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# A polymorphism of serotonin 2A receptor (5-$HT_{2A}$R) influences delay discounting

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ABSTRACT

The present study investigated the association between a polymorphism of the serotonin 2A receptor (5-$HT_{2A}$R) gene and the form of impulsive choice known as delay discounting. Using a hypothetical situation, we asked Japanese participants to choose between receiving (or paying) a different amount of money immediately or with a specified delay (one week, two weeks, one month, six months, one year, five years, or 25 years), and estimated the parameters of intertemporal choice models (exponential, hyperbolic, hyperbolic with exponent, and quasi-hyperbolic). Regardless of the genotypes, the hyperbolic with exponent model, which always indicated minimum AICc (Akaike Information Criterion with small sample correction), fitted better the observed data than the other models. Future gains were discounted more steeply than future losses. Moreover, as expected, individuals with the AA genotype of the 5-$HT_{2A}$R A-1438G polymorphism discounted the future more steeply than did individuals with the GG genotype, although this effect was limited to only gains. The findings implied individual differences based on the A-1438G polymorphism in the modulation of serotonin in the reward valuation underlying delay discounting.



## 1. Introduction

Impulsivity is generally considered a dysfunctional trait and is associated with poor self-control (e.g., Baumeister, 2002), aggressive behavior (e.g., Barratt, 1994), substance dependence (e.g., Wills, Vaccaro, & McNamara, 1994), and psychiatric disorders (e.g., Moeller, Barratt, Dougherty, Schmitz, & Swann, 2001). Thus far, a wide array of studies on impulsive behavior has been conducted (see Bari & Robbins, 2013 for a review), particularly in terms of motor response inhibition (e.g., Horn, Dolan, Elliott, Deakin, & Woodruff, 2003) and impulsive choice (e.g., Winstanley, Theobald, Cardinal, & Robbins, 2006). Although impulsivity is a multidimensional construct, this study focuses on delay discounting—i.e., one's tendency to discount the value of rewards that are obtained at some later point in time. This delay discounting reveals people's preference for immediate, smaller gains over larger, delayed gains (e.g., $10 today vs. $20 after one year). Although individual differences in the delay discounting tendency have been documented, to our knowledge, the genetic underpinnings of such individual differences have not been intensively investigated. Thus, we targeted a polymorphism of the serotonin 2A receptor (5-$HT_{2A}$R) gene and examined its impact on delay discounting.

### 1.1. Delay discounting

Classical economic theory presupposes an exponential model that assumes an exponential decay of the subjective value of a reward along with the delay. The exponential discounting function is written as follows (e.g., Samuelson, 1937):

$$V(D) = \frac{V(0)}{\exp(kD)} \quad (1)$$

where V(D) is the subjective value of a reward (or payment) at delay D, and k is a free parameter that represents the discount rate. This function predicts that individuals have time-consistent preferences. Suppose that one prefers $10 today to $11 tomorrow. If this person has time-consistent preferences, he/she prefers $10 earned *x* days later to $11 earned $(x + 1)$ days later.

Nevertheless, empirical evidence suggests that delay discounting often exhibits time-inconsistent patterns and that the reduction in the subjective value of an outcome is much steeper in the early phase of delay and becomes more gradual as the delay gets longer (e.g., Ainslie, 1975; Mazur, 1987). For instance, people tend to prefer to receive $450 immediately rather than to receive $500 after one week, whereas they prefer to receive $500 after five years and one week rather than to receive $450 after five years. Although the length of the delay is identical in both cases (i.e., one week), people's preferences for the two options are

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reversed. It has been pointed out that a hyperbolic function better describe such time-inconsistent choice behavior (e.g., Kirby, 1997).

The equation is

$$V(D) = \frac{V(0)}{1 + kD} \quad (2)$$

where D and k represent delay and discount rate, respectively.

Moreover, more general forms of the hyperbolic equation have been suggested. For example, Rodriguez and Logue (1988) proposed an equation in which an exponent is added to the delay (see also Rachlin, 2006).

$$V(D) = \frac{V(0)}{1 + kD^S} \quad (3)$$

The exponent S, which is a power-function parameter, suggests individual differences in sensitivity of V (D) / V (0) to D. When S = 1, the equation is identical to the hyperbolic Eq. (2). On the other hand, when S is <1, the decrease of V (D) / V (0) over the course of the delay diminishes faster than it does in the (simple) hyperbolic model.

Such a time-inconsistent delay discounting pattern has also been expressed by an equation based on quasi-hyperbolic discounting (e.g., Laibson, 1997).

$$V(D) = \begin{cases} V(0) \text{ when } D = 0 \\ V(0)\beta\delta^D \text{ when } D>0 \end{cases} \quad (4)$$

When $\beta$ and $\delta$ are <1, the equation indicates that subjective value decreases more in the near term, whereas it decreases less in the long term. When $\beta = 1$, the equation is similar to the exponential Eq. (1). Thus, $\delta$ corresponds to an individual's discount rate, whereas $\beta$ suggests the degree to which an individual values present outcomes relative to future outcomes.

### 1.2. Serotonin and delay discounting

Previous research, including animal studies, has suggested that the serotonergic system regulates inhibitory control, so that a reduction in serotonin function is associated with impulsivity. Lower levels of serotonin increase delay discounting rates in rats (Mobini, Chiang, Ho, Bradshaw, & Szabadi, 2000) and humans (Schweighofer et al., 2008). Serotonin depletion also leads to a failure to wait for delayed but large reinforce in rats (e.g., Wogar, Bradshaw, & Szabadi, 1993). Moreover, using microdialysis, Winstanley, Theobald, Dalley, Cardinal, and Robbins (2006) showed that an increase in 5-HT efflux was found in the medial prefrontal cortex (mPFC) during delay discounting. Furthermore, Tanaka et al. (2007) found that activity of the ventral parts of the striatum was linked to steeper delay discounting of future gains in participants with low serotonin levels, whereas activity of the dorsal parts of the striatum was linked to less delay discounting in participants with high serotonin levels. Although the specific mechanisms through which the serotonergic system interacts with the activities of neural substrates (e.g., mPFC and striatum) are still unclear, the involvement of the serotonergic system in regulating impulsive behaviors has been established (Miyazaki, Miyazaki, & Doya, 2012).

The 5-$HT_{2A}$ receptor is one type of 5-HT receptors. Although it is widely distributed in the brain, it is concentrated in the cerebral cortex (Varnas, Halldin, & Hall, 2004). Associations between the 5-$HT_{2A}$R gene and substance abuse disorders have been reported (Cao et al., 2014). Moreover, 5-$HT_{2A}$R binding in the prefrontal cortex is associated with aggression in suicide subjects (Oquendo, Currier, & Mann, 2006), which implies a relationship between the 5-$HT_{2A}$R gene and impulsivity. Polymorphisms of the 5-$HT_{2A}$R gene are also associated with impulsivity. For example, focusing on one of the polymorphisms on this gene, A-1438G (rs6311), Preuss, Koller, Bondy, Bahlmann, and Soyka (2001) demonstrated an association between alcohol dependence with the AA genotype and impulsivity. In addition, by administering a go/no-go task to healthy participants, Nomura et al. (2006) showed that individuals with the AA genotype found it more difficult to withhold to-be-withheld stimuli and made more commission errors than did individuals with the GG genotype. This suggests greater difficulty for individuals with the AA genotype in motor response inhibition.

### 1.3. The present study

Although the associations between the A-1438G polymorphism in the 5-$HT_{2A}$R gene and impulsive behaviors have been suggested using subtypes of impulsivity measures, such as motor response inhibition (e.g., Nomura et al., 2006), no studies have directly examined the effect of this polymorphism on delay discounting. Although delay discounting is considered a type of impulsivity, it might be more regulated by overlapping but different neural mechanisms than other types of impulsivity (Brewer & Potenza, 2008). This study thus examined whether the A-1438G polymorphism in the 5-$HT_{2A}$R gene influences a particular type of impulsivity, delay discounting.

In this study, we examined the extent to which Japanese participants discounted future gains and losses, as it is known that people tend to discount future gains more than future losses—the sign effect (e.g., Frederick, Loewenstein, & O'donoghue, 2002). We then estimated parameters of exponential, hyperbolic, hyperbolic with exponent, and quasi-hyperbolic models for each group of the genotypes of A-1438G polymorphism in the 5-$HT_{2A}$R gene. We expected that individuals with the AA genotype would more heavily discount the future than G carriers.

## 2. Method

### 2.1. Participants

Two hundreds and twelve Japanese undergraduate students (112 females and 100 males, $M_{age} = 19.25$, $SD = 0.99$) at Kobe University participated in this study. They were recruited through a psychology subject pool in the university. This study was conducted as part of a half-day experiment, which included the administration of questionnaires on a wide range of topics, such as the self, emotion, cognition, and interpersonal behaviors. In addition, the session included behavioral game experiments. Participants were paid 4000 yen (about $40) plus some bonuses based on the results of the behavioral games. The study was reviewed and approved by the Experimental Research Ethics Committee at the Graduate School of Humanities at Kobe University.

### 2.2. Procedures

This study focused on a decision-making task that included hypothetical gains and losses. Participants were asked to make a series of 1120 hypothetical binary choices under the assumption that their choices involved real money. Each choice consisted of two alternatives: (a) receiving (or paying) a certain amount of money immediately or (b) receiving (or paying) the fixed amount of 100,000 yen (about $1000) after a certain period of delay. The immediate option (a) was always presented in the left column and the delayed option (b) was always presented in the right column. Participants were asked to choose whether they preferred option (a) or (b). In (a), the immediate options varied from 0 to 97,500 yen, with an increment of 2500 yen (i.e., in 2.5% increments); thus, there were 40 variants. There were seven periods of delay: one week, two weeks, one month, six months, one year, five years, and 25 years. A single page of this task included 40 choices: the 40 immediate options were compared with the fixed amount of 100,000 yen at one of the seven periods of delay. For instance, in the case of gain after a one-week delay, participants were instructed as follows: "If you had to choose one of two alternatives, whether you receive the money indicated in the left column today or the money indicated in the right column after one week, which of the alternatives would you choose? For each of the cases numbered one to 40, please circle the amount of money you prefer." The order of the 40 immediate options (ascending vs. descending) was a within-participant factor. The domain of the choice (gain vs.

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