

## Catechol-O-methyl transferase Val108/158Met genotype influences the striatum volume in healthy subjects: A voxel-based morphometry study at 3T MRI.

Keita Watanabe<sup>1</sup>, Shingo Kakeda<sup>1</sup>, Reiji Yoshimura<sup>2</sup>, Abe Osamu<sup>3</sup>, Ide Satoru<sup>1</sup>, Rieko Watanabe<sup>1</sup>, Asuka Katsuki<sup>2</sup>, Wakako Umene-Nakano<sup>2</sup>, Jun Nakamura<sup>2</sup>, and Yukunori Korogi<sup>1</sup>

<sup>1</sup>Radiology, University of Occupational and Environmental Health, Fukuoka, Japan, Kitakyushu, Fukuoka, Japan, <sup>2</sup>Psychiatry, University of Occupational and Environmental Health, Fukuoka, Japan, Japan, <sup>3</sup>Nihon University School of Medicine, Tokyo, Japan

### PURPOSE

Catechol-O-methyltransferase (COMT) is a methylation enzyme engaged in the degradation of dopamine by catalyzing the transfer of a methyl group from S-adenosylmethionine. Although COMT appears to be concentrated especially in the prefrontal cortex (PFC) and medial temporal lobe, the recent studies using functional MRI showed that COMT impact on brain activation is not limited to the PFC and medial temporal lobe, but extending into the striatum in healthy subjects<sup>1</sup>. We investigated the relationship between the Val108/158Met COMT genotype and striatum volume.

### MATERIALS AND METHODS

Forty-eight healthy subjects were recruited via an interview conducted by the psychiatrist using the Structured Clinical Interview for DSM-IV, nonpatient edition. They were divided by the COMT genotype: 27 with Valine (Val)/Val, 18 with Val/Methionine (Met), 3 with Met/Met. The MR imaging data were obtained with all cases using 3D-SPGR (a three-dimensional fast spoiled gradient recalled acquisition with steady state) at 3T MRI. Image processing for VBM was conducted using SPM8 (Statistical Parametric Mapping 8). The DARTEL (Diffeomorphic Anatomical Registration Through Exponential Lie Algebra) toolbox was used in a high-dimensional normalization protocol. Effects of COMT genotype in relation to brain morphology were evaluated.

### RESULTS

The volume of the bilateral caudate head and body was significantly larger for the Val/Met than for the Val/Val individuals [right: false-discovery rate (FDR)-corrected  $p = 0.026$ , left: FDR-corrected  $p = 0.035$ ] (Fig.).

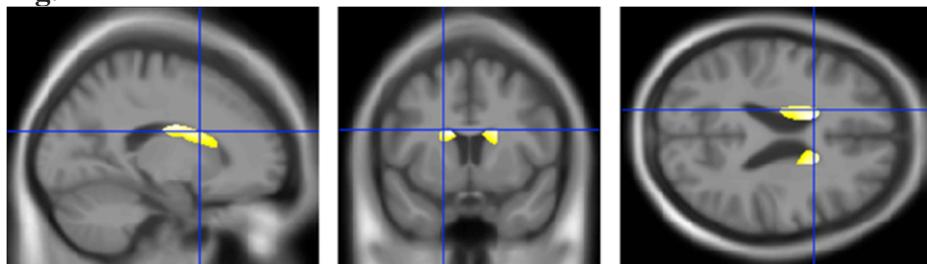
### DISCUSSION

Our data implies that genetic variation of COMT may affect the caudate volume. Previous study has reported that Met polymorphism (Val/Met and Met/Met genotype) have higher levels of dopamine in the frontal lobe<sup>2</sup>. In contrast, another report has demonstrated that Met polymorphism also has an opposite effect (lower levels of dopamine) on the caudate<sup>3-4</sup>. The caudate volume difference between genotypes in our study may be explained by the neurotrophic and/or neurotoxic effects of varying levels of dopamine caused by COMT activity.

### CONCLUSION

The COMT genotype affects the caudate volume, which may relate to the differences of dopamine level in the striatum.

### Fig.



### REFERENCES

- 1) Krugel, et al. PNAS 106(42): 17951-17956.
- 2) Matsumoto, et al. Neuropsychopharmacology 28(8): 1521-1530.
- 3) Drabant, et al. Arch. Gen. Psychiatry 63(12), 1396-1406.
- 4) Tunbridge, et al. Behave. Neurosci. 8, 119-140.

Larger caudate volume in the Val/Met individuals than the Val/Val individuals  
The SPM  $\{t\}$  is displayed in T1-weighted images. Significantly larger volumes of the bilateral caudate head and body are observed in the Val/Met individuals