refractory depression, we have compared BDNF levels in frontal cortex, hippocampus, and amygdala in each group of animals. In addition, we have measured BDNF and BDNF expression related microRNA (miRNA206) contents in all exosome and brain-derived exosome in the peripheral blood, aimed at the identification of peripheral molecular dynamics that specifically reflect the changes in the brain. All experiments have carried out according to the approval of the Sapporo Medical University Animal Care and Use Committee with consideration so as not to give unnecessary pain to the animal.

We have found that blood BDNF levels of refractory depression (7.4 ng/ml ± 1.50) showed significantly higher ($p<0.05$) than the controls (5.6 ng/ml ± 1.02) and simple depression models (4.5 ng/ml ± 0.84), and antidepressant tended to increase the BDNF levels in depression model (6.2 ng/ml ± 1.54), but reduced in refractory depression models (5.6 ng/ml ± 1.38). Furthermore, interestingly, the variation of blood BDNF levels and the way of the changes in the exosome is different. In considering the clinical report that indicated higher levels of blood BDNF in the non-reactive group of antidepressant treatment prior to administration, we are continuing analysis to identify the pathological mechanism that is common to the intractable depression.

PS199

Contrasting expression patterns of inflammation-related genes in mouse models of depression and psychosis

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Abstract

Previously, we showed the existence of pseudo-immature brain cell states in the dentate gyrus (DG) of mouse models of psychiatric disorders, including schizophrenia and bipolar disorder. It was also demonstrated that some brain cells can undergo rejuvenation in response to the external stimulation, such as treatment with antidepressant (fluoxetine; FLX), pilocarpine-induced seizure, and physiological stimulation. Pseudo-immature brain cell states are often associated with inflammation. Recently, via bioinformatics analysis, we indicated transcriptomic "hypermaturity" in the DG of mice overexpressing the glucocorticoid receptor (GRov mice), which show increased depression-like and anxiety-like behaviors and are considered potential animal models for mood disorders, and the hippocampus of the glutamate dehydrogenase 1 (Glud1) transgenic mice and mice treated with PF-04447943, a selective phosphodiesterase-9 (PDE9) inhibitor. However, it is largely unknown whether there is any common molecular basis for "hypermature" and pseudo-immature brains. Here, we compared genome-wide gene expressions in the DG of GRov mice with those in inflammation by using a bioinformatics tool, NextBio. The gene expression patterns in the DG of GRov mice showed statistically significant similarity to those in the inflammation-associated events, such as poly(I:C) infection and colitis. Among genes that were upregulated or downregulated in "hypermature" brains, there were significant enrichments in signal pathways related to inflammation and immune reactions. Both these enrichments were also observed for pseudo-immature brains. Of the inflammation and immune–related genes in the pseudo-immature brains, the number of upregulated genes was significantly greater than that of downregulated genes. In contrast, in the "hypermature" brains, downregulations were dominant to upregulations in the inflammation and immune–related genes. These observations indicate that inflammation is commonly involved in both pseudo-immature and "hypermature" brains, and each of them may represent unique inflammation-related events.

PS200

Effects of p11 on BDNF-induced changes in dendritic outgrowth and spine formation in primary hippocampal cells

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Abstract

Objectives: p11 (S100A10) is a key regulator of depression-like behaviors and antidepressant drug response in rodent models. Recent studies suggest that p11 mediates the behavioral antidepressant action of brain-derived neurotrophic factor (BDNF) in rodents. BDNF improves neural plasticity, which is linked to the cellular actions of antidepressant drugs. In the present study, we investigated whether p11 regulated BDNF action on neural plasticity *in vitro*.

Methods: We generated primary hippocampal cultures. p11 expression, dendritic outgrowth, and spine formation were investigated under toxic conditions induced by B27 deprivation, which causes hippocampal cell death.

Results: B27 deprivation significantly decreased p11 expression. Treatment with BDNF significantly prevented the B27 deprivation-induced decrease in p11 levels in a concentration-dependent manner, whereas these concentrations had no effect on control cultures. B27 deprivation significantly reduced the total outgrowth of hippocampal dendrites and spine number. BDNF increased dendritic outgrowth and spine number in conditions with or without B27. Furthermore, p11 knockdown through small interfering RNA (siRNA) transfection blocked these effects. Specially, overexpression of p11 in B27-deprived cells increased dendritic outgrowth and spine number, and treatment with BDNF potentiated these effects.

Conclusions: Taken together, our data suggest that BDNF-induced improvement in neural plasticity may depend on the regulation of p11 in hippocampal cells. These results provide evidence to strengthen the theoretical basis of a role for p11 in BDNF-induced antidepressant action.

Keywords: p11, BDNF, hippocampus, dendritic outgrowth, spine formation

PS201

EphB2 in the medial prefrontal cortex regulates vulnerability to stress

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