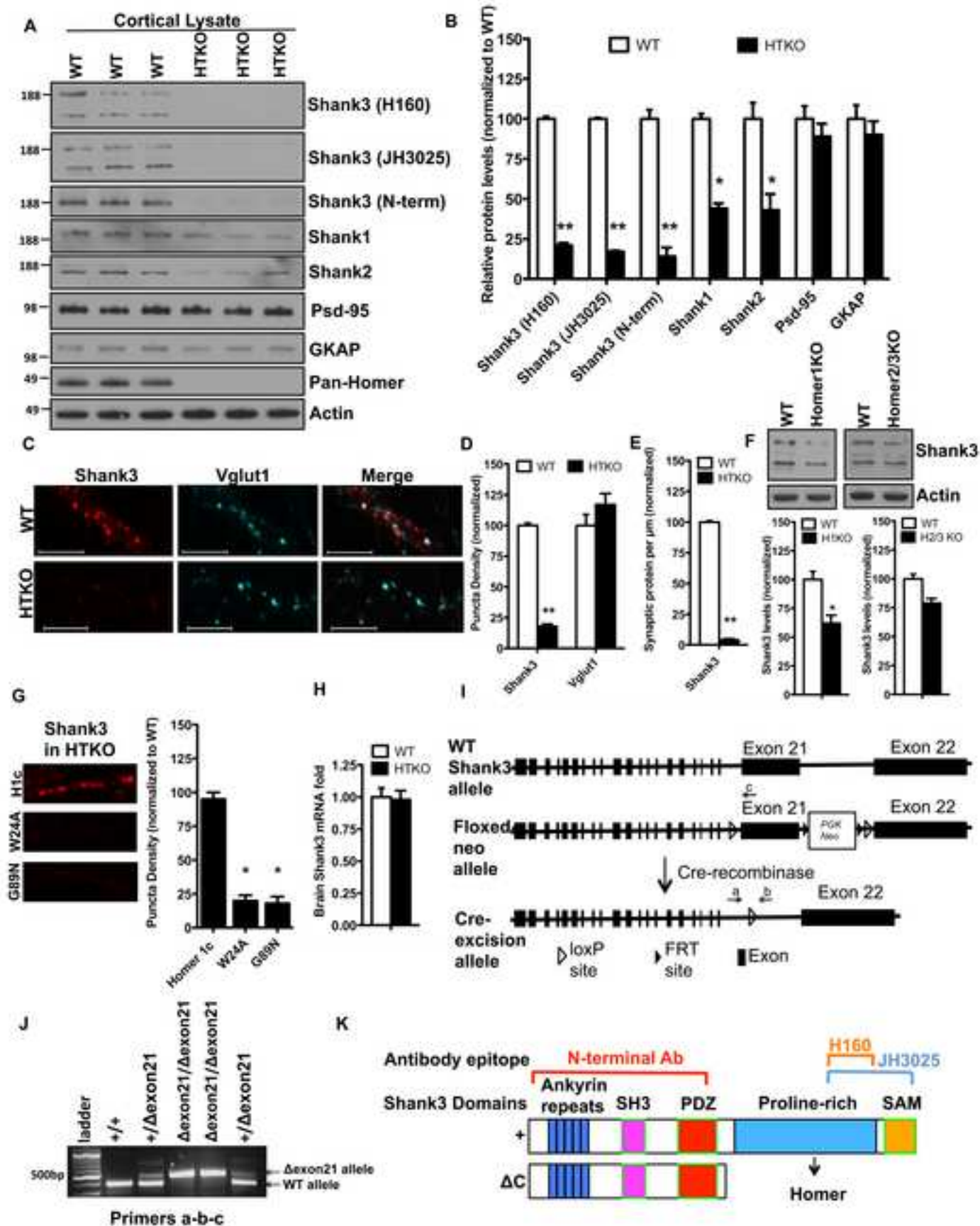
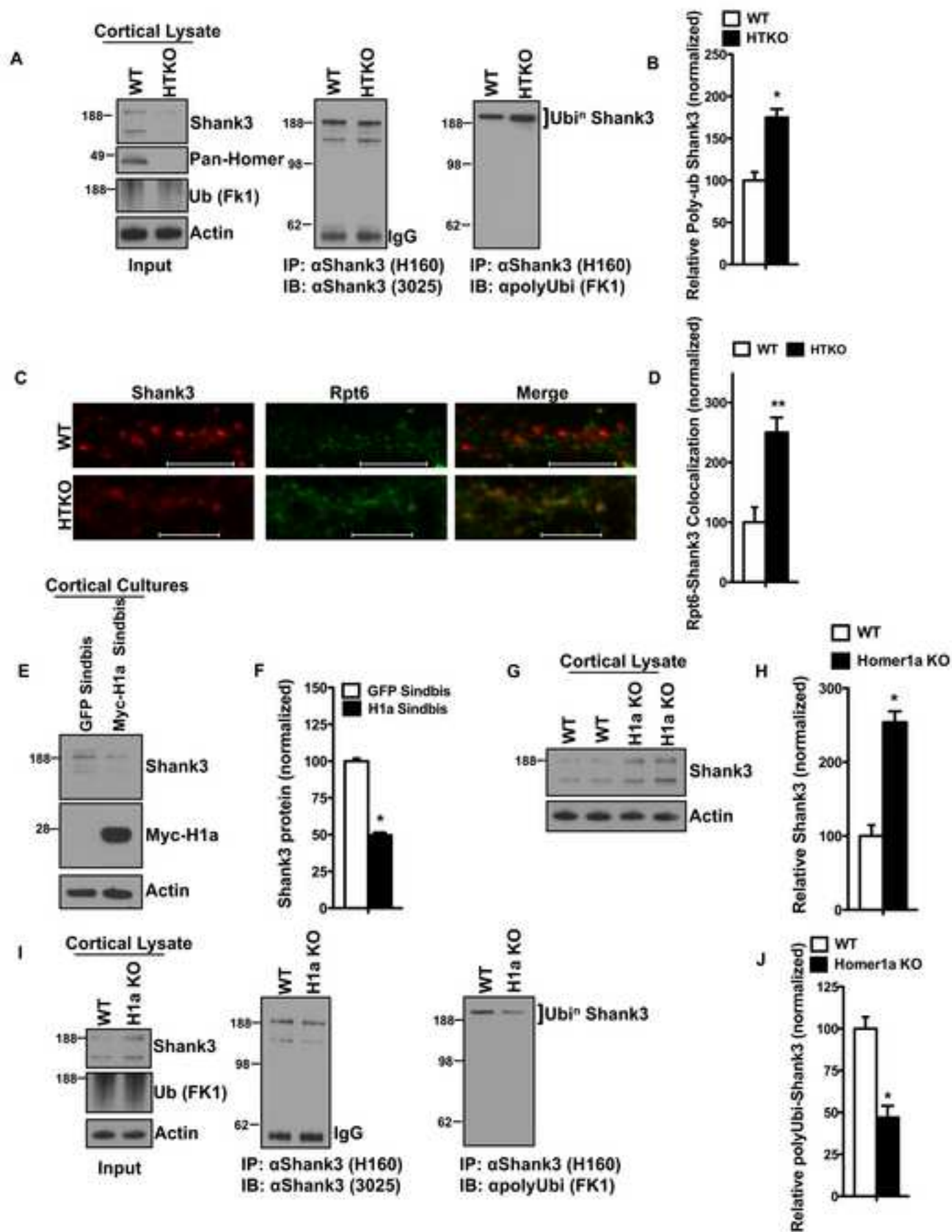


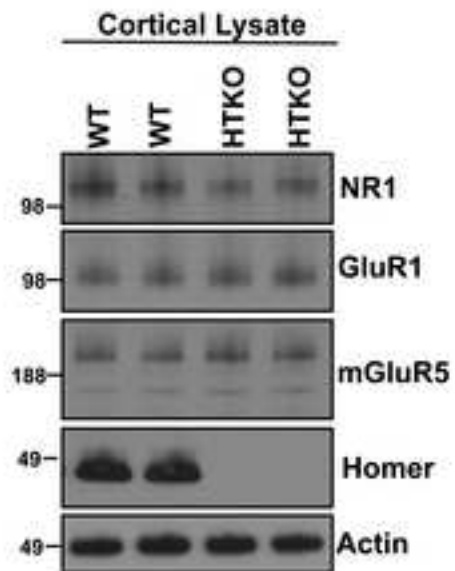
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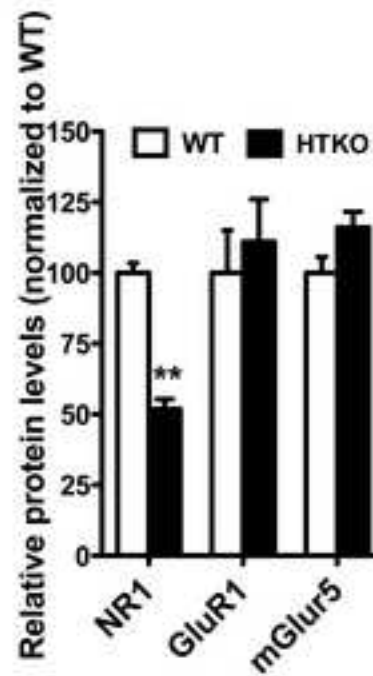




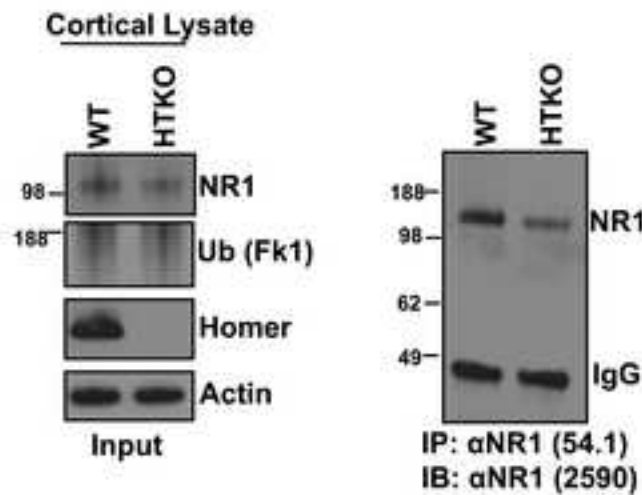
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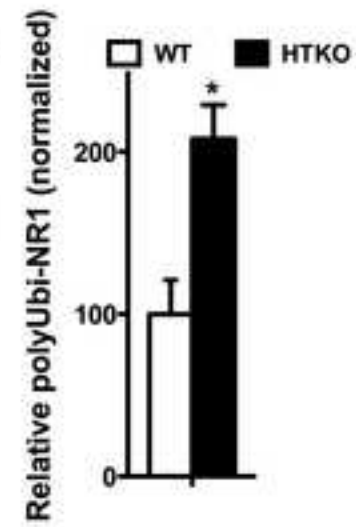
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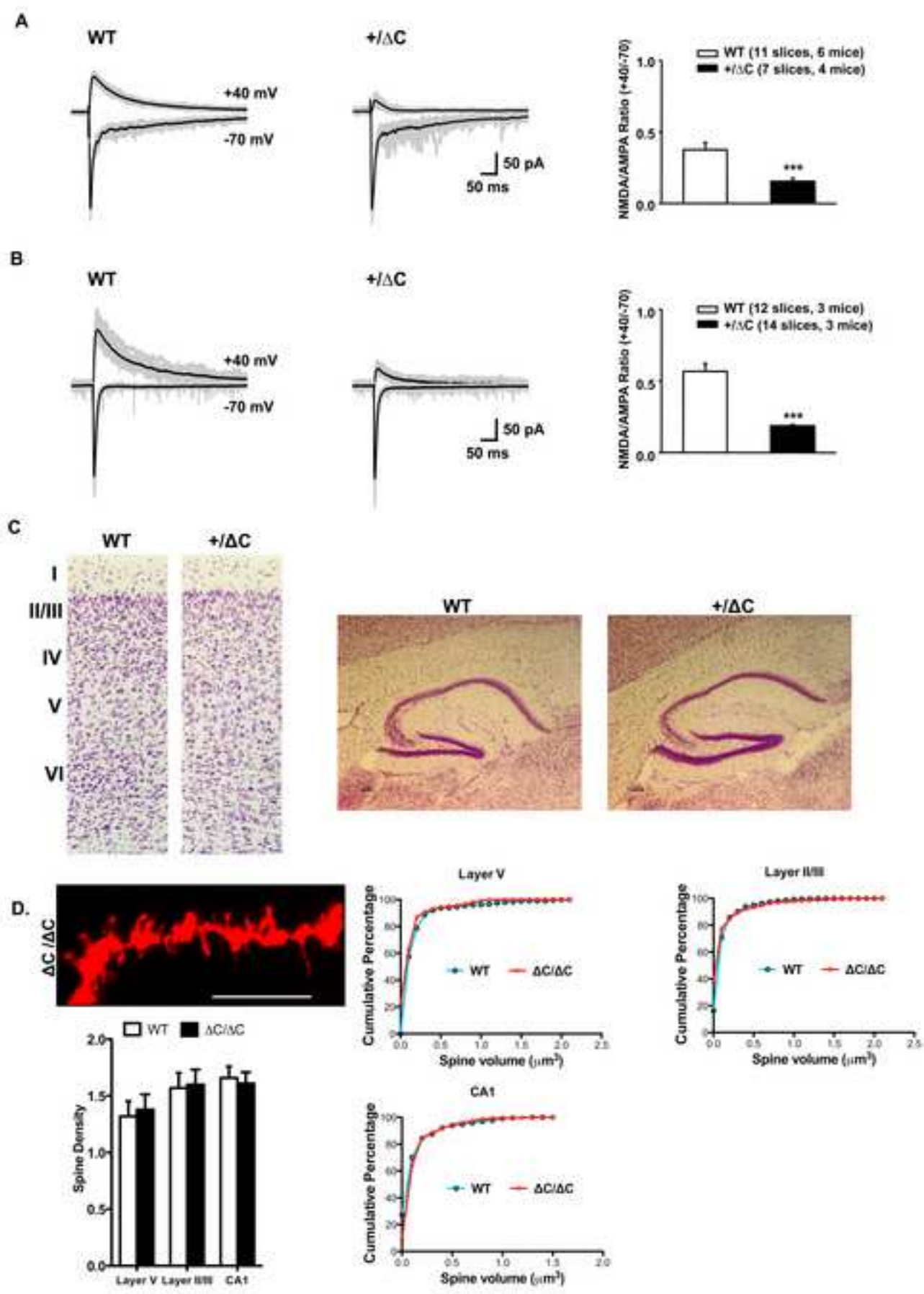


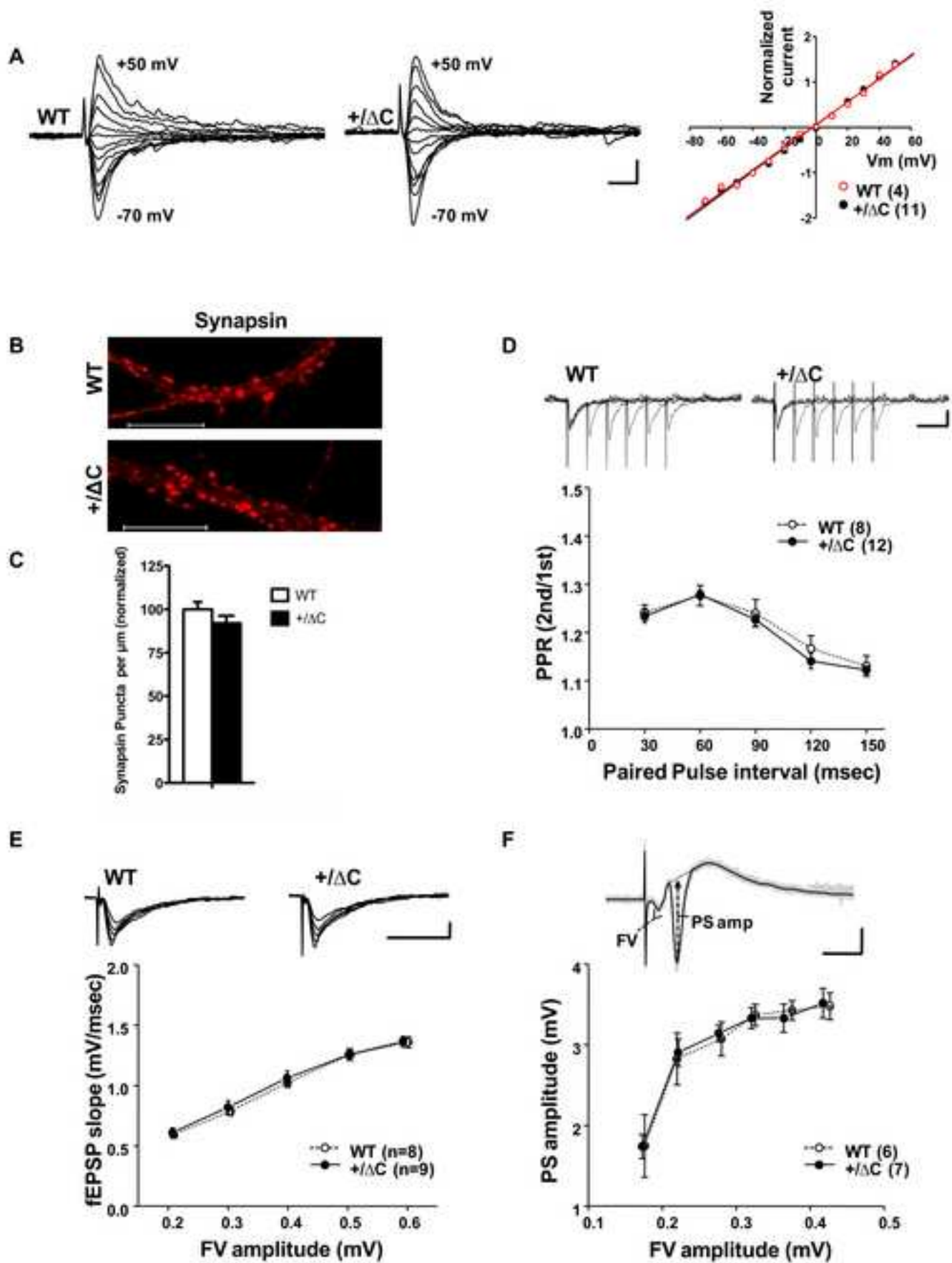
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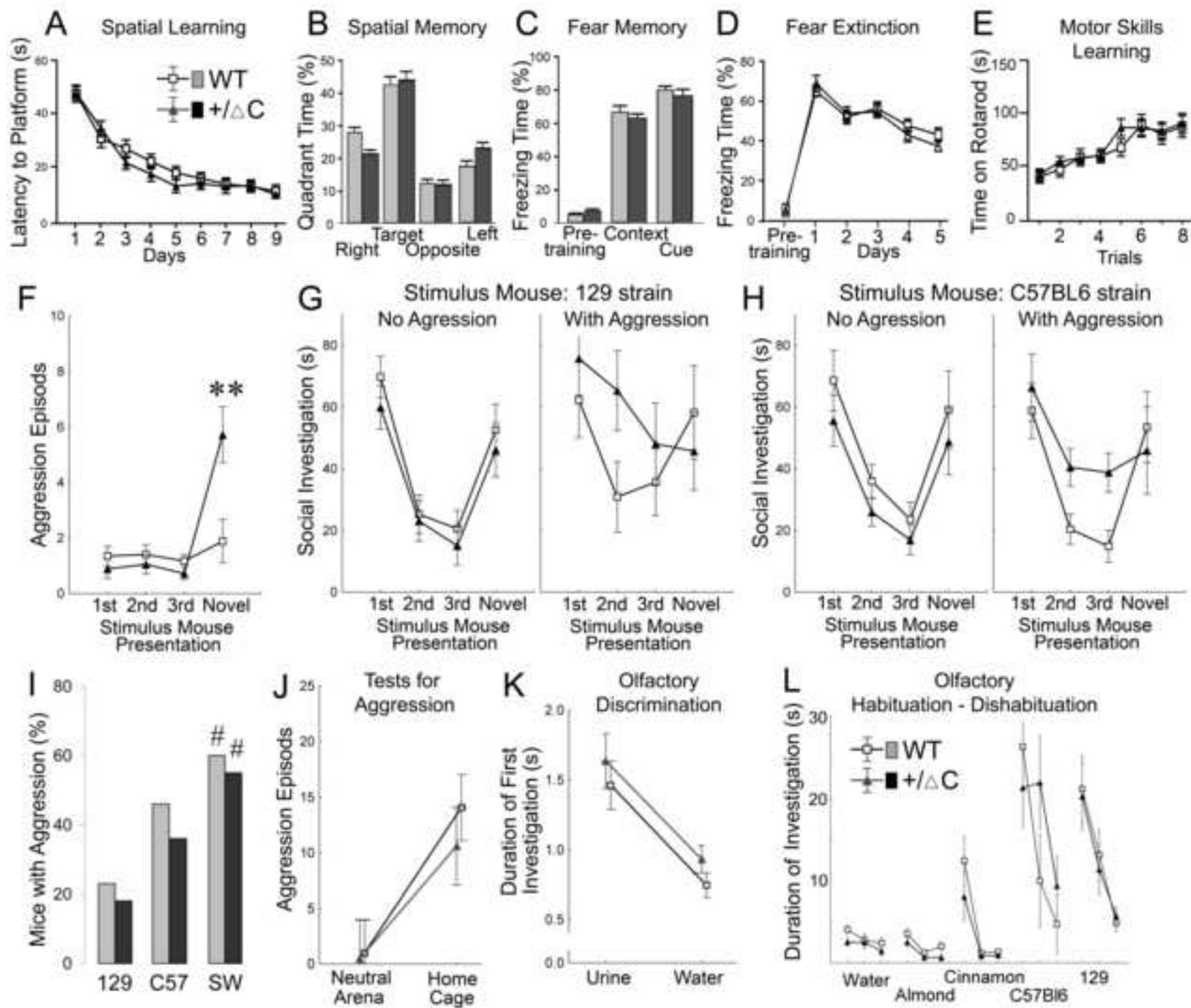


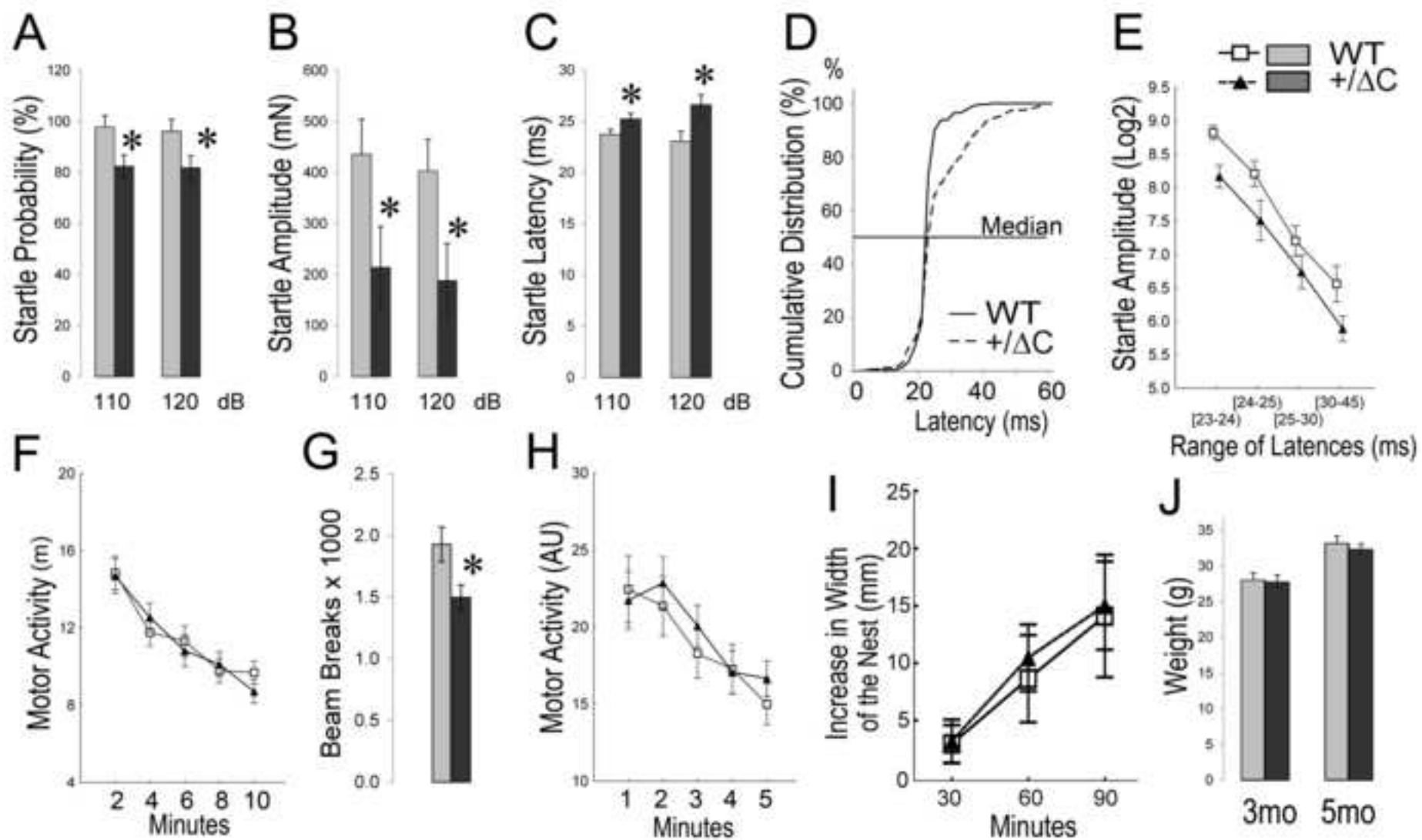
D











Shank3 is a neuronal protein that functions at excitatory synapses in developing and adult brain. Mutations of Shank3 are linked to autism spectrum disorders. Here we create a transgenic mouse that mimics human mutations of Shank3, and reveal how mutant Shank3 protein causes degradation of synaptic NMDA type glutamate receptors to alter synaptic functions important for information processing. Shank3 mutant mice show autism-like behavioral deficits together with schizophrenia-like phenotypes that are consistent with glutamate receptor changes. The study defines a biochemical pathway leading to NMDA glutamate receptor degradation, and suggests this may be shared in other autism and schizophrenia disorders.

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