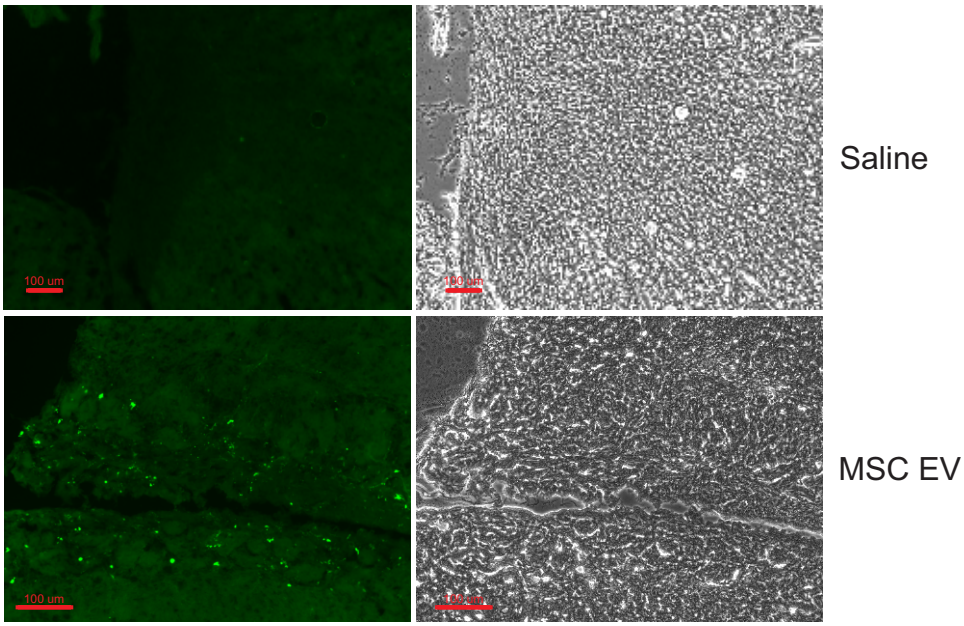
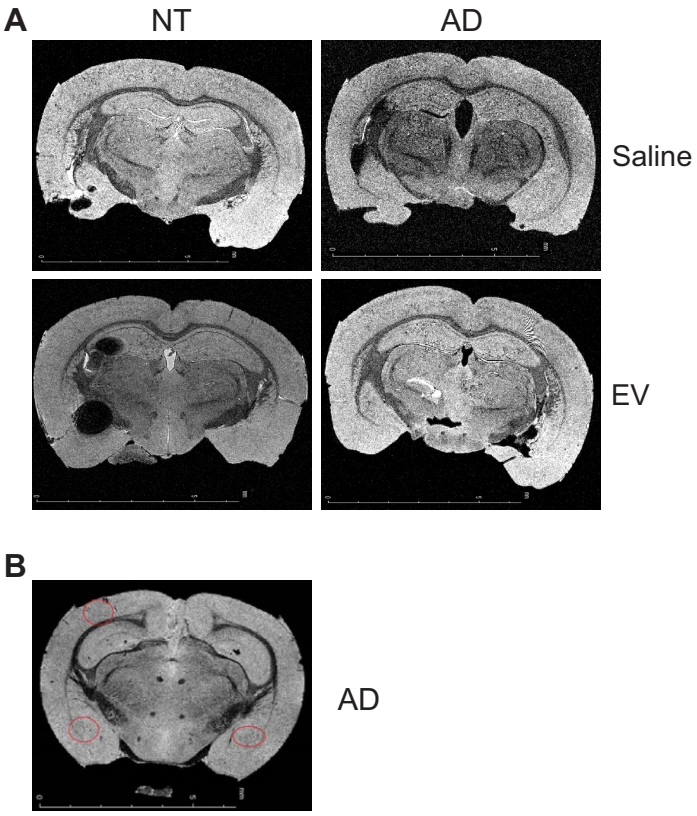
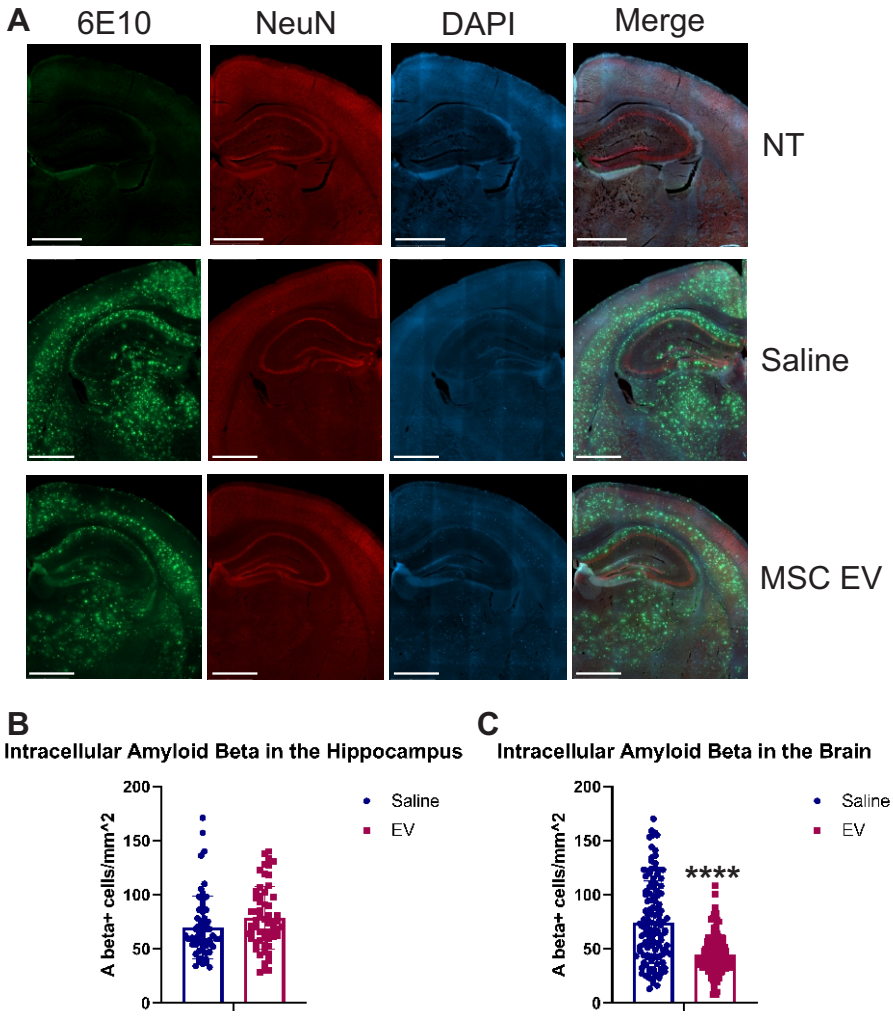


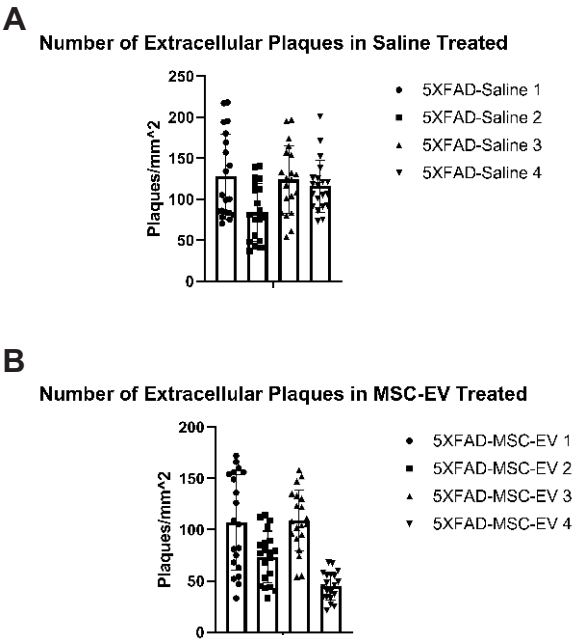
Supplemental Figure 1: Intranasal treatment of hMSC-derived EVs cross the blood-brain barrier. Two-month-old mice were given saline with Vybrant Dio dye, or EVs stained with Vybrant Dio. 24 h after administration, mice were euthanized, and sections were taken and imaged with Keyence BZ-X800. Right side imaged with fluorescence; left side imaged with brightfield.



Supplemental Figure 2: MRI shows a lack of plaque formation at four months of age. (A) MRI images of four-month-old NT or 5XFAD mice with saline or hMSC-EV treatment. (B) MRI image of a 6-month-old 5XFAD mouse. Plaques are circled in red.



Supplemental Figure 3: Treatment with hMSC-EVs decreased intracellular amyloid-beta outside of the HPC but not in the HPC of 5XFAD mice. (A) Representative staining of brains with 6E10, NeuN, and DAPI. Scale bar = 1 mm. (B) 20 one mm2 images were taken from the HPC of 4 different mice and quantified using ImageJ. (C) 30 one mm2 images were taken throughout the cortex, excluding HPC, and quantified using ImageJ. ****P < 0.0001.



Supplemental Figure 4: The number of extracellular plaques for each mouse. 20 one mm2 images were taken from the HPC of 4 different mice and plaque density was quantified using ImageJ. (A) Number of plaques per mouse in the saline treated. (B) Number of plaques per mouse in the hMSC-EV treated.