

## 安定した統合失調症患者においてリスペリドンおよびオランザピンの減量が認知機能に与える影響: オープンラベル無作為化比較試験

### Effects of Risperidone and Olanzapine Dose Reduction on Cognitive Function in Stable Patients with Schizophrenia: An Open-label, Randomized, Controlled, Pilot Study

竹内 啓善<sup>1,2</sup>、鈴木 健文<sup>1,3</sup>、GARY REMINGTON<sup>2,4</sup>、ROBERT BIES<sup>5,6,7</sup>、阿部 貴行<sup>8</sup>、  
ARIEL GRAFF-GUERRERO<sup>4,5,9</sup>、渡邊衡一郎<sup>10</sup>、三村 将<sup>1</sup>、内田 裕之<sup>1,5</sup>

1 慶應義塾大学医学部精神・神経科学教室、2 Schizophrenia Division, Complex Mental Illness Program, Centre for Addiction and Mental Health, Toronto, ON, Canada、3 井之頭病院

4 Campbell Family Mental Health Research Institute, Centre for Addiction and Mental Health, Toronto, ON, Canada、

5 Geriatric Mental Health Program, Centre for Addiction and Mental Health, Toronto, ON, Canada

6 Division of Clinical Pharmacology, Indiana University School of Medicine, Indianapolis, IN, USA

7 Indiana Clinical and Translational Sciences Institute, Indianapolis, IN, USA

8 慶應義塾大学医学部クリニカルリサーチセンター

9 Multimodal Imaging Group, Research Imaging Centre and Campbell Institute, Centre for Addiction and Mental Health, Toronto, ON, Canada、10 杏林大学医学部精神神経科学教室

[Schizophrenia Bulletin 2013. 39. 5. 993-998]

Background: Cognitive impairment is one of the core features in schizophrenia, which is closely related to functional impairment. Despite tremendous efforts to develop pro-cognitive drugs for schizophrenia, no cognitive enhancer is currently available. Beneficial effects of antipsychotic medication on cognition have remained controversial. In fact, both typical and atypical antipsychotics have been shown to induce cognitive impairment across various domains in healthy subjects, and higher dose of antipsychotics or excessive dopaminergic blockade impairs cognitive function in patients with schizophrenia, even treated with atypical antipsychotics. However, impact of dose reduction of atypical antipsychotics on cognitive function has not been investigated in stable patients with schizophrenia.

Methods: In this open-label, 28-week, randomized controlled trial, stable patients with schizophrenia treated with risperidone or olanzapine were randomly assigned to the reduction group (dose reduced by 50% in 4 weeks and then maintained) or maintenance group (dose kept constant). Assessments at baseline and week 28 included the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), Positive and Negative Syndrome Scale (PANSS), and Drug-Induced Extrapyramidal Symptoms Scale (DIEPSS).

Results: Sixty-one patients were enrolled; 2 of 31 (6.5%) and 5 of 30 (16.7%) patients prematurely withdrew from the study in the reduction and maintenance groups, respectively. While no significant differences in change in the PANSS total score were observed between the two groups, the reduction group showed significantly greater improvements in the RBANS and DIEPSS total scores compared to the maintenance group (mean±SD, +7.0±7.1 vs. -0.1±8.0, P<0.001; -0.9±1.7 vs. +0.1±1.2, P=0.010, respectively).

Conclusions: Dose reduction of risperidone or olanzapine by half could improve cognitive function without significantly increasing the risk of worsening in clinical psychopathology for stable patients with schizophrenia over six months.