

D-Aspartate uptake into cultured rat pinealocytes and the concomitant effect on L-aspartate levels and melatonin secretion

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Abstract

Significant amounts of D-aspartate (Asp) are found in mammalian tissues and D-Asp is presumed to play some significant, but as yet undefined physiological role. However, it is not known whether D-Asp is synthesized in mammals. In this study, we addressed this issue in cultured rat pinealocytes, parenchymal cells of the pineal gland, which contain significant amounts of D-Asp. Biosynthesis of D-Asp was found to be minimal to non-existent in cultured rat pinealocytes. We then investigated the mechanism of uptake of D-Asp into these cells and its consequent effect on cell function. D-Asp was efficiently taken up into cells, in a time- and dose-dependent manner. Interestingly, the L-Asp levels in the cells and media decreased concomitantly with the uptake of D-Asp. This decrease was not due to D-Asp cytotoxicity, since the cellular levels of other amino acids were not affected. D-Serine and D-alanine were not taken up efficiently into the cells and the cellular levels of L-serine and L-alanine were unchanged. Also, immunocytochemical staining with anti-D-Asp antibody showed that D-Asp, which had been taken up into the cells, was dispersed throughout the cytoplasm. In response to norepinephrine stimulation, pinealocytes, which had been pretreated with D-Asp released D-Asp as well as L-Asp. In these cells, norepinephrine-induced secretion of melatonin, a pineal hormone, was suppressed. The mechanism of this suppression is discussed here.