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Mechanosensitivity in axon growth and guidance[1]

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In the developing nervous system, axons respond to a diverse array of cues to generate the intricate connection network required for proper function. The growth cone, a highly motile structure at the tip of a growing axon, integrates information about the local environment and modulates outgrowth and guidance, but little is known about effects of external mechanical cues and internal mechanical forces on growth cone behavior. We have investigated axon outgrowth and force generation on soft elastic substrates for dorsal root ganglion (DRG) neurons (from the peripheral nervous system) and hippocampal neurons (from the central) to see how the mechanics of the microenvironment affect different populations. We find that force generation and stiffness-dependent outgrowth are strongly dependent on cell type. We also observe very different internal dynamics and substrate coupling in the two populations, suggesting that the difference in force generation is due to stronger adhesions and therefore stronger substrate engagement in the peripheral nervous system neurons. We will discuss the biological origins of these differences, and recent analyses of the dynamic aspects of growth cone force generation and the implications for the role of mechanosensitivity in axon guidance.

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