Journal of Alzheimer's Disease 19 (2010) 1–6

IOS Press

Supplementary Material

Lithium Treatment Arrests the Development of Neurofibrillary Tangles in Mutant Tau Transgenic Mice with Advanced Neurofibrillary Pathology

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Accepted 31 August 2009

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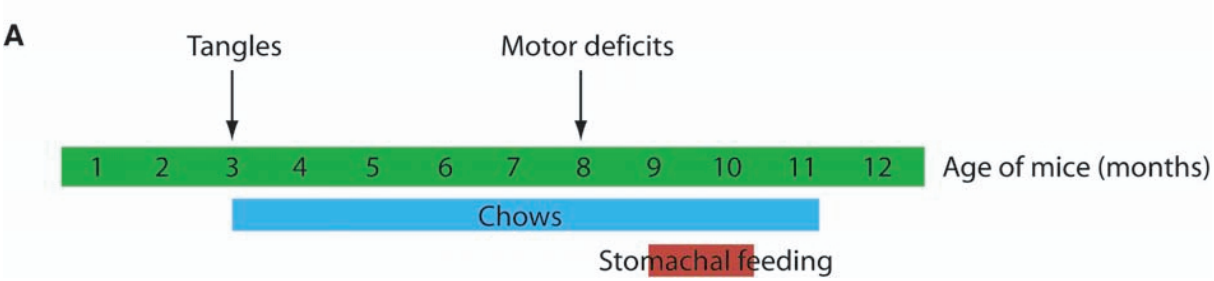
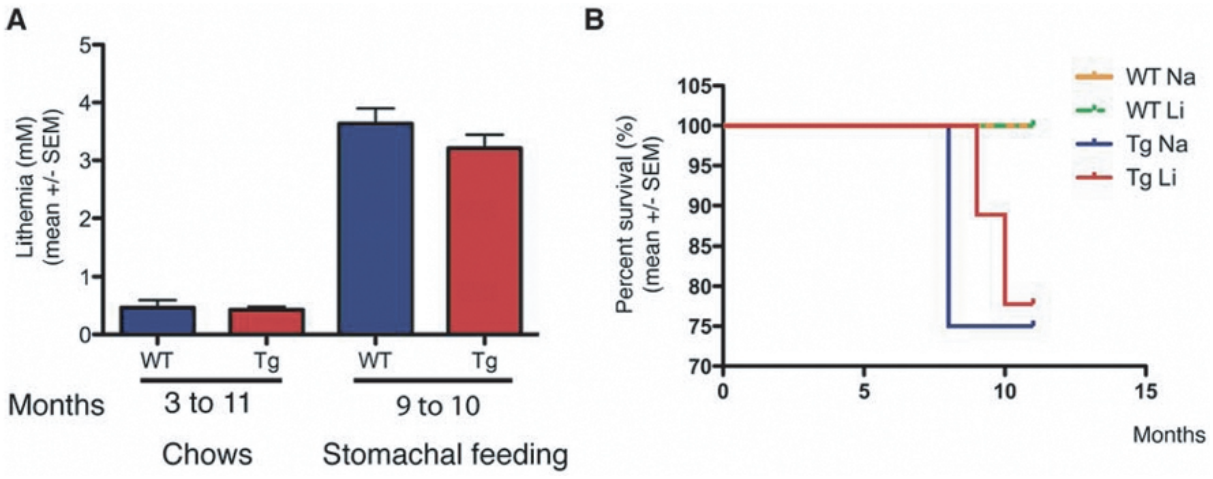
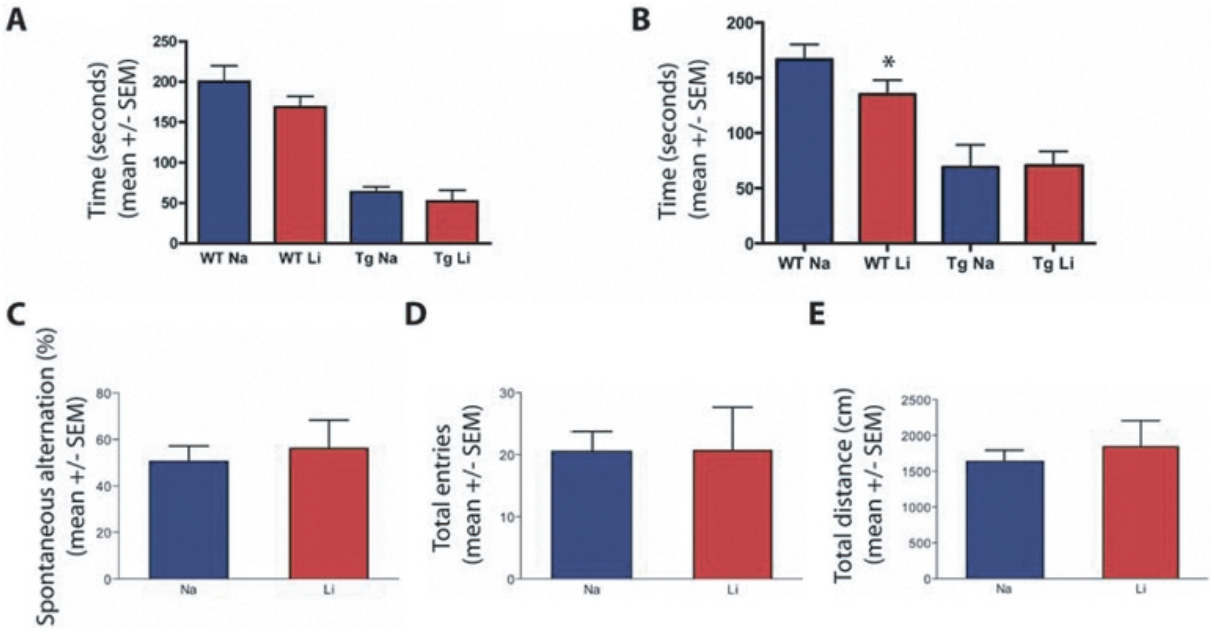
ISSN 1387-2877/10/$27.50



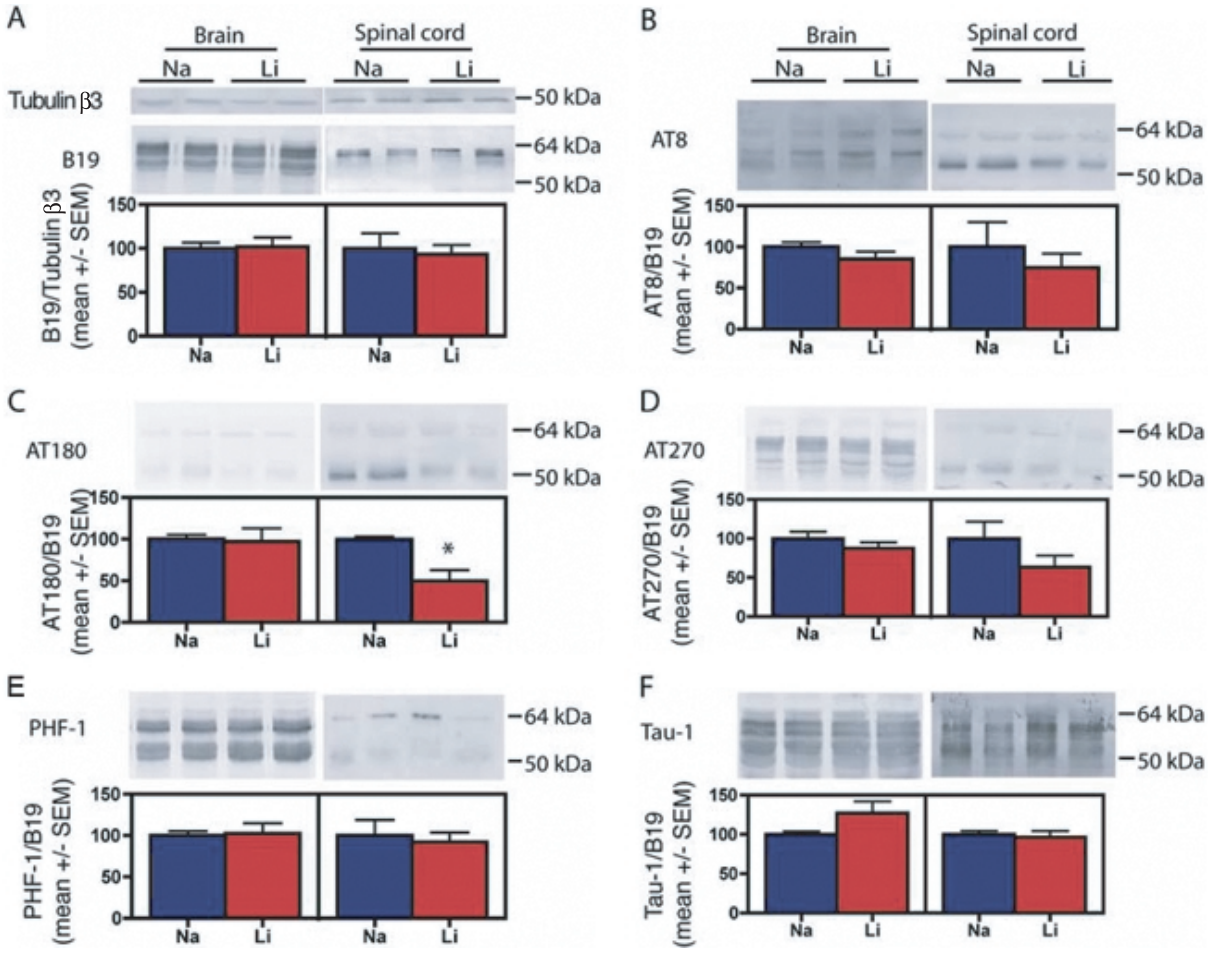
Supplemental Figure 1. Time-line of lithium treatment of wild-type and Tg30tau mice, from 3 to 11 months with chows and from 9 to 10 months by oral gavage.



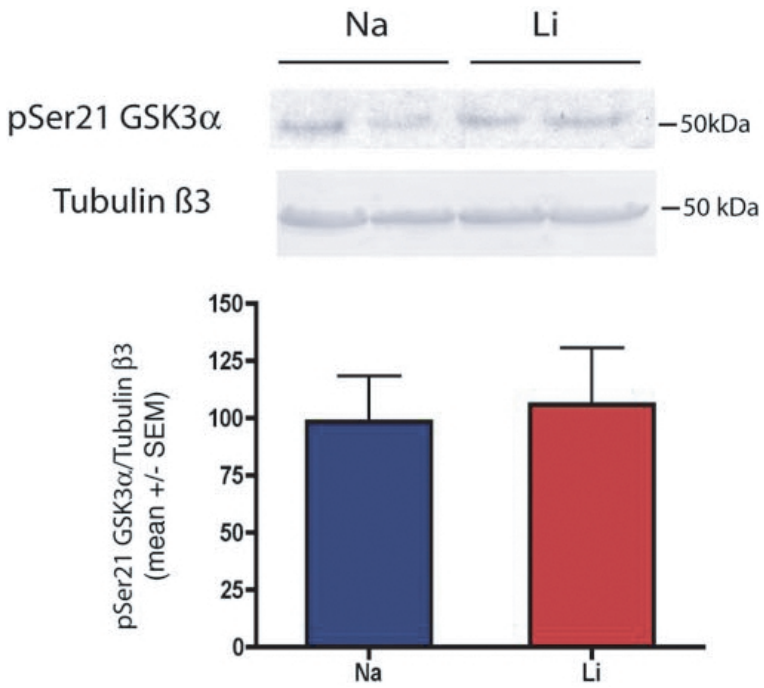
Supplemental Figure 2. (A) Lithium levels in blood of wild-type (WT) and Tg30tau (Tg) mice treated with lithium carbonate from 3 to 11 months by chows feeding (WT: $n = 3$; Tg: $n = 15$) of for one month (from 9 to 10 months) by oral gavage (WT: $n = 15$; Tg: $n = 14$). (B) Survival curves of WT and Tg30tau mice fed with chows containing sodium (WT: $n = 4$; Tg: $n = 11$) or lithium (WT: $n = 3$; Tg: $n = 15$) carbonate from 3 to 11 months of age. The survival percentages were not significantly different between sodium- and lithium-treated mice.



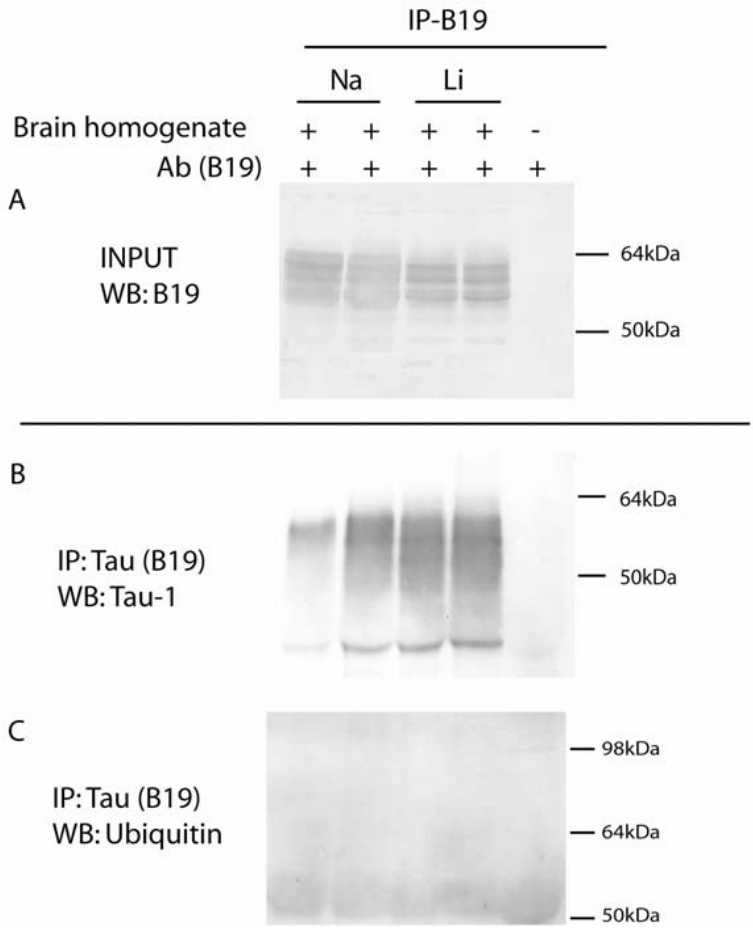
Supplemental Figure 3. Effect of lithium on motor function and working memory. (A and B) Rotarod motor testing of mice fed with sodium or lithium carbonate in chows from 3 to 11 months of age (A) and by oral gavage from 9 to 10 months of age (B). Lithium treatment impaired the motor abilities of aged wild-type mice but motor abilities were not different between sodium- and lithium-treated transgenic mice ($n = 13 - 16$). (C, D, E) Y maze testing of transgenic mice fed with sodium or lithium carbonate by oral gavage from 9 to 10 months of age. Spontaneous alternation scores (C), total entries (D) and total run distance (E) were not different between sodium and lithium treated mice. ($n = 4$). $^{*}p < 0.05$, by one-way ANOVA.



Supplemental Figure 4. Immunoblots of brain and spinal cord homogenates of Tg30tau mice treated (chows feeding from 3 to 11 months) with sodium (Na) ($n = 13$) or lithium (Li) ($n = 13$) carbonate, with the β-tubulin and the B19 anti-tau antibodies (A), and the phosphotau antibodies AT8 (B), AT180 (C), AT270 (D), PHF-1 (E), and tau-1 (F). Phosphotau immunoreactivities were normalized to the B19 tau immunoreactivity. Immunoreactivity of phosphotau was not significantly altered by chow feeding both in the brain and in the spinal cord with the AT8, AT270, PHF-1, and tau-1 antibodies. The signal of AT180 was significantly altered in the spinal cord. * $p < 0.05$, by unpaired Student t test.



Supplemental Figure 5. Effect of lithium on levels of phosphorylation of GSK-3α. Representative immunoblots with the pSer9/21 GSK-3 antibody of brain homogenates of Tg30tau mice treated (oral gavage) with sodium (Na) ($n = 14$) or lithium (Li) ($n = 14$) carbonate. The levels of pSer21 GSK-3α, normalized to tubulin β3, are not significantly different between sodium- and lithium-treated mice. The number on the right of blots refers to the positions of molecular weight markers: 50 kDa (alcohol dehydrogenase).



Supplemental Figure 6. Ubiquitin immunoreactivity of tau in lithium- and sodium-treated animals (oral gavage). (A) Representative immunoblots with the B19 tau antibody of brain homogenates (input used for tau immunoprecipitation) of Tg30tau mice treated (oral gavage) with sodium (Na) or lithium (Li). (B and C) Representative immunoblots of tau immunoprecipitated (IP) with the B19 tau antibody from brain homogenates of Tg30tau mice treated (oral gavage) with sodium (Na) or lithium (Li). Immunoprecipitated tau was analyzed by Western blotting with the tau-1 antibody (B) or the ubiquitin antibody (C). The numbers on the right of blots refer to the positions of molecular weight markers: 50 kDa (alcohol dehydrogenase), 64 kDa (glutamic dehydrogenase).