

Bradykinin promotes neuron-generating division of neural progenitor cells through ERK activation.

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Authors: Micheli M Pillat, Claudiana Lameu, Cleber A Trujillo, Talita Glaser, Angelica R Cappellari, Priscilla D Negraes, Ana M O Battastini, Telma T Schwindt, Alysson R Muotri, Henning Ulrich

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Public Summary:

In this work we showed a potential molecular pathway that controls the bradykinin system during the proliferation and differentiation of neural stem cells.

Scientific Abstract:

During brain development, cells proliferate, migrate and differentiate in highly accurate patterns. In this context, published results indicate that bradykinin functions in neural fate determination, favoring neurogenesis and migration. However, mechanisms underlying bradykinin function are yet to be explored. Our findings indicate a previously unidentified role for bradykinin action in inducing neuron-generating division in vitro and in vivo, given that bradykinin lengthened the G1-phase of the neural progenitor cells (NPC) cycle and increased TIS21 (also known as PC3 and BTG2) expression in hippocampus from newborn mice. This role, triggered by activation of the kinin-B2 receptor, was conditioned by ERK1/2 activation. Moreover, immunohistochemistry analysis of hippocampal dentate gyrus showed that the percentage of Ki67(+) cells markedly increased in bradykinin-treated mice, and ERK1/2 inhibition affected this neurogenic response. The progress of neurogenesis depended on sustained ERK phosphorylation and resulted in ERK1/2 translocation to the nucleus in NPCs and PC12 cells, changing expression of genes such as Hes1 and Ngn2 (also known as Neurog2). In agreement with the function of ERK in integrating signaling pathways, effects of bradykinin in stimulating neurogenesis were reversed following removal of protein kinase C (PKC)-mediated sustained phosphorylation.

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