

STIMULATION OF EPHRIN B INDUCES MODIFICATIONS OF HIPPOCAMPAL SYNAPTIC PLASTICITY IN NEONATAL AND ADULT RATS

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Eph receptors and their ligands, ephrins, are involved in mechanisms regulating synaptic plasticity both during development and in the adulthood. We have recently found that ephrinB2 co-immunoprecipitates with group-I metabotropic glutamate receptors (mGlu1 and mGlu5 receptors) in different brain regions, and that activation of ephrinB2 by a clustered form of its receptor, EphB1, amplifies mGlu1-receptor stimulated polyphosphoinositide hydrolysis [1]. Hence, we have hypothesized that a functional interaction between ephrinB2 and group-I mGlu receptors can be involved in the induction of long-term changes in synaptic activity. We used transverse hippocampal slices prepared from postnatal days 7-9 and 4-week old rats. Perfusion of slices with a chimeric Fc/EphB1 clustered with an anti-Fc IgG induced a small long-lasting depression of synaptic activity (~20% of the baseline). Application of the selective group-I mGlu receptor agonist, 3,5-dihydroxyphenylglycine (DHPG, 10 μ M) for 20 minutes, instead induced a short-term depression (STD) of synaptic activity. Co-application of DHPG and clustered EphB1 resulted in a prolonged synaptic depression, which was still substantial after 60 min. This effect was completely blocked when clustered EphB1 was applied in the presence of DHPG and the mGlu5 receptor antagonist MPEP (10 μ M). Application of MPEP could also prevent the small depression of synaptic activity induced by clustered EphB1 alone, suggesting that depression requires the endogenous activation of mGlu5 receptors. Our results raise the interesting possibility that an interaction between group-I mGlu receptors and ephrin/EphB receptors contributes to the regulation of synaptic plasticity in the developing and adult hippocampus.

1. Calò L, Bruno V, Spinsanti P, Molinari G, Korkhov V, Esposito Z, Patane M, Melchiorri D, Freissmuth M, Nicoletti F. (2005) *J Neurosci.* 25(9):2245-54