NRG-1/ERBB PATHWAY IS MODULATED IN SCHWANN CELL-SPECIFIC GABA-B1 RECEPTOR NULL MICE

ABSTRACT

Poster Instructions

Title	NRG-1/ERBB PATHWAY IS MODULATED IN SCHWANN CELL-SPECIFIC GABA-B1 RECEPTOR NULL MICE Room: Poster Area - Session: B08 - Abstract Number: FENS-1939 - Poster Board Number: B083
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In the last years great interest has been addressed to the investigation of the molecular mechanisms underlying the regulation of Schwann cells (SC) differentiation. Our recent data suggest that the metabotropic ?-aminobutyric acid type B (GABA-B) receptor is involved in SC differentiation mainly towards the state of non-myelinating SC. In order to investigate the mechanism regulating this process we used a model of conditional knockout mice, in which GABA-B1 receptor was selectively deleted in SC. By means of qRT-PCR and western blot analysis we studied the NRG/ErbB receptor complex in 3- and 6-months old male mice, assessing the expression of NRG-1 type I and type III, their ErbB2/ErbB3 receptors and the intracellular kinase Erk2 (involved in ErbB signal transduction). In 3-months old mice GABA-B1 receptor deletion correlates with a down-regulation of NRG-1 type III, concomitantly with an up-regulation of ErbB2/ErbB3 and phosphorylated-Erk2 (pErk2), the latter being a key regulator of SC differentiation. These changes are accompanied with alterations of myelin protein expression, morphology and behavioural measurements. Overall, several morphometric parameters are altered in these mice. Indeed, increased number of irregular fibres and rise in myelin thickness, associated to a greater number of Remak bundles, unmyelinated axons and small DRG neurons, are observed. The GABA-B1 conditional mice also show hyperalgesia and allodynia, with walking alterations. Altogether, our findings suggest an involvement of GABA-B receptor and NRG/ErbB signalling in SC maturation towards the non-myelinating phenotype. (Granted by Ass. Française Contre les Myopathies n°16342-2012)