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Growth Cone Biomechanics in Peripheral and Central Nervous System Neurons JEFFREY URBACH, DANIEL KOCH, WILL ROSOFF, Georgetown University, HERBERT GELLER, NIH — The growth cone, a highly motile structure at the tip of an 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 mediated guidance. We have investigated neurite outgrowth, traction forces and cytoskeletal substrate coupling 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 the biomechanics of DRG neurons are dramatically different from hippocampal, with DRG neurons displaying relatively large, steady traction forces and maximal outgrowth and forces on substrates of intermediate stiffness, while hippocampal neurons display weak, intermittent forces and limited dependence of outgrowth and forces on substrate stiffness. DRG growth cones have slower rates of retrograde actin flow and higher density of localized paxillin (a protein associated with substrate adhesion complexes) compared to hippocampal neurons, suggesting that the difference in force generation is due to stronger adhesions and therefore stronger substrate coupling in DRG growth cones.

Jeffrey Urbach
Georgetown University

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