Salivary alpha-amylase levels and temporal discounting for primary reward under a simulated life-threatening condition

Taiki Takahashi [1], Koki Ikeda [2], Toshikazu Hasegawa[2]

1. Department of Behavioral Science, Faculty of Letters, Hokkaido University, N.10, W.7, Kita-ku, Sapporo, 060-0810, Japan
2. Department of Cognitive and Behavioral Science, Graduate School of Arts and Sciences, University of Tokyo, 3-8-1 Komaba, Meguro, Tokyo, 153-8902, Japan

Correspondence to: Taiki Takahashi: taikitakahashi@gmail.com

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Abstract

OBJECTIVES: This study was aimed to examine the relationships between salivary alpha-amylase (sAA, a non-invasive biological marker of adrenergic activities) levels and hyperbolic discounting for primary reward under simulated life-threatening condition, which is of interest in psychoneuroendocrinology and neuroeconomics of visceral influences on behavior.

METHODS: We assessed degrees to which delayed primary reward (i.e., water) was discounted (hyperbolic discount rates) in 31 healthy male students. Participants' sAA were also assessed.

RESULTS: We observed a positive correlation between sAA and hyperbolic discounting for primary reward.

CONCLUSIONS: The result indicates that threat-induced visceral urge acutely prompts impulsivity in temporal discounting.

1.2. INTRODUCTION

Impulsivity is a core deficit in neuropsychiatric disorders such as attention-deficit-hyperactivity disorders (ADHD), psychopathy, and addiction (Arnsten and Li 2005, Cardinal 2006, Winstanley *et al.* 2006, Kirby *et al.* 1999, Ohmura *et al.* 2005, Monterosso *et al.* 2007). As such, neuropsychological functioning associated with impulsivity has attracted much attention. In this study, we operationalized impulsive behavior as a strong devaluation of delayed primary reward (i.e., water), leading to a preference of small immediate rewards over large delayed ones (delay discounting), following a standard behavioral paradigm in neurobiochemical and neuroeconomic studies of impulsivity (Cardinal 2006, Kirby *et al.* 1999, Ohmura *et al.* 2005).

Neuropharmacological investigations have demonstrated that monoamines (e.g., dopamine and serotonin) in the central nervous system and drug dependence-induced synaptic modifications in dopaminergic reward circuitry modulate delay discounting behavior (Cardinal 2006, Mobini *et al.* 2000). We have also previously reported that severity of nicotine addiction is positively associated with the degree to which smokers discount delayed monetary gains (but not losses) (Ohmura *et al.* 2005). We have also conducted neuroendocrinological studies on intertemporal choice and observed that chronic levels of cortisol (a stress hormone) (Takahashi 2004), testosterone (a male hormone) (Takahashi *et al.* 2006), salivary alpha-amylase levels (Takahashi *et al.* 2007) are related to discounting of delayed monetary gains in men. However, it is yet to be elucidated how acute

ORIGINAL ARTICLE

adrenergic activitations in the brain are associated with impulsivity and self-control in intertemporal choice, although behavioral economic studies proposed that acutely-induced visceral urges tend to make people experience a feeling of being "out of control" (Loewenstein 1996).

Recent progress in non-invasive measurement of neuroendocrine and neuroactive substances in saliva has made it possible to measure salivary alpha-amylase (sAA) levels, which may reflect (nor)adrenergic and SAM (sympathetic-adrenal-medullary) activities (van Stegeren *et al.* 2006, Yamaguchi *et al.* 2006, Takahashi *et al.* 2007a). It has been demonstrated that sAA elevation is one of the stress-response types which have pathways distinct from HPA (hypothalamic-pituitary-adrenal) axis (van Stegeren *et al.* 2006, Yamaguchi *et al.* 2006). It may now be important to examine the relationship between impulsivity and acute adrenergic/SAM activations in a more extensive manner.

In this study we therefore examined relationships between sAA levels and delay discounting for primary reward under a simulated life-threatening condition, in healthy male students, by utilizing well-established Kirby's MCQ (monetary choice questionnaire), with modification, for the assessment of subjects' discounting rates for water (Kirby *et al.* 1999).

2. METHOD

2.1. Participants and saliva collection

A total of 31 healthy male students (age: 21±3.4) participated in the present study. It should be noticed that, to avoid influences of chronic nicotine-induced neuroadaptation on discounting behavior, only non-smokers were included in the study. Further, subjects with physical or psychiatric illnesses were excluded. Each participant collected two saliva samples in the afternoon (14:00–18:00). The participants were asked to refrain from the consumption of alcohol beginning from the night before the samples were collected and, as far as possible, to obtain sufficient sleep. They were also instructed to maintain an interval of 6 h after brushing their teeth, at least 1 h after eating or drinking any fluid other than water, and 30 min after any strenuous exercise while collecting the samples of saliva. The detailed methodology of sAA measurement is denoted below. In order to induce visceral activation under a simulated life-threatening condition, subjects were required to read a hypothetical story regarding a traveler without having water for drinking who got lost in the vast desert under a strong sunlight. Participants were instructed to imagine as if the thirsty traveler in the story were themselves. After an exposure to the hypothetical life threat, participants also answered Kirby's questionnaire modified for the assessment of hyperbolic discount rate for water (explained below). This study was approved by the ethical committee on the use of human subjects at the Graduate School of Arts and Sciences, the University of Tokyo.

2.2. MATERIALS

2.2.1. Kirby's MCQ (monetary choice questionnaire) for primary reward

We adopted the same procedure for assessing subject's discount rates as previous neuroendocrinological and neuroimaging studies of intertemporal choice (Monterosso *et al.* 2007). Studies in neuropsychopharmacology, psychoneuroendocrinology, and behavioral neuroeconomics have repeatedly observed that human and animal subject's delay discounting is well described by the hyperbolic discount function (Cardinal 2006, Kirby *et al.* 1999):

$$V(D)=1/(1+kD) \qquad \text{(equation 1)}$$

where V(D) is a subjective value of delayed rewards at delay time D, and k (a hyperbolic discount rate) is a free parameter indicating subject's impulsivity in intertemporal choice (larger k values correspond to more rapid/steeper discounting; while smaller k values indicate self-control in intertemporal choice). In order to assess subject's discount rate k for water, as defined in equation 1, modified Kirby's MCQ (Kirby *et al.* 1999) was used. The modified Kirby's MCQ consists of 9 (=[the number of questions in the original MCQ for three different magnitudes=27]/3) questions relating to a choice between smaller immediate primary rewards and larger but delayed primary rewards (e.g. "Would you prefer 19mL of water now or 25 mL of water in 53 seconds?"). According to the standard analysis procedure of MCQ, established by Kirby and colleagues (Kirby *et al.* 1999), we calculated subjects' discounting rates (i.e. k) for primary reward. We then examined relationships between the hyperbolic discount rates of water and sAA levels.

2.2.2. Salivary alpha-amylase (sAA) assay

For measuring SAM system activity, we employed the same methodology as Yamaguchi *et al.*'s investigation into the relationships between sAA and driver's fatigue with a commercial hand-held monitor of sympathetic nervous system indicated as sAA levels (Yamaguchi *et al.* 2006). This monitor (cocoro meter, Nipro Co. Ltd, Japan), being sold for personal assessment of psychosocial stress levels, utilizes a reagent paper containing 2-chloro-4-nitrophenyl-4-O-beta-d-galactopyranosylmaltoside (Gal-G2-CNP), a substrate for amylase. When Gal-G2-CNP is hydrolyzed by amylase, the hydrolyzed product (CNP) changes emission wavelengths (reflectance) with time. The collecting paper was directly inserted into an oral cavity, and approximately 20–30 microL of saliva was collected from under the tongue within 10–30 s. Thus, the reflectance 30 s after the initial time was automatically measured by the optical device. A total of one minute was enough to measure the

salivary amylase activity. We have measured sAA levels twice in this manner and averaged sAA levels were defined as subject's resting sAA levels. Because sAA levels (measured with the monitor) over 61 kU/L is the maximal stress reaction level (too high sAA as resting levels), we have removed two subjects with sAA higher than 61 kU/L.

2.3. Data analysis and statistical procedure

Following Kirby's procedure (Kirby *et al.* 1999), discount rates were calculated as denoted above. We then conducted Spearman's rank correlation analysis between sAA and discount rates. Data are expressed in terms of Mean ± SEM. Significance level is set at 0.05 throughout.

3. RESULTS

Relationship between salivary alpha-amylase (sAA) level and discount rate

Pearson's correlation analysis showed a significant positive correlation between sAA, and the logged discount rates for primary reward (Spearman's rho = 0.378, p = 0.043). In other words, subjects with strong sAA activation under the simulated life-threatening condition were more impulsive in intertemporal choice. The average sAA level was 30.5± 0.8 kU/L.

4. DISCUSSION

To our knowledge, this study is the first to demonstrate a positive relationship between acute sAA activations and delay discounting of primary rewards. Our results suggest that subjects with acute strong SAM response (as indicated with sAA) are more impulsive in intertemporal choice on primary rewards. Recent findings suggest that enhanced sAA levels may be associated with hyper-activation of beta-adrenergic pathways (van Stegeren *et al.* 2006). Furthermore, we have previously observed that chronic sAA levels were inversely related to impulsive intertemporal choice (Takahashi *et al.* 2007). Therefore, it is speculated that acute ("phasic") and chronic ("tonic") activations of adrenergic systems in the brain may oppositely modulate impulsivity in temporal discounting. With respect to neuroeconomics, it has been proposed that people act against their self-interest in full knowledge of doing so, when visceral urges (e.g., thirst, fear, sexual desire, and hunger) influences their behavior (Loewenstein 1996). Future studies in neuroeconomics should employ other types of neuroendocrinological markers of such visceral factors.

We now discuss limitations of our present study. We employed only male subjects in the present study. Because it is possible there is a gender difference in the relationships between sAA and impulsivity in intertemporal choice, females' sAA-discount rate relationships must be examined.

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