Erratum

Erratum: Larson et al., "Soluble α-Synuclein Is a Novel Modulator of Alzheimer's Disease Pathophysiology"

In the article "Soluble α-Synuclein Is a Novel Modulator of Alzheimer's Disease Pathophysiology," by Megan E. Larson, Mathew A. Sherman, Susan Greimel, Michael Kuskowski, Julie A. Schneider, David A. Bennett, and Sylvain E. Lesné, which appeared on pages 10253–10266 of the July 25, 2012 issue, Western blots in Figures 1, *A* and *B*, 2*B*, and 5*A* were processed inappropriately, and therefore the published figures appeared incorrectly. The authors regret these errors and note that the scientific conclusions of the article were not affected. The corrected figures and their legends, which were not changed, appear below.

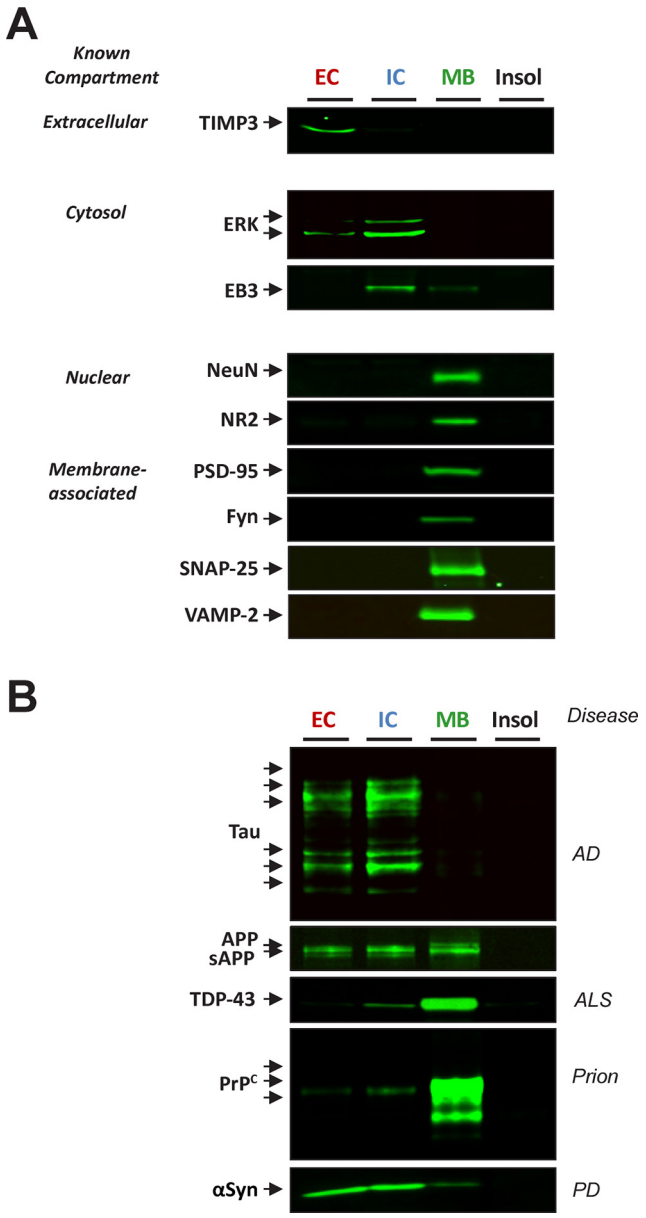

Figure 1. Characterization of the four-step protein extraction protocol using human brain tissue. ***A***, Selected brain tissue (0.5 mm^3 of inferior temporal gyrus of a control brain) was subjected to serial extractions allowing the segregation of proteins based on their cellular compartmentalization. Examples of obtained segregation for human proteins with known compartmentalization are shown. ***B***, Extraction profile for selected disease-related proteins. TIMP3, Tissue inhibitor of metalloproteinase-3; ERK, extracellular signal-regulated kinase; EB3, end-binding protein-3; NeuN, neuronal nuclei; GluN2, glutamate NMDA receptor subunit 2; PSD-95, postsynaptic density protein-95; Fyn, Fyn kinase; SNAP-25, synaptosomal-associated protein 25; VAMP-2, vesicle-associated membrane protein 2; sAPP/APP, soluble/full-length amyloid precursor protein; ALS, amyotrophic lateral sclerosis; PD, Parkinson's disease; Insol, insoluble.

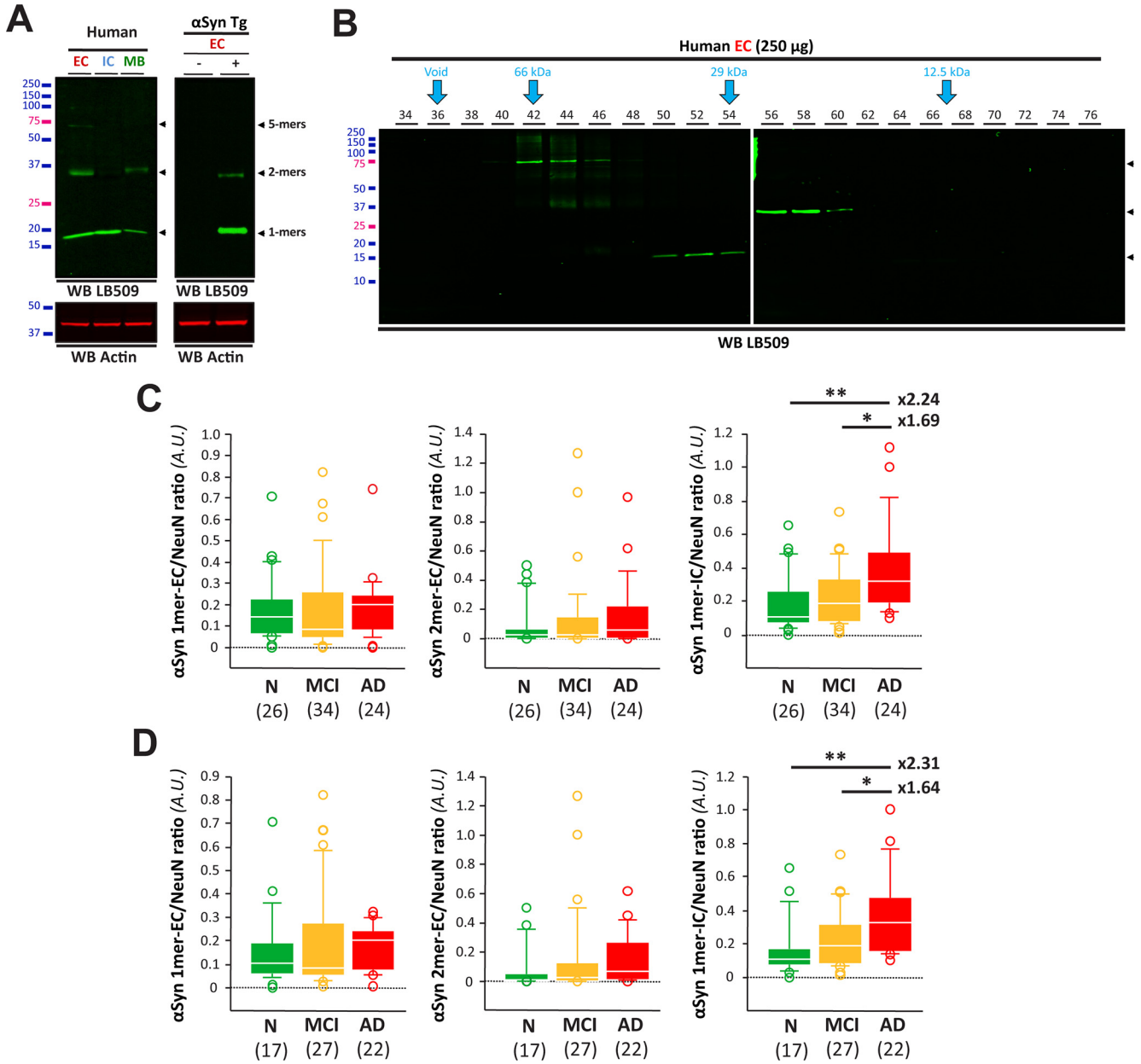

Figure 2. Increase in soluble αSyn in AD brain in the absence of Lewy bodies/neurites. ***A***, Western blot (WB) analyses of soluble αSyn species in EC-, IC-, or MB-enriched fractions using LB509. Similar results were obtained with 4D6 or Syn1 (not shown). Both transgenic and wild-type littermates from line G2.3-A53T (αSyn Tg) used were 10 months of age. ***B***, Gel filtration combined with SDS-PAGE confirmed the presence of SDS-resistant αSyn soluble assemblies. ***C***, Quantification of monomeric and oligomeric αSyn species in the inferior temporal cortex of subjects with NCI, MCI, or AD. Whereas monomeric and dimeric αSyn-EC remained unchanged across groups, monomeric αSyn-IC levels were significantly higher in AD than in MCI and NCI brain tissues. ***D***, In total absence of LB pathology, αSyn-IC monomers were increased by more than twofold in AD compared with controls. Italicized numbers in parentheses indicate group sizes. NCI is shown in green, MCI is shown in orange, and AD in indicated by red boxes. In box plots of all figures, the bar inside the box indicates the median; the upper and lower limits of boxes represent the 75th and 25th percentiles, respectively; and bars flanking the box represent the 95th and fifth percentiles. $*p < 0.05$; $**p < 0.01$. ***N***, no cognitive impairment.

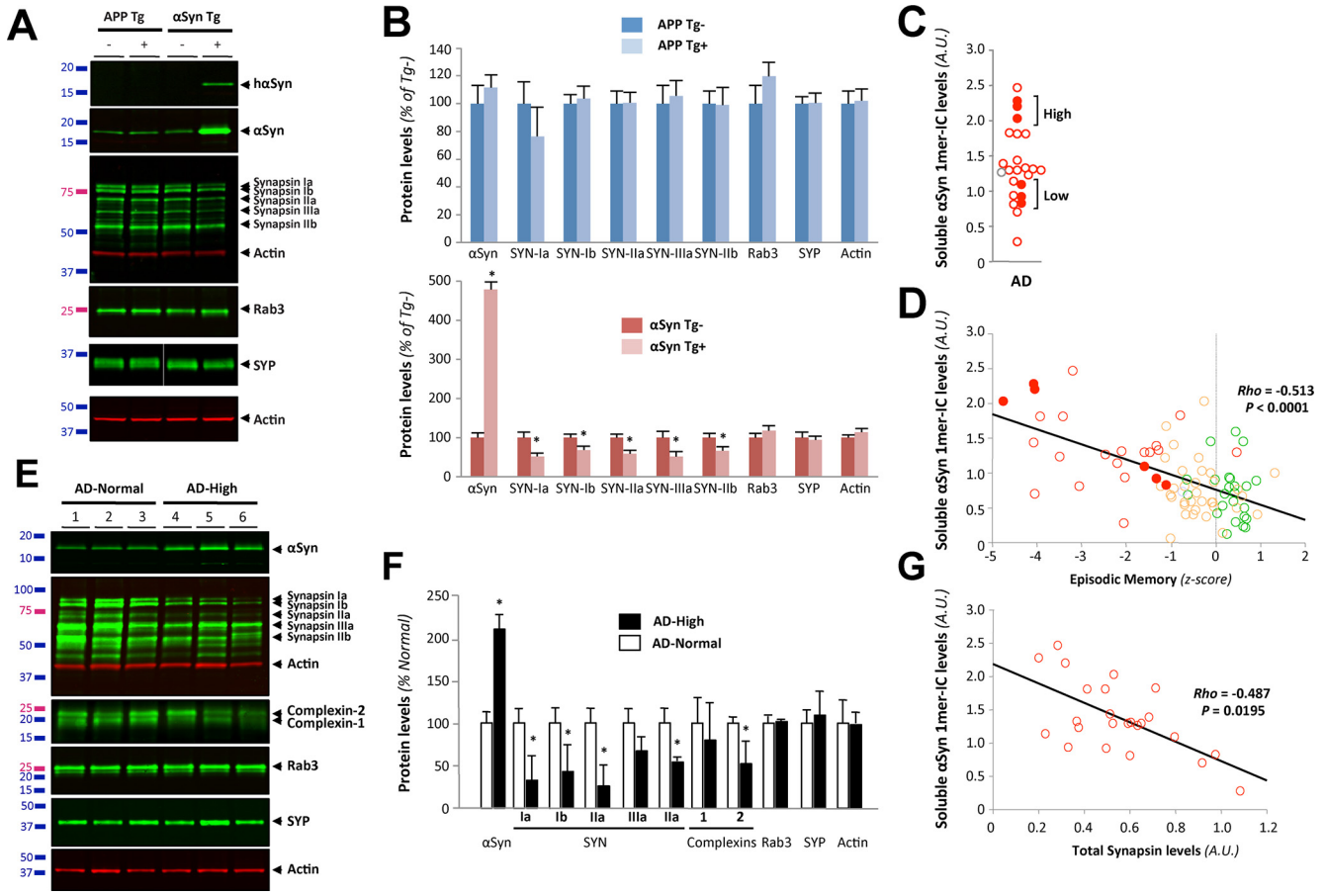

Figure 5. A twofold increase in soluble αSyn is associated with a selective decrease in vesicular proteins in AD. ***A***, Western blot (WB) analysis of brain extracts from 17-month-old Tg2576 (APP Tg) and 10-month-old TgG2.3-A53T (αSyn Tg) brain tissue using infrared-conjugated secondary antibodies shows a selective reduction in synapsins in αSyn Tg. Rab3, synaptophysin, and actin levels were unchanged in both lines. ***B***, Quantification of protein levels detected in both lines revealed specific decreases in synapsins in αSyn Tg mice ($n = 3$/group). ***C***, Scatterplot of soluble αSyn levels in the ITG of subjects with AD. Measurements reflect the quantification of αSyn by WB after SDS-PAGE using the antibody LB509. Selected AD subjects were chosen to compose two groups ($n = 3$ per group) whose soluble αSyn ratio equaled 2. They are referred to as AD-High and AD-Normal and are indicated by filled red circles. ***D***, Linear regression depicting the relationship between episodic memory and the levels of monomeric αSyn in the IC fraction measured by SDS-PAGE. Filled circles indicate specimens selected for analyses of vesicular presynaptic proteins (Figs. 3 and 4). Note that the AD subjects with a twofold elevated αSyn are more impaired than AD subjects with lower αSyn expression. ***E***, Quantitative WB analysis of brain extracts from AD brain tissue with normal (AD-Normal) or high (AD-High) (twofold increase) αSyn-IC levels shows a reduction in synapsins and complexins but not Rab3 or synaptophysin. ***F***, Quantification confirms the observed changes in ***B***. Values represent mean $\pm$ SD ($n = 3$). ***G***, Regression analyses between total synapsin protein expression and "monomeric" αSyn in all AD cases ($n = 24$) indicated a negative correlation (Spearman ρ).

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