(Accepted for publication August 25, 2015.)

In Reply:
We thank Kla et al. for their interest and comments on our recent publication in Anesthesiology. They raise concerns about the generalizability of the results of our study conducted in young and healthy patients, considering (1) the prevalence of elderly or diabetic patients in surgical patients and (2) the pupillary autonomic dysfunction associated with these two conditions.

Elderly patients make up a significant proportion of the surgical population in the United States and worldwide. According to the Centers for Disease Control and Prevention, 37.4% of inpatient procedures were performed in patients older than 65 yr in 2010. However, it also indicates that almost two thirds of these procedures were performed in patients younger than 65 yr. The rates of diagnosed diabetes in the civilian population in 2010 were 1.7% between 0 and 44 yr and 12.2% between 45 and 64 yr. These numbers highlight that the pupillary dilation reflex amplitude evoked by a standardized noxious test to predict movement to surgical stimulation and individualized administration of general anesthesia could be used in a significant proportion of inpatient procedures.

Studies reporting pupillary autonomic dysfunction in elderly or diabetic patients have examined the changes in pupillary diameter elicited by light/darkness or by mydriatic/myotic eye drops. The effects of these two conditions on the changes in pupillary diameter elicited by noxious stimuli such as an electrical current have not yet been examined. The nature and characteristics of the stimuli used affect the amplitude of the pupillary response, and further investigations should examine the consequences of pupillary autonomic dysfunction on the pupillary dilation reflex to pain in these populations.

Contrary to volatile agents and the minimum alveolar concentration, there is currently no available tool in the United States to predict the absence of response to noxious stimuli when using total intravenous anesthesia. Target-controlled infusions of hypnotic and opioid allowing real-time calculation of effect-site concentrations of both agents are available in Europe but not yet in the United States. This underscores the urgent need for further research in this area to help anesthesiologists in the administration of total intravenous anesthesia.

As indicated by Larson and Gupta in the accompanying editorial, our study should be viewed as a first step toward “real-time individualized intravenous anesthetics,” and “additional studies examining this pupillary test to predict nonmovement in a more diverse population” are warranted.

Competing Interests
The authors declare no competing interests.

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Trials and Observations: A Friendly Pointer on the Language of Study Design

To the Editor:
I appreciate the fine efforts of Silbert et al. to improve our knowledge about patients at risk for postoperative cognitive dysfunction. However, the language used to describe their investigation would benefit from additional precision to improve interpretation and uptake of the study by the readership. Following are a few friendly clarifications.

This letter was sent to the author of the referenced article, who declined to reply.
The authors use the word “trial” to describe their study. It is not a trial. A trial is “a research activity that involves the administration of a test regimen to humans to evaluate its efficacy and safety.” Because there was no administration or assignment of exposure, this study was observational and not experimental. All trials, it should be noted, are prospective. Using the terms “prospective” and “trial” together, although increasingly common, is redundant to the point of risking confusion among readers.3

Although the authors report that their trial was registered at the Australian Clinical Trials Registry, the study was described there as an observational study. Registration of observational studies at “clinical trials” registries such as ClinicalTrials.gov is an increasingly common, and good, scientific practice.

The authors use the words “prospective” and “observational” to describe their study. This is accurate, and the study should be interpreted as such.

The authors also refer to “patients” and “controls” in their study, terms that may lead some to assume it is a case-control study. This is not correct. In a case-control study, the cases and controls are selected based on the outcome. In this fine study, controls were selected based on the exposure. They may be referred to as groups with and without the exposure to surgery or surgical and nonsurgical patients. So why was the word “controls” selected? Perhaps the confusion about trials is to blame, because in trials, one group of patients is commonly referred to as a control group.

These details of language are critically important because language describes design, and design informs interpretation. Again, I congratulate the authors on this contribution to the literature and anticipate their future work.

Competing Interests
The author declares no competing interests.

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