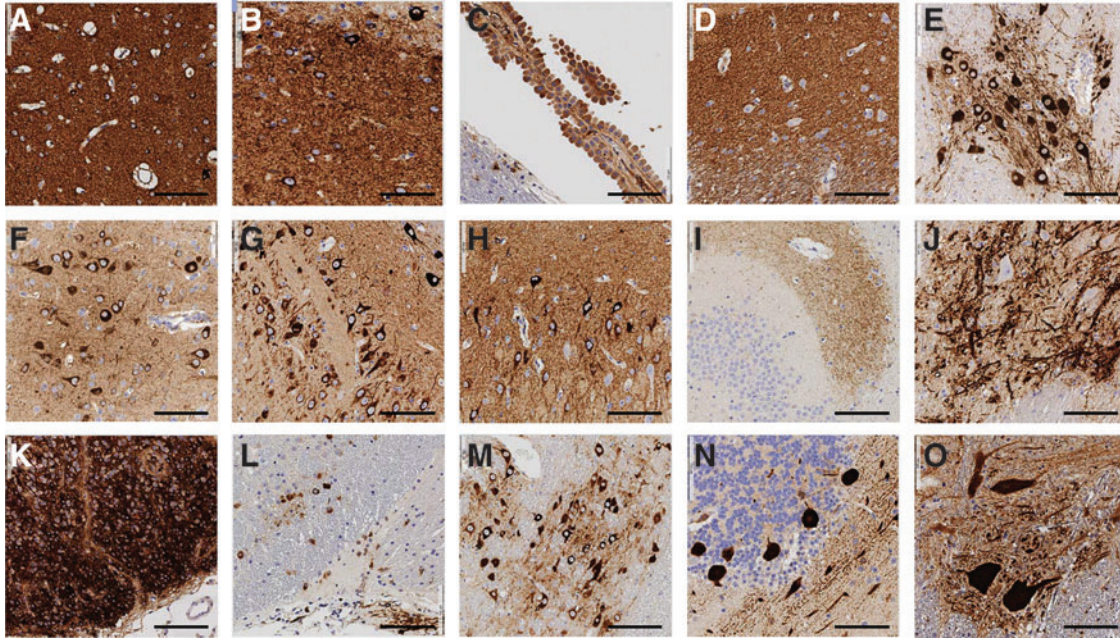
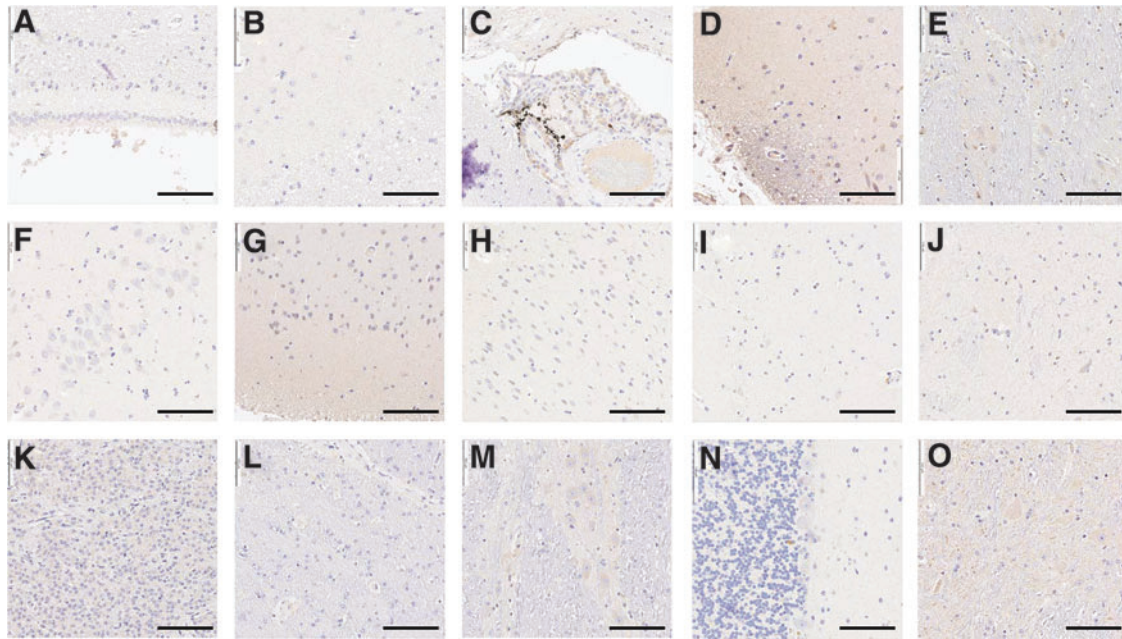


**Supplementary Figure S3.** IHC assessment of expression of ApoE2-HA in the NHP CNS following delivery of AAVrh.10hAPOE2-HA by the intracisternal route. Shown are multiple images displaying expression of ApoE2 across the CNS. The animals were euthanized 8 weeks post surgery and vector administration. Left hemispheres were sectioned into 24–25 coronal sections (3mm) following formalin fixation. IHC staining for APOE2-HA in brain slices was performed with anti-HA antibodies and 3,3'-diaminobenzidine (DAB) chromogen (brown stain), with blue indicating nuclei (hematoxylin counterstain). Representative images from various brain substructures are displayed. **(A–E)** Areas around the frontal and mid-brain. **(F–I)** Areas around the hippocampal region. **(J–O)** Areas around the posterior brain and spinal cord. **(A)** Frontal horn of lateral ventricle—adjacent to site of administration for intraventricular route. **(B)** Caudate nucleus. **(C)** Choroid plexus. **(D)** Anterior olfactory nucleus. **(E)** Thalamic reticular nucleus. **(F)** Parahippocampal cortex. **(G)** Entorhinal cortex. **(H)** Parasubiculum. **(I)** Dentate gyrus/CA1 of hippocampus. **(J)** Lateral hypothalamus. **(K)** Pineal body. **(L)** Stria terminalis. **(M)** Pontine gray. **(N)** Cerebellum—rostral to site of intracisternal administration. **(O)** Lumbar spinal cord—gray nuclei. *Middle panels (F–I)* are regions associated with early AD in humans (hippocampus, entorhinal/parahippocampal cortex). Brain structures identified using Nissl stained coronal brain sections from [brainsmap.org](http://brainsmap.org). Scale bar = 100  $\mu$ m.



**Supplementary Figure S4.** IHC assessment of expression of ApoE2-HA in the NHP CNS following delivery of AAVrh.10hAPOE2-HA by the intraventricular route. Shown are multiple images displaying expression of ApoE2 across the CNS. The animals were euthanized at 8 weeks post surgery and vector administration. Left hemispheres were sectioned into 24–25 coronal sections (3 mm) following formalin fixation. IHC staining for APOE2-HA in brain slices was performed with anti-HA antibodies and 3,3'-DAB chromogen (brown stain), with blue indicating nuclei (hematoxylin counterstained). Representative images are displayed. **(A–E)** Areas around the frontal and mid-brain. **(F–I)** Areas around the hippocampal region. **(J–O)** Areas around the posterior brain and spinal cord. **(A)** Frontal horn of lateral ventricle—adjacent to site of administration for intraventricular route. **(B)** Caudate nucleus. **(C)** Choroid plexus. **(D)** Anterior olfactory nucleus. **(E)** Thalamic reticular nucleus. **(F)** Parahippocampal cortex. **(G)** Entorhinal cortex. **(H)** Parasubiculum. **(I)** Dentate gyrus/CA1 of hippocampus. **(J)** Lateral hypothalamus. **(K)** Pineal body. **(L)** Stria terminalis. **(M)** Pontine gray. **(N)** Cerebellum—rostral to site of intracisternal administration. **(O)** Lumbar spinal cord—gray nuclei. Panels **(F–I)** are regions associated with early AD in humans (hippocampus, entorhinal/parahippocampal cortex). Brain structures identified using Nissl stained coronal brain sections from brainsmap.org. Scale bar = 100  $\mu$ m.





**Supplementary Figure S5.** Control immunohistochemistry assessment of HA in non-treated control NHP CNS. Anti-HA staining and expression of ApoE2 in the CNS of non-treated NHP. Similar to Supplementary Figs. S3 and S4, IHC staining for APOE2-HA in brain slices was performed with anti-HA antibodies. Representative images from various brain substructures are displayed matched to the areas shown in Supplementary Figs. S3 and S4. **(A–E)** Areas around the frontal and mid-brain. **(F–I)** Areas around the hippocampal region. **(J–O)** Areas around the brain posterior and spinal cord. **(A)** Frontal horn of lateral ventricle—adjacent to site of administration for intraventricular route. **(B)** Caudate nucleus. **(C)** Choroid plexus. **(D)** Anterior olfactory nucleus. **(E)** Thalamic reticular nucleus. **(F)** Parahippocampal cortex. **(G)** Entorhinal cortex. **(H)** Parasubiculum. **(I)** Dentate gyrus/CA1 of hippocampus. **(J)** Lateral hypothalamus. **(K)** Pineal body. **(L)** Stria terminalis. **(M)** Pontine gray. **(N)** Cerebellum—rostral to site of intracisternal administration. **(O)** Lumbar spinal cord—gray nuclei. Panels **(F–I)** are regions associated with early AD in humans (hippocampus, entorhinal/parahippocampal cortex). Brain structures identified using Nissl stained coronal brain sections from brainsmap.org. Bar = 100  $\mu$ m.