# An alternative splicing switch shapes neurexin repertoires in principal neurons versus interneurons in the mouse hippocampus.

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The unique anatomical and functional features of principal and interneuron populations are critical for the appropriate function of neuronal circuits. Cell type-specific properties are encoded by selective gene expression programs that shape molecular repertoires and synaptic protein complexes. However, the nature of such programs, particularly for post-transcriptional regulation at the level of alternative splicing is only beginning to emerge. We here demonstrate that transcripts encoding the synaptic adhesion molecules neurexin-1,2,3 are commonly expressed in principal cells and interneurons of the mouse hippocampus but undergo highly differential, cell type-specific alternative splicing. Principal cell-specific neurexin splice isoforms depend on the RNA-binding protein Slm2. By contrast, most parvalbumin-positive (PV(+)) interneurons lack Slm2, express a different neurexin splice isoform and co-express the corresponding splice isoform-specific neurexin ligand Cbln4. Conditional ablation of Nrxn alternative splice insertions selectively in PV(+) cells results in elevated hippocampal network activity and impairment in a learning task. Thus, PV-cell-specific alternative splicing of neurexins is critical for neuronal circuit function.

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