mice. Male ddY mice were treated with nicotine (1 mg/kg, i.p.), and the intensity and duration of nicotine-induced tremor was evaluated over 10 min. Anti-essential tremor agents were given 15 min before the nicotine injection. The medications for human essential tremor, propranolol (a β receptor antagonist), diazepam (benzodiazepine receptor agonist) and phenobarbital (a $GABA_A$ receptor stimulant), all significantly reduced the duration and intensity of nicotine-induced tremor. In contrast, neither medication for parkinsonian tremor, trihexyphenidyl (a muscarinic receptor antagonist), L-DOPA (a dopamine precursor) nor bromocriptine (a D_2 receptor agonist) affected nicotine-induced tremor. These results show that nicotine-induced tremor mimics essential tremor not only for the causative site (inferior olive), but also for the responses to anti-tremor agents, suggesting both tremor types share the common tremorgenic mechanisms.

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VGF overexpression mice exhibited several behavioral abnormalities with disruption of brain organization: implication in mental disorders.

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Abstract

Objective: Recently, the number of patients suffered from mental disorders has been increased with increase of stress. The two hit hypothesis proposed that mental disorders, such as schizophrenia, bipolar and depression, may be caused by the damage in both of developmental and adult stage. VGF nerve growth factor inducible (VGF) is a neuropeptide induced by nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF) and so on. It is also known that this peptide is related to brain function in both of developmental and adult stages. Additionally, the expression of VGF is changed in patients with these diseases. However, detailed mechanism of VGF action in brain is still unknown. In the present study, we generated mice in which VGF expression is increased and investigated the roles of VGF in the central nervous system.

Methods: To investigate the role of VGF, we investigated several behavioral phenotypes using several behavioral tests, such as locomotor activity test, open field test, Y-maze test, tail suspension test, forced swimming test, and social interaction test and organization of the brain.

Results: These adult VGF overexpression mice showed (a) hyperactivity in home cage and novel environment, working memory impairment, lower sociality, higher depressive state compared with age-matched wildtype mice, (b) decreased the brain weight without the change of body weight, and (c) increased the lateral ventricle volume compared with wild-type mice.

Conclusion: These results suggest that VGF is implicated in several mental behaviors and the formation of the brain, and this transgenic mice provide good insight to research of mental disorders.

Policy of Full Disclosure: None.

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Modulation by cerebellar D3 receptors of dyskinesia induction in rats

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Abstract

Dopaminergic neurotransmission is mediated by multiple dopamine receptors, D_1 ~ D_5. Dopamine D_3 receptors are highly expressed in the cerebellum; however, their pathophysiological functions are not fully understood. We previously demonstrated that cerebellar D_3 receptors modulate the incidence of extrapyramidal motor disorders (Prog. Neuro-Psychopharmacol. Biol. Psychiatry, 50, 157, 2014). In the present study, we conducted microinjection study to clarify the role of cerebellar D_3 receptors in modulating D_1 agonist-induced oral dyskinesia and L-DOPA-induced dyskinesia in rats. In normal SD rats, the D_1 agonist SKF-38393 dose-dependently elicited vacuous chewing movements (VCM), which was blocked by SCH-23390 (D_1 antagonist) and haloperidol (antipsychotic drug). Microinjection of the preferential D_3 agonist 7-OH-DPAT into lobe 9 of the cerebellum significantly inhibited SKF-38393-induced VCM. The inhibition of VCM by 7-OH-DPAT occurred in a dose-dependent manner and was blocked by simultaneous treatment with U-99194A (D_3 antagonist). In the unilateral 6-OHDA lesioned hemiparkinsonian rat model, chronic L-DOPA treatment elicited intensive dyskinesia including axial, forelimb and orolingual dyskinesia. However, microinjection of 7-OH-DPAT into lobe 9 of the cerebellum failed to alleviate L-DOPA-induced dyskinesia. The present results illustrate the important role of cerebellar D_3 receptors in modulating D_1 receptor-mediated dyskinesia, implying that stimulation of cerebellar D_3 receptors can ameliorate tardive dyskinesia in the treatment of schizophrenia.

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Empathic deficits in a mouse model of autism spectrum disorder

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Abstract

Empathy, a high-level cognitive process, is believed to exist exclusively in humans; however, recent evidence has demonstrated empathy-like behaviors in rodents. The rodent models provide experimental platforms to investigate the neural basis for empathy and help elucidating the mechanisms underlying pathological conditions, such as autism spectrum disorders (ASDs). People with ASD have social impairments and often lack the ability to fully understand emotions in others, however, the neural substrates for the deficits remain largely unknown. In this study, we developed a fear observational system in which a mouse (observer) exhibits freezing behavior, a form of fear responses, through observation of another freezing mouse (demonstrator) that receives repetitive electrical foot shocks. We found that observers showed higher freezing responses when they had received a priming foot shock, suggesting that empathy-based behavior of mice is enhanced by a previous similar experience. Next, we investigated the relationship between neuronal populations that were active during the direct shock experience and observation of the other's shocks in neocortical regions involved in pain coding. To detect neural activities with cellular resolution, we used a biochemical technique called catFISH. The neuronal populations that were active during the priming shock were significantly overlapped with those engaged in the fear observation, indicating that neural networks involved in firsthand and vicarious experiences are shared at the single-cell level. We then examined empathetic behaviors in ASD model mice. The ASD model was produced by intraperitoneal injection of poly(I:C) into pregnant females. In ASD model mice, observational fear was not enhanced by a priming foot shook, and this behavioral deficit was rescued by sub-chronic injection