Review of: "Synapse Weakening-Induced Caspase-3 Activity Confers Specificity to Microglia-Mediated Synapse Elimination"

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Potential competing interests: No potential competing interests to declare.

This is laborious work that uses a large amount of image data to show that caspase-3 activity is required for synapse selection during growth. The analysis of image data is inherently difficult, but the problem is well circumvented by an excellent idea.

https://www.sciencedirect.com/science/article/pii/S0889159123001575
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC16023/
There seems to be no reference to these papers, but is some of the content relevant?
Why not mention them in the discussion?

Figures S1-3 are important for understanding, so shouldn't they be incorporated rather than supplanted? In fact, it is now incorporated, so there is no point in labeling it as a supplement, is there? This is a minor but important measure to avoid confusing the reader.

Comparing images statistically is a rather difficult problem, but I think it is an excellent idea to create a threshold and compare them to a zero one. That's basically how we're getting the data here. I agree with the way the tests are applied and the fact that multiple testing is not used. However, rather than two-tailed t-tests, shouldn't we take logarithmic values and get two-tailed t-tests? It would be nice if they actually did so. If the data are lognormally distributed, as is the case with this and S12, which will be discussed later, it is not very appropriate to perform the t-test as it is. This is because the test assumes normally distributed numbers. If it is not being done now, taking the logarithm will probably make the p-value a little smaller.

Although a topic slightly off the main topic of organizing synapses during growth, the AD story is interesting in a different way.

Fig. 7B and D, shouldn't these be put together? I would like to see a direct comparison between Casp3 plus and minus, including testing. In that case, a combination of ANOVA and TukeyHSD would be a good idea. Similarly, A and C and B to D for S12 and S15 should also be compiled.

Incidentally, the S12 data, are they not lognormally distributed? Wouldn't the data be more coherent if the y-axis was shown as log? Please take a moment to check.