

5. Kohl BA, Schwartz S: Surgery in the patient with endocrine dysfunction. *Med Clin North Am* 2009; 93:1031–47
6. Fulk GW, Bower A, McBride K, Boatright R: Sympathetic denervation of the iris dilator in noninsulin-dependent diabetes. *Optom Vis Sci* 1991; 68:954–6
7. Karachaliou F, Karavanaki K, Greenwood R, Baum JD: Consistency of pupillary abnormality in children and adolescents with diabetes. *Diabet Med* 1997; 14:849–53
8. Pittasch D, Lobmann R, Behrens-Baumann W, Lehnert H: Pupil signs of sympathetic autonomic neuropathy in patients with type 1 diabetes. *Diabetes Care* 2002; 25:1545–50
9. Bitsios P, Prettyman R, Szabadi E: Changes in autonomic function with age: A study of pupillary kinetics in healthy young and old people. *Age Ageing* 1996; 25:432–8

(Accepted for publication August 25, 2015.)

### In Reply:

We thank Kla *et al.* for their interest and comments on our recent publication in *ANESTHESIOLOGY*.<sup>1</sup> 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.<sup>2</sup> 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.<sup>3</sup> These numbers highlight that the pupillary dilatation reflex amplitude evoked by a standardized noxious test to predict movement response 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.<sup>4,5</sup> 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 dilatation reflex to pain in these populations.<sup>6</sup>

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.<sup>7</sup> 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<sup>8</sup> 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.

**Jean Guglielminotti, M.D., Ph.D., Dan Longrois, M.D., Ph.D.** Assistance Publique - Hôpitaux de Paris, Hôpital Bichat-Claude Bernard, Paris Cedex, France (J.G.). jean.guglielminotti@bch.aphp.fr

### References

1. Guglielminotti J, Grillot N, Paule M, Mentré F, Servin F, Montravers P, Longrois D: Prediction of movement to surgical stimulation by the pupillary dilatation reflex amplitude evoked by a standardized noxious test. *ANESTHESIOLOGY* 2015; 122:985–93
2. Centers for Disease Control and Prevention: Inpatient surgery 2010. Available at: <http://www.cdc.gov/nchs/fastats/inpatient-surgery.htm>. Accessed August 14, 2015
3. Centers for Disease Control and Prevention: Rate per 100 of civilian, noninstitutionalized population with diagnosed diabetes, by age, United States, 1980–2011. Available at: <http://www.cdc.gov/diabetes/statistics/prev/national/figbyage.htm>. Accessed August 16, 2015
4. Cahill M, Eustace P, de Jesus V: Pupillary autonomic denervation with increasing duration of diabetes mellitus. *Br J Ophthalmol* 2001; 85:1225–30
5. Bitsios P, Prettyman R, Szabadi E: Changes in autonomic function with age: A study of pupillary kinetics in healthy young and old people. *Age Ageing* 1996; 25:432–8
6. Larson MD, Behrends M: Portable infrared pupillometry: A review. *Anesth Analg* 2015; 120:1242–53
7. Egan TD, Shafer SL: Target-controlled infusions for intravenous anesthetics: Surfing USA not! *ANESTHESIOLOGY* 2003; 99:1039–41
8. Larson MD, Gupta DK: Pupillary reflex dilation to predict movement: A step forward toward real-time individualized intravenous anesthetics. *ANESTHESIOLOGY* 2015; 122:961–3

(Accepted for publication August 25, 2015.)

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

### To the Editor:

I appreciate the fine efforts of Silbert *et al.*<sup>1</sup> 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.