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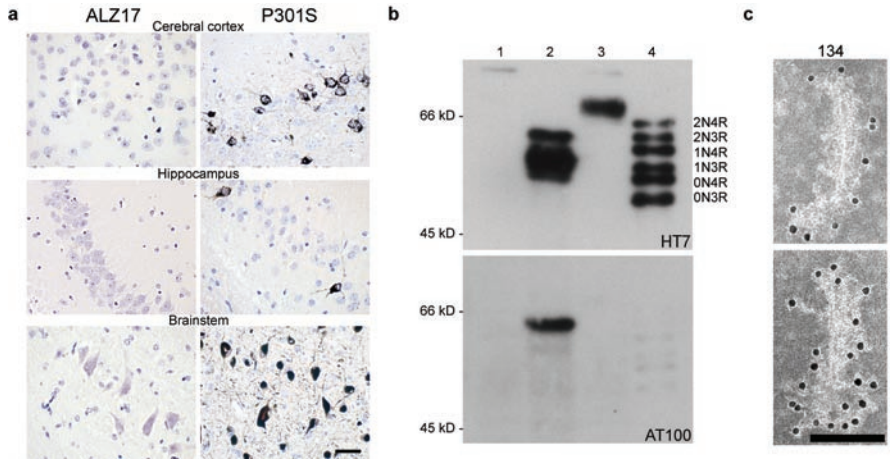


Figure S1 Transgenic mouse lines ALZ17, human P301S tau and characterization of mouse brain extracts. (**a**) Gallyas-Braak staining of cerebral cortex, hippocampus and brainstem of an 18 month-old ALZ17 mouse (left) and a 5 month-old mouse transgenic for human P301S tau (right). Note the absence of silver staining in the ALZ17 mouse and the strong staining in the P301S mouse. The sections were counterstained with haematoxylin. Scale bar, 50 μm (same magnification in all panels). (**b**) Immunoblotting of mouse brain extracts with anti-tau antibodies HT7 (specific for human tau, phosphorylation-independent) and AT100 (phosphorylation-dependent). Lanes: 1, brain extract (125 μg tissue) from non-transgenic control mouse; 2, brain extract used for injection (125 μg tissue) from a 5 month old mouse transgenic for human P301S tau; 3, forebrain extract (125 μg tissue) from 18 month-old ALZ17 mouse; 4, recombinant human tau isoform mixture (10 ng). (**c**) Immunoelectron microscopy using anti-tau serum BR134 to decorate filaments in the brain extract used for injection. Scale bar, 100 nm. The full scan of the Western blot data is available in the Supplementary Information, Fig. S7.

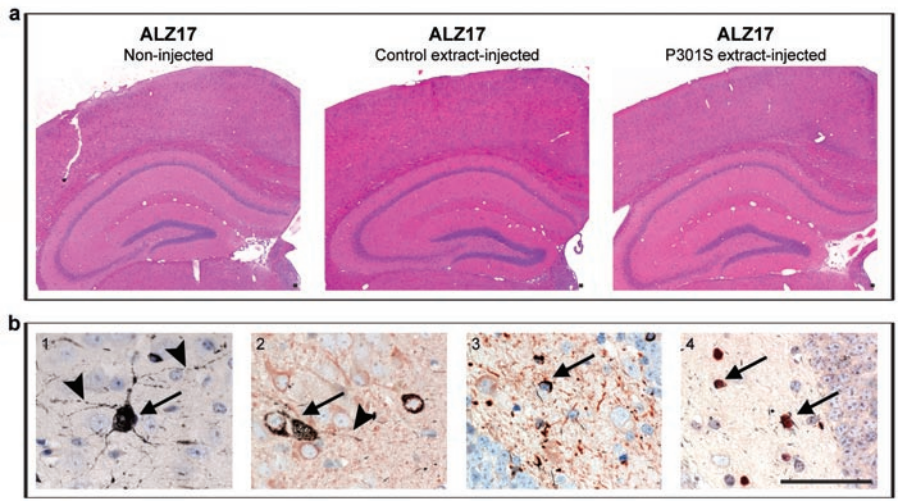


Figure S2 Injection sites and tau pathology. (**a**) H&E staining of corresponding hippocampal levels of non-injected ALZ17 animals (left), ALZ17 mouse injected with control brain extract (middle) and ALZ17 mouse injected with P301S tau brain extract (right). Scale bar, 50 µm (same magnification in all panels). (**b**) Different types of filamentous tau pathology in ALZ17 brains injected with P301S tau brain extract: (1) neurofibrillary tangle (arrow) and neuropil threads (arrowheads) visualized by silver staining; (2,3) double staining with silver and AT8 (red) shows neurofibrillary tangles (2, arrow), neuropil threads (2, arrowhead) and coiled bodies (3, arrow). (4) Double staining of coiled bodies (arrows) with silver and antibody Olig2 (red). The sections were counterstained with haematoxylin. Scale bar, 50 µm (same magnification in all panels).

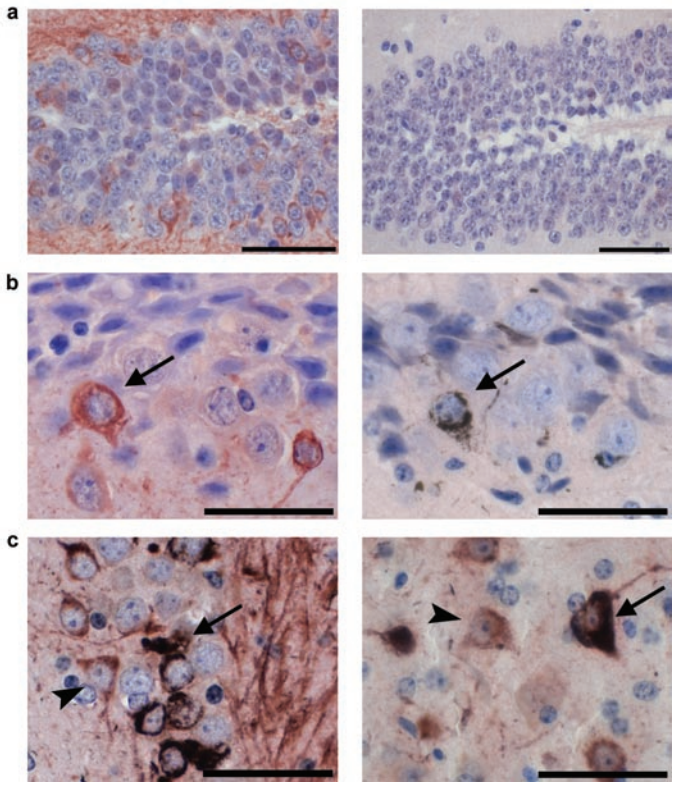


Figure S3 Inclusions in ALZ17 mice injected with P301S brain extract contain tau with N-terminal inserts. (**a**) BR189 staining (specific for tau isoforms with both N-terminal inserts) of the dentate gyrus of an 18-month-old ALZ17 mouse (left) and a 6-month-old homozygous P301S mouse (right). Note the absence of staining in the P301S mouse and the staining of pretangle pathology in the ALZ17 mouse. (**b**) BR304 staining (specific for tau isoforms with the first N-terminal insert; left) and Gallyas-Braak silver staining (right) of the CA3 region of the hippocampus of an ALZ17 mouse 15 months after injection with P301S brain extract. The images are of serial brain sections. The arrows point to a BR304-positive neuron which is also stained by the Gallyas-Braak method. (**c**) Double staining with BR304 and Gallyas-Braak (left) and with BR189 and Gallyas-Braak (right) of the hippocampus of an ALZ17 mouse 15 months after injection with P301S brain extract. Darker neurons (arrows) are double stained for Gallyas-Braak and BR304 (left) or Gallyas-Braak and BR189 (right), indicative of tangles. Single-stained neurons (arrowheads) with BR304 (left) or BR189 (right) represent pretangles. The sections were counterstained with haematoxylin. Scale bars, 50 μm.

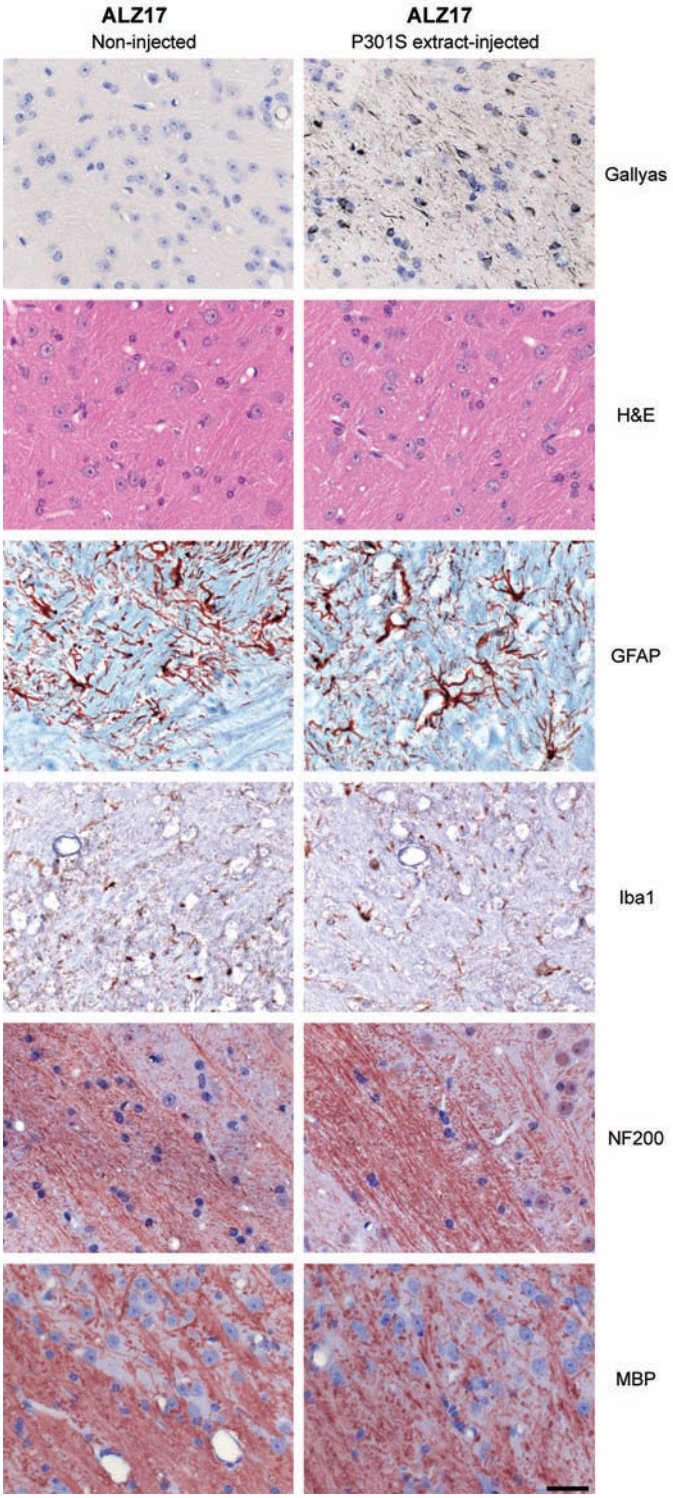


Figure S4 Comparison between non-injected (left) and P301S extract-injected (right) ALZ17 mice (15 months post-injection). High magnification of the thalamic region of ALZ17 animals in which Gallyas-Braak silver staining detects threads and coiled bodies (top). Various stains do not reveal overt neurodegeneration (H&E), astrogliosis (GFAP), microgliosis (Iba1), neurofilament alterations (NF200) or myelin changes (MBP) in ALZ17 mice injected with P301S brain extract. The sections were counterstained with haematoxylin. Scale bar, 50 μm (same magnification in all panels).

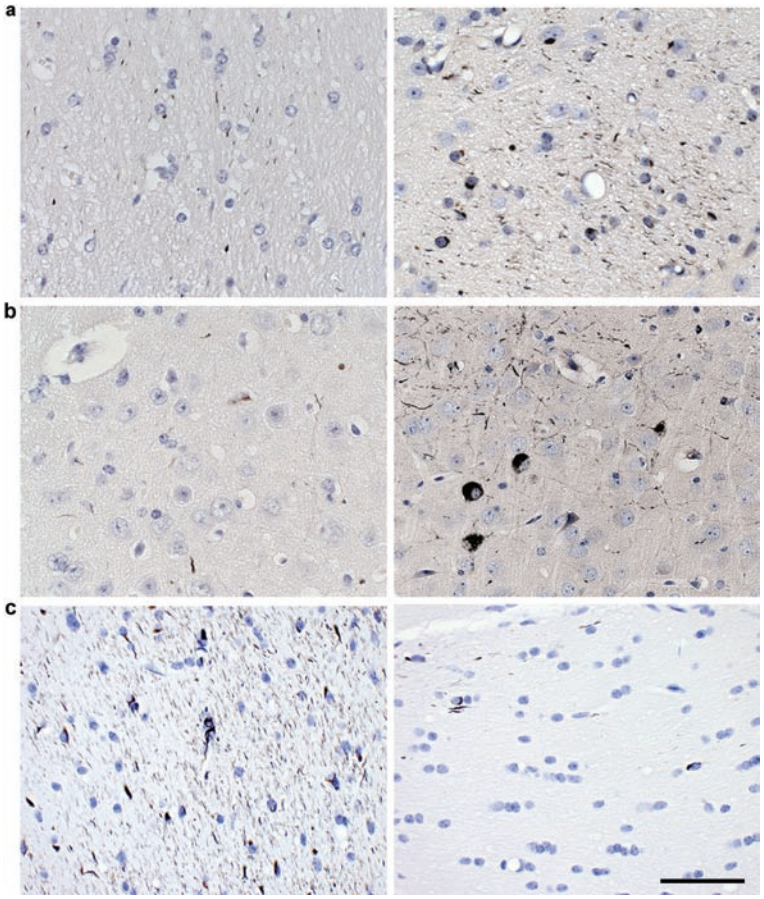


Figure S5 Spreading of filamentous tau pathology. (**a**) Anterior to the injection level (section 1.7 mm from injection level). Gallyas-Braak staining of the fimbria from ALZ17 mice 6 months (left) and 15 months (right) after the injection of brain extract from mice transgenic for human P301S tau. The sections were counterstained with haematoxylin. Scale bar, 50 μm (same magnification in all panels). (**b**) Posterior to the injection level (section 1.3 mm from injection level). Gallyas-Braak staining of the polymorphic layer of the hippocampus from ALZ17 mice 6 months (left) and 15 months (right) after the injection of brain extract from mice transgenic for human P301S tau. The sections were counterstained with haematoxylin. Scale bar, 50 μm (same magnification in all panels). (**c**) Modest contralateral spreading of filamentous tau pathology. Gallyas-Braak staining of the ipsilateral (left) and contralateral (right) fimbria of an ALZ17 mouse 15 months after the unilateral injection of brain extract from mice transgenic for human P301S tau (injection level). Note the few scattered silver-positive lesions on the contralateral side. The sections were counterstained with haematoxylin. Scale bar, 50 μm (same magnification in all panels).

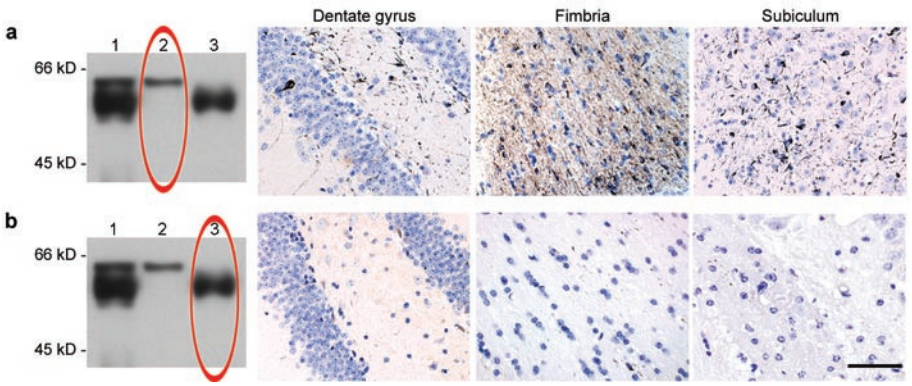
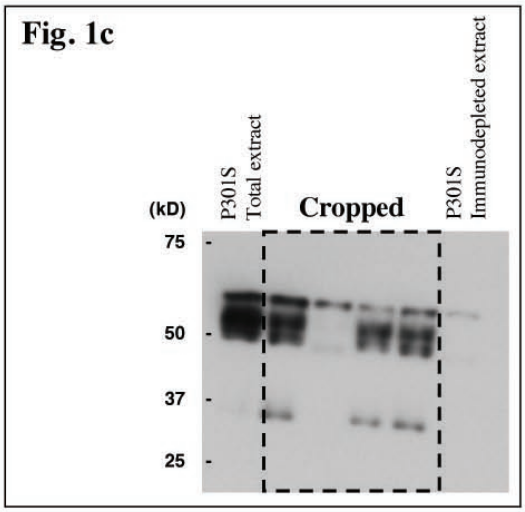
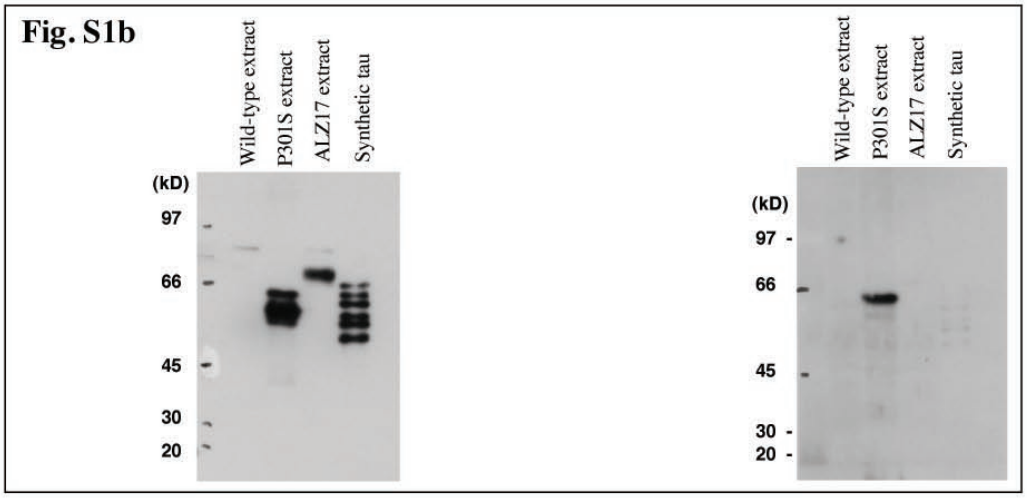


Figure S6 Injection of human P301S tau brain extract containing either insoluble or soluble tau into ALZ17 mice. (**a**) Major induction of filamentous tau pathology after injection of insoluble tau into ALZ17 mice. Left: Western blot using anti-tau antibody HT7 of total human P301S tau brain extract (lane 1), P301S brain extract containing insoluble tau (lane 2) and P301S brain extract containing soluble tau (lane 3). Right: Gallyas-Braak staining of dentate gyrus, fimbria and subiculum of an ALZ17 mouse 12 months after the injection of insoluble tau. (**b**) Minor induction of filamentous tau pathology after injection of soluble tau into ALZ17 mice. Left: Western blot with anti-tau antibody HT7 of total human P301S tau brain extract (lane 1), P301S brain extract containing insoluble tau (lane 2) and P301S brain extract containing soluble tau (lane 3). Right: Gallyas-Braak staining of dentate gyrus, fimbria and subiculum of an ALZ17 mouse 12 months after the injection of soluble tau. The sections were counterstained with haematoxylin. Scale bar, 50 μm (same magnification in all panels). The full scan of the Western blot data is available in the Supplementary Information, Fig. S7.





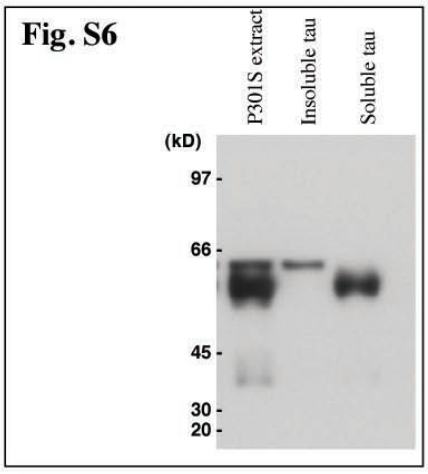


Figure S7 Full scans of the Western blot data shown in Figure 1, Figure S1 and Figure S6.