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Constitutively Active Myosin Light Chain Kinase Alters Axon Guidance Decisions in Drosophila Embryos

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Abstract

Conventional myosin II activity provides the motile force for axon outgrowth, but to achieve directional movement during axon pathway formation, myosin activity should be regulated by the attractive and repulsive guidance cues that guide an axon to its target. Here, evidence for this regulation is obtained by using a constitutively active Myosin Light Chain Kinase (ctMLCK) to selectively elevate myosin II activity in *Drosophila* CNS neurons. Expression of ctMLCK pan-neurally or in primarily pCC/MP2 neurons causes these axons to cross the midline incorrectly. This occurs without altering cell fates and is sensitive to mutations in the regulatory light chains. These results confirm the importance of regulating myosin II activity during axon pathway formation. Mutations in the midline repulsive ligand Slit, or its receptor Roundabout, enhance the number of ctMLCK-induced crossovers, but ctMLCK expression also partially rescues commissure formation in *commissureless* mutants, where repulsive signals remain high. Overexpression of Frazzled, the receptor for midline attractive Netrins, enhances ctMLCK-dependent crossovers, but crossovers are suppressed when Frazzled activity is reduced by using loss-of-function mutations. These results confirm that proper pathway formation requires careful regulation of MLCK and/or myosin II activity and suggest that regulation occurs in direct response to attractive and repulsive cues.

Keywords

Myosin; Myosin Light Chain Kinase; Calmodulin; motility; axon guidance; repulsion; Drosophila

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