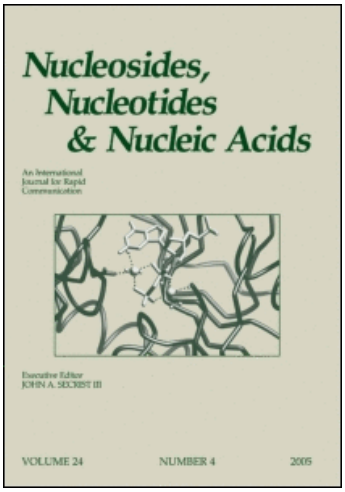

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Calcium Antagonists Modulate ^{3}H-Purine Release from Rat Striatum Glial Cultures Via Vscc-Dependent and Independent Mechanisms

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CALCIUM ANTAGONISTS MODULATE ^{3}H-PURINE RELEASE FROM RAT STRIATUM GLIAL CULTURES VIA VSCC-DEPENDENT AND INDEPENDENT MECHANISMS.

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Abstract: Electrical stimulation increased both ^{3}H-purine release and $^{45}Ca^{2+}$ influx in rat primary cultures of astrocytes. Nitrendipine and w-conotoxin reduced the first event being the ion fluxes unaffected. Only when the outward K^{+}-currents were impared, 90nM nitrendipine decreased the electrical evoked glial cell inward $^{45}Ca^{2+}$ fluxes too.

Although astrocytes are suggested to be modulators of several CNS activities their physiological role is to date yet unknown. This study was mainly aimed at the investigation of the eventual Ca^{2+} dependence of purine (P) outflow from rat striatum dissociated primary glial cultures. As previously observed, glial cells,at the 14^{th} day of culture, a time when the cells had completed their main processes of development and had reached a sufficient degree of both maturation and quiescence were able to selectively take up ^{3}H-adenosine and to release ^{3}H-P at rest and under electrical stimulation in a frequency-dependent and Na^{+}-independent manner[1]. Ca^{2+}-free medium + 1mM EGTA did not affect ^{3}H-P basal release but significantly (30% of control) reduced that one evoked by a suitable electrical stimulation (alternating polarity; 30mA/cm^{2}, 5msec duration) required to reach the maximal stimulus triggered nerotransmitter release from brain slices[2]. The effects of Ca^{2+} antagonists were tested too, since cultured glial cells were shown to be provided with voltage sensitive Ca^{2+}-channels (VSCC)[3] and high affinity binding sites for nitrendipine, an antagonist for L-type of VSCCs. However it was worth underlining that Ca^{2+} antagonists had been also reported to interfere with an increasing number of membrane cell mechanisms, thus their effect on basal and evoked $^{45}Ca^{2+}$ currents into

the cultures had to be evaluated too. 10-90nM nitrendipine reduced the evoked ^{3}H-P release beginning from the concentration of 30nM. At the dose of 90nM the drug caused an inhibition (45% of control) similar to that induced by the culture pretreatment with 100nM w-conotoxin (w-CgTX), a toxin reported to antagonize the different types of VSCCs. The simultaneous treatment with 90nM nitrendipine and 100nM w-CgTX did not cause any additive effect. Unexpectedly neither nitrendipine (from 90nM to 30 μM) nor 100nM w-CgTX were able to inhibit the astrocyte inward $^{45}Ca^{2+}$ currents which, under the electrical stimulation rised in a frequency-dependent manner. Since in glial cells, however, electrophysiological studies demonstrated that the recording of action potentials is stricly linked to K^{+} ion currents and more precisely to the blockade of Ca^{2+}-mediated outward K^{+} fluxes[3], the possibility that the lacking effect of Ca^{2+} antagonists was related to the experimental condition could not be ruled out. In this view, a study is in progress and particularly, some modification of the applied stimulus is going to be made. It seems reasonable to carry on in these terms on the basis of some preliminary data obtained by testing the effect of tetraethylammonium (TEA), a blocker of Ca^{2+}-activated outward K^{+} currents, and of K^{+} removal on cultured astrocyte $^{45}Ca^{2+}$ influx. In these experimental conditions 90nM nitrendipine succeeded in significantly reducing the electrically-evoked inward $^{45}Ca^{2+}$ currents. These findings suggest that ^{3}H-P release from dissociated primary glial cultures is corelated to Ca^{2+} transmembrane fluxes. The Ca^{2+}-dependence seems to be functionally linked to the efficiency of the outward K^{+} current and only when these mechanisms are impared it seems that a role for VSCCs could be suggested. However, it cannot be underestimated neither that Ca^{2+}-antagonists exert an inhibitory effect on ^{3}H-P release independent from their capability of influencing the VSCC-fluxes nor that voltage operated channels with not yet identified characteristics like those recently unmasked in different tissue preparations exist.

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