The receptor guanylyl cyclase Npr2 is essential for sensory axon bifurcation within the spinal cord.

Abstract:
Sensory axonal projections into the spinal cord display a highly stereotyped pattern of T- or Y-shaped axon bifurcation at the dorsal root entry zone (DREZ). Here, we provide evidence that embryonic mice with an inactive receptor guanylyl cyclase Npr2 or deficient for cyclic guanosine monophosphate-dependent protein kinase I (cGKI) lack the bifurcation of sensory axons at the DREZ, i.e., the ingrowing axon either turns rostrally or caudally. This bifurcation error is maintained to mature stages. In contrast, interstitial branching of collaterals from primary stem axons remains unaffected, indicating that bifurcation and interstitial branching are processes regulated by a distinct molecular mechanism. At a functional level, the distorted axonal branching at the DREZ is accompanied by reduced synaptic input, as revealed by patch clamp recordings of neurons in the superficial layers of the spinal cord. Hence, our data demonstrate that Npr2 and cGKI are essential constituents of the signaling pathway underlying axonal bifurcation at the DREZ and neuronal connectivity in the dorsal spinal cord.