Correlation of 4'-[methyl-^{11}C]-thiothymidine uptake with human equilibrative nucleoside transporter-1 and thymidine kinase-1 expressions in patients with newly diagnosed gliomas.

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Abstract

OBJECTIVE:

We examined expressions of human equilibrative nucleoside transporter-1 (hENT1) and thymidine kinase-1 (TK1), the key enzyme in 4'-[methyl-^{11}C]-thiothymidine (4DST) phosphorylation, to elucidate the mechanism of 4DST uptake in patients with newly diagnosed gliomas.

METHODS:

A total of 19 patients with newly diagnosed gliomas were examined with 4DST PET. Tumor lesions were identified as areas of focally increased uptake, exceeding that of normal brain background. For semi-quantitative analysis, tumor-to-contralateral normal brain tissue (T/N) ratio was determined by dividing the maximal standardized uptake value (SUV) for tumor by that of the mean SUV for reference tissue. The expressions of hENT1, TK1 and Ki-67 in tumor specimens were examined by immunohistochemistry and compared with 4DST T/N ratio.

RESULTS:

All but two gliomas showed focally increased 4DST uptake. All gliomas showed hENT1 staining, except one grade II glioma, which was also not visualized on 4DST PET. A significant correlation was observed between T/N ratio and hENT1 score ($\rho = 0.90$, $p < 0.001$). All gliomas showed TK1 staining, except two gliomas which were also not

visualized on 4DST PET. There was a significant correlation between T/N ratio and TK1 score ($\rho = 0.92$, $p < 0.001$). There was a significant correlation between T/N ratio and Ki-67 index ($\rho = 0.50$, $p < 0.03$).

CONCLUSION:

Results of this preliminary study indicate that expressions of hENT1 and TK1 appear to be important determinants of 4DST uptake in newly diagnosed gliomas.

KEYWORDS:

4DST; Glioma; PET; TK1; hENT1