The impacts of Val158Met in Catechol-*O*-methyltransferase (*COMT*) gene on moral permissibility and empathic concern

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ABSTRACT

Dopamine levels in the brain influence emotional experiences and empathic responses to others' misfortune. Inspired by roles of Catechol-O-methyltransferase (COMT) in dopamine degradation and the link between moral judgment and empathic responses, this study investigated to what extent the Val158Met polymorphism of *COMT* gene contributes to individual differences in moral permissibility and empathic dispositions. One thousand two hundred and seventy-two Chinese Han college students, who were differentiated with the *COMT* Val158Met (rs4680) polymorphism, rated permissibility of harm in moral dilemmas and scored their empathic dispositions with Interpersonal Reactivity Index. The results showed a significant association between *COMT* Val158Met and the moral permissibility of committing harm. Individuals with the Val/Val genotype, which is associated with lower levels of dopamine, endorsed impersonal harm as more impermissible than those with the Val/Met and Met/Met genotypes. Results also showed that individuals with the Val/Val genotype showed higher empathic concern for others' misfortune. The findings provide the first evidence for the link between *COMT* gene and the moral permissibility, highlighting the roles of dopamine in social cognition.

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1. Introduction

Utilitarian moral judgment refers to the evaluation or opinion that whether it is permissible to preserve a greater number of people's well-being by sacrificing fewer individuals' interests (Conway and Gawronski, 2013; Greene, Morelli, Lowenberg, Nystrom, and Cohen, 2008). Moral judgment is related to many aspects of our life such as strategic interactions among members who experienced interest conflict (Krebs, 2008) and socio-normative judgments (Prehn et al., 2008). Studies indicated that a conflict between deliberative cost-benefit analysis and emotional aversion guides the permissibility of moral judgment, in which the inclination for maximizing more individuals' benefits and the lower level of emotional aversion make people endorse committing harm as more permissible (Conway and Gawronski, 2013). These psychological findings implicated that the biological processes involved in emotional aversion and deliberative cost-benefit analysis possibly modulate the moral permissibility of utilitarian moral judgment. In this study, we tested the contribution of a genetic factor to individual differences in views of moral permissibility.

Views of the moral permissibility of committing harm strikingly varied among individuals. For instance, the permissibility is significantly associated with the levels of oxytocin (Scheele et al., 2014), testosterone (Chen, Decety, Huang, Chen, and Cheng, 2016; Montoya et al., 2013), and serotonin in the brain (Crockett, Clark, Hauser, and Robbins, 2010; A. A. Marsh et al., 2011), which partly attributes to these neuromodulators modulating the balance between emotional aversion and cost-benefit analysis of moral judgment. Dopamine may also be involved in moral judgment given its roles in harm aversion of moral decision making (Crockett et al., 2015) and the cost-benefit analysis of economic decision making (Dan and Howard, 2011; Phillips, Walton, and Jhou, 2007). Thus, in this study we investigated whether Catechol-*O*-methyltransferase gene, which modulates levels of dopamine in the brain, underpins the individual differences in moral permissibility.

The Catechol-*O*-methyltransferase (COMT) enzyme degrades dopamine in the prefrontal cortex (Weinshilboum, 1988). This enzyme is encoded by *COMT* gene. Within this gene, a common functional polymorphism in codon 158 (Val158Met), leading to an amino acid substitution of valine (Val) for methionine (Met), results in the Met/Met genotype showing 40% less enzymatic activity than that of the Val/Val genotype (Bilder, Volavka, Lachman, and Grace, 2004; Chen et al.,

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2004; Lachman et al., 1996). Thus, the Val allele is expected to associate with lower levels of dopamine than the Met homozygote.

Recent studies indicated that *COMT* Val158Met is associated with emotional processes. For instance, this polymorphism modulates individual's emotional regulation in decision making. Subjects with the Val/Val genotype, compared with the Met/Met genotype, are more able to use their emotional experiences to guide choices in the Iowa Gambling Task (Malloy-Diniz et al., 2013; van den Bos, Homberg, Gijsbers, den Heijer, and Cuppen, 2009), which suggests that the Val/Val genotype could reduce individuals' emotional aversion in loss and enhance the skills of guiding their emotion in decision making. Moreover, a meta-analysis of 27 studies indicated that individuals with the Val/Val genotype show higher levels of harm avoidance than those with the Met/Met genotype (Lee and Prescott, 2014). This result suggests that, for individuals with the Val/Val genotype, the harm avoidance possibly leads to greater negative emotional responses such as fear and aversion to harm (Baeken et al., 2014; Schuerbeek, Baeken, Luypaert, Raedt, and Mey, 2014; Yoshino, Kimura, Yoshida, Takahashi, and Nomura, 2005; Zhang et al., 2013). Therefore, this study examine to what extent *COMT* Val158Met underpins individual difference in utilitarian moral judgment (Greene, Nystrom, Engell, Darley, and Cohen, 2004; Greene, Sommerville, Nystrom, Darley, and Cohen, 2001). Given that individuals with the Val/Val genotype show higher levels of harm avoidance and effectively guide on emotional aversion to loss in decision making, we predict that those with the Val/Val genotype report lower permissibility of utilitarian moral judgment.

Previous studies have evidenced negative correlations between utilitarian moral judgment and empathy (Gleichgerrcht and Young, 2013; Patil and Silani, 2014). Empathy refers to the ability to understand and experience others' mental states (Davis, 1983). This ability is fundamental to experiencing concern for the victim's pain and understanding the agent's intention in moral dilemmas (Molnar-Szakacs, 2011; Patil, Melsbach, Hennig-Fast, and Silani, 2016). For instance, the lower empathic concern leads to decline in perceived significance of harm norms (Patil, 2015), by which the individuals with lower levels of empathic concern (i.e. *feeling of affection and concern in response to other's misfortune*) show higher proportion of utilitarian moral judgment (Gleichgerrcht and Young, 2013; Patil and Silani, 2014). Therefore, given the roles of empathy in moral judgment and the association of *COMT* with the ability of understanding other's mental states (Poletti et al., 2013; Xia, Wu, and Su, 2012), as well as the link of the lower dopamine levels with higher empathic responses (Gong, Liu, Li, and Zhou, 2014), this study also investigated modulations of *COMT* Val158Met on individual differences in empathic dispositions, with predication of individuals having the Val allele would show higher empathic ability.

2. Methods

To discover whether individuals with the Val actually have this provision we presume, 1272 Han Chinese college students were recruited. They were differentiated with this polymorphism, and rated permissibility of harm in moral dilemmas and empathic dispositions with Interpersonal Reactivity Index. In all, we designed this study that consists of the following procedures.

2.1. Participants

College students ($N = 1272$; 67.2% female; mean age = 19.30 ± 1.81 years) were recruited. These participants were ethnic Han Chinese without any known ancestors of other ethnic origin. Participants signed informed consent before taking part.

2.2. Moral permissibility assessment

Sixteen hypothetical moral dilemmas (Greene et al., 2001; Greene et al., 2004) were used to assess participants' view of the moral permissibility of harm. These moral dilemmas were differentiated as eight personal scenarios and eight impersonal scenarios. The personal moral scenarios were those involving serious bodily harm to one or more particular individuals, where the harm was not the result of deflecting an existing threat (e.g., *a runaway trolley is about to run over and kill five people, and a bystander is standing on a footbridge next to a large stranger. The bystander's body would be too light to stop the train, but he can push the large stranger onto the tracks, to save the five people by killing him. Is it permissible to push the man?*) (Greene et al., 2001), whereas the impersonal moral scenarios involves indirect or remote harm (e.g., *a runaway trolley is about to run over and kill five people, and a bystander can throw a switch to turn the trolley onto a sidetrack, where it will kill only one person. Is it permissible to throw the switch?*) (Greene et al., 2001). In this paper-pencil test, the scenarios were presented on answer sheets. The participants rated what extent it was permissible of harming one innocent person to save others, with a 7-point Likert scale (totally unacceptable = 1 to perfectly acceptable = 7). The order in which the participants completed the moral permissibility ratings was fixed across individuals.

2.3. Empathic dispositions assessment

Empathic dispositions were measured with the Chinese version (Rong, Sun, Huang, Cai, and Li, 2010) of the 28-item Interpersonal Reactivity Index (IRI) (Davis, 1983). This scale consists of four subscales: Perspective Taking, Fantasy, Empathic Concern, and Personal Distress. Fantasy subscale assesses the extent to which people immerse themselves in fictitious character's feelings and actions; Empathic Concern measures other-oriented feelings of sympathy and concern for unfortunate others; Perspective Taking evaluates the cognitive propensity to spontaneously adopt the viewpoint of others; Personal Distress taps self-oriented feelings of personal anxiety and unease in tense interpersonal settings. The scoring procedure was consistent with Davis' suggestion (Davis, 1983). For each item, the respondent scored on a 5-point Likert scale, with 0 indicating 'does not describe me well' and 4 indicating 'describes me very well'. The internal consistency of IRI, as measured with Cronbach's α, was 0.715 in this sample. This assessment was followed by moral permissibility rating.

2.4. Genotyping

We extracted genomic DNA from hair follicle cells with Chelex-100 method (de Lamballerie, Chapel, Vignoli, and Zandotti, 1994). The *COMT* Val158Met polymorphism was amplified by polymerase chain reaction (PCR) with upstream primer, 5′-CCAGCGGATGGTGGATTTCGCACGC-3′ and downstream primer 5′-TGGGGGGGTCTTTCCTCAGCC-3′ (Gong et al., 2013). The PCR system contained 2.50 μl reaction MIX (Golden Easy PCR System, TIANGEN), 0.50 μl DNA template, 2.00 μl ddH$_2$O, and 0.50 μl (25 pmol/μl) primers. The PCR reaction began with a 4 min denaturation at 94 °C, followed by 30 cycles of 94 °C for 30 s, 63.5 °C for 30 s, 72 °C for 30 s, and a final extension at 72 °C for 3 min. The PCR product was incubated using restriction enzyme MluI (FERMENTAS, MBI) at 37 °C in a 5.0 μl digested mixture (2.0 μl PCR products, 0.4 μl MluI (10 U/μl), 0.4 μl R buffer, and 2.2 μl ddH$_2$O). The digested mixture was analyzed by using 8% polyacrylamide gel electrophoresis with 200 voltages for 2.5 h, followed by silver staining. The genotypes were scanned with the Multi-Spectral imaging System. In our sample, the distribution of genotypes (Val/Val = 746, Val/Met = 452, Met/Met = 74) showed no deviation from Hardy-Weinberg equilibrium, $\chi^2 = 0.229$, $p = 0.632$.