

**Response to the reviewer 1's comments:**

**Point 1.** The introduction requires mention of the characteristics of the murine models used.

**Answer:** Thank you for your comment. According to the reviewer's comment, we have additionally mentioned the characteristics of the 6xTg-AD models in the introduction section (page 2 lines 76-79) of the resubmitted manuscript and highlighted it in red.

**Point 2.** The paragraph beginning on line 83 describes the results using a TSPO-specific radiotracer and reference is made to Figure 1. However, Figure 1 describes the experimental scheme, the images of flutemetamol, and the quantification of flutemetamol uptake. On the other hand, the caption of Figure 1 indicates that these are representative images of Flutemetamol and DPA714 but there is no image of DPA17.

**Answer:** Thank you for your kind comment. According to the reviewer's comment, we have modified the caption of figure 1.

**Point 3.** On line 105 the asterisk must be before p

**Answer:** Thank you for your kind reminder. According to the reviewer's comment, we have edited it.

**Point 4.** The caption of Figure 1 seems to be for Figure 2. Revise all the captions

**Answer:** Thank you very much for your comment. According to the reviewer's comment, we have carefully checked and modified the captions of all figures.

**Point 5.** On line 143, "WT mice brains. Counterstained...." spare the point

**Answer:** Thank you for your comment. According to the reviewer's comment, we have modified that sentence.

**Point 6.** All the correlation graphs are too small. The labels at X and Y axes is difficult to read

**Answer:** Thank you for your kind comment. According to the reviewer's comment, we have increased the size of graphs including the X and Y axes in all figures.

**Point 7.** The caption of figure 3 indicates that the figures show results for animals of 2, 4 and 8 months. Nevertheless the images are only for 2 month-old animals. The other ages are shown at the supplemental figure. This description confuses the reader since it expresses something that is not seen in the image.

**Answer:** Thank you for your important comment. According to the reviewer's comment, we have modified the caption of figure 3.

**Point 8.** In addition, at line 182 it says that brain tissues are immunostained with 6E10 Ab; this is a mistake since the panel C is stained with TSPO Ab. Also, at the line 192 appear symbols like ## and "dolar" however these symbols do not appear in the figure. In line 185 it is indicated that panel c shows the correlation between DPA714 and TSPO, but that correlation appears in panel D

**Answer:** Thank you for your detailed comment. According to the reviewer's comment, we have modified the antibody name and symbol in the caption of figure 3 as appropriate.

**Point 9.** lines 195 and 196 the title doesn't make sense "...PET imaging detected age-related and AD-associated elevation in brain tau"

**Answer:** Thank you for your comment. According to the reviewer's comment, we have modified the title such as *"In vivo [ $^{18}\text{F}$ ]THK5351 and [ $^{18}\text{F}$ ]MK6240 PET imaging detected AD-associated elevation in brain tau"*