Tohoku Univ. Technology

PPARα agonists that improve cognitive function

New drug discovery seeds for psychiatric disorders such as schizophrenia

Overview

Recent large-scale genomic and postmortem brain analyses have indicated that synaptic dysgenesis may be involved in the pathogenesis of schizophrenia, but the detailed mechanisms remain unclear. Drugs mainly blocking dopamine D2 receptors have been used for the treatment of schizophrenia, but they are mainly used for symptomatic treatment and have insufficient effects on negative symptoms and cognitive dysfunction. Therefore, it is desirable to develop new drugs based on new molecular mechanisms.

The inventors have discovered that the decreased function of the *PPARA* gene, which encodes the nuclear receptor PPARα, is involved in the pathogenesis of schizophrenia [1]. Since PPARα is a transcription factor that can be activated by its ligand, they considered the possibility that activation of *PPARA* might lead to the improvement of schizophrenia, and found that fenofibrate, a PPARa agonist, is actually effective in improving synaptic function [2]. In this study, they found that pemafibrate, a PPARa agonist, helps to improve cognitive function at the same time as restoring spine density in mice. The invention could lead to the discovery of novel mechanisms for schizophrenia. Furthermore, since decreased spine density and cognitive decline are similar symptoms in other psychiatric disorders such as Alzheimer's, it could also be a therapeutic agent for these disorders.

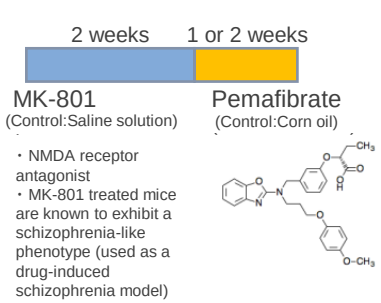
Product Application

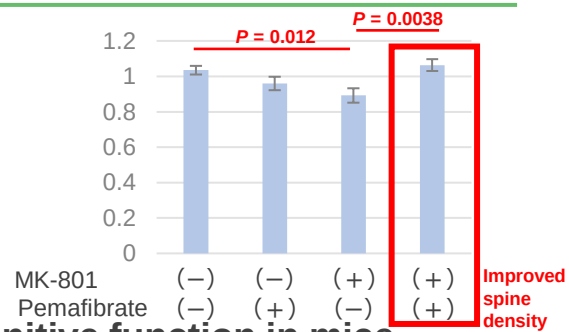
- ☐ Drugs for schizophrenia
- ☐ Drugs for Alzheimer's dementia
- ☐ Other therapeutic agents for psychiatric disorders

IP Data

IP No. : PCT/JP2023/023819
Inventor : MAEKAWA Motoko, OWADA Yuji
Admin No. : T22-091

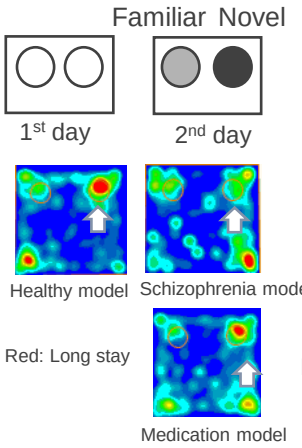
Spine density evaluation test in mice

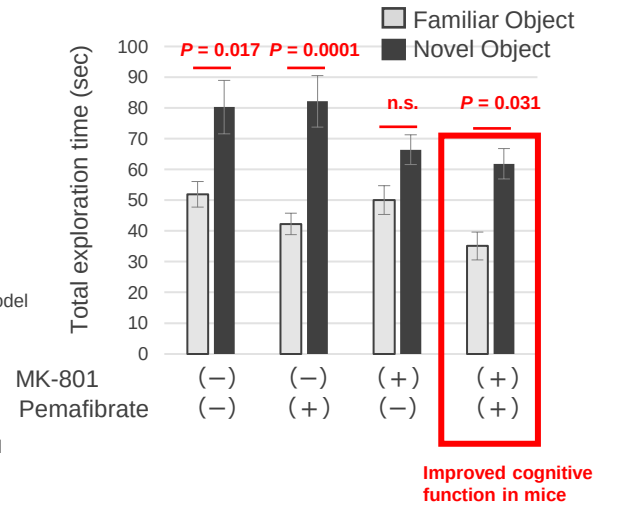




Assessment of cognitive function in mice

Novel object recognition test :
Studies of cognitive function in mice
Less time to approach novel objects in schizophrenia model animals (cognitive decline)





Related Works

[1] Maekawa M, et al. Transl Psychiatry. 2017; 7:e1229.
[2] Wada Y, et al. EBioMedicine, 2020; 62 : 103130.

Contact

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