations have an increased incidence of postoperative delirium. Such patients appear to exhibit a phenotype of anaesthetic sensitivity, which might predispose them to adverse cognitive outcomes.

Keywords: anaesthesia; brain waves/drug effects; delirium/aetiology; electroencephalography/instrumentation

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Editor's key points

- An association of postoperative delirium with heightened sensitivity to volatile anaesthetics was tested in a single centre retrospective analysis of 618 noncardiac surgery patients.
- Patients with electroencephalogram suppression at lower anaesthetic concentrations had a higher incidence of postoperative delirium.
- Greater sensitivity to volatile anaesthetics might predispose patients to postoperative delirium.

Postoperative delirium is a common surgical complication that is associated with increased morbidity, mortality, and other undesired outcomes after surgery. Delirium is characterized by a disturbance in attention and awareness that develops over a short period of time, represents a change from baseline, tends to fluctuate in severity, and is associated with an additional disturbance of cognition.[1] Patients who experience postoperative delirium often require longer stays in the intensive care unit and in the hospital.[2] After discharge, these patients have higher rates of mortality, although the evidence is insufficient to determine whether this relationship is causal.[3] These patients also incur greater healthcare costs in the year following surgery and report decreased ability to complete activities of daily living 30 days after surgery.[4,5] The pathophysiology of delirium is complex and obscure, and the aetiology is typically multifactorial, with patient vulnerability (e.g. older age), physiological perturbation (e.g. inflammation), and specific precipitants (e.g. anaesthetic agents) all likely to contribute.[6–8]

Recent studies have identified an association between electroencephalogram suppression during general anaesthesia and postoperative delirium. In addition, two randomized trials comparing bispectral index-guided anaesthesia to routine anaesthesia care have found that patients in the bispectral-index guided groups had a lower incidence of postoperative delirium.[9,10] In these and other trials, time spent with a bispectral index below a certain threshold value was an independent predictor of postoperative delirium.[9–11] Low bispectral index values can be driven by the presence of electroencephalogram suppression, an electroencephalogram feature characterized by periods of electroencephalogram suppression alternating with bursts of high-amplitude activity.[12] Two recent observational studies, including one conducted by our group, have identified an association between longer duration of intraoperative electroencephalogram suppression and postoperative delirium.[5,13] However, it is unclear whether the observed associations indicate that increased exposure to anaesthetic agents cause delirium or if underlying patient characteristics increase the risk both for electroencephalogram suppression and for postoperative delirium. Interestingly, some studies have also reported lower—not higher—average end-tidal concentration of volatile anaesthetic agent as a risk factor for postoperative delirium.[5,14] One possible explanation for such findings would be that certain patients are more sensitive to the effects of volatile anaesthetic agents, which might manifest as more-than-expected electroencephalogram suppression or other electroencephalogram features of deep anaesthesia, such as generalized slowing. Therefore we hypothesized that patients who are more likely to have electroencephalogram suppression at lower volatile anaesthetic concentrations would have a higher incidence of postoperative delirium.

Methods

To test our hypothesis, we conducted a retrospective cohort study. All patients provided written, informed consent to participate in the Systematic Assessment and Targeted Improvement of Services Following Yearlong Surgical Outcomes Surveys (SATISFY-SOS) data registry project (clinicaltrials.gov identifier NCT02032030). The Human Research Protection Office at Washington University (St. Louis, MO, USA) provided a waiver of informed consent to use data from the SATISFY-SOS registry to conduct an observational cohort study examining the association between intraoperative electroencephalogram suppression and postoperative delirium. The primary results of this study have been previously published.[5] This manuscript presents a secondary *post hoc* analysis from the aforementioned study.

Patient population

The patient population included 618 patients age 18 or older who underwent general anaesthesia for surgery at Barnes-Jewish Hospital (St. Louis, MO, USA) with planned intensive care unit admission between November 2012 and November 2013. Patients were included if they received intraoperative electroencephalogram monitoring and had at least one delirium assessment documented in the electronic medical record during the first five postoperative days. Patients undergoing neurologic surgery were excluded.

Data collection

The electroencephalogram was monitored continuously during surgery using a BIS Quatro sensor (Covidien, Dublin, Ireland) which employs a single frontal electroencephalogram channel (FP1 to F7). This monitor calculates the suppression ratio (SR), which describes the percentage of the preceding 63 s for which the electroencephalogram amplitude was less than 5 μV. The SR was captured at a rate of once per minute using MetaVision software (iMDSoft, Needham, MA, USA). Data points with a signal quality index <50% were excluded. The end-tidal anaesthetic concentration (ETAC) and bispectral index values were also captured once per minute using MetaVision software.

Postoperative delirium was measured using the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU).[15] In our institution, nurses in the surgical intensive care units routinely perform CAM-ICU assessments on all patients every 12 h unless the patient is sedated to a Richmond Agitation-Sedation Scale score of −4 or −5. Delirium assessments were not conducted on the hospital ward after patients were discharged from the intensive care unit. A patient was defined as experiencing postoperative delirium if one or more positive CAM-ICU assessments were documented in the electronic medical record between postoperative Day 1 and postoperative Day 5.

Definition of sensitivity to volatile anaesthetic agents

Patients who experienced electroencephalogram suppression at relatively lower concentrations of volatile anaesthetics were

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