suspend use of isoflurane maintenance anesthetic in elderly patients.

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References

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In Reply:
Thank you for your attention and good suggestion regarding our article.¹ In clinical practice, we have observed that even if known factors had been excluded, there were still some patients who suffered from postoperative cognitive dysfunction—even to the extent that there is a handful of patients who suffered from long-term postoperative cognitive dysfunction. We hypothesized that there must be some other factors that we did not know about, this is why we designed this clinical trial. Because the incidence of postoperative cognitive dysfunction is low, to analyze the reason for this, a large sample is needed.

Sometimes postoperative cognitive dysfunction that occurred because of anesthesia is reversible, but the cognitive dysfunction resulting from some diseases (such as Alzheimer disease) is not reversible. The essence of the cognitive dysfunction is different, even if the Mini-Mental State Examination score is same.

There is no nitrous oxide in the inhaled anesthesia group. To focus on the association between postoperative cognitive dysfunction and apolipoprotein E4, some sections of results were deleted during the process of modification. Apolipoprotein E single nucleotide polymorphism varies among people with different ethnic backgrounds and living in different regions. The current study was conducted in patients who are of Han ethnicity residing in northwest China; thus, inevitable limitation exists in our research findings. The scientific results would be more universal if performed and verified in much more diverse territories and ethnic groups. We hope to see more similar or different results.

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Feedback Control Is Engineering, Let’s Treat It as Such

To the Editor:
As a practicing anesthesiologist with a Ph.D. in control systems engineering, I feel compelled to comment on both the merits and hazards of closed-loop control (CLC) in the operating room, as discussed in the February 2012 article by Liu et al.¹ and the accompanying editorial.²

CLC is a mature field of engineering with well established standards of analysis, design, and reporting – points missing from Liu et al.’s article and the accompanying editorial. This absence suggests unfamiliarity with the hazards of CLC, which include the risk of introducing instability where none existed before.

My main criticism of Liu et al.’s work is that there is no evidence that the appropriate groundwork was done to ensure that the control algorithm was safe (stable) before entering the operating room. Minimizing the hazards of CLC requires a thorough stability analysis before implementation. By way of comparison, it is as important to precede CLC operational testing with computer modeling and simulation studies as it is to precede human drug trials with animal modeling and testing. Testing under extremes of “physiologically challenging conditions such as hypertension, hypotension, morbid obesity, in pediatric patients, or during major surgery such as cardiac surgery or lung transplantation,” as the authors propose for their next clinical trial (see Discussion¹), should have been done by simulation before the first clinical trial.

Controller design is the key to ultimate success and acceptance of any closed-loop strategy. There are dozens of ways to design closed-loop algorithms. Of all of the available approaches, it is noteworthy that the authors decided to use the PID, or proportional, integral, derivative, approach. The details of how PID controllers work are not important for this point of discussion. The important issue is that the PID approach is the most basic and unsophisticated of algorithms—the first one learned by every CLC engineer in their first undergraduate control course—and is suitable for some simple mechanical, electrical, or hydraulic systems (e.g., automo-
bile cruise control), but not for complicated, time-variant, nonlinear systems with time delays (e.g., the surgical patient).

Lastly, Liu et al.’s article lacks the necessary engineering detail to evaluate the work. By piecing together comments from the present paper and previous work,3,4 it is possible, however, to determine that the controller is in fact not a PID controller. Instead, the authors used empirical methods to develop look-up tables and logic trees to mimic the proportional (P) and derivative (D) terms of a classic PID while ignoring the integral (I) term altogether. The result is that the control algorithm looks more like a crude expert system than a PID controller. An expert system of this type is what would result from a survey of anesthesiologists asked what they would do with propofol and remifentanil infusion rates given particular entropy values.

In conclusion, what the authors have done is replace the human anesthesiologist with an ideal, empirically derived, computer anesthesiologist dedicated to the one task of maintaining a set entropy value. For this menial task, the computer wins. For the advancement of closed-loop control design in the operating room, no one wins.

Studies using CLC have the potential to significantly impact our specialty and, more importantly, our patients. When considering the publication of CLC articles, the editors of ANESTHESIOLOGY must consider using a control systems engineer in the peer review process. There is precedent for recent and good systems engineering work in the anesthesia literature. I refer to the work of De Smet et al.,5,6 where the authors follow a sound engineering development strategy.

Finally, perhaps Crosby and Culley think the future bright if “a dozen operating rooms filled with patients having surgery” are managed by a “lone anesthesiologist … from a distant location.”2 In my view, this is an unholy grail. Almost every paper about “closed-loop” anesthesia discusses the similarities of our environment and the cockpit. Without doubt there is one way they are exactly alike: Patients and passengers would recoil if they were to learn that their anesthesiologist or pilot would be in abstinencia.

The ideal goal of control systems engineering in the operating room is not the elimination of anesthesia staff, but the ability to prescribe an effect rather than a dose. Imagine a future where we say “set end-tidal carbon dioxide to 36, set mean arterial pressure to 80, set heart rate to 70, set pain response to 0, set awareness to 45,” and then watch as safe, stable, robust, and reliable control algorithms adjust all fluids and anesthetics at once to achieve these results. This is a bright future, indeed.

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References

In Reply.
We thank Dr. Looke for his interest in our recently published article.1 Space constraints preclude a full description of the in silico and animal studies that we performed before introduction of our controller in the operating room. We followed these different steps: the State Entropy (SE) and the Response Entropy were recorded simultaneously in surgical patients anesthetized using a target-controlled infusion of propofol and remifentanil; a controller guided by the entropy monitor similar to the controller developed for the Bispectral monitor was developed and implemented2; the controller was tuned during laboratory simulation; to obtain the agreement of the relevant French regulatory office for the clinical study, a risk assessment was performed and followed by an open-loop pilot study in swine3; fine-tuning was tested in a previous pilot study in 10 subjects.

However, simulation studies cannot evaluate the controller’s performance in surgical patients. In fact, simulation can only determine whether the controller respects command such as to administer or to stop a bolus of propofol. For example, in the same patient a bolus of 20 mg propofol has virtually no effect before induction, yet can reduce SE in the same patient when anesthetized. Furthermore, SE can increase when noxious surgical stimuli are applied to the patient without any change in the control status. And finally, although simulation studies are necessary for administrative clearance, there is little relationship between performance in silico or in animal studies and performance in anesthetized surgical patients because the transfer function remains unknown. Thus, a controller’s performance can only be evaluated clinically in comparison with a suitable control group.