# Dopamine and Cognitive Control: The Influence of Spontaneous Eyeblink Rate and Dopamine Gene Polymorphisms on Perseveration and Distractibility

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One fundamental problem of intelligent organisms pursuing goal-directed behavior is how to dynamically regulate the balance between maintenance and flexibility. The authors show that central dopaminergic activity, as indicated by spontaneous eyeblink rate and dopamine gene polymorphisms, plays an important role in the modulation of this balance. Seventy-two young adults were examined. Participants with high blink rates showed increased cognitive flexibility but decreased cognitive stability compared with participants with low blink rates. This pattern of results was even more pronounced for carriers of the *DRD4* exon III 4/7 genotype, even though no main effects were found for *DRD4* and *COMT* polymorphisms. Results converge with neuropsychological models that suggest a modulatory role of prefrontal dopaminergic activity for processes of cognitive control.

*Keywords:* cognitive control, task switching, dopamine gene polymorphism, *DRD4*, spontaneous eyeblink rate

To pursue goal-directed behavior in a constantly changing environment, intelligent agents are generally confronted with two fundamental demands: On the one hand, they have to maintain and protect current goals over time and shield intentions against possible distraction. On the other hand, they must be able to flexibly switch between goals and to update working memory whenever significant changes occur (Braver & Cohen, 2000; Dreisbach & Goschke, 2004; Goschke, 2003). These challenges—stable maintenance and flexible switching—impose antagonistic constraints on cognitive control processes: An organism that was not able to protect intentions and goals from interfering stimuli and prepotent but inadequate responses would suffer from distractibility and impulsivity; an organism that was not able to flexibly switch a currently active cognitive set would suffer from perseveration and behavioral rigidity (see Goschke, 2003, for a discussion of these control dilemmas).

Dreisbach and Goschke (2004) showed that the flexibility–stability dilemma, (i.e., the balance between maintenance and switching) is modulated by positive affect. To this end, we introduced the following paradigm (which was also used in our current study) that made it possible to detect the costs and benefits of increased cognitive flexibility under positive affect. First, participants were trained to respond to target stimuli appearing in a prespecified color while ignoring distractor stimuli in a different color. Then participants were transferred to one of two switching conditions. In one condition, they had to respond to stimuli in a new color while distractors appeared in the previous target color. In this so-called perseveration condition, increased flexibility should facilitate the disengagement from the formerly relevant task, presumably supported by a bias toward novel stimuli, thereby leading to decreased switch costs. In the second condition—the learned irrelevance condition—participants had to respond to stimuli in the previously to-be-ignored color while distractors appeared in a new color. In this condition, increased flexibility should again bias participants' attention toward novel stimuli, which, in this case, should produce increased switch costs. In accordance with the hypothesis, the authors found reduced switch costs in the perseveration condition under positive affect compared with neutral or negative affect. In addition, they found increased switch costs in the learned irrelevance condition under positive affect compared with negative or neutral affect (see Figure 1).

Taken together, the results of that study showed that mild positive affect, induced by means of short presentation of affective picture stimuli, enhanced cognitive flexibility but at the same time incurred a cost in terms of reduced stability or increased distract-
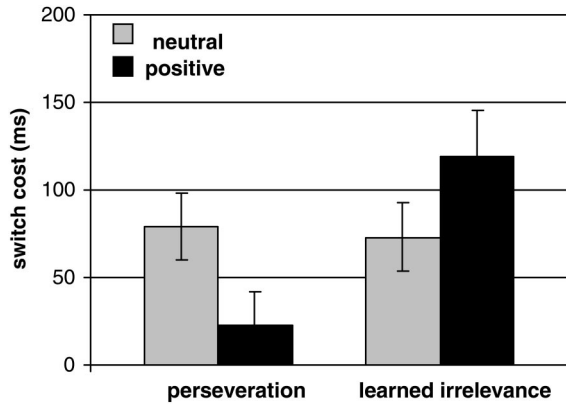
*Figure 1.* Mean response time switch cost (in milliseconds) as a function of transfer condition and affect. Adapted from "How Positive Affect Modulates Cognitive Control: Reduced Perseveration at the Cost of Increased Distractibility," by G. Dreisbach and T. Goschke, 2004, *Journal of Experimental Psychology: Learning, Memory, and Cognition, 30,* p. 346. Copyright 2004 by the American Psychological Association.

ibility, respectively. Dreisbach and Goschke (2004) hypothesized that this affective modulation of cognitive control processes might have been due to moderate increases in dopamine (DA) activity in prefrontal areas in response to positive affective picture stimuli.

The idea of an affective modulation of cognitive control through altered DA activity converges with common theories that suggest a link among positive affect, DA, and cognitive control. There exists growing evidence that positive affect has an influence on a broad range of cognitive processes, generally leading to higher cognitive flexibility (Greene & Noice, 1988; Isen & Daubman, 1984; Isen, Daubman, & Nowicki, 1987; Isen, Niedenthal, & Cantor, 1992; Kuhl & Kazén, 1999; Phillips, Bull, Adams, & Fraser, 2002). In the light of these studies, Ashby and colleagues (Ashby, Isen, & Turken, 1999; Ashby, Valentin, & Turken, 2002) assumed that the cognitive effects of positive affect are modulated by increased brain DA levels in prefrontal areas, as a result of which the ability to overcome dominant responses is enhanced and cognitive flexibility is increased. Further support for the linkage between dopaminergic activity and cognitive control comes from Cohen et al. (Braver & Cohen, 2000; Cohen, Braver, & Brown, 2002). These authors propose that phasic increases of DA in prefrontal cortex (PFC), elicited by reward-predicting stimuli, serve as a gating signal, thereby triggering the updating of working memory and facilitating a switch of cognitive set. A third line of evidence for the linkage between DA and cognitive control derives from a neuropsychological study (Owen et al., 1993) that compared the performance of Parkinson's disease patients on and off L-dopa (a preproduct of dopamine, able to pass the blood–brain barrier) in two different task-switching conditions. Whereas DA medication did increase flexibility (as indicated by reduced perseveration when a task switch required patients to ignore a previously relevant stimulus dimension), it did not improve performance when a task switch required patients to attend to a formerly ignored stimulus dimension.

In conclusion, DA appears to be one possible candidate to dynamically regulate the just-mentioned cognitive control issue: the stability-flexibility dilemma. In this study, we want to collect

further evidence for the modulatory effects of DA on cognitive control. To this end, we used the set-switching paradigm as described above (Dreisbach & Goschke, 2004), which makes it possible to detect the costs and benefits of increased cognitive flexibility. However, instead of manipulating dopaminergic activity indirectly by an affect induction procedure, we additionally used neurobiological measures of dopaminergic activity, namely the spontaneous eyeblink rate (EBR) and dopaminergic gene polymorphisms.

The EBR is a functional marker of central dopaminergic function (Blin, Masson, Azulay, Fondarai, & Serratrice, 1990; Karson, 1983; Kleven & Koek, 1996; Sax & Strakowski, 1998; Taylor et al., 1999) and has been shown to be a sensitive mirror of general cognitive factors like attention and activation (Brookings, Wilson, & Swain, 1996; Elsworth et al., 1991). The assumed link between DA and EBR is further supported by a study showing that EBR is increased in primates by DA agonists and is reduced in patients with Parkinson's disease (cf. Swerdlow et al., 2003). This latter result suggests that EBR is directly correlated with reduced DA activity in subcortical areas, which, as outlined above, can lead to specific switching deficits (see Owen et al., 1993). More specifically and most important with respect to our own study, there exists evidence that the EBR is inversely related to stereotyped behavior (Bodfish, Powell, Golden, & Lewis, 1995; MacLean et al., 1985), which can be interpreted in terms of reduced cognitive flexibility. This latter result is completely in line with the aforementioned theories of DA and cognitive control in that it shows that reduced dopaminergic activity, as indicated by lower EBR, attenuates cognitive flexibility.

The main purpose of the present study was to show that performance in a set switching paradigm is modulated by central dopaminergic activity as measured by the spontaneous blink rate. Our specific hypothesis was that participants with a high EBR, compared with those with a low EBR, would show increased cognitive flexibility (i.e., reduced switch cost in the perseveration condition) but decreased cognitive stability (i.e., increased switch cost in the learned irrelevance condition).

The second purpose of our study was to explore the differential effects of gene polymorphisms related to DA activity, namely the catechol *O*-methyltransferase (*COMT*) gene and the D₄ dopamine receptor (*DRD4*) gene exon III polymorphisms. COMT is an enzyme that plays a critical role in the metabolic degradation of DA in the prefrontal cortex, thereby influencing the response of prefrontal neurons during working memory tasks. The *COMT* gene contains a functional polymorphism, Val158Met, which has repeatedly been shown to influence performance on a neurocognitive test thought to rely on prefrontal activity: the Wisconsin Card Sorting Test (WCST; Milner, 1963). Carriers of the low-activity Met allele made significantly less perseverative errors in the WCST, a result that was shown for both a patient group diagnosed with schizophrenia and normal controls (Bilder et al., 2002; Egan et al., 2001; Malhotra et al., 2002). However, another study did not find differential effects of the Val158Met polymorphism on tasks relying on prefrontal processes (Fossela et al., 2002). As for the current study, it will be interesting to clarify whether or not carriers of the Met variant will show less perseveration compared with carriers of the Val variant in our set-switching paradigm.

The second candidate gene included in our study is the *DRD4* exon III polymorphism. Several studies reported a role of *DRD4*

exon III variability in human behavior, personality, and psychiatric disorders (e.g., attention-deficit/hyperactivity disorder [ADHD], which is characterized by attentional deficiencies, motor hyperactivity, and impulsivity; Oak, Oldenhof, & Van Tol, 2000). In other words, ADHD patients show decreased cognitive control, which may also implicate an effect of the *DRD4* gene variation on our paradigm (Barkley, 1997). Several studies demonstrated an association between ADHD and *DRD4* allele 7 (Rowe et al., 1998; Smalley et al., 1998; Swanson et al., 1998; Tahir et al., 2000). However, about as many studies did not find an association between *DRD4* and ADHD (Castellanous et al., 1998; Hawie et al., 2000; Kotler et al., 2000). The same controversial results have been reported for the assumed link between the *DRD4* polymorphism and the personality trait novelty seeking. Whereas some studies found increased novelty seeking scores for carriers of the *DRD4* exon III 7-repeat allele (Ebstein et al., 1996; Noble et al., 1998; Strobel, Wehr, Michel, & Brocke, 1999), others did not (e.g., Malhotra et al., 1996; Pogue-Geile, Ferell, Deka, Debski, & Manuck, 1998; Strobel et al., 2002; Strobel, Spinath, Angleitner, Riemann, & Lesch, 2003). However, Strobel, Lesch, Jatzke, Petzold, and Brocke (2003) found higher novelty-seeking scores in carriers of the 7-repeat allele compared with individuals without the 7-repeat allele but only in the absence of the short allele of the serotonin transporter gene promoter-linked polymorphic region (5–HTTLPR) and the *COMT* Val/Val genotype. If there actually exists a link between the *DRD4* exon III polymorphism and novelty seeking, we expect that carriers of the 7-repeat allele would show decreased switch cost in the perseveration condition (because a bias toward novel stimuli will direct the attention to the target color) but increased switch cost in the learned irrelevance condition (because a bias toward novel stimuli in this case would direct attention toward the distractor color).

The primary aim of the current study is to show that participants with increased DA activity (as indicated by spontaneous EBR) will show reduced switch cost in the perseveration condition and increased switch costs in the learned irrelevance condition. Participants with low versus high EBR will be identified using median split. Thus, we can ensure that, even though participants cannot be assigned to a low versus high blink group beforehand, group sizes will be equal. Our secondary aim is to further explore the role of two DA candidate genes, *COMT* and *DRD4*, on processes of cognitive control.

## Method

### Participants

Seventy-two undergraduates (40 women, 32 men; mean age = 22.3 years, *SD* = 2.8, range = 18–30 years) from the Dresden University of Technology participated for partial fulfillment of course credit or a financial reward. Participants signed an informed consent form and were debriefed after the session. All participants were German; those with grandparents from other countries were excluded to avoid confusion with possible biases as a result of genetic heterogeneity. Furthermore, participants with a known history of drug abuse or psychopathology and those who were taking medication were excluded.

### Materials and Procedure

On each trial, two stimuli, either two digits (2, 3, 4, 5, 6, 7, 8, and 9) or two letters (A, E, O, U, K, M, R, and S), were presented simultaneously one above the other in different colors (digits could appear in the colors olive, purple, and gray, whereas letters could appear in red, blue, and yellow). Participants were instructed to respond to the stimulus appearing in a prespecified color (e.g., red) and to ignore the other stimulus, which always appeared in a constant different color (e.g., blue). The location (above–below) of the target was determined at random.

In a given block of trials, participants performed either a letter categorization task, which required them to indicate whether the target letter was a consonant or a vowel, or a digit categorization task, which required them to indicate whether a target digit was odd or even. Participants had to press a left key if the stimulus was a consonant or even and a right key if the stimulus was a vowel or odd. Feedback was only given for errors, in which case the intertrial interval was extended to 2,000 ms. Targets and distractors were either response compatible (i.e., consonant and odd or vowel and even) or response-incompatible (i.e., consonant and even or vowel and odd). Stimulus presentation was completely randomized with two constraints: (a) Target and distractor were never identical, resulting in 25% more incompatible than compatible trials, and (b) the first stimulus after the switch was always incompatible.

Each block consisted of 60 trials. After 40 trials an instructional cue indicated a switch of the target color. Participants had been informed of this rule change at the beginning of the experiment. In the learned irrelevance condition, participants had to switch to the formerly ignored color while distractors appeared in a new color that had not appeared before. In the perseveration condition, participants had to switch to a new color that had not appeared before while distractors appeared in the formerly relevant color (see Figure 2). For instance, if in the training phase the target color was red and distractor color was blue, in the learned irrelevance condition the target color was switched to blue and the distractor color to yellow, whereas in the perseveration condition the target color was switched to yellow and the distractor color to red. The task (letter vs. digit categorization) was not switched within a block.
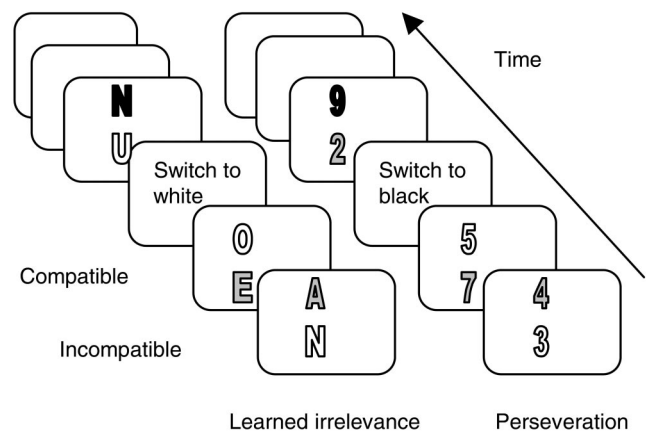


*Figure 2.* Examples for Trials 39–41 in both switch conditions. The shaded stimuli are the target stimuli before the switch. In the learned irrelevance condition, the former distractor color (here white) becomes the target and the new color (here black) becomes the distractor after the switch, whereas in the perseveration condition, the former target (here shaded) becomes the distractor and the new color becomes the target. For better comparability with the original study by Dreisbach and Goschke (2004), each trial was preceded by a neutral affect picture (250 ms) derived from the International Affective Picture System (Lang et al., 1998). From "How Positive Affect Modulates Cognitive Control: Reduced Perseveration at the Cost of Increased Distractibility," by G. Dreisbach and T. Goschke, 2004, *Journal of Experimental Psychology: Learning, Memory, and Cognition, 30,* p. 345. Copyright 2004 by the American Psychological Association.

For the sake of better comparability between the original paradigm as used by Dreisbach and Goschke (2004), in which affect was manipulated by means of pictures derived from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 1998), we presented a neutral picture before every trial for 250 ms.[1] The mean ($\pm$ SE) valence ratings from IAPS norms for these 10 neutral affect pictures were as follows: pleasant = 4.9 (.95), arousal = 2.56 (1.85). This same neutral picture set had been used in the original study (Dreisbach & Goschke, 2004).

Each participant performed three perseveration and three learned irrelevance blocks, each comprising 60 trials. Tasks (letter vs. digit categorization) and switching conditions (perseveration vs. learned irrelevance) changed every other block. The order of conditions was counterbalanced. Assignment of colors to stimuli (relevant, irrelevant, new) remained constant for a given participant but was counterbalanced across participants. Prior to the first two experimental blocks, participants performed 20 practice trials with only a single stimulus appearing in different colors.

### Eyeblink Rate

The experiment reported in this article was part of a larger study over two sessions, including EEG registration during a novelty oddball paradigm (Strobel et al., 2004). Eyeblinks were recorded for 4-min eyes-open segments under resting conditions during both recording sessions at the correspondingly same time of day. Never did we register after 7 p.m. Given that spontaneous EBR is supposed to be stable during daytime but increases in the evening (8:30 p.m., as reported by Babarto et al., 2000), this should not have caused any problems. Additionally, we asked participants beforehand to avoid alcohol and nicotine consumption and to sleep sufficiently before the experiment. Data were examined using the BrainVision Analyzer (Brain Products GmbH, Munich, Germany; http://www.brain-products.com/products/analyzer/index_analyzer.html). Continuous EEGs were divided offline into $4 \times 6$ periods of 10 s, which were visually inspected to count the blinks. The medians across the 4-min segments were residualized separately for the recording sessions for duration of sleep, room temperature, and relative humidity. Because the resulting values did not differ between sessions (Wilcoxon's test, $p = .889$), they were averaged to obtain a more reliable EBR measure. To minimize influences of demographic variables on the EBR, the measure was residualized for age and gender, especially because women exhibited a higher tonic EBR than men (Wilcoxon's test, $p = .008$). The residuals were median split to obtain a dichotomous measure suitable as an independent variable in subsequent analyses of variance (ANOVAs).[2] Six participants were excluded from this procedure because they tried to avoid blinking during the recording. Thus, 33 participants with low EBR presumably reflecting low dopaminergic tone could be compared with 33 participants with high EBR and hence high dopaminergic tone.

### Genotyping

Buccal samples were obtained and DNA was extracted using the Buc-calAmp system (Epicenter Technologies, Omaha, NE). *DRD4* genotypes were determined as described earlier (Ebstein et al., 1996). The allele frequencies for *DRD4* exon III were as follows: 2 repeat, 6.9%; 3 repeat, 6.3%; 4 repeat, 60.8%; 5 repeat, 2.8%; 6 repeat, 0.7%; 7 repeat, 22.2%; 8 repeat, 0.7%. On the basis of functional considerations (Oak et al., 2000), participants were chosen for further analyses if they had either the 4/4 or the 4/7 genotype ($N = 24$, and $N = 20$, respectively).[3]

*COMT* variants (Met/Met, Val/Met, Val/Val) were determined as previously described (Eisenberg et al., 1999). Sixteen participants were identified as Val/Val, 37 as Val/Met, and 14 as Met/Met.

### Design

A 2 (EBR: high vs. low) $\times$ 2 (transfer condition: perseveration vs. learned irrelevance) $\times$ 2 (compatibility: compatible vs. incompatible) design was used. EBR was a between-subjects variable, and the others were manipulated within participants. The *COMT* and *DRD4* genotypes were determined as already described and served as additional group factors.

## Results

As mentioned, 6 participants had to be excluded from the analysis because they tried to avoid blinking during the registration of the EBR. Additionally, the response time (RT) data of 2 participants were lost as a result of technical problems, leaving a total data set of 64 (40 women, 24 men; mean age = 22.3 years, $SD = 2.8$, range = 18–30 years).

### EBR and RT Data

Incorrect responses (mean error rate = 3.11%) and RTs exceeding 2,000 ms (additional 2.39%) were excluded from the analyses. For each of the six experimental blocks, means of the remaining RTs and errors were computed for consecutive intervals of five trials, separately for response-compatible and response-incompatible trials. The critical comparison is between the two intervals immediately before the target color switch (Trials 36–40) and immediately after the switch (Trials 41–46). (Analyses with larger intervals of 10 trials did not substantially alter the results.) Switch costs were computed as the difference between postswitch and preswitch trials for RT and error data, respectively. All following analyses rely on these mean switch costs. Data were collapsed over the three blocks of each switch condition.

To test our primary hypothesis of whether high blink rates go along with reduced switch cost in the perseveration condition and increased switch cost in the learned irrelevance condition, a 2 (EBR: high vs. low) $\times$ 2 (compatibility: compatible vs. incompatible) $\times$ 2 (transfer-condition: perseveration vs. learned irrelevance) ANOVA was computed, with EBR as a between-subjects factor. This analysis yielded a significant main effect for compat-

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[1] The experiment reported here was part of a larger study running over two sessions with approximately 1 week in between. Beforehand, we had to decide whether to present neutral or positive pictures in the first or the second session, respectively. Random presentation (half the participants receive positive pictures in the first session and neutral pictures in the second session and vice versa) was not possible because we did not know the distribution of the genetic variants in advance and thus would have risked having sample sizes that were too small. We, therefore, decided to present neutral pictures in the first session to examine whether a high EBR and specific dopaminergic gene polymorphisms have the same influence on behavioral performance as did positive pictures in the original study by Dreisbach and Goschke (2004). For exploratory reasons, we still ran the same experiment with positive pictures in the second session, being aware that performance there would be completely confounded with practice effects. Actually, practice effects in the second session were so strong that the data are hard to interpret, especially given the fact that novelty plays an important role in this paradigm. We, therefore, do not present these data; results can be obtained on request.

[2] Using a median split without the reported corrections yielded qualitatively the same results.

[3] Obviously, but fortunately, the frequencies of the *DRD4* 4/4 and 4/7 genotypes in our study do not mirror the usually reported distribution in the population, thereby resulting in nearly equal group sizes.

ibility, $F(1, 62) = 24.19$, $MSE = 7934.96$, $p < .001$, $\eta^2 = .28$.[4] The transfer condition slightly failed to reach statistical significance ($p = .059$, $\eta^2 = .05$). EBR was far from reliable ($F < 0.11$, $p > .7$). Compatible trials were generally faster than incompatible trials, but because no interaction with any other factor was found ($p > .15$) data in Figure 3 were collapsed over compatible and incompatible trials. As predicted, high blinkers show reduced switch cost in the perseveration condition but increased switch cost in the learned irrelevance condition. This observation is substantiated by a significant EBR × Transfer Condition interaction, $F(1, 62) = 4.1$, $MSE = 13642.11$, $p < .05$, $\eta^2 = .06$. All further interactions did not prove reliable (all $ps > .5$).

### EBR and Error Data

Error data were entered into a 2 (EBR) × 2 (compatibility) × 2 (transfer condition) ANOVA, with EBR as a between-subjects factor. Neither the main effects nor the interactions proved reliable (all $ps > .19$). Only a marginal EBR × Compatibility interaction ($p = .07$) was detected, with a tendency of high blinkers to reach a stronger compatibility effect than low blinkers.

### DRD4 and RT Data

Twenty-four participants with *DRD4* 4/4 genotypes and 20 with *DRD4* 4/7 genotypes were included in the analysis. For these remaining 43 participants, a 2 (*DRD4*: 4/4 vs. 4/7) × 2 (compatibility) × 2 (transfer condition) ANOVA did not show any effects of the *DRD4* polymorphism on task performance. Main effect and all interactions were far from reliable (all $ps > .4$).

### DRD4 and Error Data

With mean error cost as dependent measure, the 2 (*DRD4*) × 2 (compatibility) × 2 (transfer condition) ANOVA yielded a significant *DRD4* × Transfer Condition interaction, $F(1, 42) = 4.1$, $MSE = 43.93$, $p < .5$, $\eta^2 = .09$. Whereas participants of the *DRD4* 4/4 genotype had comparable error cost in the perseveration and learned irrelevance conditions (0.58% and 0.68%, respectively), the 4/7 genotype had higher cost in the perseveration condition (2.6%) but lower, even negative, cost in the learned irrelevance

condition ($-1.5\%$). Admittedly, the error rate is extremely low, which makes the interpretation of the significance of these results difficult.

### COMT and RT Data

Sixteen participants were identified as Val/Val, 37 as Val/Met, and 14 as Met/Met genotype. A 3 (*COMT*: Val/Val, Val/Met, Met/Met) × 2 (compatibility) × 2 (transfer condition) ANOVA with *COMT* polymorphism as a between-subjects factor did not yield a significant main effect for *COMT* ($p > .9$), nor did *COMT* interact with any other factor (all $ps > .7$).

### COMT and Error Data

The same null effect was found for the error data (main effect, $p > .9$; all interactions, $p > .3$).

One possible reason for the discrepant results reported in the literature and our null effects for *DRD4* and *COMT* might be that several genetic factors interact, such that the observation of only one polymorphism in isolation might have led to erroneous conclusions (see, e.g., Comings, 1998). We, therefore, explored our data for possible interactions among *COMT*, *DRD4* exon III, and EBR. It was not possible to test for a *COMT* × *DRD4* interaction because some cells were only occupied by 1 participant (see Table 1 for further cell sizes). The *COMT* × EBR × Transfer Condition interaction was far from statistical significance ($F < 1$; $p = .69$). Given the small sample size, this null effect is not conclusive. However, we found the following interesting interaction: With RT data, a 2 (EBR) × 2 (*DRD4*) × 2 (compatibility) × 2 (transfer condition) ANOVA yielded a significant EBR × *DRD4* × Transfer Condition interaction, $F(1, 39) = 11.34$, $MSE = 9730.74$, $p < .01$, $\eta^2 = .23$.

Figure 4 depicts mean switch costs of this interaction. The most prominent feature of the data pattern is the performance of the subgroup with a high blink rate and a *DRD4* 4/7 genotype. Perseveration costs of this subgroup drop near to zero, whereas this same group reaches highest switch cost in the learned irrelevance condition. This result is descriptively mirrored for the *DRD4* 4/4 subgroup; however, performance of the genotype 4/4 subgroup does not differ between high and low blinkers (all $ps > .3$).

## Discussion

Our results support the idea that dopamine plays a critical role in the modulation of cognitive control. The obtained disordinal interaction, indicated by the marked attenuation of perseverative behavior in combination with impaired performance in the learned irrelevance condition in the high blink rate group, suggests that central dopaminergic activity enhances cognitive flexibility but also incurs a complementary cost in the form of increased distractibility. Although participants with high blink rates had fewer problems in switching to a new task dimension when the formerly task-relevant stimuli served as distractor, they showed an RT increase when switching to a formerly irrelevant task dimension in the face of novel distractors. One possible explanation for these results is that increased dopaminergic activity in the high blink
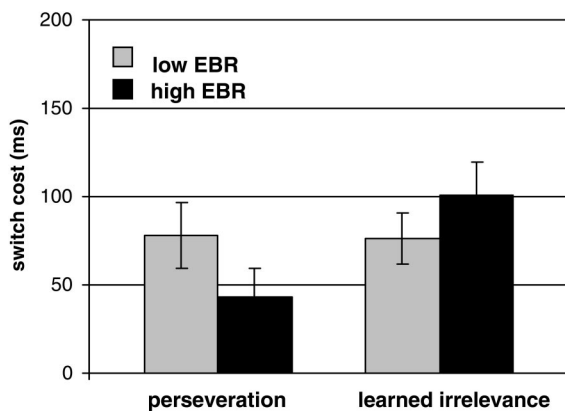


*Figure 3.* Mean response time switch cost (in milliseconds) as a function of eyeblink rate (EBR) and transfer condition.

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[4] Here and later we report partial $\eta^2$.

group biases attention toward novel stimuli, thereby reducing perseveration but simultaneously increasing distractibility. The data pattern of the present study (see Figure 3) obviously mirrors the results of the original study by Dreisbach and Goschke (2004; see Figure 1). The high blinkers in the present study show the same data pattern as the positive affect group, suggesting that the effects of positive affect are mediated by increased dopaminergic activity. This finding converges with the theories mentioned in the introduction that suggest a link among DA, positive affect, and cognitive control (Ashby et al., 1999, 2002; Cohen et al., 2002).

As for the *DRD4* exon III and *COMT* polymorphisms, we found no evidence for the assumed link between *DRD4* and novelty seeking (at least in the learned irrelevance condition of the current paradigm) or for the assumed link between *COMT* and perseveration. However, the significant threefold *DRD4* × EBR × Transfer Condition interaction shows that the data pattern of reduced switch cost in the perseveration condition and increased cost in the learned irrelevance condition is even more pronounced given a high blink rate and the DRD 4/7 genotype. Thus, it seems that the effects found for high blinkers are especially prominent for the DRD 4/7 genotype.

We, therefore, are tempted to take this interaction between blink rate and *DRD4* exon III polymorphism as one possible reason for the controversial findings of a linkage among *DRD4*, ADHD, and novelty seeking. It is possible, but highly speculative, that the reported equivocal effects of *DRD4* were, unbeknownst to the researchers, mediated by factors other than the *DRD4* genotype (e.g., by central dopaminergic activity). However, one should bear in mind the small sample size in the single subgroups (4/4 low blink: 8; 4/4 high blink: 15; 4/7 low blink: 11 and 4/7 high blink: 9), such that these preliminary results should be taken with caution. Note, however, that according to Cohen (1977) the effect size of this interaction was very large with $f = .54$, resulting in an estimated power of .93 (Faul & Erdfelder, 1992). Of course, the observed interaction might still be regarded as a false-positive finding and thus awaits independent replication. However, support for the behavioral relevance of the observed Blink Rate × *DRD4* interaction comes from an EEG study in our lab using the same sample, which showed no direct effect of *DRD4* on the novelty P3 (an EKP component that is thought to reflect processes of cognitive control) but the same disordinal EBR × *DRD4* interaction with the novelty P3 (Strobel et al., 2004). Nonetheless, we suggest that the reported interaction Blink Rate × *DRD4* should be taken as exploratory to generate hypotheses for future research.

**Table 1**
*Number of Participants With High and Low Blink Rate and the Corresponding Genotype Available for the Additional Analysis*

| Genotype | EBR low | EBR high |
|---|---|---|
| *DRD* 4/4 | 8 | 15 |
| *DRD* 4/7 | 11 | 9 |
| *COMT* Val/Val | 4 | 9 |
| *COMT* Val/Met | 21 | 14 |
| *COMT* Met/Met | 6 | 8 |

*Note.* The means of columns and rows do not necessarily sum up to the mean available in the single analyses, because for some participants whose EBR data were not available the genotypic information was. EBR = eyeblink rate.
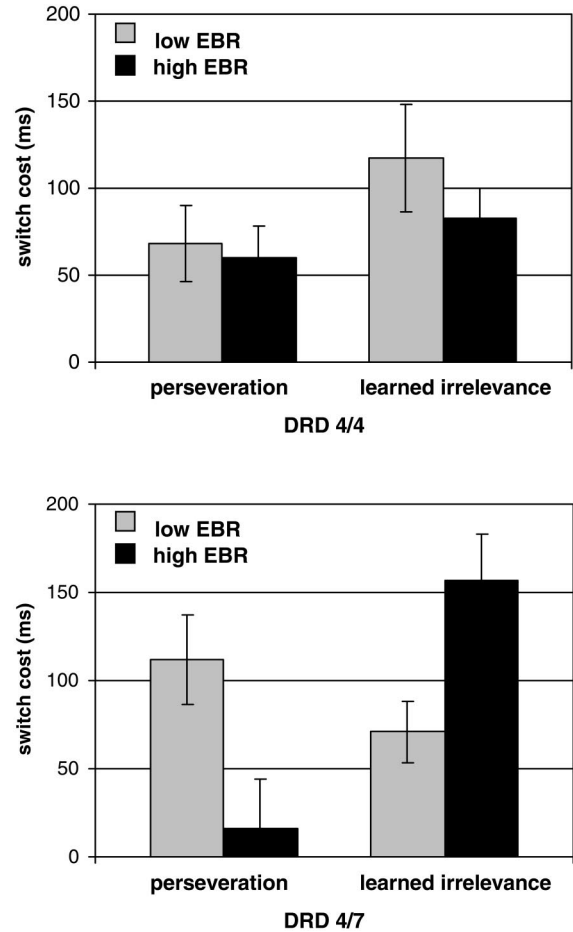


*Figure 4.* Mean response time switch cost (ms) as a function of eyeblink rate (EBR), *DRD4* exon III genotype, and transfer condition.

In conclusion, adaptive action in a constantly changing environment requires the dynamic regulation of flexible switching on the one hand and successful shielding against distraction on the other. We found further evidence for the modulatory role of central DA activity, as indicated by spontaneous eyeblink rate and the *DRD4* polymorphism, for the regulation of this flexibility–stability dilemma. Future research is clearly needed to learn more about the reciprocal influence of neurogenetic and neurobiological markers of dopaminergic activity and cognitive control.

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