# Taq1A polymorphism in the dopamine D2 receptor gene predicts brain metabolic response to aripiprazole in healthy male volunteers

Euitae Kim[a], Jun Soo Kwon[a,d], Yong-Wook Shin[a], Jae Sung Lee[b], Won Jun Kang[b], Hang Joon Jo[e], Jong-Min Lee[e], Kyung-Sang Yu[f], Do-Hyung Kang[a], Joo-Youn Cho[c], In-Jin Jang[c] and Sang-Goo Shin[c]

***Objective*** **The Taq1A polymorphism in the dopamine D2 receptor (DRD2) gene has been reported to be associated with the pharmacodynamics of antipsychotic drugs. We investigated the metabolic response of glucose in the brain to aripiprazole in relation to the DRD2 Taq1A polymorphism.**

***Methods*** **Twenty healthy male volunteers were recruited and were divided into two groups of 10 participants, according to their DRD2 genotypes (A1A1, $n=10$; A2A2, $n=10$). The volunteers received single oral doses of aripiprazole (10 mg) and a placebo, following a single-blind, placebo-controlled, randomized, two-way crossover study design. Brain glucose metabolism was assessed using positron emission tomography, scanned with $^{18}$F-fluorodeoxyglucose 12 h after the administration of the drug or placebo.**

***Results*** **In voxel-based analysis using SPM2, volunteers with the A2A2 genotype showed decreased metabolism in the right middle frontal gyrus, the left middle and inferior frontal gyrus, the right and left inferior temporal gyrus, and the right cingulate gyrus, and increased metabolism in the pons. In contrast, volunteers with the A1A1 genotype exhibited increased metabolism in the right caudate head, and no brain region showed decreased metabolism. In a region-of-interest analysis, significant interactions between drug and genotype were observed in the right medial orbitofrontal gyrus and the left caudate nucleus.**

***Conclusions*** **This suggests that DRD2 Taq1A polymorphism status may be associated with the clinical response to aripiprazole.** ***Pharmacogenetics and Genomics*** **18:91–97 © 2008 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Departments of [a]Psychiatry, [b]Nuclear Medicine, [c]Pharmacology and Clinical Pharmacology Unit, Seoul National University College of Medicine, [d]Clinical Cognitive Neuroscience Center, SNU-MRC, [e]Department of Biomedical Engineering, Hanyang University, Sungdong and [f]Department of Clinical Pharmacology and Clinical Trial Center, Seoul National University College of Medicine and Hospital, Seoul, Korea

Correspondence to Professor Jun Soo Kwon, MD, PhD, Department of Psychiatry, Seoul National University College of Medicine, 28 Yeongon-dong, Chongno-gu, Seoul 110-744, Korea
Tel: +82 2 2072 2972; fax: +82 2 747 9063;
e-mail: kwonjs@plaza.snu.ac.kr

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## Introduction

Pharmacogenetic studies have demonstrated associations between allelic variation and the effects of antipsychotic drugs [1], which raises the possibility for tailored medicine in the treatment of schizophrenia.

In recent years, pharmacogenetic approaches, combined with brain imaging, have offered the potential for understanding the clinical response to antipsychotic drugs. For example, polymorphisms in cytochrome P450 enzymes were reported to influence the delta power response to aripiprazole in quantitative electroencephalography [2]. Potkin *et al.* [3] used positron emission tomography (PET) to show that brain metabolic and clinical response to clozapine differed according to the dopamine D1 receptor (DRD1) genotype.

Aripiprazole has been the focus of much clinical attention, because of its unique receptor profile as a dopamine partial agonist. It has been demonstrated to be safe, effective, and well tolerated for the treatment of positive and negative symptoms in patients with schizophrenia and schizoaffective disorder [4,5]. Interindividual variations in clinical responses to aripiprazole, however, have been reported. Several reports demonstrated the worsening of psychotic symptoms in patients taking aripiprazole [6–9], but some patients showed symptomatic improvement with adverse effects such as extrapyramidal symptoms, even at low doses [6]. The variation in clinical response to aripiprazole gives pause to the clinicians prescribing it, but there are as yet no criteria by which to predict the response. Thus, further research is needed with regard to interindividual variability in drug responses and pharmacogenetic factors.

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Aripiprazole has a high affinity for the dopamine D2 receptor (DRD2), which raises the possibility that polymorphisms in the DRD2 gene may exert some influence on the pharmacodynamics of aripiprazole. Indeed, although the association between a Taq1A polymorphism in the DRD2 gene and variations in antipsychotic response has not been universally replicated, the DRD2 Taq1A polymorphism has been reported to affect the clinical response to antipsychotic drugs with high affinity for DRD2. Specifically, patients homozygous for the wild-type allele (A2A2) showed poorer clinical responses to haloperidol, compared with heterozygous patients (A1A2) [10]. Moreover, nemonapride, a selective dopamine antagonist, also exhibited more favorable therapeutic effects in schizophrenic patients with the A1 allele [11]. Given these results, the response to aripiprazole may differ according to the DRD2 Taq1A polymorphism.

We determined whether the DRD2 Taq1A polymorphism affects the pharmacodynamics of aripiprazole in healthy male volunteers, using brain $^{18}$F-fluorodeoxyglucose (FDG) uptake as a pharmacodynamic biomarker.

## Methods

### Volunteers

With approval from the Institutional Review Board of Seoul National University Hospital, Seoul, Korea, 20 right-handed, healthy, male volunteers participated in this study. After complete description of the study to the volunteers, written informed consent was obtained. The volunteers came from a group of 162 participants who had consented to the use of their genetic information before this study. Screening tests included a complete blood count, blood electrolyte analysis, urine analysis, electrocardiography, and a psychiatric interview. Volunteers with medical and/or psychiatric disease were excluded.

The 20 volunteers were divided into two groups of 10 participants, according to their DRD2 genotype (A1A1, $n = 10$; A2A2, $n = 10$). The mean age ($\pm$ SD) of the subjects was $23.4 \pm 1.2$ years (A1A1: $22.8 \pm 0.8$ years; A2A2: $24.1 \pm 1.3$ years). The mean body weight and height were $71.9 \pm 12.2$ kg (A1A1: $74.8 \pm 12.6$ kg; A2A2: $68.9 \pm 11.6$ kg) and $174.3 \pm 5.6$ cm (A1A1: $174.9 \pm 3.5$ cm; A2A2: $173.7 \pm 7.3$ cm), respectively. All the volunteers in the study had been drug-free for at least 1 month and consumed neither alcohol nor caffeine for at least 2 days before the administration of aripiprazole and placebo.

### Study design

The study was conducted according to a single-blind, placebo-controlled, randomized, two-way crossover design (Fig. 1).

The volunteers stayed overnight in the Clinical Trial Center, Seoul National University Hospital before PET scanning and received single oral doses of aripiprazole (10 mg) or placebo at 20 : 00 h. PET scans were obtained 12 h after drug administration. At least 2 weeks elapsed between aripiprazole and placebo administration.

Blood samples for the measurement of aripiprazole and its metabolite (OPC-14857) were obtained just before and 12 h after the administration of aripiprazole and placebo.

To ensure a standard mental status during the period of FDG uptake, the volunteers were engaged in a continuous performance task (CPT). Specifically, red and blue triangles and squares were presented one at a time on a visual display unit, and the volunteer was instructed to press a button as quickly as possible whenever a red square was presented consecutively after a red triangle.

### DRD2 Taq1A genotyping

Genomic DNA was extracted from the peripheral whole blood of each volunteer, using a Qiagen DNA extraction kit (Qiagen, Hilden, Germany), according to the manufacturer's instructions.

The presence of the A1 and A2 allele was evaluated via polymerase chain reaction (PCR) and single base extension, using SNaPshot analysis. The following primers were used for PCR amplification: 5′-GCTGGC CAAGTTGTCTAAAT-3′ (forward) and 5′-TGGAGCTG TGAACTGGACT-3′ (reverse). For SNaPshot analysis, the PCR products were purified using exonuclease I and shrimp alkaline phosphatase (USB, Cleveland, Ohio, USA) and then mixed with AmpliTaq DNA polymerase, four fluorescently labeled dideoxynucleotides, each of the primers for single base extension, and the reaction buffer from an ABI PRISM SNaPshot Multiplex Kit

**Fig. 1**

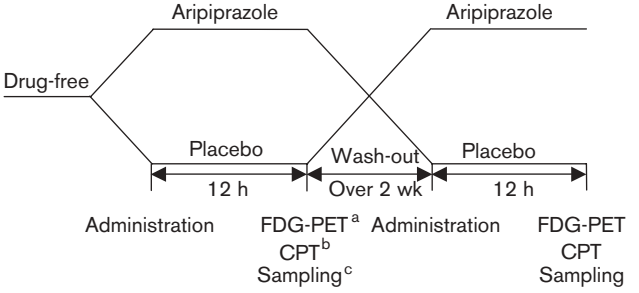



Diagram for study protocol in each genotype group. (a) Positron emission tomography scanned with $^{18}$F-Fluorodeoxyglucose. (b) Continuous performance task. (c) Blood sampling for the measurement of aripiprazole and it metabolite (OPC-14857).

(Applied Biosystems, Foster City, California, USA), according to the manufacturer's protocols. The primer used for single base extension was 5′-CACAGCCATCCT CAAAGTGCTGGTC-3′ for the Taq1A polymorphism. This primer was extended over 25 cycles of 96°C for 10 s, 50°C for 5 s, and 60°C for 30 s. The amplicons were then analyzed using an ABI PRISM 3700 Automated Sequencer (Applied Biosystems). DNA sequences proximal to the polymorphic sites were verified via direct sequencing.

### Positron emission topography scanning procedure and image analysis

All volunteers underwent repeated FDG-PET scans 12 h after administration of aripiprazole and placebo using an ECAT EXACT 47 scanner (Siemens-CTI, Knoxville, Tennessee, USA). The obtained data were reconstructed in a $128 \times 128 \times 47$ matrix with a pixel size of $2.1 \times 2.1 \times 3.4$ mm by means of a filtered back-projection algorithm employing a Shepp-Logan filter, with a cut-off frequency of 0.3 cycles/pixel.

Spatial preprocessing and statistical analysis were performed using the SPM2 software (Institute of Neurology, University College London, UK). All reconstructed images were spatially normalized into the MNI (Montreal Neurological Institute, McGill University, Canada) standard template to remove the intersubject anatomical variability. An affine transformation was performed, and the subtle transformed image and the template were removed using the nonlinear registration method, with the weighted sum of the predefined smooth basis functions used in a discrete cosine transformation. Spatially normalized images were smoothed by convolution with an isotropic Gaussian kernel, with 16 mm full width, at half-maximum, to increase the signal-to-noise ratio and accommodate variations in subtle anatomical structures. Variation between scans in mean global image intensity was removed by proportional scaling, using SPM2.

Mean intensities in the frontal lobe (inferior, middle and superior frontal gyrus, insula, precentral gyrus, lateral and medial orbitofrontal gyrus, medial frontal gyrus), temporal lobe (amygdala, hippocampal formation, parahippocampal gyrus, inferior, middle and superior temporal gyrus), caudate nucleus, and cingulate gyrus, where the metabolic activity differed according to the genotype in the voxel-based analysis, were quantified to test the interaction between drug and genotype by averaging regional intensities, which were weighted using the probabilistic maps of these regions [12,13]. Probability-weighted mean FDG uptake for each region was calculated using the following equation, $\Sigma(C_i \cdot P_i)/\Sigma P_i$, in which $C_i$ represents for the value of $i$th voxel in the spatially normalized PET image, and $P_i$ the probability value of $i$th voxel in the probabilistic maps predefined in the same standard stereotaxic space.

### Statistical analysis

In voxel-based analysis, the post-aripiprazole image was aligned with the post-placebo image as a control. Significant changes in regional cerebral glucose metabolism after aripiprazole administration were estimated using a paired $t$-test at every voxel. The threshold of statistical significance was defined as a $P$ value below 0.001 (uncorrected, one-tailed) and contiguous voxels above 150.

A method based on Gaussian random field theory is frequently used to perform to correct multiple comparisons. An alternative method using $P$ value and contiguous number of voxels can be employed as seen in the present study. This method is more sensitive to detect intensity change than the criteria after correction based on Gausian random field theory.

In our separate analysis using SPM2 based on the genotype, we could observe the difference in frontal metabolic response to aripiprazole according to the genotype even after the correction for multiple comparisons. Nonetheless, we defined the threshold of statistical significance as a $P$ value below 0.001 (uncorrected, one-tailed) and contiguous voxels above 150, because voxel-based analysis carries a meaning of screening for region-of-interest (ROI) analysis to assess an interaction between drug and genotype.

In the ROI analysis, SAS GLM procedure was employed for repeated measures analyses of a between-subjects by within-subjects interaction of genotype by drug.

CPT parameters were also analyzed using SAS GLM procedure.

## Results

The mean plasma levels of aripiprazole and its metabolite (OPC-14857) were $34.2 \pm 6.5$ ng/ml (A1A1: $34.2 \pm 7.0$ ng/ml; A2A2: $34.2 \pm 6.4$ ng/ml) and $2.3 \pm 1.2$ ng/ml (A1A1: $2.3 \pm 1.0$ ng/ml; A2A2: $2.4 \pm 1.4$ ng/ml), respectively. The plasma levels were not different between the genotypes (aripiprazole: $t = 0.007$, d.f. = 18, $P = 0.995$; OPC-14857: $t = 0.321$, d.f. = 18, $P = 0.752$).

CPT parameters analyzed included reaction time (RT), standard deviation of RT (SD_RT), and number of false response (FR). No significant differences were noted between the groups in the CPT parameters after the administration of placebo (RT: $t = -0.331$, d.f. = 18, $P = 0.745$; SD_RT: $t = 0.246$, d.f. = 18, $P = 0.809$; FR: $t = -0.179$, d.f. = 18, $P = 0.860$). After the administration of aripiprazole, SD_RT and FR were increased (RT: F = 0.691, d.f. = 1, $P = 0.417$; SD_RT: F = 7.209, d.f. = 1, $P = 0.015$; FR: F = 9.598, d.f. = 1, $P = 0.006$), but the interaction between genotype and drug was not observed

(RT: F = 0.261, d.f. = 1, $P = 0.616$; SD_RT: F = 1.285, d.f. = 1, $P = 0.272$; FR: F = 1.627, d.f. = 1, $P = 0.218$).

### Aripiprazole changed $^{18}$F-fluorodeoxyglucose uptake in the brain

In a pooled analysis with the A1A1 and A2A2 genotypes, there were extensive changes in FDG uptake after the administration of aripiprazole compared with the placebo (Table 1, Fig. 2). Aripiprazole decreased FDG uptake in the right middle and medial frontal gyrus, the left middle temporal gyrus, and the right cingulate gyrus, and increased FDG uptake in the left superior temporal gyrus, and the pons ($P < 0.001$, uncorrected, voxel > 150). These changes remained statistically significant after correction for multiple comparisons, based on the theory of random Gaussian fields ($P < 0.05$, corrected, voxel > 150).

### Effects of DRD2 Taq1A genotype

In voxel-based analysis, FDG uptake after the administration of aripiprazole differed according to the DRD2 Taq1A genotype (Table 2, Fig. 2). Volunteers with the A2A2 genotype exhibited a significant reduction in FDG uptake in the right middle frontal gyrus, the left middle and inferior frontal gyrus, the right and left inferior temporal gyrus, and the right cingulate gyrus, but these findings were not observed in volunteers with the A1A1 genotype. Increased FDG uptake was observed in the right caudate head of volunteers with the A1A1 genotype, and in the pons of volunteers with the A2A2 genotype.

Considering the plasma level of aripiprazole and its metabolite as a covariate, ROI analysis was conducted to evaluate the interaction between drug and genotype. The frontal lobe (inferior, middle, and superior frontal gyrus, insula, precentral gyrus, lateral and medial orbitofrontal gyrus, medial frontal gyrus), temporal lobe (amygdala, hippocampal formation, parahippocampal gyrus, inferior, middle, and superior temporal gyrus), caudate nucleus, cingulate gyrus, and pons, where the voxel-based analysis raised the possibility that the interaction could be observed, were chosen for ROI analysis. Significant interaction between drug and genotype was observed in the right medial orbitofrontal gyrus (F = 4.834, d.f. = 1, $P = 0.044$) (Fig. 3a) and the left caudate nucleus (F = 5.867, d.f. = 1, $P = 0.029$) (Fig. 3b).

The mean intensity of the post-placebo in the right medial orbitofrontal gyrus was significantly different by the DRD2 Taq1A genotype (F = 8.350, d.f. = 1, $P = 0.010$), but that of the post-aripiprazole was not (F = 0.810, d.f. = 1, $P = 0.381$). The mean intensities of the post-placebo and the post-aripiprazole in the left caudate nucleus were not different according to the DRD2 Taq1A genotypes (placebo: F = 1.747, d.f. = 1, $P = 0.204$; aripiprazole: F = 0.022, d.f. = 1, $P = 0.883$).

## Discussion

Pooled analysis revealed that aripiprazole reduced metabolic activity in the frontal lobe. This result is consistent with the findings of previous studies regarding typical antipsychotic drugs [14–17]. Atypical antipsychotic drugs such as olanzapine, risperidone, and clozapine have also been reported to induce metabolic decreases in the frontal lobe [18–20]. A separate analysis found that metabolic change in the frontal lobe differed depending on the DRD2 Taq1A genotype. Volunteers with the A2A2 genotype showed a frontal metabolic decrease that was similar to that seen in the pooled analysis, but volunteers with the A1A1 genotype did not. As the A2 allele is more frequent in the population [21], previous results that are consistent with the pooled analysis results may primarily reflect brain metabolic changes in volunteers with the A2 allele.

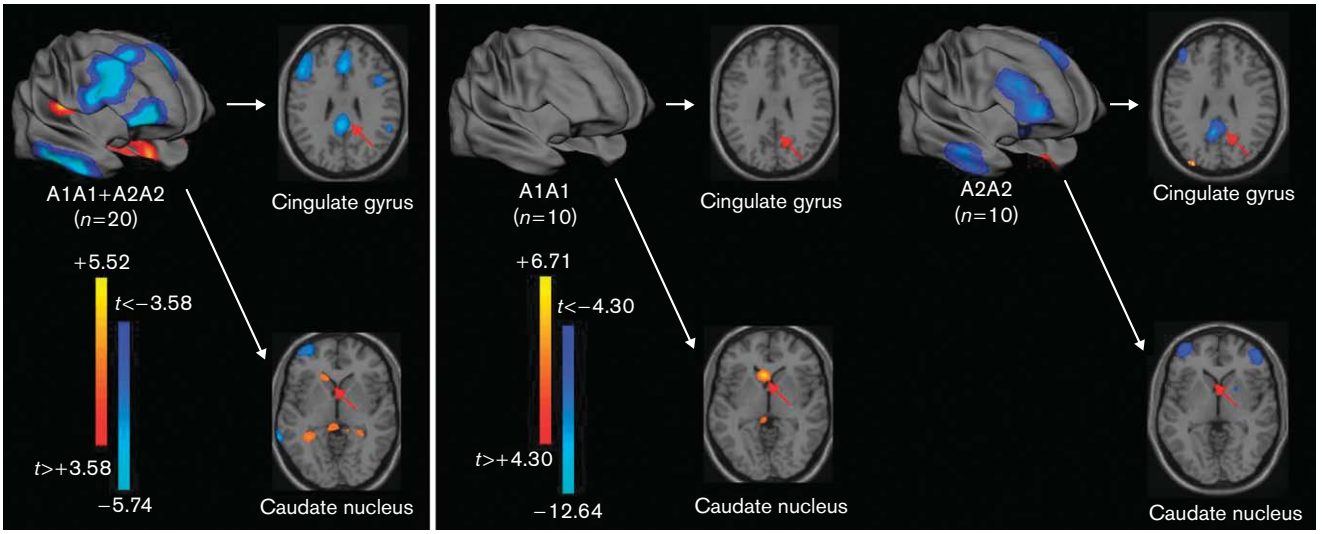
Changes in frontal activity, expressed in terms of glucose metabolic rate, after the administration of antipsychotic drugs have been associated with the effects of antipsychotic drugs. Bartlett *et al.* [22] reported that haloperidol challenge caused widespread metabolic decreases in patients without symptomatic improvement, but not in patients with symptomatic improvement. It was also reported that risperidone reduced metabolic activity in the frontal lobe, and that decreased activity in the medial frontal cortex correlated with improvement of positive symptoms [23]. These results, although somewhat contradictory, suggest that decreases in frontal lobe metabolism by antipsychotic drugs may be related to

**Table 1 Change in FDG uptake after the administration of aripiprazole in pooled analysis**

| Region | MNI coordinate | | | Highest *Z* value | Cluster size (voxels) | Uncorrected *P* value | Corrected *P* value |
|---|---|---|---|---|---|---|---|
| | *x* | *y* | *z* | | | | |
| Decreased uptake | | | | | | | |
| Right middle frontal gyrus (BA10) | 48 | 54 | 0 | 4.17 | 1290 | <0.001 | 0.027 |
| Right medial frontal gyrus | 2 | 24 | 44 | 3.96 | 3359 | <0.001 | 0.027 |
| Right cingulate gyrus (BA31) | 2 | −44 | 36 | 3.87 | 526 | <0.001 | 0.028 |
| Left middle temporal gyrus (BA21) | −62 | −40 | −14 | 4.32 | 495 | <0.001 | 0.027 |
| Increased uptake | | | | | | | |
| Pons | −12 | −22 | −36 | 4.22 | 5327 | <0.001 | 0.041 |
| Left superior temporal gyrus | −60 | 10 | −16 | 4.12 | 217 | <0.001 | 0.041 |

BA, Broadmann area; FDG, $^{18}$F-fluorodeoxyglucose; MNI, Montreal Neurological Institute.

**Fig. 2**




Brain metabolic changes after administration of aripiprazole compared with placebo. Color bar shows *t* value. Red colors indicate areas that have significantly increased metabolism after administration of aripiprazole compared with placebo whereas blue colors indicate areas that have significantly decreased metabolism. The threshold of statistical significance was defined as a *P*-value below 0.001 (uncorrected, one-tailed) and contiguous voxels above 150. Left column shows voxels with significant metabolic change in pooled analysis with the A1A1 and A2A2 genotypes. Middle and right columns show voxels with significant metabolic change in separate analysis, based on the DRD2 Taq1A genotype. Two cross-sectional plates in each column are including two notable areas indicated by red arrows (cingulate gyrus and caudate nucleus).

**Table 2 Change in FDG uptake after the administration of aripiprazole according to the DRD2 Taq1A genotype**

| Region | MNI coordinate | | | Highest *Z* value | Cluster size (voxels) | Uncorrected *P* value | Corrected *P* value |
|---|---|---|---|---|---|---|---|
| | *x* | *y* | *z* | | | | |
| (a) A1A1 genotype | | | | | | | |
| Decreased uptake | | | | | | | |
| None | | | | | | | |
| Increased uptake | | | | | | | |
| Right caudate head | 7 | 18 | 6 | 3.94 | 363 | <0.001 | 0.435 |
| (b) A2A2 genotype | | | | | | | |
| Decreased uptake | | | | | | | |
| Right middle frontal gyrus (BA11) | 34 | 36 | −24 | 4.88 | 432 | <0.001 | 0.010 |
| Right middle frontal gyrus (BA10) | 46 | 58 | 0 | 4.04 | 742 | <0.001 | 0.029 |
| Right inferior temporal gyrus (BA21) | 58 | −6 | −20 | 3.63 | 244 | <0.001 | 0.052 |
| Right cingulate gyrus (BA23) | 6 | −52 | 26 | 5.06 | 615 | <0.001 | 0.010 |
| Left middle frontal gyrus (BA11) | −28 | 40 | −22 | 3.85 | 336 | <0.001 | 0.040 |
| Left inferior frontal gyrus (BA10) | −46 | 50 | 2 | 4.49 | 537 | <0.001 | 0.015 |
| Left inferior temporal gyrus (BA20) | −60 | −40 | −24 | 4.20 | 172 | <0.001 | 0.022 |
| Increased uptake | | | | | | | |
| Pons | −12 | −24 | −36 | 3.93 | 610 | <0.001 | 0.172 |

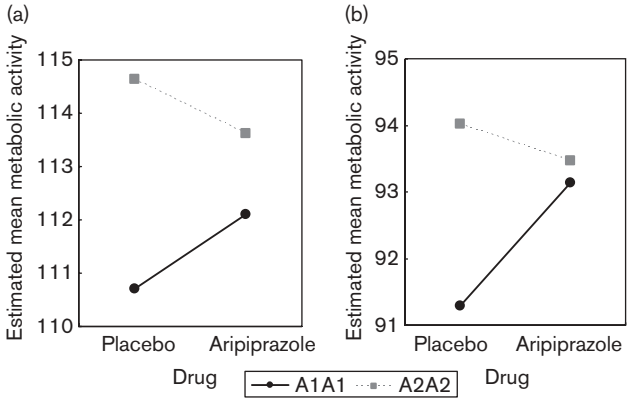
BA, Broadmann area; FDG, $^{18}$F-fluorodeoxyglucose.

their effects, though it is unclear whether the effects are positive or negative.

From this point of view, the DRD2 Taq1A polymorphism, which affected the frontal metabolic response to aripiprazole, could influence the clinical response in patients treated with aripiprazole. Several studies have demonstrated that symptomatic improvement after treatment with antipsychotic drugs, such as haloperidol and nemonapride, was associated with the DRD2 Taq1A genotype [1,10,11]. This study did not include patients with schizophrenia, and could not evaluate therapeutic response. These limitations warrant further pharmacogenetic studies regarding the relationship between the DRD2 Taq1A genotype and the clinical response to aripiprazole in patients with schizophrenia.

In contrast to volunteers with the A2A2 genotype, voxel-based analysis revealed that volunteers with the A1A1 genotype exhibited metabolic increase in the caudate head. In ROI analysis of the left caudate nucleus, the changes in intensity after the aripiprazole administration

**Fig. 3**




Estimated mean metabolic activity in the right medial orbitofrontal gyrus (a) and the left caudate nucleus (b). The activity is estimated when global mean activity in whole gray matter is 100. Interactions between genotype and drug were observed (a: F=4.834, d.f.=1, $P$=0.044; b F=5.867, d.f.=1, $P$=0.029).

were also significantly different according to the DRD2 Taq1A genotype.

In treatment with antipsychotic drugs, metabolic increases in the basal ganglia, including the putamen and caudate nucleus, appear to be related to the extrapyramidal symptoms induced by these drugs. It has been reported that typical antipsychotic drugs, which induce extrapyramidal symptoms more frequently than atypical antipsychotic drugs, increased metabolic activity in the basal ganglia [15–17]. In addition, patients with increased metabolism in the dorsal putamen showed higher scores in the Abnormal Involuntary Movement Scale, and clinical diagnosis of tardive dyskinesia showed a significant positive correlation with the metabolic rate in the caudate nucleus [24]. Such previous results raise the possibility that volunteers with the A1A1 genotype could be more vulnerable to extrapyramidal symptoms in treatment with aripiprazole than volunteers with the A2A2 genotype.

As seen in Fig. 3, frontal metabolic activity after the administration of placebo was lower in the volunteers with the A1A1 genotype than the volunteers with the A2A2 genotype. This is consistent with the finding of previous PET study [25]. The metabolic difference at baseline may result from the difference in dopaminergic activity depending on the DRD2 Taq1A genotype. As brain regional energy metabolism reflects primarily metabolic activity of nerve terminals within the region [26,27], the volunteers with the A1A1 genotype, expressing lower density of DRD2 [21], may exhibit reduced metabolic activity at baseline.

The Taq1A polymorphism resides in non-coding region of DRD2 gene, but recent report has identified that the Taq1A polymorphism lies within a novel kinase gene, named ankyrin repeat and kinase domain containing 1 (ANKK1) and causes an amino acid substitution within the 11th ankyrin repeat of ANKK1, which, although unlikely to affect structural integrity, may influence substrate-binding specificity [28]. The exact function of ANKK1 gene and its association with the DRD2 gene remains to be answered. At the present, we cannot conclude whether the effect of the Taq1A polymorphism on the metabolic response to aripiprazole is the direct functional effects of the Taq1A polymorphism acting through the amino acid substitution of the ANKK1 or the indirect effects of other single nucleotide polymorphism, which is in linkage disequilibrium with the Taq1A polymorphism.

A recent report gave some clues about the indirect effects of the Taq1A polymorphism, mediated by other polymorphism, on the brain metabolic response [29,30]. It has been reported that the Taq1A polymorphism is in linkage disequilibrium with C957T, a synonymous mutation in DRD2 gene. C957T affects messenger ribonucleic acid (mRNA) folding, leading to a decrease in mRNA stability and translation, and changes dopamine-induced upregulation of DRD2 expression.

This molecular mechanism may give rise to difference in the DRD2 density and baseline metabolism in brain according to the DRD2 Taq1A genotype, which could, in part, influence brain metabolic change after the administration of aripiprazole.

In summary, the DRD2 Taq1A polymorphism affected the brain metabolic response to aripiprazole in healthy male volunteers. This different metabolic response could influence the clinical response in patients with schizophrenia who are taking aripiprazole.

As we are predicting clinical responses in patients by examining metabolic responses in healthy volunteers, the prediction should be interpreted with caution. One reason is that, because of the pathophysiology of schizophrenia and long-term exposure to antipsychotic drugs, patients with schizophrenia are different in their brain metabolism and receptor status from healthy volunteers [31–33]. Another reason for caution is that our findings were observations made after a single administration of aripiprazole. Long-term treatment with aripiprazole could have a different effect on brain metabolism.

In addition, the association between the Taq1A polymorphism and the antipsychotic response has not been universally replicated. The inconsistency can result from genetic heterogeneity across different ethnic and racial population [34]. To confirm the present result, it should be replicated in other ethnic groups.

Nonetheless, this report is the first pharmacogenetic evaluations with aripiprazole using FDG-PET, and will help our understanding of the variability in clinical response to aripiprazole, in addition to guiding further clinical evaluations of this topic.

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Disclosures: none.

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