

## **Abstract**

Line 22: Rats were anesthetized with 1% pentobarbital and maintained with 3% sevoflurane.

Line 22-23: Use complete terms before abbreviation in the abstract and in the rest of the manuscript do the same.

## **Introduction**

Lines 50-53: The sentence seems too long and I suggest modifying it so it can be easier connected to the first sentence of the introduction.

Line 54: I suggest splitting the sentence and using an alternative instead. For example: „Although the pathophysiological mechanism of POCD is still unclear. Studies increasingly (or progressively) believe...”

Line 61: In my opinion, this part of the sentence can be replaced by: „in order to (or may help to) prevent cognitive dysfunction”.

Lines 67-68: instead of „and” the author should write „therefore”. I suggest removing „phenotype” words and writing out of the bracket because in this way the sentence seems unfinished.

Line 70: Full stop instead of a semicolon.

Lines 72-75: „that” from the beginning of the sentence is not necessary. This sentence is too long so I suggest rewriting it or split on 2.

Line 80: typo

Line 89: I would suggest a semicolon instead of a comma before „sinomenine”. From my point of view, that will format the sentence much more adequately.

Lines 93-97: I can anticipate the meaning of this sentence but I strongly suggest rewriting it because in this way it would be very confusing to the readers.

Lines 100-101: „In summary, in this study..” is too much in the same sentence. I suggest removing „In summary”. Furthermore, „surgical anesthesia” is a more proper term that you can find in the text below.

## **Materials and methods**

I would suggest merging subtitles under this section. For example: staining methods could be placed and explained under one subtitle divided into paragraphs; cognitive testing also can be placed under the same subtitle, etc.

Line 108: It is not correct to start any sentence with a number.

Line 112: Can you provide me with information about the preanesthetic preparation of the rat? What does the „could not hold water” exactly mean? Why were they subjected to fasting before anesthesia? It is well known that the rats do not require any food restriction and if it is necessary in some cases, which must be no longer than 3 hours. It is very important to explain this in the text as well so further studies do not make the same mistake.

Line 116: typo. What does of pentobarbital you use per kilogram? The pentobarbital is often diluted before administration to make a concentration less than 10 mg/ml. Did you provide the same?

Line 119: What is “the left lateral ventricle of the rats” means?

Line 120: PBS solution was injected in the same way as lentivirus?

Line 123: Can you please explain why the authors used 30% oxygen? Is that concentration also common for patients in humane medicine in your country? In such case, how did you prepare and checked oxygen concentration (mixed with air or you did not use medical pure oxygen)? Were they in an anesthesia chamber or you performed endotracheal intubation; what was the FGF formulation accordingly? The second sentence needs correction. Rats’ euthanasia performed after cognitive testing?

Lines 128-133: This paragraph needs correction. Please rewrite it because the first sentence is way too long and it can be divided into shorter parts.

Line 135: As I asked before, is this done before euthanasia or ten animals were randomly selected for cognitive testing while others are euthanized?

Line 137: “on days 1 and 5” is more correct if I can guess you performed testing only twice. In this way, it seems you tested them every day for five days. If I am wrong, then consider writing as “from day 1 to 5”. The sentence is also too long.

Line 148: on days 12 and 13.

Line 149: what type of surgery you performed earlier? If you performed any, it is a must to explain the analgesic approach in the text.

Line 154: The sentence starts with number again. “The testing” is much more appropriate than “training” in my opinion.

Line 171: Separate the sentence – typo.

## **Results**

If the journal’s rules do not require separation under the Result section, it would be a better option to delete subtitles and make this section one text divided into paragraphs.

Was there any rat with any kind of anesthesia complication during the experiment? It is important to mention in the result section and consider do those potential complications can affect overall results which can be described in the Discussion.

Line 215: The number of the subtitle is missing.

Line 222: Consider rewriting the sentence and to start differently than “We then...” You can choose “Expression of C/EBPalpha protein after surgical anesthesia in aged rats was examined”.

Line 224: On several points the authors mentioned surgery, but do you mean surgical anesthesia? If it is surgical anesthesia which is refer to the anesthesia depth, please replace the term in the whole text.

Lines 234, 249, and 287: “general anesthesia”

Line 240: New sentence starting so remove the semicolon.

Line 275-277: “receiving surgery with anesthesia” is not the correct term.

Line 288: Consider starting the sentence differently.

Line 296: Consider using alternative instead of training.

### **Discussion**

Please consider explaining anesthesia complication and their impact on the results, if there was any of course.

Line 306: Start the sentence with “Sevoflurane has ...” and rewrite the rest of it accordingly.

Line 309: typo

Line 311-312: the part of the sentence between commas can be deleted.

Line 314: “more likely than ...” should go at the end of the same sentence. Please replace.

Line 316: Compared to propofol.

### **Conclusions**

In my opinion, you should state how safe is sevoflurane for elderly patients by your results and suggest using alternatives instead of this drug if there is a clinical need.