Indispensability of glial glutamate transporters during a neurodevelopmental period to cognitive behaviors and brain development

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[Purpose] Impairments of neural cells and networks as a consequence of glutaminergic dysfunctions occurring in neurodevelopment are involved in the onset of psychiatric disorders during adolescence or early adulthood. In the present study, we investigated the influence of functional decreases of glial glutamate transporters in neurodevelopment pharmacologically on the cognitive behaviors and glutamatergic functions in adolescent mice.

[Methods] Early postnatal mice were microinjected DL-threo- β -benzyloxyaspartate (DL-TBOA: 5 nmol, i.c.v.), a glial glutamate transporter inhibitor 4 times every other day. In mice administered DL-TBOA at the age of 8 weeks, cognitive and glutamatergic functions or neuronal morphology were evaluated.

[Results] Mice injected DL-TBOA at the age of 8 weeks, showed visual recognition memory impairment, decreased ability of glutamate release, cell size and the number of dendritic spines, or increased GLT-1 and GLAST proteins in the PFC or cerebral cortex. No difference for PCP response was between mice injected vehicle and DL-TBOA.

[Conclusions] These results indicated that dysfunctions of glial glutamate transporters in neurodevelopment developed the impairment of cognitive behaviors accompanying abnormalities of glutamatergic neuronal functions and neuronal morphology in adolescence.