EFFECTIVENESS OF SELECTIVE ADENOSINE A2A RECEPTOR ANTAGONIST ISTRADEFYLLINE ON THE MOTOR SYMPTOMS OF PARKINSON’S DISEASE CORRELATES WITH THE INTRACORTICAL INHIBITION REVEALED BY TRANSCRANIAL MAGNETIC STIMULATION

Murase N., Masuda Y., Takata M., Kuwata Y., Sainouchi M., Goto M., Ohtai R., Nakamura M.*
* Neurology department, National Hospital Organization Kyoto Medical Center, Kyoto city, Japan

Summary
(1) Istradefylline, a selective antagonist to the adenosine A2A receptor on the GABAergic medium spiny neurons in the striatum, reduces the duration of off-state in Parkinson’s disease (PD).
(2) Its effectiveness correlated with short-interval intracortical inhibition (SICI) studied by transcranial magnetic stimulation, which is a marker of cortical GABAergic inhibition in the M1.
(3) SICI may be an useful predictor of the effectiveness of istradefylline.

Introduction and Aim

PD patients show the hyperactivity of adenosine A2A receptor (Mishina et al., Plos One 2011, Calon F et al., Brain 2004), leading to LTD in the cortex.

Istradefylline is a selective antagonist to the adenosine A2A receptor in the striatum. It is used to reduce the duration of off-state in Parkinson’s disease (PD) and an insurance coverage drug in Japan.

We explored whether the effect of istradefylline in the striatum may relate with the cortical inhibitory system.

Patients and Methods

Subjects
Sixteen patients (12 females, mean age 72.0±7.6 yo) who gave IC participated in this study. (Two subjects were added to the group shown in the abstract.)

SICI study
Short Interval Intracortical Inhibition (SICI) studied by transcranial magnetic stimulation reflects GABAergic inhibition in M1.

Motor Evoked Potential (MEP) on APB of the non-dominant hand, on state

Statistical Analysis
Wilcoxon signed-rank test was used to access the effectiveness of istradefylline. Spearman’s rank-order correlation was to evaluate the correlation between SICI and effectiveness of istradefylline.

Results
1. UPDRS part III off-state was improved from 28.3±13.6 to 24.3±13.7.4 (p=0.002, n=16).
2. SICI before istradefylline administration correlated with the effect (UPDRS part III off-state Before -After) (r=-0.79, p<0.05).

Discussion
• In the PD model rat, abnormal synchronized activity in the substantia nigra, thalamus and motor cortex is reduced by applying GABA antagonist picrotoxin in the thalamus (Brazhnik E et al., J Neuroscience 2016). Our result suggests the GABAergic system in the basal ganglia also effect to the motor cortex through the abnormally synchronized network in PD.
• Limitation: TMS was only available on the unaffected side during on state.

Conclusion
SICI may be a sensitive index to predict the effectiveness of istradefylline.

COI disclosure information
Nagako Murase, MD, PhD
I have no financial relationships to disclose.