

# Cognitive control and the COMT Val<sup>158</sup>Met polymorphism: genetic modulation of videogame training and transfer to task-switching efficiency

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**Abstract** The study investigated whether successful transfer of game-based cognitive improvements to untrained tasks might be modulated by preexisting neurodevelopmental factors, such as genetic variability related to the catechol-O-methyltransferase (COMT)—an enzyme responsible for the degradation of dopamine. The COMT Val<sup>158</sup>Met genotype may differentially affect cognitive stability and flexibility, and we hypothesized that Val/Val homozygous individuals (who possess low prefrontal dopamine levels) show more pronounced cognitive flexibility than Met/-carriers (who possess high prefrontal dopamine levels). We trained participants, genotyped for the COMT Val<sup>158</sup>Met polymorphism on playing “Half-Life 2”, a first-person shooter game which has been shown to improve cognitive flexibility. Pre-training (baseline) and post-training measures of cognitive flexibility were acquired by means of a task-switching paradigm. As expected, Val/Val homozygous individuals showed larger beneficial transfer effects than Met/-carriers. Our findings support the idea that genetic predisposition modulates transfer effects and that playing first-person shooter games

promotes cognitive flexibility in individuals with a suitable genetic predisposition.

## Introduction

The interest in the influence of videogame experience on our daily life is constantly growing. In our society, entertainment and technology go hand-in-hand and game developers and designers strive at optimizing the gaming experience and satisfying the needs of players.

In the past decade, there has been an increasing interest in the possible cognitive benefits that playing video games may have on players. Videogame-players (VGPs) have been reported to show better performance in both easy and difficult visual search tasks (Castel, Pratt & Drummond, 2005) and a more efficient distribution of visuo-spatial attention capacity (Green and Bavelier 2006b). VGPs exhibit a general increase of visual acuity across all eccentricities tested (Green & Bavelier, 2007), and show an increment in the number of objects that can be detained (Green & Bavelier, 2006a). Along the same lines, Green and Bavelier (2003) conducted a series of experiments suggesting that video game playing experience enhances the capacity of the players’ visual attentional system.

Recently, several studies have also focused whether and to which degree experience with videogames generalizes to cognitive control, that is, to people’s capacity to control their thoughts and goal-directed behavior. VGPs [all playing first-person shooter (FPS) games] and NVGPs performed on a task-switching paradigm that provides a relatively well-established measure of cognitive flexibility. As predicted, VGPs showed smaller switching costs (i.e., greater cognitive flexibility) than NVGPs. The results support the idea that playing FPS games promotes

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cognitive flexibility (Colzato, van Leeuwen, van den Wildenberg & Hommel, 2010a). In line with these findings, Karle, Watter and Shedden (2010), Boot, Kramer, Simons, Fabiani and Gratton (2008), Strobach, Frensch and Schubert (2012) and Green, Sugarman, Medford, Klobusicky and Bavelier (2012), using different paradigms, found VGPs to switch faster between tasks (note, however, that in some of these studies gaming was associated with a general drop of reaction times, which allows for less specific interpretations; see Green et al., 2012). Moreover, VGPs were found to be faster and more accurate in the monitoring and updating of WM than NVGPs (Colzato, van den Wildenberg, Zmigrod & Hommel, 2013).

So far, studies have neglected to take into account the role of individual differences in explaining the relationship between gaming experience and other cognitive abilities. The purpose of the present study was to investigate whether the successful transfer to untrained tasks is modulated by preexisting neuro-developmental factors. Individual differences may affect the degree to which individuals can benefit from cognitive training: individuals with a certain genetic predispositions may take advantage from a given type of training, whereas individuals with another predisposition may not.

Particularly, promising in this respect seems to be the genetic variability related to levels of dopamine (DA), a key neurotransmitter in the regulation of executive functions in the prefrontal cortex (PFC). The enzyme catechol-*O*-methyltransferase (COMT) is responsible for the degradation of DA in the synaptic cleft. A single nucleotide polymorphism (SNP), leading to a valine (Val) to methionine (Met) substitution (Val<sup>158</sup>Met), in the coding region of the COMT gene has been shown to influence the activity of the enzyme at body temperature (Lachman et al., 1996). The low-activity Met allele results in slower inactivation of extracellular DA within the brain, being associated with higher DA in the PFC for the Met/-carriers than for Val/Val homozygous individuals (Chen et al., 2004).

Interestingly, recent reports have suggested that the Val<sup>158</sup>Met genotype may differentially affect cognitive stability (defined as the maintenance of task-relevant representations) and flexibility (defined as the ability to adapt, update, and shift between informational states)—two major, but partially antagonistic functions of cognitive control (Cools & D'Esposito, 2010). In particular, Met/-carriers might be comparatively high in cognitive stability but comparatively low in cognitive flexibility (see Cools, 2006, for a review). Bilder, Volavka, Lachman and Grace (2004) discussed the effects of the COMT polymorphism on DA transmission in terms of a distinction between tonic and phasic DA processes. According to their analysis, phasic DA levels are not directly affected by COMT, which is thought to primarily eliminate extracellular DA. In

contrast, COMT does exert direct metabolic control over tonic extrasynaptic DA levels, which are less influenced by reuptake. Along these lines, Val/Val homozygous individuals may exhibit lower tonic DA transmission in the PFC and the striatum, but higher phasic DA transmission in the striatum. In contrast, Met/-carriers show higher tonic DA transmission in the PFC and the striatum, but lower phasic DA transmission in the striatum. In sum, Val/Val homozygous individuals are assumed to be associated with low tonic and high phasic DA levels, and Met/-carriers with high tonic and low phasic DA levels.

Consistent with these findings, Ettinger et al. (2008) observed associations between COMT polymorphism and BOLD response during prosaccade (index of cognitive stability) and antisaccade task performance (index of cognitive flexibility) supporting the idea that the Val allele is associated with greater brain flexibility performance, while the Met allele is associated with greater brain stability performance. According to Cools (2006), the same high DA levels in the PFC (as in the case of the Met/-carriers) which are beneficial for the stability of representations may reduce the ability to flexibly alter cognitive representations. Low DA levels in the PFC (as in the case of Val/Val homozygous) may in turn be beneficial for the flexible alteration of cognitive representations, but at the same time impair the ability to maintain representations in the face of intervening distractors.

Evidence for such interplay has been reported by Nolan, Bilder, Lachman and Volavka (2004). They showed that, in a reversal learning task, Val/Val homozygous individuals exhibit worse performance than Met/Met homozygous individuals at the acquisition stage but outperform them at the reversal stage, suggesting that their genetic predisposition impairs cognitive stability but enhances cognitive flexibility. Consistent with this picture, in animals, PFC DA depletion improves performance on an attentional set-shifting task (which requires the ability to alter behavior according to changes in dimensional relevance of multidimensional stimuli) while increasing distractibility (Roberts et al, 1994), whereas DA depletion in the striatum reduced distractibility (Crofts et al, 2001). More converging evidence has been provided by Colzato, Waszak, Nieuwenhuis, Posthuma and Hommel (2010b). In a task-switching paradigm, Met/-carriers showed larger switching costs (i.e., less cognitive flexibility) than Val/Val homozygous individuals. The findings support, again, the idea that low prefrontal dopamine levels promote cognitive flexibility.

Recently, Cools and D'Esposito (2010) have suggested that the balance between cognitive flexibility and stability depends on the adjustment of processing in the circuits connecting the PFC with the striatum through DA. DA in the striatum is supposed to promote flexibility by allowing the updating of novel relevant representations, whereas DA

in the PFC is proposed to support stability by increasing distractor resistance. These two processes seem to interact with each other: too much flexibility may be associated with distractibility, while too much stability may imply inflexibility—one of the major control dilemmas discussed by Goschke (2000).

To test whether individual differences regarding DA may mediate the efficiency of brain training in cognitive flexibility, we trained young healthy participants, genotyped for the COMT Val<sup>158</sup>Met polymorphism, on playing “Half-Life 2” (HL2), a FPS game that has been shown to improve the ability to switch between tasks (Colzato et al., 2010a). Pre-training (baseline) and post-training measures of cognitive flexibility were acquired by means of the task-switching paradigm. The amount of the time needed to switch between two different tasks can be taken to indicate the efficiency in adapting and restructuring cognitive representations, so that smaller switching costs would reflect a higher level of cognitive flexibility (Monsell, 2003).

Considering the evidence that Val/Val homozygous individuals (who possess low prefrontal dopamine levels) show more pronounced cognitive flexibility than Met-carriers (who possess high prefrontal dopamine levels) (Colzato et al., 2010b), we expected DA variability to account for individual differences in the transfer to performance in cognitive flexibility. Accordingly, we expected Val/Val homozygous individuals to show larger beneficial transfer effects than Met-carriers.

## Methods

### Participants

One hundred young healthy adults with little to no video-game experience served as participants for partial fulfillment of course credit or a financial reward. The sample was drawn from 186 adults in the Leiden and Rotterdam metropolitan area (The Netherlands), who volunteered to participate in studies of behavioral genetics.

Following Clark, Fleck and Mitro (2011) and Colzato et al. (2013), participants filled in a video game questionnaire, as part of a large test battery that assessed their familiarity with several video game genres (e.g., FPS, role-playing, puzzle) over several time frames. Their responses were used to classify them as experienced video game players (VGPs), individuals with little to no videogame experience (NVGPs), or “neither” (participants who did not fully qualify as NVGP were not included in this study). Following Colzato et al. (2013), a week after the completion of the test battery, based on the results of the questionnaire, the participants classified as NVGPs were invited to take part in the testing session.

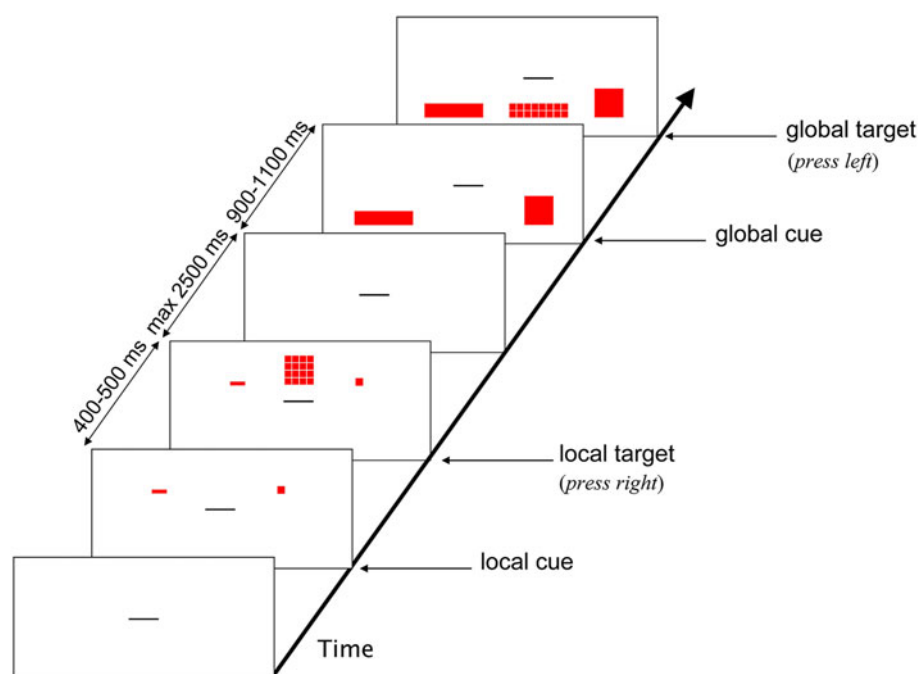
Four participants withdrew from the study. For two participants the COMT Val<sup>158</sup>Met polymorphism was not available. Exclusion criteria were any major medical illness that could affect brain function, current substance abuse, neurological conditions, a history of head injury, and a personal history of psychiatric medical treatment. Written informed consent was obtained from all participants after the nature of the study was explained to them; the protocol was approved by the ethical committee of the Leiden University Institute for Psychological Research.

### Apparatus, stimuli, and task

The experiment was controlled by a PC attached to a 17-inch monitor with a refresh rate of 100 Hz. Responses were made by pressing the “Z” or “?” of the QWERTY computer keyboard with the left and right index finger, respectively. The target stimuli were adopted from Colzato et al. (2010a) and consisted of geometric figures. Larger (global) rectangles/squares consisted of smaller (local) rectangles or squares. Global stimuli (i.e., squares or rectangles;  $93 \times 93$  or  $41 \times 189$  pixels, respectively) were composed of many smaller “local” stimuli (i.e., squares or rectangles;  $21 \times 21$  or  $8 \times 46$  pixels, respectively). The space between the local elements of a stimulus was 3 pixels. A global square consisted of 16 small squares or 16 small rectangles; a global rectangle consisted of 16 small squares or 16 small rectangles. The “local” and “global” cues were the same size as the global and local stimuli and were presented at 189 pixels from the center of the computer screen.

Participants responded to randomly presented rectangles or squares by pressing a left or right response button, respectively. Three blocks of trials were administered, two training blocks in which the instruction (global or local) was constant across all trials, followed by the experimental block in which participants switched between the global and the local task. In one of the two training blocks, participants responded to the local figure, in the other block they responded to the global figure. The order of the training blocks was randomized across participants and each block consisted of 50 trials. In the third block consisting of 160 trials, participants alternated between predictable sequences of four “local” and four “global” trials. A cue indicated to which dimension (global or local) the participants should respond. Cues that related to the global (local) dimension consisted of a big (small) square, presented at one side of the target stimulus, and a big (small) rectangle, presented at the other side of the target stimulus (see Fig. 1). The color of cues and target was red. Both remained on the screen until a response was given or 2,500 ms had passed. The time interval between presentation of the cue and of the target stimulus varied between

**Fig. 1** Illustration of the sequence of events in a trial of the switch blocks



400 and 500 ms and the interval between responses and the next presentation of the cue varied between 900 and 1,100 ms.

#### Video game of cognitive intervention: Half-Life 2

The online intervention game was the best-selling Half-Life 2 (HL2) game, a single-player science fiction FPS game broken into chapters. The main character is Gordon Freeman, a rebel scientist, who is fighting against a brutal police state in the fictitious City 17, somewhere in Eastern Europe. HL2 is situated in a 3D environment and requires frequent switching between multiple tasks. To play HL2, every participant received a personal account from <http://Store.steampowered.com>, an online game platform. To play HL2 via the participant's account the following requirements needed to be met: the installation of steam set-up and a PC with Windows XP, Vista or 7; 512 MB RAM, 1 Ghz or faster processor; Intel Mac, OS X version Leopard 10.5.8, Snow Leopard 10.6.3 or higher; 1 GB disk space and an internet connection preferable broadband. Once the participant started to play HL2, by logging into the personal account, the site automatically opened the "store" page, where information about the time played in total and the chapter reached by the participant could be found. Lab assistants logged every day into the personal account of the participants to closely monitor the performance and the continuity of time played by the participants (note, however, that the monitoring system did not allow excluding that someone else played instead of the participant). In case of failure to meet the criteria of playing one

30-min intervention session per day, the participants were reminded to do that by the lab assistants by means of e-mail and/or SMS.

#### DNA laboratory analysis

Genomic DNA was extracted from saliva samples using the Oragene<sup>TM</sup> DNA self-collection kit following the manufacturer's instructions (DNA Genotek, Inc., 2006). The SNP Val<sup>158</sup>Met of the COMT gene was genotyped using applied biosystems (AB) TaqMan technology. The Val<sup>158</sup>Met COMT polymorphism was assayed by polymerase using primers 5'-TCGTGGACGCCGTGATT-CAGG-3' and 5'-AGGTCTGACAACGGGTCAGGC-3'. Following Colzato et al. (2010a), the genotype was scored by two independent readers by comparison to sequence-verified standards. To obtain two equally sized subsamples to investigate the effect of COMT Val<sup>158</sup>Met polymorphism on cognitive flexibility we combined Val/Met heterozygotes and Met/Met homozygotes to create the group of Met/-carriers, see Table 1.

#### Procedure and design

All participants were tested individually. After each game round, data were saved through the personal account by Store.steampowered.com. Before and after the 3-week intervention, the task-switching paradigm measuring cognitive flexibility was administered. In addition, in the pre-test, individual IQs were determined by means of a 30-min reasoning-based intelligence test: the Raven Standard

**Table 1** Sample and genotype-specific demographics, chapters reached in playing Half-Life 2 (HL2), time played (h), and mean response latencies (ms), error rates (%), switch costs (alternation–

repetition), and transfer effect (switch costs pre-test–switch costs post-test) for Met/-Carriers and Val/Val Homozygous individuals

Variables (SE)	Met/-carriers ( <i>n</i> = 38)		Val/Val Homozygous ( <i>n</i> = 56)	
Sex (M:F)	18:20		27:29	
Age	22.1 (3.1)		21.3 (2.7)	
IQ	119.8 (3.6)		118.6 (3.8)	
Chapters in HL2*	5.4 (2.1)		6.7 (3.2)	
Time played	10.17 (0.1)		10.15 (0.1)	
Assessment	Pre-test	Post-test	Pre-test	Post-test
<b>Repetition</b>				
Reaction times (ms)	365 (6.1)	340 (6.3)	364 (5.0)	345 (5.2)
Error rates (%)	5.8 (0.6)	7.0 (0.6)	4.8 (0.5)	5.5 (0.5)
<b>Alternation</b>				
Reaction times (ms)	404 (8.4)	374 (8.3)	406 (6.9)	369 (6.9)
Error rates (%)	5.4 (0.8)	6.2 (0.9)	5.2 (0.7)	4.8 (0.5)
<b>Switch costs</b>				
Reaction times (ms)	39	34	42	24
Error rates (%)	−0.4	−0.8	−0.4	−0.7
<b>Transfer effect</b>				
Reaction times (ms)*	5		18 <sup>†</sup>	

Standard errors in parentheses

Significant group difference: \*  $p < 0.05$ Significant transfer effect: <sup>†</sup>  $p < 0.05$ 

Progressive Matrices (SPM). The SPM assesses the individual's ability to create perceptual relations and to reason by analogy independent of language and formal schooling; it is a standard, widely used test to measure Spearman's  $g$  factor and of fluid intelligence in particular (Raven, Court & Raven 1988). The pre- and post-test assessment was separated by an intervention period of three weeks. Participants were instructed to complete one 30-min intervention session per day, resulting in a total of approximately 10 h of training. Compliance was confirmed by analysis of the recorded progression data, as indexed by the chapters reached in playing HL2 and time played.

### Statistical analysis

First, repeated-measures ANOVAs were performed for analyses of age, IQ, sex, time played and chapters reached in playing HL2 differences between genotype groups. Second, the effect of COMT genotype in predicting individual differences in the efficiency of brain training was assessed by means of ANOVAs using target level (global vs. local), the congruency between the stimuli on the two levels (congruent vs. incongruent), task switch (i.e., same vs. different target level as in previous trial: task repetition vs. alternation) and assessment (pre-test vs. post-test) as

within and COMT (Val/Val homozygous vs. Met/-carriers) as between-subject factor. Finally, to assess whether the magnitude of switch costs (alternation–repetition) in the post-test session was proportional to the amount of chapters reached in playing HL2, Pearson correlation coefficients were performed. A significance level of  $p < 0.05$  was adopted for all tests.

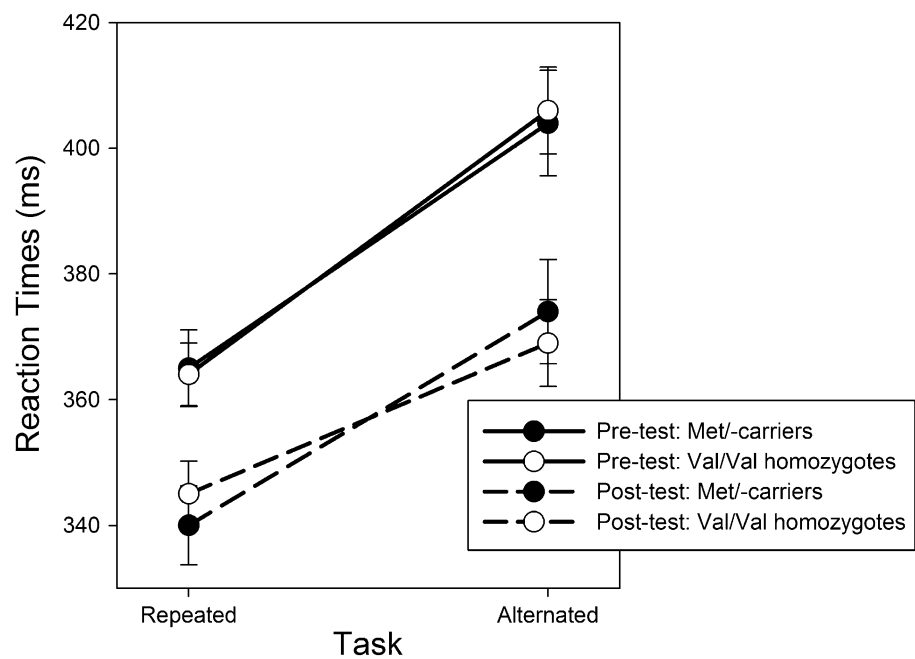
### Results

No significant differences were found among genotype frequencies with respect to age, sex, IQ and time played,  $F < 1$ , see Table 1. The genotype frequency from our cohort of participants did not deviate from Hardy–Weinberg equilibrium ( $p < 0.10$ ). As expected, Val/Val homozygotes reached significantly more chapters in playing HL2 than Met/-carriers,  $F(1,92) = 5.21$ ,  $p < 0.05$ ,  $MSE = 7.883$ ,  $\eta^2 p = 0.05$ .

Table 1 provides an overview of the outcomes for reaction times (RTs) and proportion errors (PEs). Four standard main effects were obtained: First, the effect of session,  $F(1,92) = 82.46$ ,  $p < 0.0001$ ,  $MSE = 4,329.63$ ,  $\eta^2 p = 0.47$ , showed that participants were becoming faster from pre-test to post-test (385 vs. 357 ms). Second, the



**Fig. 2** Mean Reaction Times (ms) as a function of group (Met/-carriers vs. Val/Val Homozygous individuals), task switch (i.e., same vs. different target level as in previous trial: task repetition vs. alternation) and session (pre-test vs. post-test). Standard errors of the difference between task repetition and alternation trials are represented by the error bars



effect of switch,  $F(1,92) = 222.05$ ,  $p < 0.00001$ ,  $MSE = 1,956.11$ ,  $\eta^2p = 0.71$ , was due to faster responses with task repetitions than with task alternations (357 vs. 388 ms). Third, the effect of target level,  $F(1,92) = 546.55$ ,  $p < 0.00001$ ,  $MSE = 1,114.95$ ,  $\eta^2p = 0.86$ , reflected the well-known global preference (Navon, 1977), that is, faster responses to globally than locally defined targets (350 vs. 391 ms). Fourth, the congruency effect,  $F(1,92) = 180.12$ ,  $p < 0.0001$ ,  $MSE = 753.61$ ,  $\eta^2p = 0.66$ , indicated interference from the non-target level, that is, faster responses if the stimulus at the currently irrelevant level was congruent with the present target than if that stimulus was incongruent (361 vs. 380 ms).

The two main effects of session and switch were involved in a two-way interaction,  $F(1,92) = 15.31$ ,  $p < 0.001$ ,  $MSE = 695.50$ ,  $\eta^2p = 0.14$  and in a three-way interaction involving COMT,  $F(1,92) = 5.76$ ,  $p < 0.05$ ,  $MSE = 695.50$ ,  $\eta^2p = 0.06$ , (see Fig. 2). Separate ANOVAs per genotype showed that only for Val/Val homozygotes the interaction of session and switch was significant,  $F(1,55) = 26.78$ ,  $p < 0.0001$ ,  $MSE = 640.37$ ,  $\eta^2p = 0.33$ , whereas it was not for Met/-carriers,  $F < 1$ ; i.e., the 18-ms transfer effect in the Val/Val homozygotes was significant while the 5-ms transfer effect in the Met/-carriers was not. Hence, as expected, only Val/Val homozygotes significantly benefited from playing FPS games showing decreased switching costs in the post-test compared to the pre-test assessment. Moreover,  $t$  tests for the obtained switch costs effect revealed that there was a significant difference between Met/-carriers and Val/Val homozygotes,  $t(92) = 2.00$ ,  $p = 0.05$  at post-test, but not at pre-test assessment,  $t(92) = 0.57$ ,  $p = 0.60$ .

The analysis of the error rates revealed two reliable main effects. First, the effect of congruency,  $F(1,92) = 152.06$ ,  $p < 0.00001$ ,  $MSE = 90.31$ ,  $\eta^2p = 0.62$ , reflecting the interference of the irrelevant target level, as indicated by a smaller proportion of errors on congruent as compared to incongruent trials (2.5 vs. 8.7 %). Second, the effect of target level,  $F(1,92) = 41.70$ ,  $p < 0.0001$ ,  $MSE = 57.25$ ,  $\eta^2p = 0.31$ , suggesting less errors to globally than locally defined targets (3.1 vs. 5.1 %). No other effect was significant.

Finally, the magnitude of switch costs in the post-test session was not significantly correlated with the amount of chapters reached in playing HL2,  $r(94) = -0.17$ ,  $p = 0.10$ , even though it followed the expected trend: progression in the game eventually associated with reduction in switch costs. This potential trend was evident for Val/Val homozygotes,  $r(56) = -0.22$ ,  $p = 0.10$ , but not for Met/-carriers,  $r(38) = -0.09$ ,  $p = 0.59$ .

## Conclusions

Our findings suggest that successful transfer of videogame training to untrained tasks is modulated by preexisting neuro-developmental factors, such as genetic variability related to levels of DA—the key neuromodulator underlying cognitive flexibility. As expected, Val/Val homozygous individuals showed larger beneficial transfer effects than Met/-carriers. Thus, FPS game training seems to have helped Val/Val homozygous individuals to extend, or make more efficient use of their cognitive-control resources for switching between tasks. Given that no significant

differences were found among genotype frequencies by age, sex, time played or estimated IQ, we can rule out an account of our results in these terms. Particularly important was the matching of the age range and intelligence: cognitive flexibility is known to be related to general/fluid intelligence (Colzato, van Wouwe, Lavender & Hommel, 2006) and to decline with increasing age (Kray, Li & Lindenberger, 2002). Given that the cue-target interval used in the present study was rather long, it should not be surprising that no effect of genetic variability on switching between tasks was found at the pre-test assessment. Indeed, in our previous study we found reliable COMT effects only for short task-preparation times (Colzato et al., 2010b). Moreover, given that only NVGPs were included in the study, our results cannot be explained in terms of previous experience with video gaming.

It is interesting to note that the training-induced benefit that Val/Val homozygous individuals showed in the task-switching paradigm was accompanied by comparable benefits in the videogame task being trained (indexed by the chapters reached in playing HL2). For one, it is important to point out that this cannot be considered a confounding variable—as it might seem at first sight. This is because Val/Val homozygotes were able to reach the higher gaming performance in the same time that was available to Met carriers, so that it does not represent more practice but a higher acquired skill or ability level. And this is indeed to be expected: if practicing video gaming taps into the same cognitive skill that underlies efficient task-switching, practicing one of the two should lead to better performance in both—which is what our findings demonstrate. For another, our findings also show that this relatively far transfer of cognitive skill is not a direct function of training but depends on the genetic set-up. Hence, our outcomes support the idea that playing FPS games promotes cognitive flexibility (Colzato et al., 2010a) in individuals with a suitable genetic predisposition.

Even though our finding may be limited to cognitive flexibility and need thus to be interpreted with caution, it does provide support for the idea that genetic predispositions modulate transfer effects. These results are in line with two previous studies. First, Brehmer et al. (2009) found that DAT 9/10-repeat carriers, individuals with a beneficial genetic predisposition in WM (Schott et al. 2006), profited more from WM training than DAT 10-repeat homozygous carriers because of more available striatal DA. Second, Colzato, van Muiden, Band & Hommel (2011) showed that genetic variability related to levels of BDNF modulates successful transfer to untrained tasks in attentional processes in elderly people.

We speculate that individual differences related to genetic variability affect the degree to which white matter will become plastic as a result of brain training. Indeed, it

is known that learning and transfer increases the plasticity and connectivity of cognitive processes (Takeuchi et al., 2010) and that genetic predisposition modulates the brain's structural connectivity (Marenco & Radulescu 2010). Future research needs to bring together these two interconnected research lines to better understand how genetic variability modulates transfer effects of cognitive functions.

The observation that the COMT polymorphism predicts transfer performance on an index of cognitive flexibility (Monsell 2003; Miyake et al. 2000) reinforces the idea of a crucial role of dopaminergic pathways in cognitive flexibility in general and the theoretical considerations of Bilder, Volavka, Lachman and Grace (2004) and of Cools (2006) in particular. As hypothesized by these authors, cognitive flexibility might benefit from relatively low DA levels in PFC (as in Val/Val homozygous individuals) but suffer from relatively high DA levels in PFC (as in Met/-carriers). With regard to the bigger picture, our observations are also in line with the hypothesis by Cools and D'Esposito (2010) that low DA level in PFC promote flexibility by facilitating the update of information in working memory (such as the current task set).

It is important to acknowledge and consider a number of limitations resulting from the design of our study. For one, the sample size of the current study was rather small as compared to other investigations of genetic variation; it would thus be important to replicate our preliminary results with a larger sample. For another, the fact that only one particular videogame was used to train participants did not allow a comparison with the impact of other video games. Accordingly, we are unable to identify those elements of the game that were crucial for producing the transfer effect. Moreover, the lack of a control group (without any training or with some kind of “neutral” or domain-general training) does not allow us to determine how specific the game-produced transfer effect really was (Boot, Kramer, Simons, Fabiani, & Gratton, 2011). In particular, even though our findings clearly demonstrate that genetic variability can predict individual differences in the efficiency of brain training in principle, we cannot be sure whether the transfer effect obtained for Met/-carriers represents a true baseline that could also be obtained without videogame training. At the same time, however, the fact that the genetic effect on transfer was mirrored in gaming performance does suggest a rather strong relationship between the skills relevant for the chosen videogame and executive control in task-switching: both seem to draw on shared cognitive resources and these resources seem to be related to the COMT polymorphism.

Apart from considering other games and types of training, future research needs to extend these preliminary findings to other control functions. Particularly relevant would be the “updating” (and monitoring) of WM

representations (Miyake et al., 2000), which seems also to be promoted by playing FPS games (Colzato et al., 2013). In any case, our findings strongly suggest that the pessimistic conclusions of Owen et al. (2010) regarding the efficiency of brain trainers might have been premature, at least with respect to cognitive flexibility.

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