【別紙２】

論文名：Neurobehavioral deficits of epidermal growth factor-overexpressing transgenic mice: impact on dopamine metabolism.

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Epidermal growth factor (EGF) and its family member neuregulin-1 are implicated in the etiology of schizophrenia. Our recent pharmacological studies indicate that EGF injections to neonatal and adult rats both induce neurobehavioral deficits relevant to schizophrenia. We, however, did not evaluate the genetic impact of EGF transgene on neurobehavioral traits. Here we analyzed transgenic mice carrying the transgene of mouse EGF cDNA. As compared to control littermates, heterozygous EGF transgenic mice had an increase in EGF mRNA levels and showed significant decreases in prepulse inhibition and context-dependent fear learning, but there were no changes in locomotor behaviors and sound startle responses. In addition, these transgenic mice exhibited higher behavioral sensitivity to the repeated cocaine injections. There were neurochemical alterations in metabolic enzymes of dopamine (i.e., tyrosine hydroxylase, dopa decarboxylase, catechol-O-methyl transferase) and monoamine contents in various brain regions of the EGF transgenic mice, but there were no apparent neuropathological signs in the brain. The present findings rule out the indirect influence of anti-EGF antibody production on the reported behavioral deficits of EGF-injected mice. These results support the argument that aberrant hyper-signals of EGF have significant impact on mouse behavioral traits and dopamine metabolism.