Astrocytes regulate adult hippocampal neurogenesis through ephrin-B signaling.

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Public Summary:
Neurogenesis in the adult hippocampus involves activation of quiescent neural stem cells (NSCs) to yield transiently amplifying NSCs, progenitors, and, ultimately, neurons that affect learning and memory. This process is tightly controlled by microenvironmental cues, although a few endogenous factors are known to regulate neuronal differentiation. Astrocytes have been implicated, but their role in cell-cell (contact dependent) signaling in NSC niches has not been investigated. We found that ephrin-B2 presented from rodent hippocampal astrocytes regulated neurogenesis in vivo. This study demonstrates a previously unknown role for ephrin-B2 in instructing neuronal differentiation, upregulating pro-neural transcription factors independently of the known mechanism through Wnt signaling. The finding that Ephrin-B2(+) astrocytes directly promote neuronal differentiation of adult NSCs, advances our understanding of adult neurogenesis and may have future regenerative medicine implications.

Scientific Abstract:
Neurogenesis in the adult hippocampus involves activation of quiescent neural stem cells (NSCs) to yield transiently amplifying NSCs, progenitors, and, ultimately, neurons that affect learning and memory. This process is tightly controlled by microenvironmental cues, although a few endogenous factors are known to regulate neuronal differentiation. Astrocytes have been implicated, but their role in juxtacrine (that is, cell-cell contact dependent) signaling in NSC niches has not been investigated. We found that ephrin-B2 presented from rodent hippocampal astrocytes regulated neurogenesis in vivo. Furthermore, clonal analysis in NSC fate-mapping studies revealed a previously unknown role for ephrin-B2 in instructing neuronal differentiation. In addition, ephrin-B2 signaling, transduced by EphB4 receptors on NSCs, activated beta-catenin in vitro and in vivo independently of Wnt signaling and upregulated proneural transcription factors. Ephrin-B2(+) astrocytes therefore promote neuronal differentiation of adult NSCs through juxtacrine signaling, findings that advance our understanding of adult neurogenesis and may have future regenerative medicine implications.