# Cognitive Effects of Perioperative Pregabalin: Comment

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## To the Editor:

We read with interest the recent article by Myhre *et al.*[1] concerning the effects of pregabalin on cognitive function in the perioperative period. The authors note that there were significant changes in several components of the battery of tests, thus leaving the reader with the conclusion that pregabalin may cause significant detriment and demonstrably raise the risk of harm, including an increased risk of fall or behavior that would increase "risk of re-injury" (presumably wound dehiscence or other injury).[1]

As we routinely use nonopioid multimodal analgesia in our practice of perioperative pain management, we have several questions about this article and the data presented. First, was any reduction in dosage considered if the patient experienced side effects of the pregabalin? This is important as the patients were likely naïve to gabapentinoids and the dose utilized is the maximum dose that has been studied perioperatively (300 mg/day). Second, it would be helpful for the authors to note the test-retest reliability of this battery of tests and the correlation between them. The authors' conclusions suggested a significant risk, yet only two of the five tests showed any change from baseline and all of the tests were only administered once at each time point. Additionally, with approximately 20% of the patients in the control group not participating at 24 h due to pain or postoperative nausea and vomiting, could the authors comment on how stable their results would be if they assumed that these patients displayed poor function due to increased pain or an opioid effect? Third, it is unclear to the reader that a fraction of an error in two of the tests is a meaningful clinical difference at 3 to 5 days. What is the significance of 0.28 or 0.43 errors in actual practice? Finally, as the authors associate the change in executive function with an increased risk of fall in both the introduction and the discussion sections, it would be helpful for the reader to know whether this is speculative or if this event actually occurred in any patient.

### Competing Interests

The authors declare no competing interests.

### References

1. Myhre M, Jacobsen HB, Andersson S, Stubhaug A: Cognitive effects of perioperative pregabalin: Secondary exploratory analysis of a randomized placebo-controlled study. Anesthesiology 2019; 130:63–71

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# Cognitive Effects of Perioperative Pregabalin: Reply

## In Reply:

Drs. Allen and McEvoy have some very important comments and questions about our article[1] that we are happy to answer. We find that their input is valuable and relevant, and we thank them for their effort.

In their letter, they note that they routinely use nonopioid multimodal analgesia in their practice of perioperative pain management. We understand this, as pregabalin is part of that routine. One of our key messages is that pregabalin many places is used routinely perioperatively even if this is off-label use without proper documentation of efficacy and safety.[2] A quite recent editorial in Anesthesiology discussed this topic related to pregabalin in particular.[3]

Drs. Allen and McEvoy ask if any reduction in dosage of pregabalin was considered if the patient experienced side effects of pregabalin. They also comment that they believe the dose was high (300 mg/day).

The dose used is the recommended dose in several publications.[4,5] Our study differs from clinical practice, as it was a randomized and double-blinded trial, and individual titration of dose was not feasible. Of course, we had "stop rules," and possibility for unblinding in case of emergencies, but this was not needed except for one patient described in the flow chart who received only 450/600 mg pregabalin due to diplopia.[1] Besides, we think that dose reduction due to side effects is quite difficult

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