P2 RECEPTORS: NEW TRENDS IN THE CENTRAL NERVOUS SYSTEM

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Background: In the CNS, several P2 receptors for extracellular nucleotides are identified on neurons and glia cells to participate to neuron-neuron, glia-glia and glia-neuron communication (1).
Results: In this work, we describe the cellular and subcellular presence and distribution of metabotropic $P2Y_1$ receptor in rat cerebellum at two distinct developmental ages, by means of immunofluorescence-confocal and electron microscopy, as well as western blotting and direct membrane separation techniques. At postnatal day 21, we find that $P2Y_1$ receptor is abundant on neuronal fibers identified as noradrenergic by anatomical, morphological and biochemical features. $P2Y_1$ receptor immunoreactivity colocalizes with dopamine beta-hydroxylase, tyrosine hydroxylase, neurofilament light chain, synaptophysin and flotillin, but not with glial fibrillary acidic protein for astrocytes, mylin basic protein for oligodendrocytes or IB4 for microglia. Moreover, $P2Y_1$ receptor is found enriched in membrane microdomains such as lipid rafts and in cerebellar synaptic vesicles. It is visualized on synaptic varicosities by electron microscopy analysis. When examined at postnatal day 7, $P2Y_1$ receptor immunoreactivity is instead predominantly expressed not on neurons, but only on Bergmann astroglia cells, as shown by colocalization with glial fibrillary acidic protein, rather then with neuronal markers. At this age, we moreover describe that $P2Y_1$ receptor-positive Bergmann fibers wrap up doublecortin-positive granule cells which are stretching along them while migrating through the cerebellar layers.
Conclusion: Since membrane components including purinergic receptors are very well known to mediate cellular contact and apposition, our results suggest a potential and dynamic role for $P2Y_1$ protein in cell junction/communication during development. Whereas this is in part confirmatory since in platelets $P2Y_1$ receptor is already known to mediate cell contact and aggregation, this role of $P2Y_1$ receptor is a completely original finding for the CNS.

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(1) Volonté C., Amadio S., D'Ambrosi N., Colpi M., Burnstock G. (2006) Pharmacol and Therapeut. 112(1): 264-80.