DNA methylation of MAOA and MAOB in postmortem brains of subjects with schizophrenia

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Research question and background

DNA methylation is an important epigenetic modification on gene expression. Extensive methylation of CpG islands has been associated with transcriptional inactivation of selected imprinted genes and genes on the inactive X chromosome of females. MAOA and MAOB are encoded by separate genes on the X chromosome, and they exhibit distinct differences in substrate selectivity. MAOA shows a preference for serotonin, norepinephrine and epinephrine as substrates, whereas MAOB shows a preference for phenylethylamine. Both isoforms break down dopamine. We focused on DNA methylation of the promoter regions of MAOA and MAOB genes from postmortem brains of subjects with schizophrenia.

Methods and tissues used

We used postmortem frozen brain tissues from prefrontal cortex (PFC), hippocampus, occipital cortex and nucleus accumbens (NAc), from six subjects with schizophrenia from the Postmortem Brain Bank of Fukushima for Psychiatric Research, and seven normal subjects from the brain bank of The Netherlands. Schizophrenia was diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders fourth edition (DSM-IV). We determined the levels of DNA methylation using genomic DNA samples purified from the four brain areas, by a bisulfite sequencing method.

Results and conclusion

Although very few methylated CpGs of the MAOA and MAOB genes were detected in male samples, various DNA methylation patterns were present in female samples, and some differences were found in such patterns between normal subjects and subjects with schizophrenia. In the PFC, the average level of methylation of both genes was significantly higher in subjects with schizophrenia than in normal subjects. The content of highly methylated alleles of the MAOA gene in the NAc was significantly associated with schizophrenia, with similar results obtained for the MAOB gene in both the NAc and PFC. Some CpG sites showed higher levels of methylation in schizophrenia than in normal subjects. Levels of methylation were quite high in NAc and PFC in female subjects with schizophrenia compared with those in female normal subjects. It was suggested that DNA methylation of MAOA and MAOB might be involved in the pathogenesis of schizophrenia.