Research Report

Dopamine and cognitive control: The influence of spontaneous eyeblink rate, DRD4 exon III polymorphism and gender on flexibility in set-shifting

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ABSTRACT

Converging evidence suggests a modulatory role of dopamine in cognitive control. We investigated the influence of two correlates of dopaminergic activity, the spontaneous eyeblink rate and the DRD4 exon III polymorphism, and the potential impact of gender on flexibility in an attentional set-shifting paradigm. The objective of the study was to confirm previous findings of an association between high eyeblink rates and increased cognitive flexibility. These findings were replicated in 87 healthy volunteers this time using a continuous variable for eyeblink rates instead of a dichotomized variable. The interaction between eyeblink rate and DRD4 found in the previous study was lower and failed significance. Analysis of the collapsed sample of n=150 revealed a main effect of gender and an interaction of gender and eyeblink rate on cognitive control. The complete prediction model explained 26% of the total variance. These data suggest that (1) the eyeblink rate is a reliable predictor of dopamine-mediated flexibility of cognitive control and (2) it is useful to include gender as predictor in future studies of dopaminergic modulation of cognitive control.

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1. Introduction

1.1. Dopamine and cognitive control

In goal-directed behaviour, there are two antagonistic ways to deal with changes in the environment. One can either direct one's actions in virtue of the new stimulus-pattern, i.e. respond flexibly, or one can stabilise actual goals against distraction by new stimuli. Miller and Cohen (2001) proposed a central role of the prefrontal cortex (PFC) in the execution of these demands of cognitive control. A phasic burst of midbrain dopamine neurons is supposed to enhance the update of...
current representations in the PFC thereby promoting flexible cognitive control at the cost of higher distractibility. According to Schultz (1998), these bursts can be released by signals of reward which on their part can elicit positive emotional states. Consequently, several studies have associated positive affect with cognitive flexibility (e.g. Phillips et al., 2002; further details in Dreisbach et al., 2005; Dreisbach, 2006). In an attentional set-shifting paradigm, Dreisbach and Goschke (2004) observed higher flexibility, but also higher distractibility after viewing pictures of positive valence compared to neutral pictures. In an integrative attempt, Ashby et al. (1999, 2002) have proposed that the influence of positive affect on executive functions is mediated by dopamine. Growing evidence supports the idea of a dopaminergic modulation of cognitive flexibility. In attentional set-shifting tasks, application of dopamine antagonists impaired flexibility in humans (Mehta et al., 2004, 1999) and rats (Floresco et al., 2006). Patients with Parkinson’s disease, who suffer from a degeneration of dopaminergic neurons in the nigrostriatal dopamine system (Fahn and Sulzer, 2004), show impairments in an attentional set shifting task (Owen et al., 1993). Likewise, attention-deficit hyperactivity disorder (ADHD) is behaviourally associated with impairments in executive control including attentional set-shifting (Boonstra et al., 2005) and neurologically associated with a dysfunction of dopamine systems (Levy and Swanson, 2001).

1.2. Set-shifting paradigm

In order to investigate influences of individual differences in dopamine activity on processes of cognitive control of healthy volunteers, we used a modified version of the task switching paradigm (see Monsell, 2003 for a review). In task switching, participants typically have to switch between different categorization tasks. In our paradigm (Dreisbach and Goschke, 2004; Dreisbach et al., 2005) only the relevant perceptual dimension (colour) changed whereas the task remained the same throughout blocks. To avoid confusion we will therefore use the term attentional set shifting instead of task shifting. The paradigm was designed to identify the costs and benefits of increased cognitive flexibility: First, participants are trained to respond to target stimuli appearing in a prespecified colour, while ignoring distracter stimuli presented in a different colour. For instance, stimuli are digits and the task is to determine whether the grey target digit is odd or even (see Fig. 1). Then participants are transferred to one of two switching conditions. In one condition, they have to respond to stimuli in a new colour, while distracters appear in the previous target colour. In this so-called perseveration condition, increased flexibility should facilitate the disengagement from the formerly relevant stimuli, presumably supported by a bias toward novel stimuli, thereby leading to decreased switch costs. In the other condition – the learned irrelevance condition – participants have to respond to stimuli in the previously to-be-ignored colour, while distracters appear in a new colour. In this condition, increased flexibility should again bias participants’ attention toward novel stimuli, which, in this case, should produce increased switch costs. Here, high switch costs should reflect an increased distractibility by the novel stimuli.

1.3. Correlates of dopaminergic activity

The spontaneous eyeblink rate (EBR), i.e. the frequency of blinks per minute under normal (resting) conditions, has been suggested to be partly regulated by dopamine and to be altered in certain psychiatric disorders associated with dopamine dysfunction (Karson, 1983). Patients with Parkinson’s disease exhibit lower EBR, a phenomenon that is used to rate the disease’s severity (Deuschl and Goldmeier, 1998). Low EBR is also observed in patients with ADHD (Konrad et al., 2003) and stereotypic behaviour (Bodfish et al., 1995). In challenge studies, EBR is elevated by dopamine agonists and diminished by antagonists (Blin et al., 1990; Jutkiewicz and Bergman, 2004; Taylor et al., 1999). These results suggest that a high EBR is related to a high dopaminergic activity on the one hand and to flexible behaviour on the other hand. In a previous study on set-switching as described above (Fig. 2; refer to Dreisbach et al., 2005 for further details concerning theory and methods), the authors observed that healthy volunteers with high EBR exhibited decreased switch costs in the perseveration condition and increased switch costs in the learned irrelevance condition as compared to participants with low EBR. The authors assumed that increased dopaminergic activity in participants with high EBR biases their attention toward novel stimuli and thereby promote flexible but also distractible behaviour.

The DRD4 gene encodes the D4 subtype of the dopamine receptor class. In a review of 23 studies, DiMaio et al. (2003) concluded that the 7-repeat allele of the DRD4 exon III polymorphism is associated with attention-deficit hyperactivity disorder (ADHD). Furthermore, an association between the presence of the 7-repeat allele and the personality trait novelty seeking was observed (Ebstein et al., 1996), but the existence of this association is highly controversial (see Kluger et al., 2002 for a meta-analysis). However, Strobel et al. (2004)
observed an interactive influence of EBR and DRD4 exon III polymorphism on the novelty P3 of the auditory evoked potential, a measure of novelty responsiveness. Similarly, Dreisbach et al. (2005) found an interaction between EBR and the DRD4 exon III polymorphism: The aforementioned positive association between EBR and flexibility was only observed in participants with the DRD4 4/7-genotype.

1.4. Gender

There exists evidence for gender differences regarding both, the behaviour and the neurotransmitter system aimed at in the current study. The personality traits novelty seeking and sensation seeking are assumed to be modulated by dopamine (Cloninger, 1993; Zuckerman, 1994). Higher scores in men compared to women have been hypothesised and observed in both traits (e.g. Cloninger et al., 1991; Zuckerman, 1994). Moreover, in voluntary explorations, male rats seem to spend more time with novel stimuli than females (Frick and Gresack, 2003; Palanza et al., 2001; Thor et al., 1988). One might speculate that this assumed bias toward novel stimuli should lead to a more flexible set-shifting in male. Regarding dopamine, e.g. Cahill (2006) underlines the importance to consider gender differences. In female, a higher dopamine activity was reported (e.g. Becker, 1999; Kaasinen et al., 2001) and Dreisbach et al. (2005) observed a higher EBR in women (p=.008), which might be taken as a hint for higher flexibility in women. Consequently, in Dreisbach et al. (2005), EBR was residualized for gender to exclude a possible indirect influence of gender on the performance mediated through EBR. In the current study, we additionally included gender as independent predictor, albeit we cannot predict the direction of an effect based on the described findings.

In sum, the objective of the current study was to replicate the initial findings of a positive association between EBR and flexibility and to provide further evidence for the usefulness of EBR in a non-clinical context. Furthermore, we attempted to replicate the interaction between EBR and the DRD4 exon III polymorphism and to explore gender differences in the flexibility of cognitive control.

2. Results

2.1. Data analysis

The difference between the switch costs in the two switching conditions perseveration and learned irrelevance served as criteria of the multiple regressions. Switch costs were computed by averaging the reaction times (RTs) of five trials after a switch and subtracting the mean of the five trials before a switch: 

\[ \text{RT}_{\text{switch costs}} = \text{RT} \text{5 trials after switch} - \text{RT} \text{5 trials before switch} \]

Incorrect responses and RTs exceeding 2000 ms were excluded from analyses. As described above, flexibility toward new stimuli should be reflected in decreased switch costs in the perseveration and increased switch costs in the learned irrelevance condition. Thus, a high flexibility should be reflected in a high difference between the switch costs of these two conditions. This measure, the so-called switch cost difference, was computed in order to gain one single criteria for the multiple regression analyses:

\[ \text{RT}_{\text{switch cost difference}} = \text{RT}_{\text{switch costs learned irrelevance}} - \text{RT}_{\text{switch costs perseveration}} \]

2.2. Eyeblink rate (EBR)

Women had a higher EBR than men (p=.04, \( \eta^2 = .05 \)), and thus EBR was residualized for gender (next to other possible influences on EBR). Concerning the first replication hypothesis, i.e. a positive association between EBR and flexibility, a regression analysis with EBR as single predictor was conducted. The analysis revealed a positive beta weight \( \beta = .23 \) (t(85) = 2.2, p = .017, one-tailed, \( \eta^2 = .05 \), see Fig. 3), reflecting a positive association between EBR and switch cost difference and thus, flexibility. Differing from the design described here, in Dreisbach et al. (2005), we used a median-split to obtain a dichotomous measure for EBR as a suitable independent factor in analysis of variance. Using this method, replication failed significance (p = .127, \( \eta^2 = .02 \), one-tailed). However, besides some advantages like a clear illustration of interactions,
median-splitting causes a possibly severe loss of information. Results can be biased by the somehow arbitrary classification of (many) participants with results close to the median. By the use of regression analyses with EBR as metric predictor and switch cost difference as criteria, these disadvantages have been avoided. The loss of information in the regression analysis, namely the main effects of the within factors time and switching condition, were of inferior interest for our hypotheses and was therefore accepted. Re-analyses of the first sample (Dreisbach et al., 2005) with a regression analysis confirmed the significant effect of EBR on the switch cost difference ($\beta=.34$, $p=0.004$, $\eta^2 =.11$, one-tailed). For power calculations concerning the first hypothesis, based on the results of this regression, an effect size of about $\eta^2 =.11$ was expected. The power to obtain significance on a one-tailed 5% level with the current sample ($n=87$) was 95% and hence satisfactory.

2.3. EBR×DRD4 exon III polymorphism

As a second replication hypothesis, we expected the association between EBR and switch costs to be increased for the DRD4 4/7-genotype as compared to 4/4-genotype. Therefore we included EBR, DRD4 and the interaction EBR×DRD4 as predictors in the regression model. The predictor EBR×DRD4 was yielded by multiplication of the two other predictors. Since DRD4 was effect coded with DRD4 4/4=−1 and DRD4 4/7=1 and an increased positive association between EBR and switch cost difference was expected for the DRD4 4/7 genotype, a positive beta weight was expected for the interaction EBR×DRD4. The analysis showed a positive beta weight $\beta=.17$ but missed significance ($t_{(56)}=1.2$, $p=.23$, $\eta^2 =.02$, one-tailed). On a descriptive level, the stronger association of EBR and switch cost difference in carriers of the DRD4 4/7 genotype observed in Dreisbach et al. (2005), also arose in this study (DRD4 4/4: $\beta=.13$, DRD4 4/7: $\beta=.33$). There was no main effect of DRD4 ($\beta=-.14$, $t_{(56)}=-1.1$, $p=.294$, $\eta^2 =.02$). Reanalysis of the first sample (Dreisbach et al., 2005) with the regression design revealed a significant effect ($\beta=.37$, $p=.005$, $\eta^2 =.16$, one-tailed). The power to detect an effect of the same size in the current sample with participants with either DRD4 4/7 or DRD4 7/7 genotype ($n=60$) on a one-tailed 5% level was 96%.

2.4. Gender

Whereas there was a reasonable prospect for gender influences, hypotheses concerning the direction or magnitude of a possible effect seemed premature. To gain sufficient power to detect also smaller effects (than the above described), we pooled the sample of Dreisbach et al. (2005) with the current sample. No participant took part in both studies. However, participants of the first study were generally slower than participants of the second study ($p=.015$, $\eta^2 =.04$). But since no interactions with the predictors in respect to the switch cost differences were observed ($p>.37$, $\eta^2 <.01$), data of the studies were collapsed and the switch costs were residualized by study. The size of the pooled sample was $n=150$ and hence allowed to detect effects up to $\eta^2 =.05$ at a two-tailed level of

![Graph](image-url)
significance of 5% and a power of 80%. There was an imbalance in the pooled sample between women (n=109) and men (n=41). According to Kraemer and Thiemann (1987), the power in an unbalanced sample is substantially reduced only if the ratio amounts to 80:20 or more. In the pooled sample, the ratio amounts to 73:27 and therefore we assumed no severe reduction in power due to the imbalance. In the regression analysis with the predictors EBR, gender, and the interaction EBR×gender, men had higher switch cost differences than women (β=.16, t_{146}=2.1, p=.038, η²=.03). More specifically, whereas women had comparable switch costs in the two switching conditions, men were faster in the perseveration condition and slower in the learned irrelevance condition (see Fig. 4). Additionally, an interaction of EBR×perseveration condition and gender was observed (β=.24, t_{146}=2.2, p=.027, η²=.03). To determine the direction of the interaction, two regression analyses were conducted separately for women and men (predictor=EBR, Fig. 5). The association between EBR and switch cost difference was stronger in men (β=.51, t_{40}=3.7, p<.001) than in women (β=.22, t_{108}=2.2, p=.019). Additionally, the slope was steeper in men (β=.78.2) than in women (β=.23.0, t_{146}=2.2, p=.027).

2.5. Complete prediction model

Finally, a prediction model with all independent predictors and second-order interactions was conducted in order to assess explained variance within the complete prediction model. Due to genotype distribution, the size of the collapsed sample was reduced to n=103 (74 women). All effects of the separate analyses were significant and the effect sizes were larger for each respective predictor (Table 1). The complete prediction model explained 26% of the variance in switch cost difference (adjusted R²=.22).

2.6. Errors

In addition to RTs, incorrect responses were recorded. Error rates were generally low (mean error rate=3.2%) and so were error costs (0.9%). Since no group differences occurred (p>.05, η²<.05), these data will not be presented in detail.

| Table 1 – Multiple regression with predictors eyeblink rate (EBR), DRD4 exon III polymorphism, gender and second order interactions in the pooled sample (n=103) |
|-------------------------------------------------|---|---|---|---|
|                                             | β  | t   | p   | η² |
| EBR                                           | .68 | 4.72 | .000 | .19 |
| DRD4a                                         | .01 | 0.11 | .909 | .00 |
| Gender                                        | .22 | 2.46 | .016 | .06 |
| EBR×DRD4a                                     | .34 | 3.68 | .000 | .12 |
| EBR×Gender                                    | .40 | 2.82 | .006 | .08 |
| DRD4a×Gender                                  | .10 | 0.99 | .325 | .01 |

Criteria is the switch cost difference (RTswitch costs learned irrelevance −RTswitch costs perseveration). Displayed are beta weights (β), t-value, probability of error (p) and partial eta-squared (η²). R²=.26, adjusted R²=.22.

a Only genotypes 4/4 and 4/7 of the DRD4 exon III polymorphism are included.

3. Discussion

3.1. Eyelink rate (EBR) and flexibility

We confirmed a positive association between EBR and flexibility in an attentional set-shifting paradigm. Higher EBR predicted lower switch costs in the perseverance condition and higher switch costs in the learned irrelevance condition. We suggest that both conditions measure a bias toward new stimulus patterns. Whereas in the first condition, this novelty bias facilitates the switch, it complicates the switch in the second condition. The aforementioned findings concerning an association between dopamine and EBR on the one hand (Blin et al., 1990; Jutkiewicz and Bergman, 2004; Taylor et al., 1999) and set-shifting on the other (Floresco et al., 2006; Mehta et al., 2004, 1999) favour the assumption that the relation between EBR and set-shifting is mediated by dopamine. On a behavioural level, our results are in line with studies of Parkinson’s disease and ADHD which associate these disorders with impairments in set-shifting, lower EBR and dysfunction of dopamine systems (Boonsra et al., 2005; Deuschl and Goldmeier, 1998; Levy and Swanson, 2001; Owen et al., 1993). In the following, some considerations regarding both EBR and flexibility will be discussed.

The established association between Parkinson’s disease with its striatal degeneration of dopamine neurons and EBR (Deuschl and Goldmeier, 1998) could indicate that the dopaminergic regulation of EBR is associated with the nigrostriatal dopamine system. Taylor et al. (1999) applied the dopaminergic neurotoxin MPTP to monkeys and observed a high negative correlation (r=−.87) between EBR and the induced parkinsonian symptoms. Moreover, in a specific region of the striatum, namely the rostral body of the ventromedial caudate nucleus, a positive correlation between EBR and the concentration of dopamine was observed post-mortem. The authors suggested this region to have a pivotal role in regulating the EBR. In another study, MPTP-treated monkeys showed cognitive dysfunctions in terms of perseverative behaviour (Taylor et al., 1990), which is well in line with our results.

The dopaminergic influence on cognitive flexibility has already been discussed by Miller and Cohen (2001). According to these authors, a phasic burst of midbrain dopamine neurons provides a gating signal for afferents in the prefrontal cortex (PFC). This phasic dopamine release in the PFC should enhance reception of new information and hence activation of new representations and a flexible cognitive control. In this respect, Seemans et al. (2001) investigated in vitro the impact of different dopamine ligands on the modulation of GABAergic inhibition of pyramidal neurons in the PFC. The authors postulated two different dopaminergic processes, a fast one via D2-like receptors (i.e., D2, D3 and D4) and a slow one via D1-like receptors (i.e., D1 and D5). Activation of D2-like receptors should decrease the GABAergic inhibition of pyramidal neurons and thus “allow multiple representations to be activated closely in time” (Seemans et al., 2001, p. 3636). This process might converge with the described updating of the PFC (Miller and Cohen, 2001) and increased flexibility in set-shifting. The second process refers to the enhancement of the
GABAergic inhibition via activation of D_{1}-like receptors. Through this, “weakly active representations fail to be maintained, and a single or limited number of strongly active representations become very stable to subsequent interfering inputs and noise” (Durstewitz et al., 2000; Seamans et al., 2001, p. 3637). This process resembles another main function of the PFC, namely the stabilisation of active representations against distraction by irrelevant stimuli (Miller and Cohen, 2001), and might converge with reduced flexibility in the described set-shifting paradigm.

The distinct neurological mechanisms linking a dopaminergic regulation of the EBR in the caudate and a dopaminergic modulation of flexibility in the PFC are unknown so far and could be subject of future research, e.g. by experimentally manipulating dopaminergic activity. The use of a continuous EBR variable seems to be reasonable in this respect. Insofar as the decision to use a regression design instead of the former used median-split was made post-hoc, it is a limitation of the current study. However, as outlined above, the regression design appeared to be more adequate and powerful.

3.2. **DRD4 exon III polymorphism**

In Dreisbach et al. (2005) we observed a positive association between EBR and flexibility only in participants with the DRD4 4/7-genotype but not in 4/4-genotype carriers. In the present study, this interaction showed up in the same direction, but did not reach significance and was of small size ($\eta^2 = 2\%$). Therefore, based on the data of our two studies it can not be decided, whether or not there is a substantial interaction of DRD4 and EBR. To detect an effect of $\eta^2 = 2\%$ on a power level of 80%, around 300 persons would have to be tested.

3.3. **Gender and complete model**

Men had higher switch cost differences, reflecting higher flexibility (at the cost of distractibility) than women. This finding converges with some theories and findings that associate male gender with a bias toward novel stimuli (Cloninger et al., 1991; Frick and Gresack, 2003; Palanza et al., 2001; Thor et al., 1988; Zuckerman, 1994) which supports the current finding of higher flexibility in men. However, higher dopamine activity in females (e.g. Becker, 1999; Kaasinen et al., 2001) and the higher EBR in women as compared to men as reported in this article and in Dreisbach et al. (2005) would have suggested increased flexibility in women. We assume that the absolute size of the EBR is not crucial, but rather the EBR relative to the members of the own gender. This assumption is supported by the observed association of flexibility and EBR residualized by gender (see Fig. 3) and the positive regression weights reflecting this association in both gender groups (see Fig. 5). A possible, but highly speculative, solution of the apparent contradictory results of a higher dopamine activity in women but a higher flexibility in men might be provided by the other significant effect concerning gender in this study: The positive association between EBR and flexibility was stronger in men compared to women in terms of a higher effect size and additionally a steeper regression slope. This effect might reflect a higher sensitivity to the dopaminergic modulation of flexibility in attentional set-shifting in men as compared to women. This higher sensitivity in men might compensate the lower baseline level of dopamine and result in a higher absolute level of flexibility. Irrespective of the ambiguity concerning these interpretations and the underlying neurological mechanisms, the presented data imply the relevance of gender as an independent predictor in further studies of dopamine and cognitive control.

Both effects concerning gender were of small size ($\eta^2 = 3\%$) in the separate analyses and of medium size (gender: $\eta^2 = 6\%$, EBR×gender: 8%) in the complete prediction model. Examining effects of this magnitude requires very large samples to reach satisfying levels of power (see above). In this regard, the applied strategy of replicating effects with a new sample and examine new assumptions with the pooled sample of two or more consecutive studies seems to be efficient and reasonable. In the current study, the power would have been too small to detect the effects of gender. Furthermore, the systematic extension of a sample concerning the same paradigm facilitates repeated replications and an evaluation of stability and size of effects. This allows explaining stepwise systematic variance with several predictors by conducting complete models. Here, the latter revealed that EBR, gender, EBR×DRD4 and EBR×gender were independent predictors and together explained one-quarter (26%) of the variation in the performance in the attentional set-shifting paradigm. In conclusion, these data confirm the prominent role of dopamine in the modulation of flexibility and warrant further research into the underlying neurobiological mechanisms.

4. **Experimental procedures**

4.1. **Participants**

As in the Dreisbach et al. (2005) study, participants were undergraduates (n=92, 74 female, mean age=21.9 years, SD=4.3, range=18–42; Dreisbach et al., 2005: n=72, 40 female, mean age=22.3 years, SD=2.8, range=18–30) from the Dresden University of Technology who participated for partial fulfillment of course credit. Participants with a known history of drug abuse, psychopathology or who were taking medication were excluded. At the day of the experiment, participants were screened for depression (Kühner, 1997) and asked not to take in caffeine, alcohol and nicotine if possible. Experiments were conducted between 09:00 a.m. and 06:00 p.m. Participants gave informed consent and were debriefed after the session. The study was carried out in accordance with the Declaration of Helsinki and was approved by the local ethics committee.

4.2. **Eyeblink rate (EBR)**

Eyeblinks in resting EEGs were visually identified by a trained researcher (JM) and the medians across 4 segments of 1 min length were computed. The mean EBR was 10.0 blinks/min (SD=8.0). EBR was residualized for gender and other possible influences on EBR (duration of sleep, room temperature, relative humidity and age). Due to the residualization, a possible indirect influence of gender on the performance in
the set-shifting paradigm mediated through EBR was eliminated. That way, both EBR and gender were suitable as independent predictors in subsequent analyses. Five participants had to be excluded because they reported that they had avoided blinking during the recording.

4.3. Genotyping

Buccal samples were obtained and DNA was extracted using the BuccalAmp system (Epicentre Technologies, Madison, USA). DRD4 exon III genotypes were determined as described earlier (Ebstein et al., 1996). The allele frequencies for DRD4 exon III were: 2 repeat 6.9%, 3 repeat 6.3%, 4 repeat 60.8%, 5 repeat 2.8%, 6 repeat 0.7%, 7 repeat 22.2%, and 8 repeat 0.7%. Based on 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=38, and N=22, respectively).

4.4. Materials and procedure

On each trial, two stimuli, either two digits (2, 3, 4, 5, 6, 7, 8, and 9, see Fig. 1) or two letters (A, E, O, U, K, M, R, and S), were presented in the centre of the screen simultaneously one above the other in different colours (digits could appear in the colours olive, purple, and grey, whereas letters could appear in red, blue, and yellow). Participants were instructed to respond to the stimulus appearing in a prespecified colour (e.g., red) and to ignore the other stimulus, which always appeared in a constant different colour (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 categorisation task, which required them to indicate whether the target letter was a consonant or a vowel, or a digit categorisation 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. Each block consisted of 60 trials. After 40 trials an instructional cue indicated a switch of the target colour. Participants had been informed of this rule change at the beginning of the experiment.

In the perseveration condition participants had to switch to a new colour that had not appeared before, while distracters appeared in the formerly relevant colour. In the learned irrelevance condition participants had to switch to the formerly ignored colour, while distracters appeared in a new colour that had not appeared before (Fig. 1). For instance, if in the training phase the target colour was red and distracter colour was blue, in the learned irrelevance condition the target colour was switched to blue and the distracter colour to yellow, whereas in the perseveration condition the target colour was switched to yellow and the distracter colour to red. 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 IAPS (Lang et al., 1998). Each participant performed 3 perseveration and 3 learned irrelevance blocks. Tasks (letter vs. digit categorisation) and switching conditions (perseveration vs. learned irrelevance) changed every other block. The order of conditions was counterbalanced. For further details, see Dreisbach et al. (2005).

4.5. Design

Multiple regression analyses were used. Independent predictors were EBR, DRD4 exon III, gender, and the respective second order interactions. For the appropriate use in a regression analysis, the two dichotomous predictors DRD4 and gender were effect coded with DRD4 4/4-genotype = -1, DRD4 4/7-genotype = 1, women = -1, and men = 1, respectively. The second order interactions were yielded by multiplication of the two regarding predictors. Analyses were conducted with SPSS 12 (SPSS Inc., Chicago, USA) and the power analyses were conducted with GPOWER (Faul and Erdfelder, 1992).

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REFERENCES


