

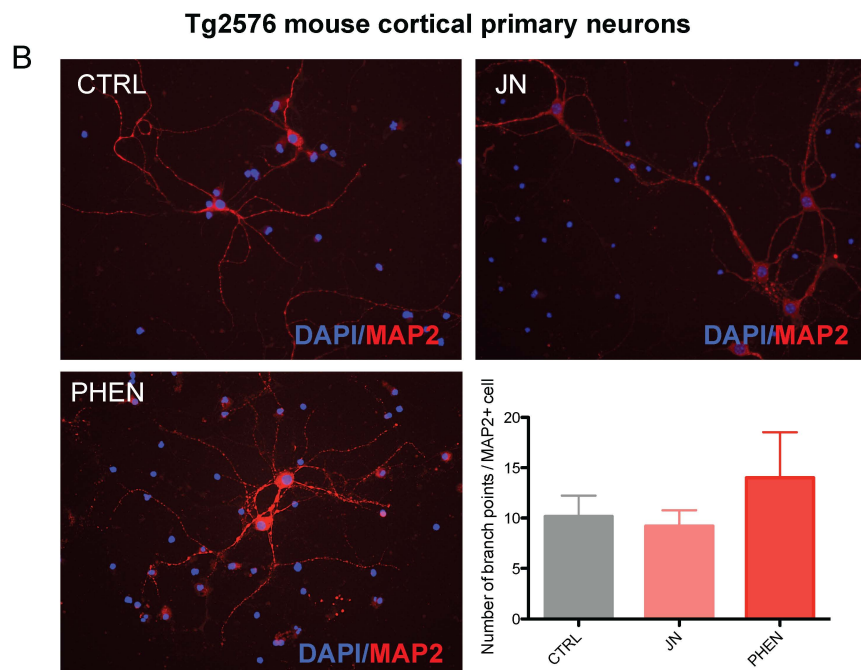
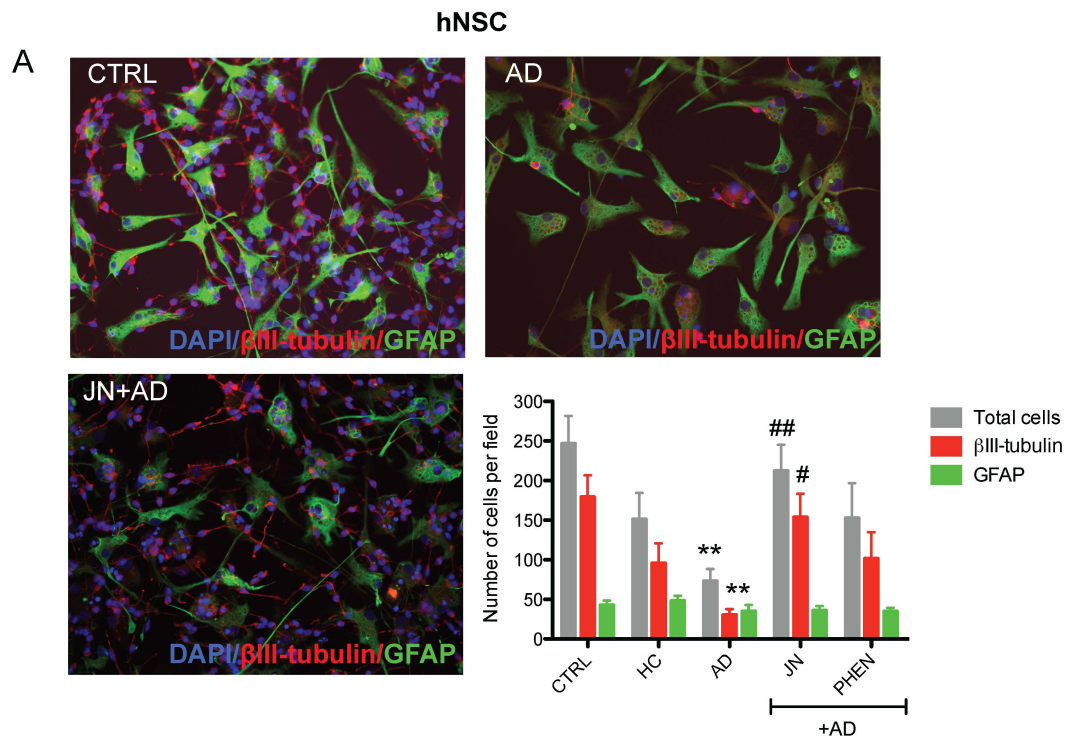
Supplemental information

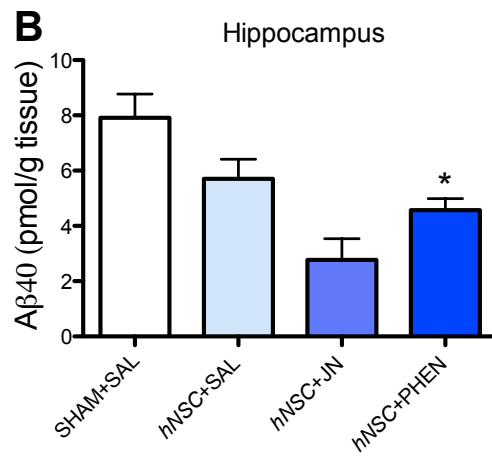
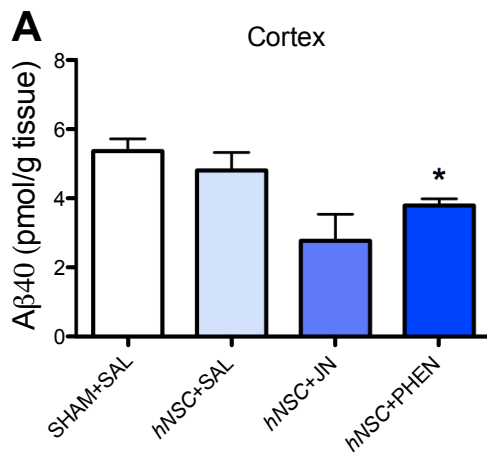
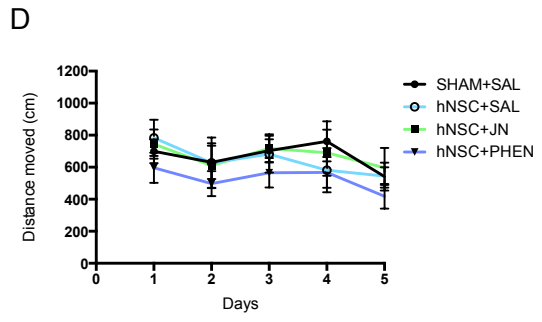
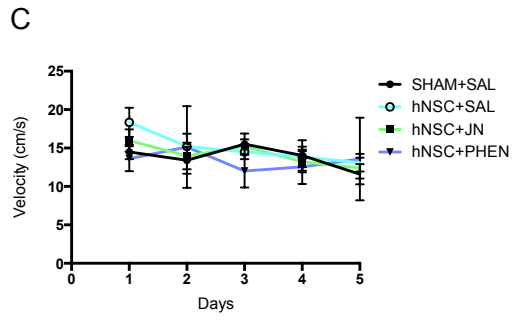
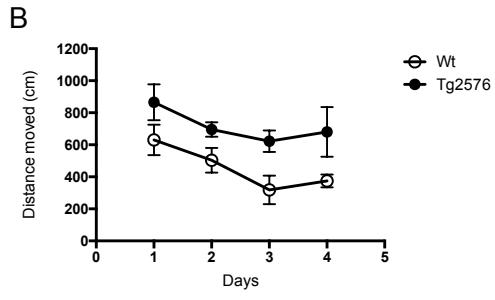
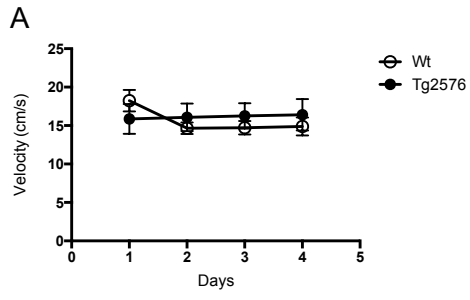
Figure S1. JN403 exerts neuroprotective actions on hNSC-derived neurons in culture. (A) Expression of neuronal marker β III-tubulin (red) and glial marker GFAP (green) in hNSCs *in vitro* after 28 days' differentiation. The hNSCs were untreated (CTRL), or exposed weekly to brain extracts from a healthy control (HC), a patient with AD (AD), AD+JN403 (JN), or AD (+)-phenserine (PHEN) Representative images of CTRL, AD, and AD+JN are outlined in (A), representative of two independent experiments with four replicate samples in each. (B) Expression of the neuronal marker MAP2 (red) and the number of branch points in untreated Tg2576 transgenic mouse primary cortex neurons in culture (CTRL) and after weekly exposure to JN403 (JN) or (+)-phenserine (PHEN) for 21 days. The data are expressed as means \pm SEM. Images of CTRL, JN and PHEN are representative of three biological replicates. ** $p < 0.01$ compared with CTRL, # $p < 0.05$, ### $p < 0.01$ compared to AD.

Figure S2. Swimming velocity and total distance swum by wildtype and Tg2576 mice in the Morris water maze. (A) Swimming velocity and (B) total distance swum by wild type (wt, n=6) and Tg2576 (APP^{swe}, n=6) mice in the Morris water maze (MWM) during 4 days of acquisition training. (C) Swimming velocity and (D) total distance swum in the MWM during 5 days of acquisition training in the follow-up for sham (vehicle)-transplanted, saline-treated (SHAM+SAL) Tg2576 mice, or mice receiving hNSC transplants and saline (hNSC+SAL), JN403 (hNSC+JN), or (+)-phenserine (hNSC+PHEN).

Figure S3. (+)-Phenserine treatment in combination with hippocampal hNSC transplantation decreases brain A β ₄₀ levels in Tg2576 mice. (A) Cortical and (B) hippocampal levels of A β ₄₀ (pmol/g tissue) measured by a sandwich ELISA assay were significantly reduced by (+)-phenserine treatment in hNSC-transplanted Tg2576 mice (hNSC+PHEN) compared to saline-treated mice receiving sham (vehicle) transplantation (SHAM+SAL). JN=JN403. *p<0.05 compared to SHAM+SAL. The data are expressed as \pm SEM.

Figures





Supplementary Table 1. Tg2576 mice included in the transplantation study according to treatment, number of animals per group, age and sex. The numbers of animals that underwent the Morris Water Maze navigation task are included in brackets. * One animal was omitted from the Morris water maze analysis, since it could not be detected by the automated video-tracking system due to its fur color. Abbreviations: human neural stem cell (hNSC), vehicle transplanted + saline treatment (SHAM+SAL), hNSC transplanted + saline treated (hNSC+SAL), hNSC transplanted + (+)-phenserine treated (hNSC+PHEN), and hNSC transplanted + JN403 treated (hNSC+JN).

Treatment	Number of mice	Age (median, min-max)	Sex (M/F)
SHAM+SAL	9	7 (6-9)	3/6
hNSC+SAL	9* (8)	7 (6-7)	3/6
hNSC+PHEN	7* (6)	7 (7-9)	2/5
hNSC+JN	5	7 (7-9)	2/3