"*Association between DNA Methylation of HTR2A Gene and Cognitive function in Schizophrenia demonstrated using multiplex families*"

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Schizophrenia, a heritable psychotic disorder, has a prevalence rate of 1% of the worldwide population and in Malaysia, the number of patients diagnosed with this disorder increased annually. Besides positive and negative symptoms, the patients usually being characterized with cognitive dysfunctions. In addition, aberrant alteration of DNA methylation at gene promoter as well exon-I regions in schizophrenia patients have been demonstrated in several studies. Gene expression studies demonstrated that *HTR2A* expression was reduced in schizophrenia patients. This study was designed to identify the methylation status of *HTR2A* exon-I in Malaysian schizophrenia patient's peripheral blood and their affected family member. This study included 13 schizophrenia families and 14 healthy control families, each with two family members. For the schizophrenia families, both of them were first-degree family members diagnosed with schizophrenia To analyze the cognitive performance of the participants, each of them was needed to complete Trail Making Test (TMT) part A and B. The genomic DNA extracted from the peripheral blood was chemically treated with bisulfite to convert the unmethylated cytosine to uracil. Methylation-specific PCR (MSP) was carried out to identify the methylation status *HTR2A* exon-I at Chr13: 46896918. The results proved that schizophrenia patients performed poorer in TMT-A and B than healthy controls. No significant difference was observed in the methylation status of *HTR2A* exon-I. The other CpG sites within the amplified sequence of *HTR2A* was unmethylated in both groups. In conclusion, our study suggested that the methylation profiles on the studied CpG site of *HTR2A* exon-1 may not associate with schizophrenia psychopathology and cognitive impairment. Inheritance of the altered methylation was observed within the majority of schizophrenia families. Our findings warrant further study involving the association of methylation of other genes such as *AKT1* with its gene expression as well as their correlation with cognitive performance in schizophrenia patients.

- *Funded by Toray Science Foundation, Japan*

Presented at the MTSF Grant Research Symposium held on 26 November 2019.