Glutamate [NMDA] receptor subunit epsilon-2, also known as N-methyl D-aspartate receptor subtype 2B (NMDAR2B or NR2B), is a protein that in humans is encoded by the GRIN2B gene.

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Stretch injury of the facet capsular ligament is a cause of neck pain, inducing axonal injury, neuronal hyperexcitability, and upregulation of pain neuromodulators. Although thresholds for pain and collagen reorganization have been defined and integrins can modulate pain signaling with joint trauma, little is known about the role of integrin signaling in neuronal dysfunction from tensile loading of the innervated capsular ligament. Using a well-characterized biomimetic collagen gel model of the capsular ligament's microstructure and innervation, a study evaluated extrasynpatic expression of N-Methyl-D-Aspartate receptor subtype 2B (GRIN2B) as a measure of neuronal dysfunction following tensile loading and determined mechanical thresholds for its upregulation in primary sensory neurons, with and without integrin inhibition.Collagen gels with dissociated dorsal root ganglion neurons (n = 16) were fabricated; a subset of gels (n = 8) was treated with the  $\beta$ 1 integrin subunit inhibitor, TC-I15. Gels were stretched to failure in tension and then immunolabeled for axonal NR2B. Inhibiting the integrin subunit does not change the failure force (p = 0.12) or displacement (p = 0.44) but does reduce expression of the  $\beta$ 1 subunit by 41% (p < 0.001) and decrease axonal NR2B expression after stretch (p = 0.018). Logistic regressions estimating the maximum principal strain threshold for neuronal dysfunction as evaluated by Analysis of Covariance determine that integrin inhibition increases (p = 0.029) the 50th percentile strain threshold (7.1%) above the threshold for upregulation in untreated gels (6.2%). These results suggest that integrin contributes to stretch-induced neuronal dysfunction via neuron-integrin-collagen interactions<sup>1)</sup>

## 1)

Singh S, Winkelstein BA. Inhibiting the  $\beta$ 1integrin subunit increases the strain threshold for neuronal dysfunction under tensile loading in collagen gels mimicking innervated ligaments. Biomech Model Mechanobiol. 2022 Mar 12. doi: 10.1007/s10237-022-01565-6. Epub ahead of print. PMID: 35279768.

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