

Figure 1A

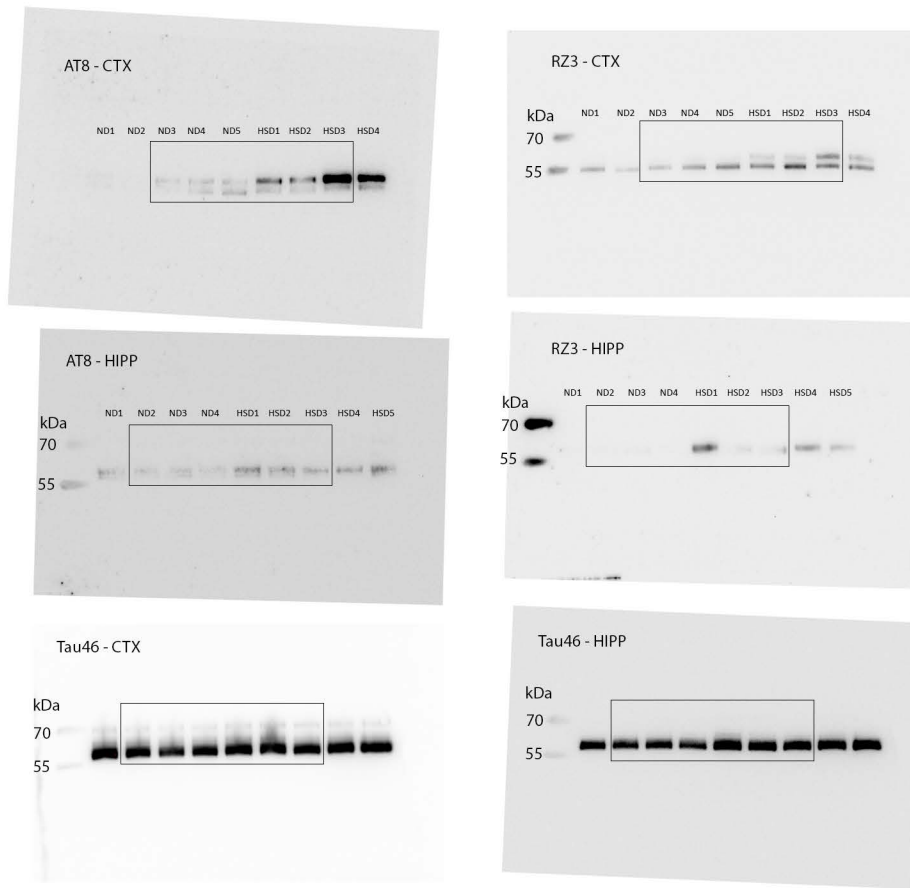
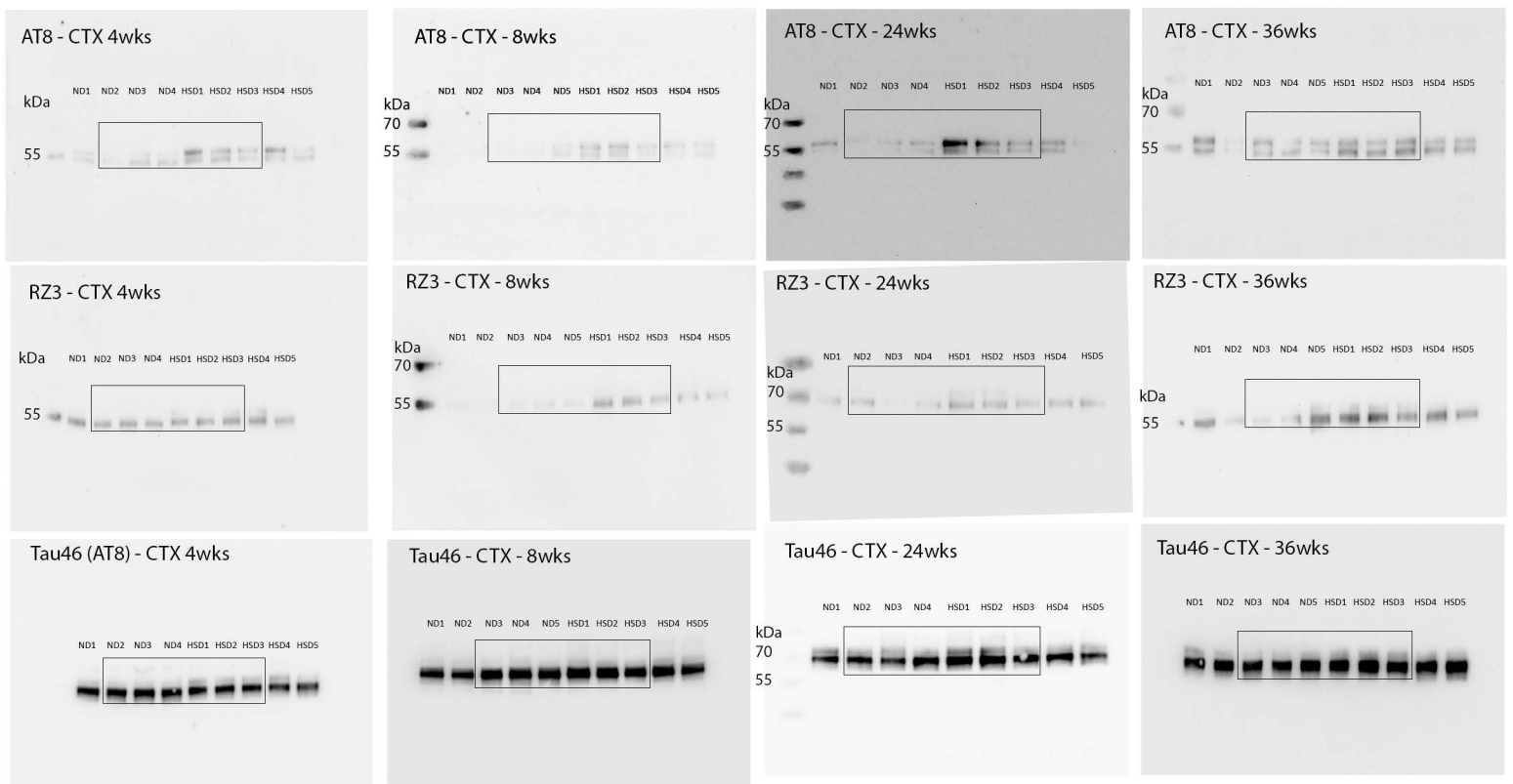


Figure 1C



Gel Source Data - Figure 1. Full Immunoblots image of Figure 1A and 1C. Membranes were incubated with AT8 or RZ3 antibody (1:500) overnight. After incubation with secondary antibody, protein bands were visualized with Clarity Western ECL Substrate (BioRad) on a Bio Rad ChemiDoc MP Imaging System. After washes with TBS/0.1% Tween-20 (TBST), membranes were incubated with anti-Tau46 antibody (1:1000) overnight. Samples from neocortex and hippocampus ($\approx 10\mu\text{g}$ of protein/lane).

Figure 1G

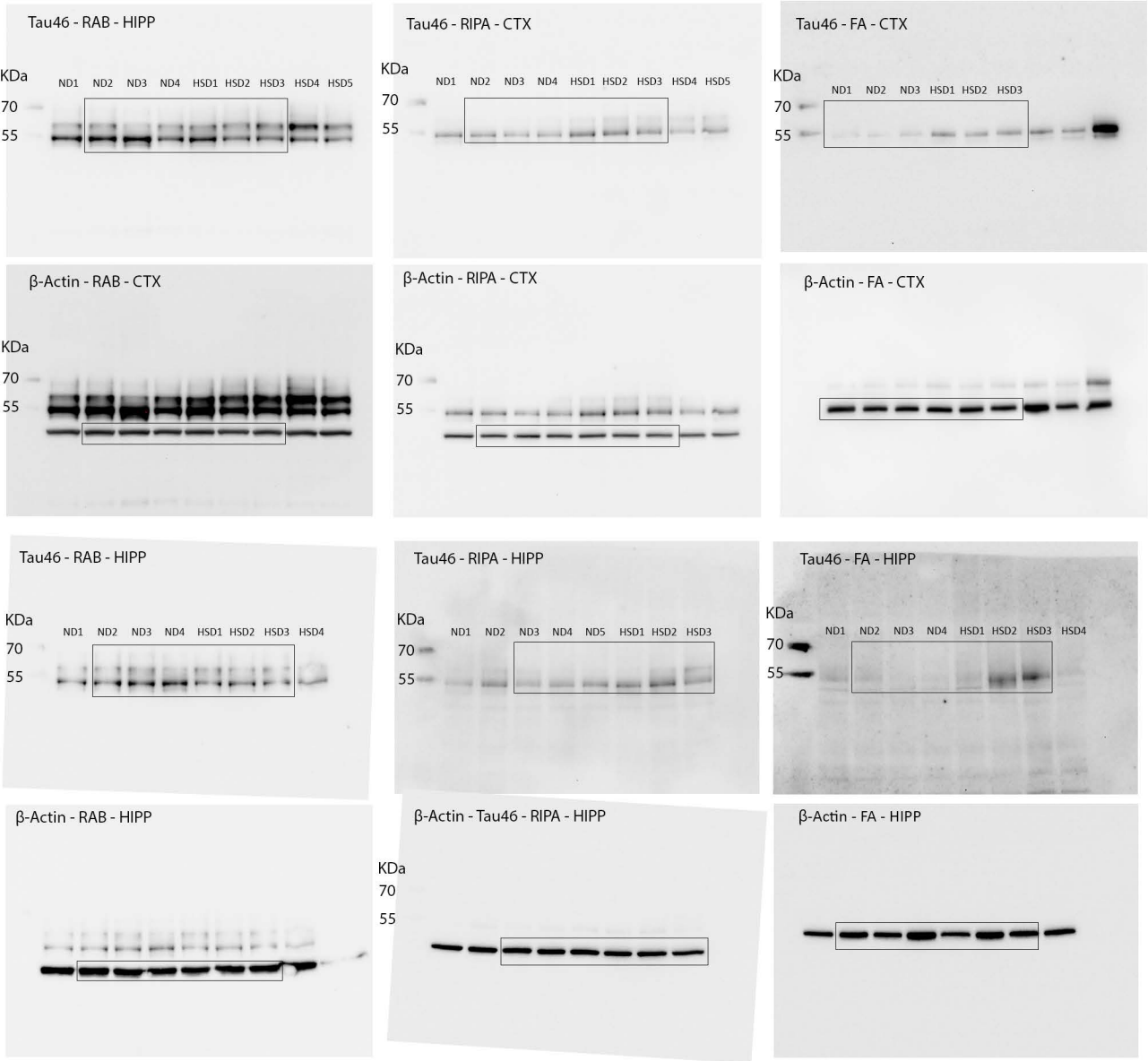
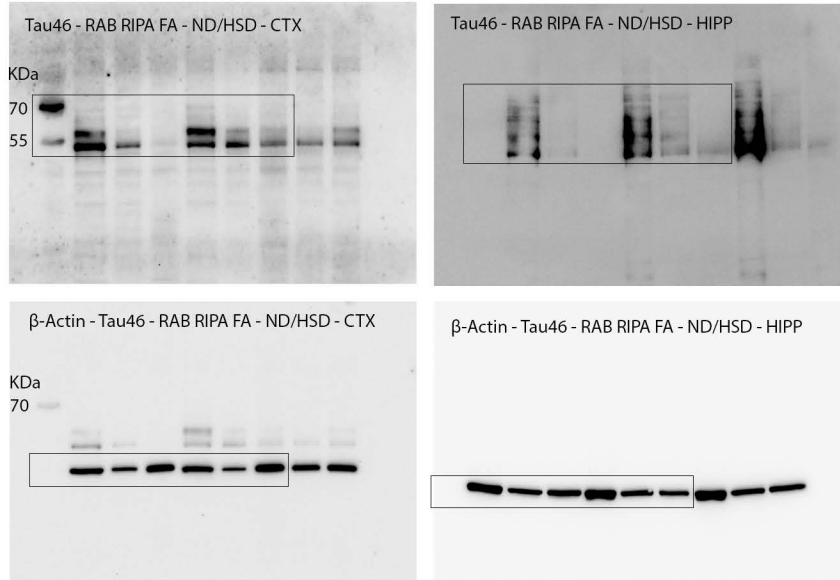


Figure 1I



Gel Source Data - Figure 1. Full Immunoblots image of Figure 1G-I. Membranes were incubated with Tau46 antibody (1:1000) overnight. After incubation with secondary antibody, protein bands were visualized with Clarity Western ECL Substrate (BioRad) on a Bio Rad ChemiDoc MP Imaging System. After washes with TBS/0.1% Tween-20 (TBST), membranes were incubated with anti- β -Actin antibody (1:50000) for 1h. Samples from RAB, RIPA and FA fractions of neocortex and hippocampus ($\approx 10\mu\text{g}$ of protein/lane).

Figure 2A-B

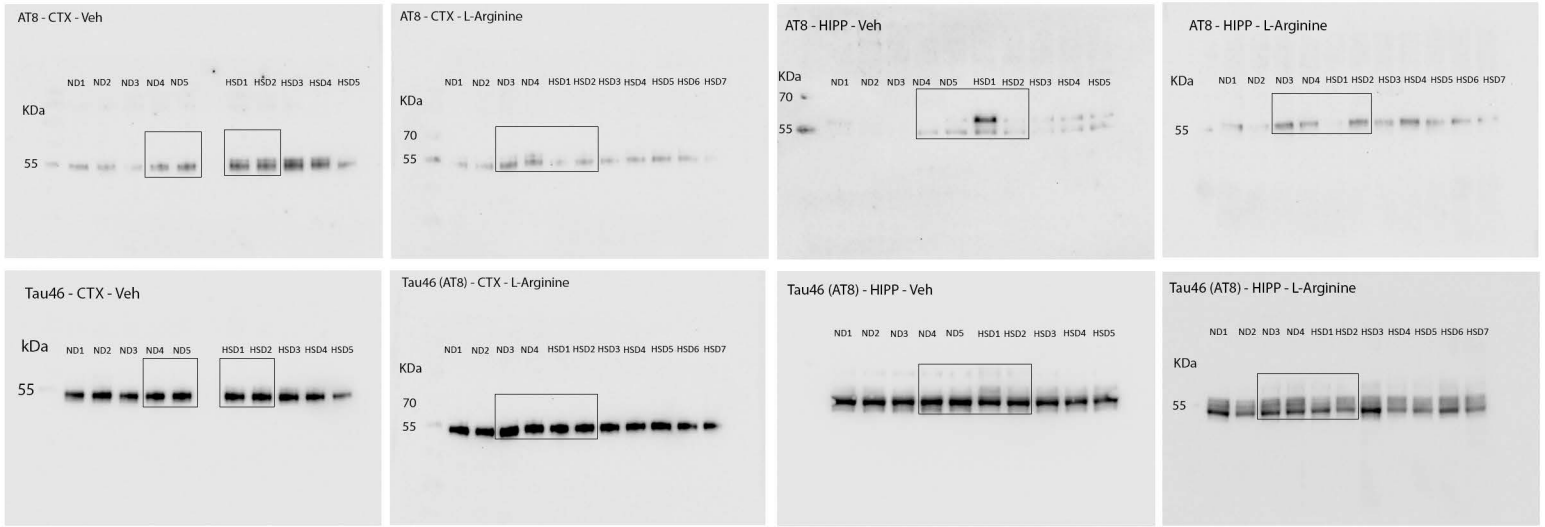


Figure 3A

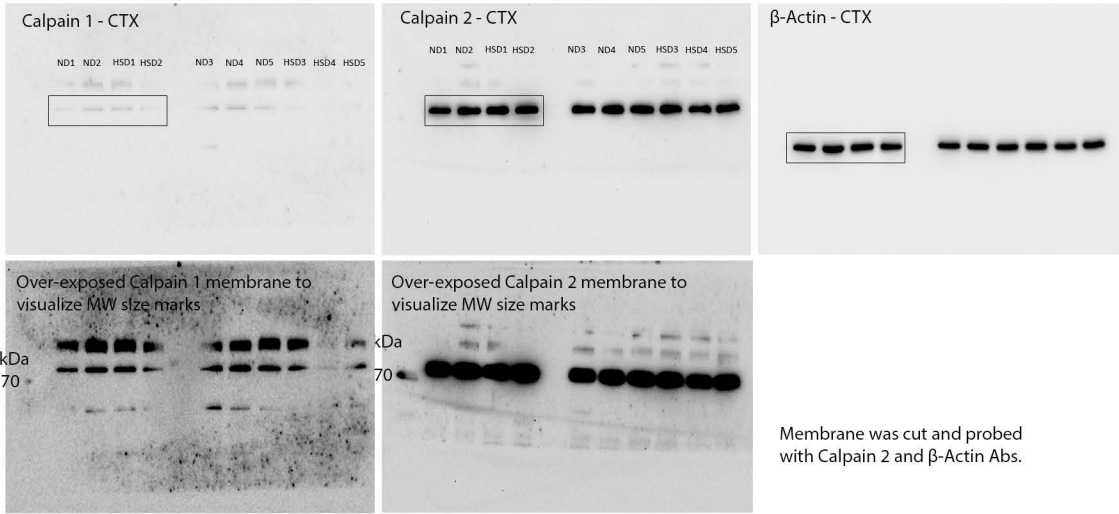
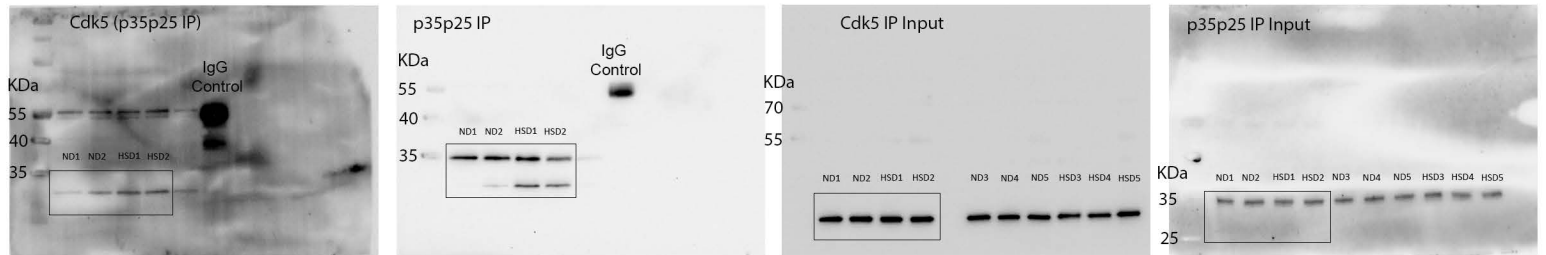


Figure 3B - Western Blotting Gels



Gel Source Data - Figure 2,3. Full Immunoblots image of panels in Figure 2A, B and 3A, B. Membranes were incubated with AT8 antibody (1:500), Calpain 1, Calpain 2, p35p25 and Cdk5 overnight. After incubation with secondary antibody, protein bands were visualized with Clarity Western ECL Substrate (BioRad) on a Bio Rad ChemiDoc MP Imaging System. After washes with TBS/0.1% Tween-20 (TBST), membranes were incubated with anti-Tau46 antibody (1:1000) overnight or β -Actin antibody (1:50000) for 1h at RT. Samples from neocortex and hippocampus ($\approx 10\mu\text{g}$ of protein/lane).

Figure 3D

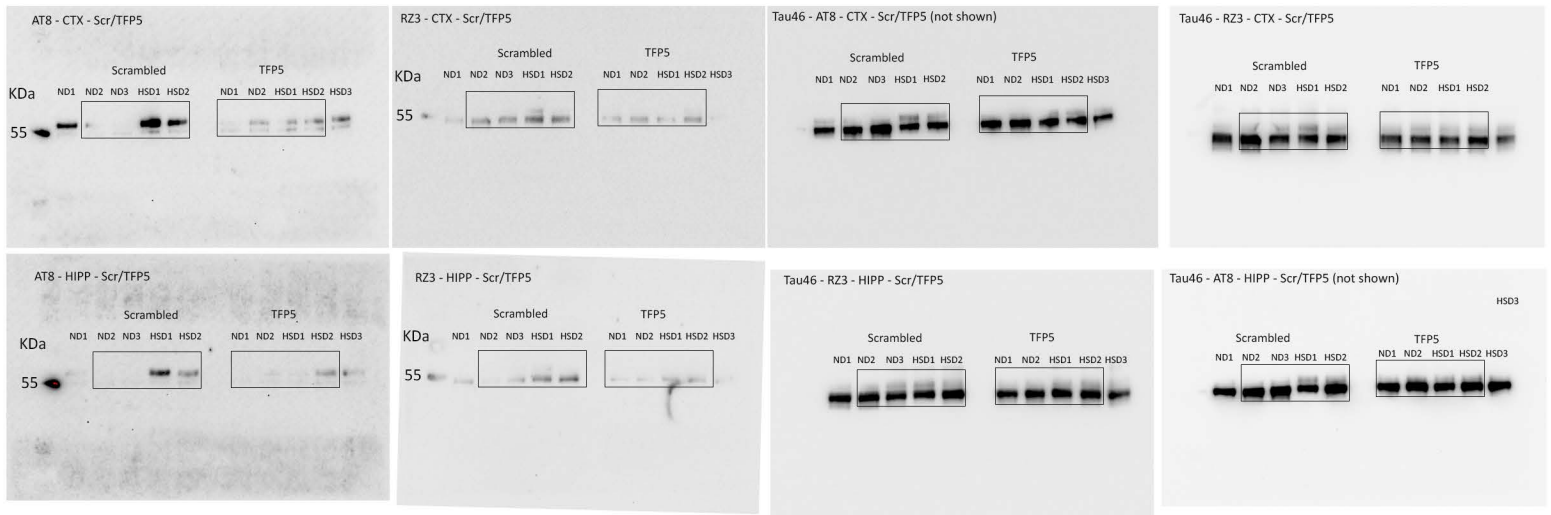


Figure 3G-H

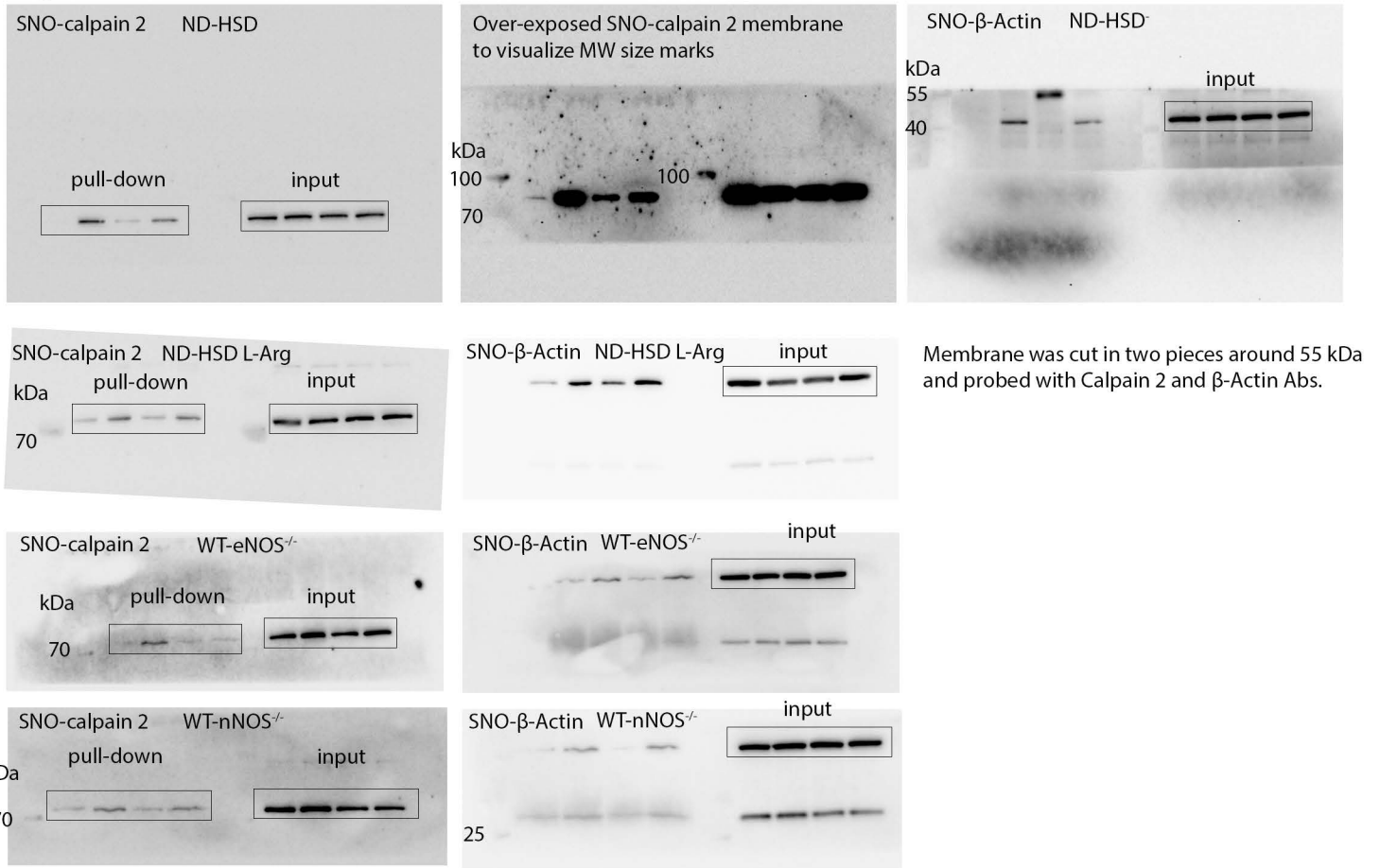
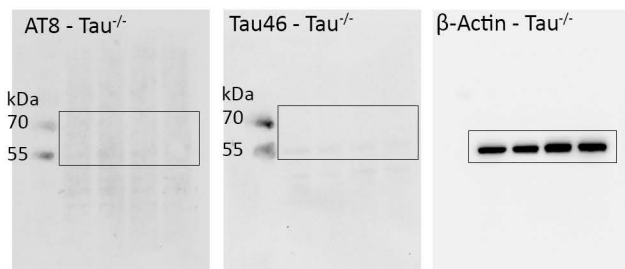
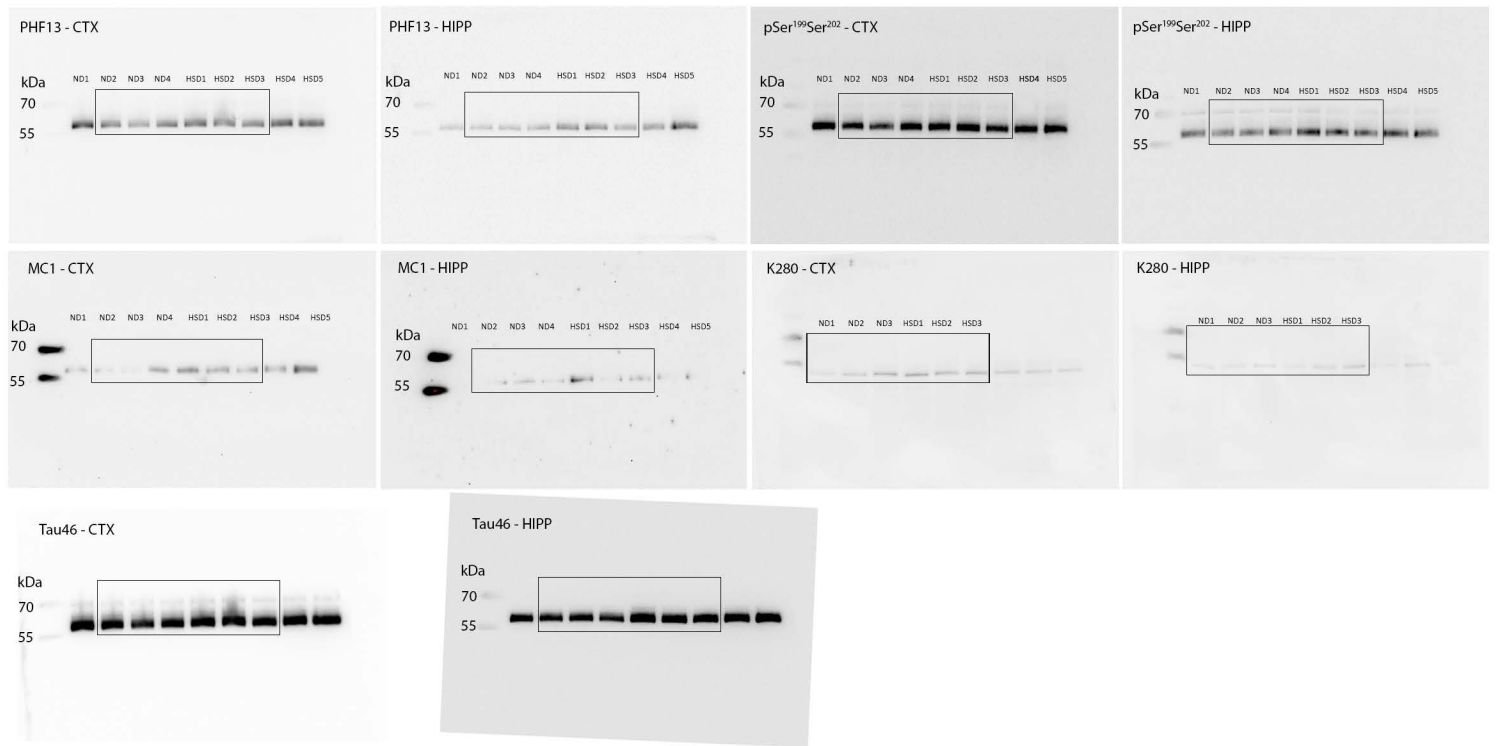


Figure 4A

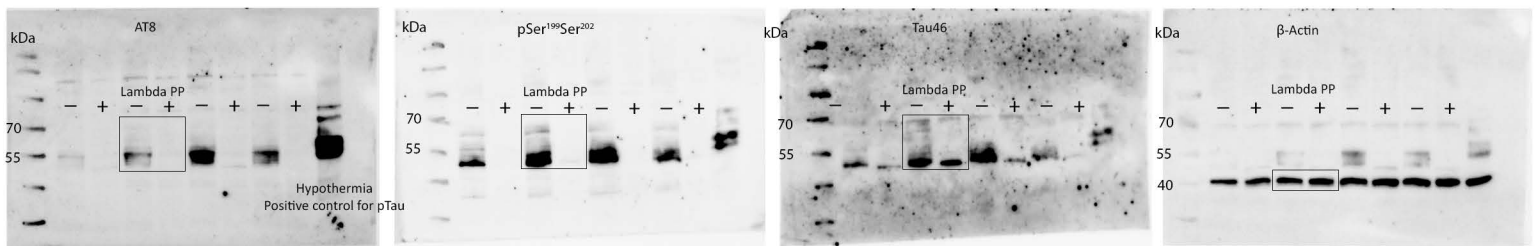


Gel Source Data - Figure 3. Full Immunoblots image of Figure 3. Membranes were incubated with AT8, RZ3, Tau46 or Calpain 2 antibody (1:1000) overnight and anti- β -Actin antibody (1:50000) for 1h at RT. After incubation with secondary antibodies, protein bands were visualized with Clarity Western ECL Substrate (BioRad) on a Bio Rad ChemiDoc MP Imaging System. Samples from neocortex and hippocampus ($\approx 10\mu\text{g}$ of protein/lane). Around 1mg of proteins (neocortex) were used for the precipitation of SNO-proteins.

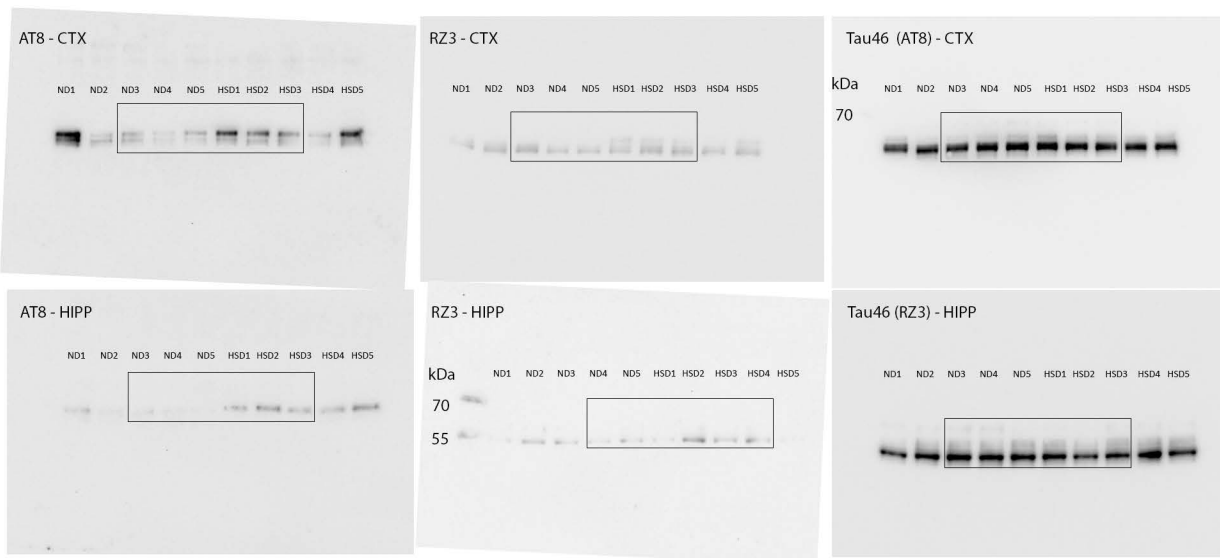
Extended Figure 1A



Extended Figure 1B

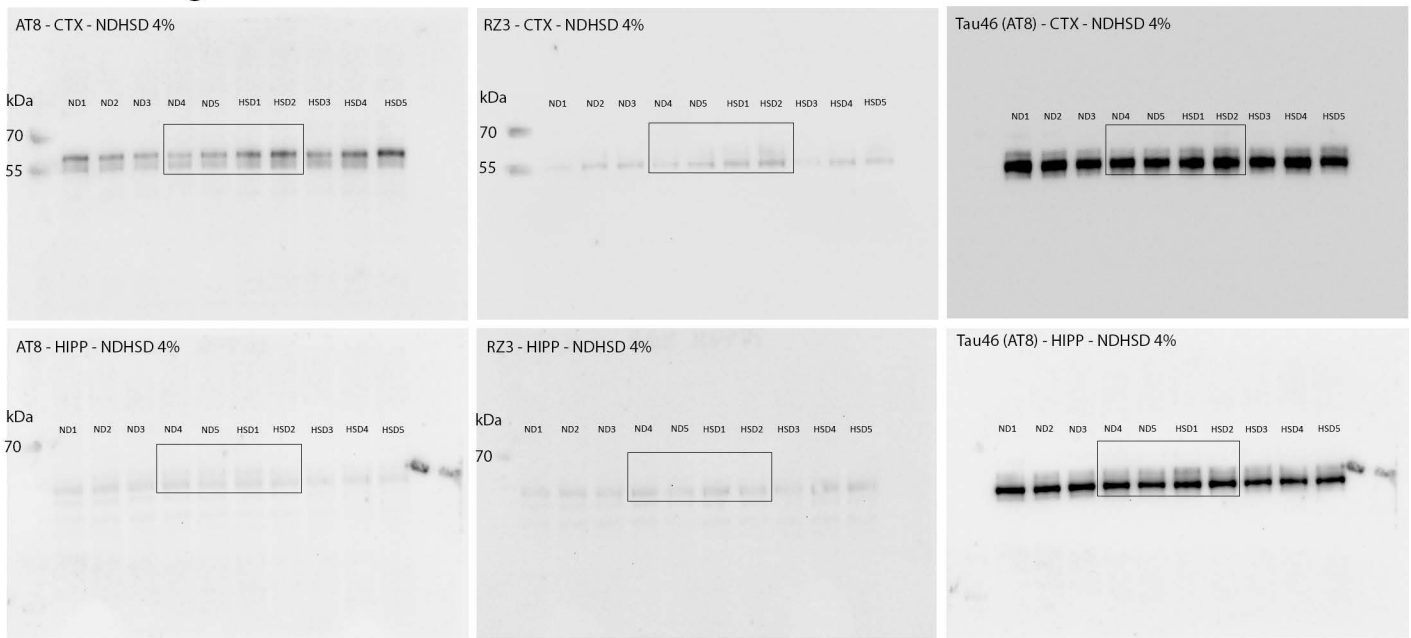


Extended Figure 1C

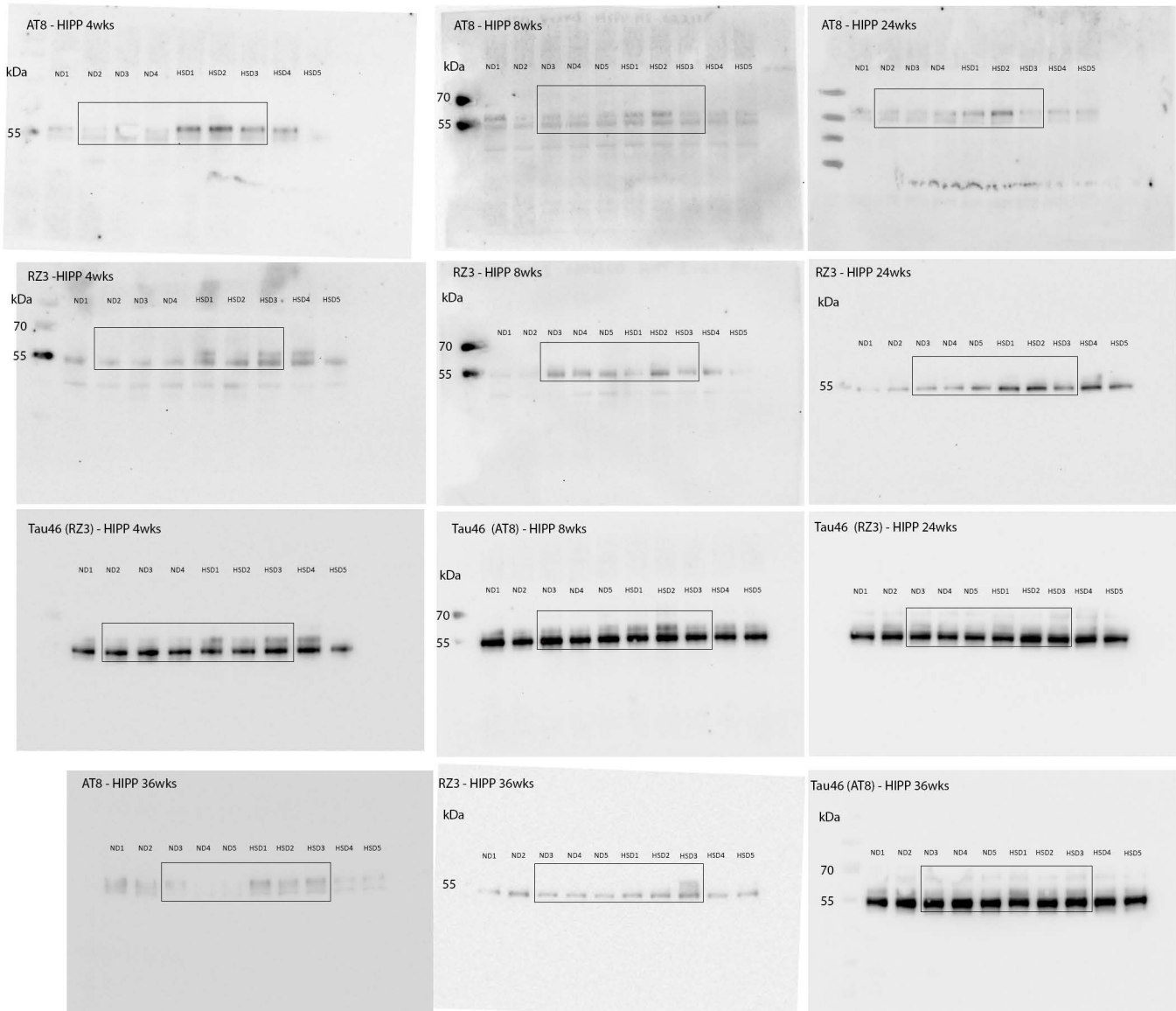


Gel Source Data - Extended Data Figure 1. Full Immunoblots image of Extended Figure 1A-C. Membranes were incubated with pTau antibody (1:500 or 1:1000) overnight. After incubation with secondary antibody, protein bands were visualized with Clarity Western ECL Substrate (BioRad) on a Bio Rad ChemiDoc MP Imaging System. After washes with TBS/0.1% Tween-20 (TBST), membranes were incubated with anti-Tau46 antibody (1:1000) overnight. Samples from neocortex and hippocampus ($\approx 10\mu\text{g}$ of protein/lane).

Extended Figure 1F

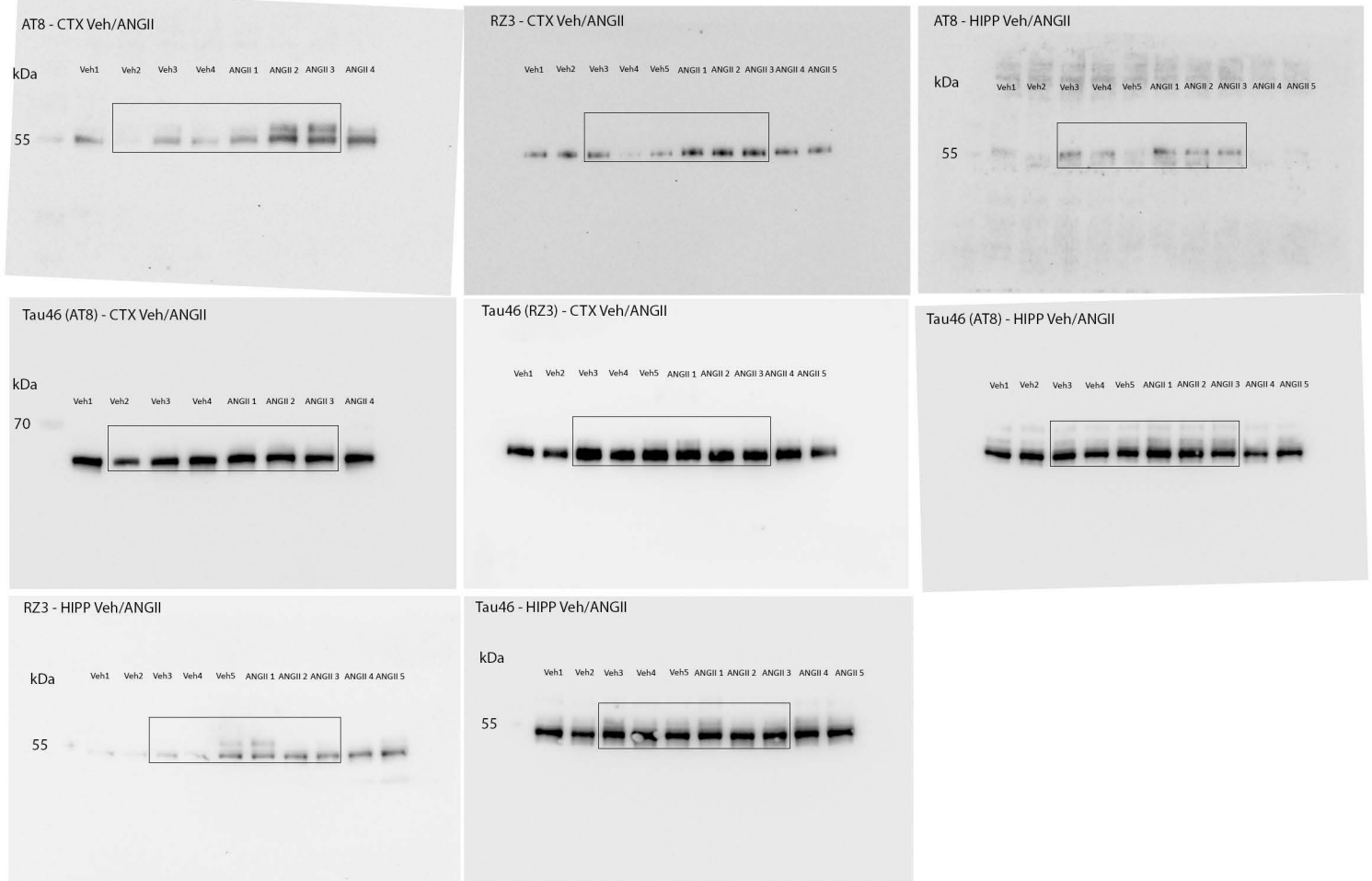


Extended Figure 1G

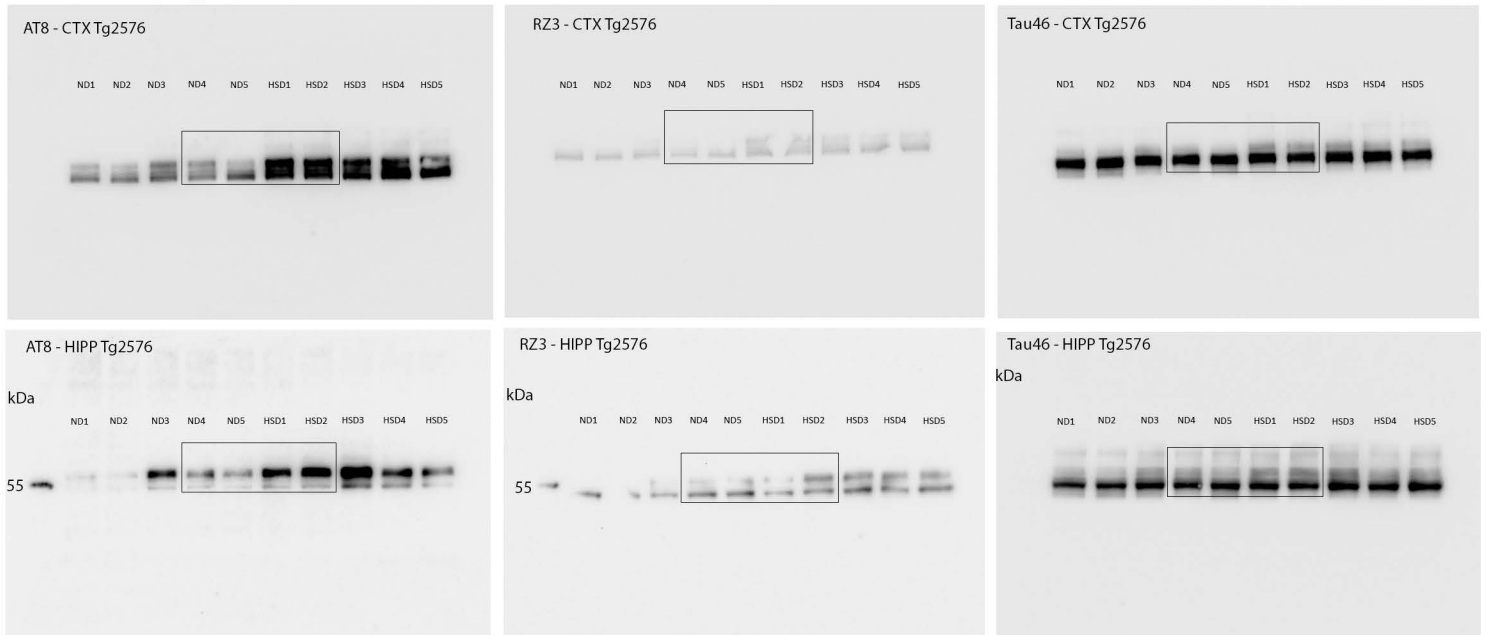


Gel Source Data - Extended Data Figure 1. Full Immunoblots image of panels in Extended Figure 1F, G. Membranes were incubated with pTau antibody (1:500 or 1:1000) overnight. After incubation with secondary antibody, protein bands were visualized with Clarity Western ECL Substrate (BioRad) on a Bio Rad ChemiDoc MP Imaging System. After washes with TBS/0.1% Tween-20 (TBST), membranes were incubated with anti-Tau46 antibody (1:1000) overnight. Samples from neocortex and hippocampus ($\approx 10\mu\text{g}$ of protein/lane).

Extended Figure 3E

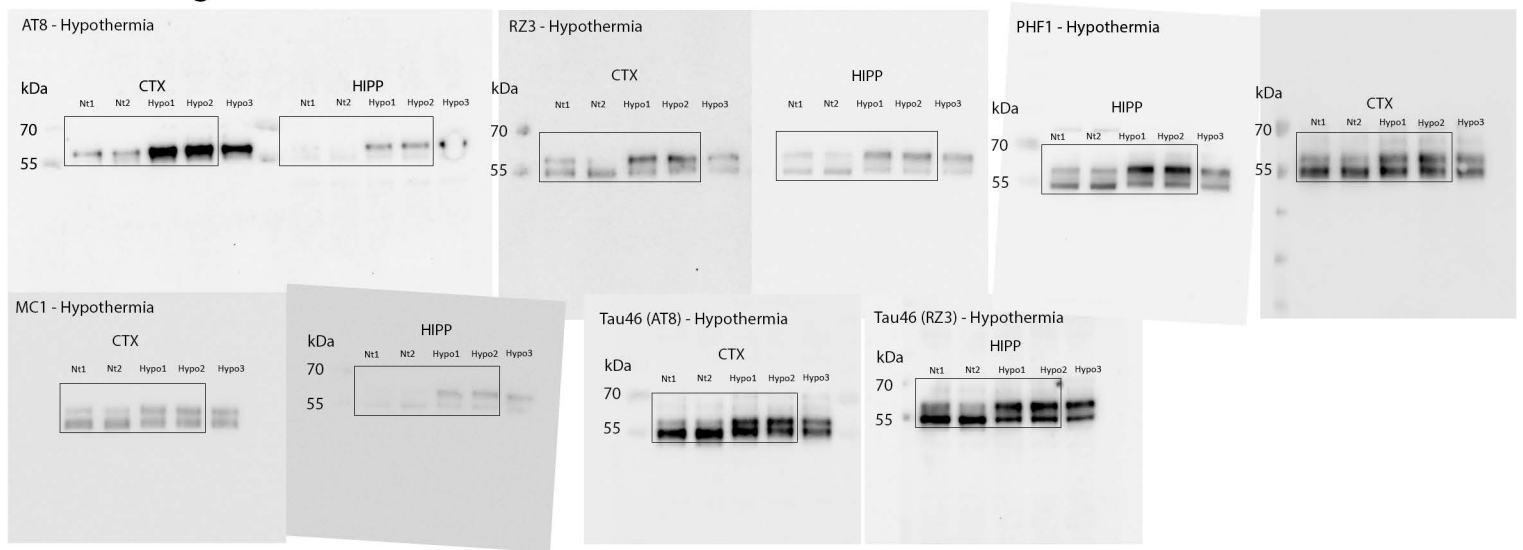


Extended Figure 3F

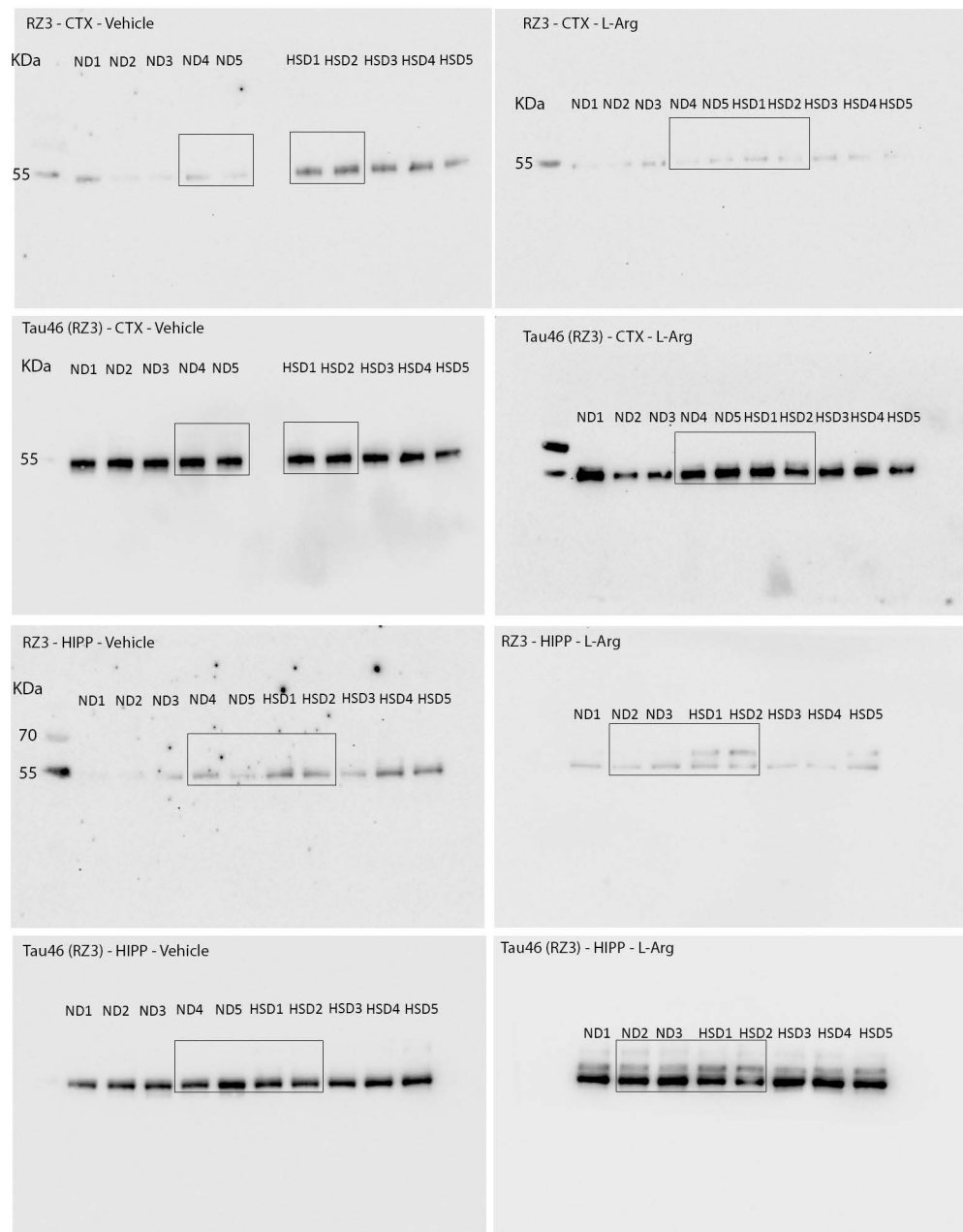


Gel Source Data - Extended Data Figure 3. Full Immunoblots image of Extended Figure 3E, F. Membranes were incubated with pTau antibody (1:500 or 1:1000) overnight. After incubation with secondary antibody, protein bands were visualized with Clarity Western ECL Substrate (BioRad) on a Bio Rad ChemiDoc MP Imaging System. After washes with TBS/0.1% Tween-20 (TBST), membranes were incubated with anti-Tau46 antibody (1:1000) overnight. Samples from neocortex and hippocampus ($\approx 10\mu\text{g}$ of protein/lane).

Extended Figure 3G

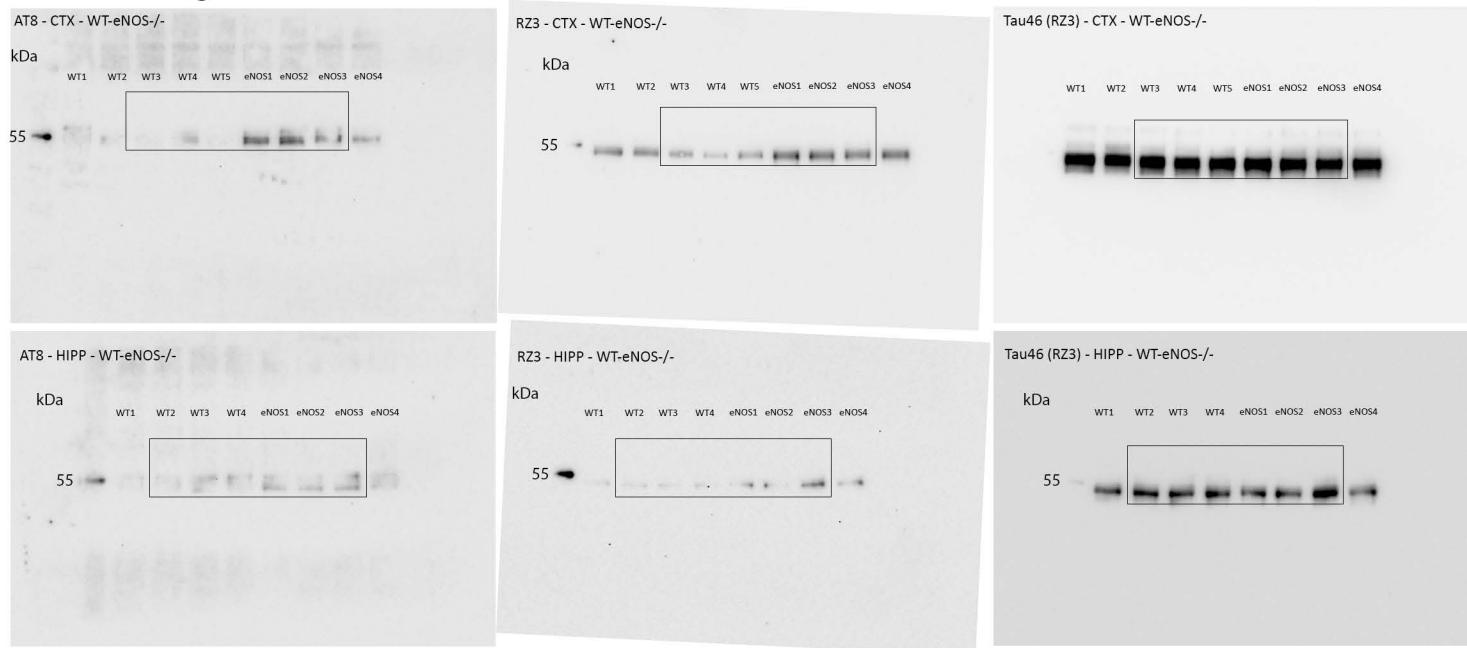


Extended Figure 4A

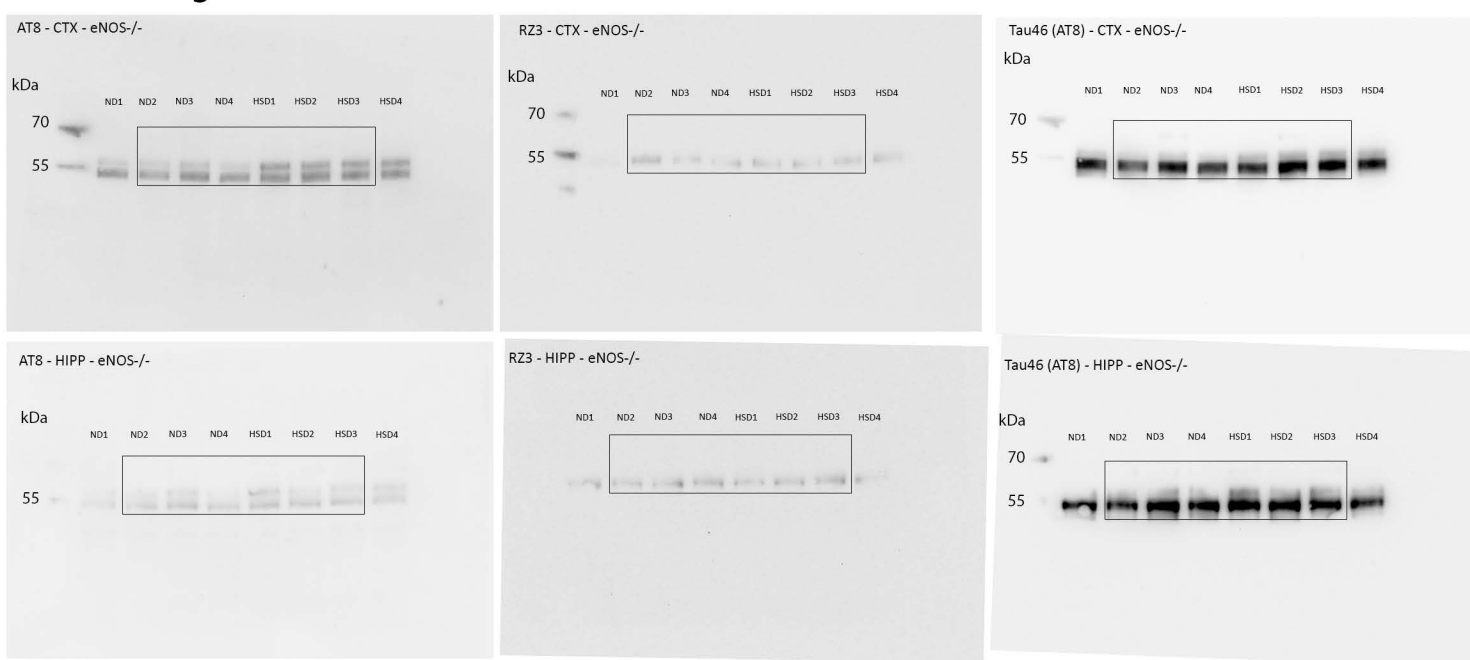


Gel Source Data - Extended Data Figure 3. Full Immunoblots image of Extended Figure 3G and 4A. Membranes were incubated with pTau antibody (1:500 or 1:1000) overnight. After incubation with secondary antibody, protein bands were visualized with Clarity Western ECL Substrate (BioRad) on a Bio Rad ChemiDoc MP Imaging System. After washes with TBS/0.1% Tween-20 (TBST), membranes were incubated with anti-Tau46 antibody (1:1000) overnight. Samples from neocortex and hippocampus ($\approx 10\mu\text{g}$ of protein/lane).

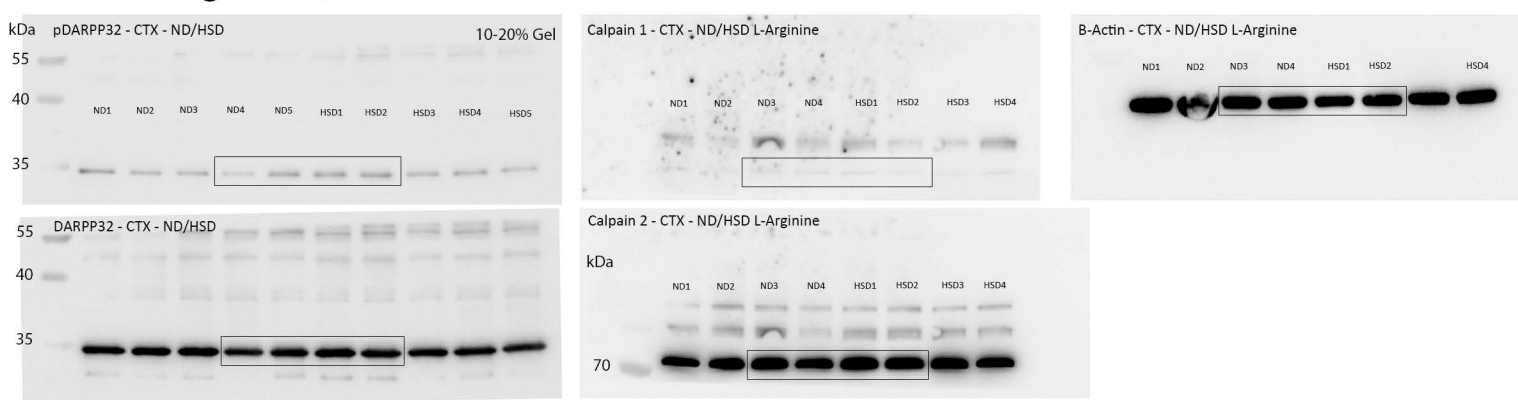
Extended Figure 4C



Extended Figure 4D

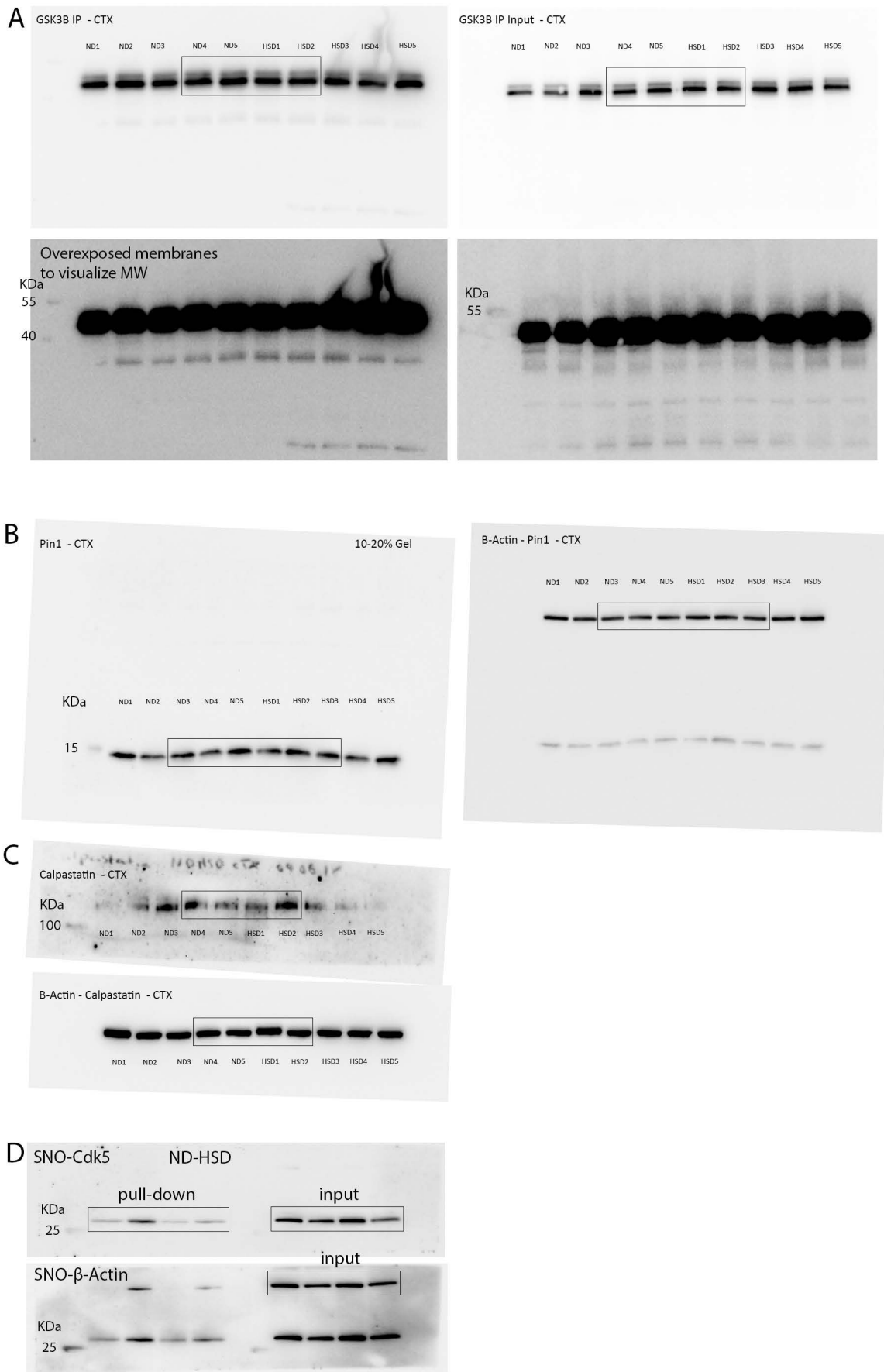


Extended Figure 4G, H



Gel Source Data - Extended Data Figure 4. Full Immunoblots image of Extended Figure 4C-H. Membranes were incubated with pTau (1:500 or 1:1000) or pDARPP32/DARPP32 (1:1000) antibodies overnight. After incubation with secondary antibody, protein bands were visualized with Clarity Western ECL Substrate (BioRad) on a Bio Rad ChemiDoc MP Imaging System. After washes with TBS/0.1% Tween-20 (TBST), membranes were incubated with anti-Tau46 antibody (1:1000) overnight. Samples from neocortex and hippocampus ($\approx 10\mu\text{g}$ of protein/lane).

Extended Figure 5



Gel Source Data - Extended Data Figure 5. Full Immunoblots image of Extended Figure 5. Membranes were incubated with primary antibodies (1:1000) overnight. After incubation with secondary antibody, protein bands were visualized with Clarity Western ECL Substrate (BioRad) on a Bio Rad ChemiDoc MP Imaging System. After washes with TBS/0.1% Tween-20 (TBST), membranes were incubated with anti- β -Actin antibody (1:50000) for 1h at RT. Samples from neocortex (\approx 10-15 μ g of protein/lane).

Figure 4E

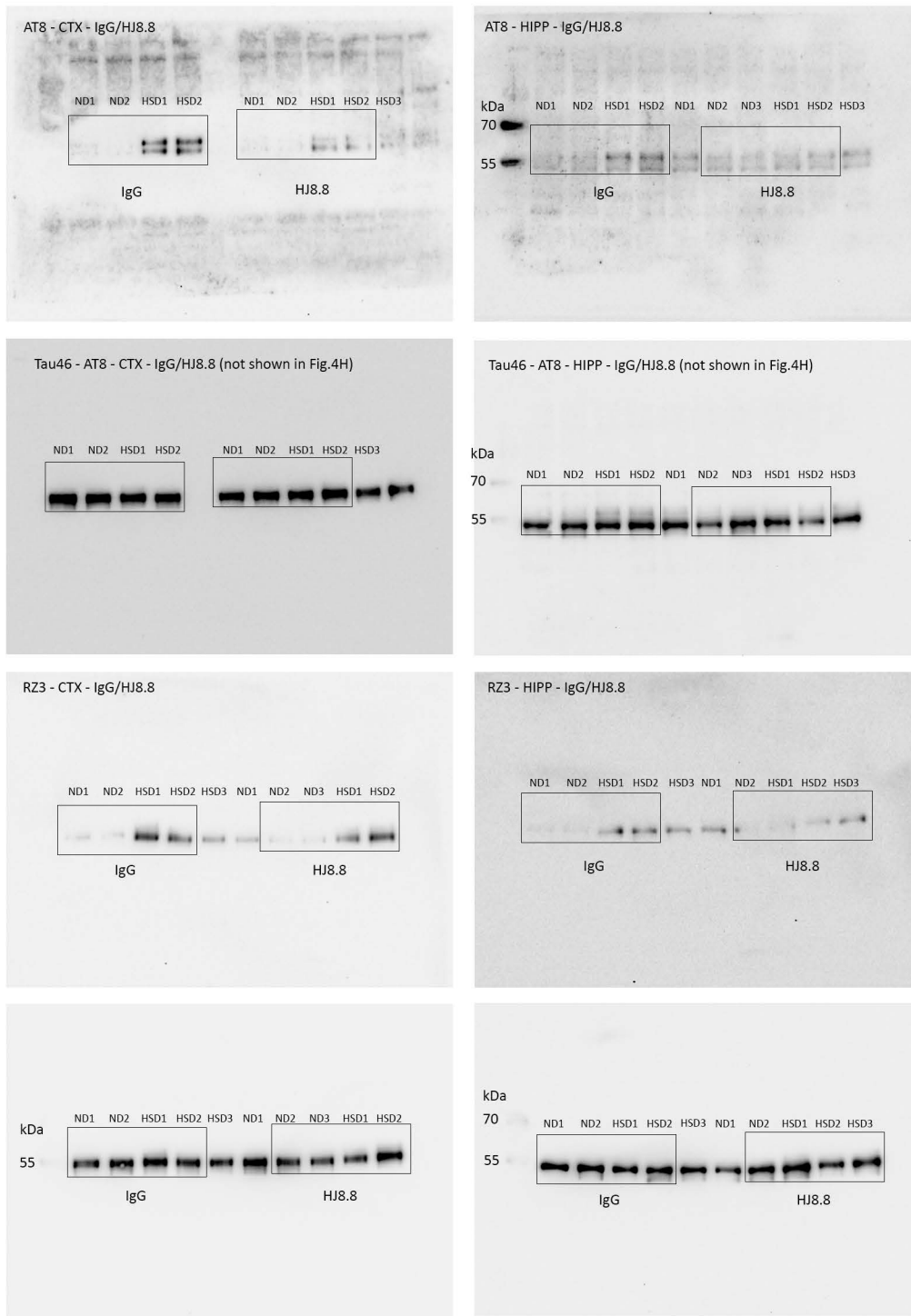
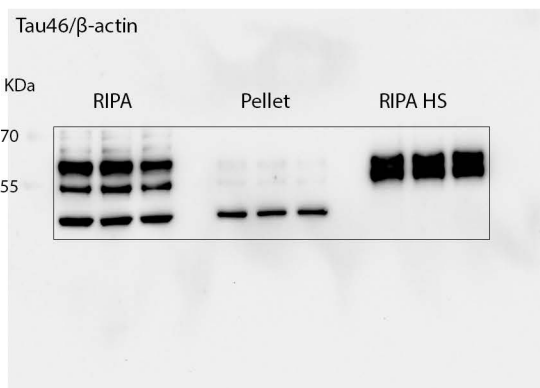


Figure 4H



Gel Source Data - Extended Data Figure 5. Full Immunoblots image of Figure 4. Membranes were incubated with AT8 or RZ3 antibody (1:500) overnight. After incubation with secondary antibody, protein bands were visualized with Clarity Western ECL Substrate (BioRad) on a Bio Rad ChemiDoc MP Imaging System. After washes with TBS/0.1% Tween-20 (TBST), membranes were incubated with anti-Tau46 antibody (1:1000) overnight. Samples from neocortex and hippocampus ($\approx 10\mu\text{g}$ of protein/lane).