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GABA Uptake by Purified Avian Müller Glia Cells in Culture

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GABA is the main inhibitory aminoacid transmitter present in neurons and glial cells. Its uptake is carried out by specific high-affinity Na^+/Cl^- dependent transporters (GATs). It has been reported in the past that, in the avian retina, [^{3}H]GABA appears to be exclusively accumulated by horizontal and amacrine cells in the inner nuclear layer, and also by ganglion cells. Purified chick Müller glia cultures were able to take up [^{3}H]GABA in a Na^+ and Cl^- dependent way. Increasing GABA concentration increases GABA uptake by these cells, reaching half-maximal transport efficiency (EC_{50}) around 0.3 mM. [^{3}H]GABA uptake by Müller glia neuronal-free cultures was not mediated by neuronal transporters since it was not blocked by NNC-711, but was inhibited by beta-alanine, a specific glial transporter inhibitor. Chick Müller glia in culture express both GAT-1 and GAT-3 GABA transporters. Although mixed neuron-glial dense cultures released GABA upon glutamate, high K^+ or veratridine stimulation, Müller glial cells did not release [^{3}H]GABA upon treatment with these agents, suggesting that different from neurons, transporter mediated GABA release is not a common mechanism operating in these cells. The data also suggest that Müller cells take up GABA unidirectionally, which may constitute an important mechanism of inactivating GABA activity mediated by neurons.

Keywords: Müller glia; GABA uptake; retina; GABA transporter; GAT; Culture

INTRODUCTION

Glia represent the most abundant group of cells in the nervous system. In recent years innumerous reports have changed the view that glial cells were only a supportive system to neurons. Thus, recent evidence show that these cells participate actively in intercellular signaling through neuro-glial communication (Perea and Araque, 2006; Todd *et al.*, 2006). Müller cells constitute the major macroglia cell population in the retina. These cells execute many of the functions associated with oligodendrocytes, astrocytes and ependymal cells in other parts of the central nervous system (Newman and Reichenbach, 1996). Recently, it was demonstrated that under certain conditions avian Müller glia can transdifferentiate and generate a few neuronal types, suggesting a plastic role for these cells in the retina (Fischer and Reh, 2001, Fischer, 2005). In addition, nearly every disease of the retina is associated with Müller glial cell reactive gliosis (Bringmann *et al.*, 2006).

Müller glia span the whole length of the retina and contribute for the formation of the inner and outer limiting membranes of the tissue. Moreover they also extend processes into the inner and outer

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