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Abstract

Research shows that genetics and effortful control play an important role in the link between parenting and problem behavior. However, little is known about how these factors act simultaneously. This article used a moderated mediation model to examine whether effortful control mediated the link between parenting and externalizing problem behavior, and whether dopaminergic genes (i.e., polygenic index score including DAT1, DRD2, DRD4, COMT) moderated this link. Two three-wave studies were conducted on community samples (adolescents: Study 1: N= 457; M_{age}= 15.74; Study 2: N= 221; M_{age}= 12.84). There was no mediation by effortful control, but a moderation by dopaminergic reactivity was observed. Despite inconsistent evidence, this article indicates that the development of externalizing problem behavior is subject to genetic characteristics and parenting.

Introduction

Given the multiple changes in adolescence (e.g. puberty, identity formation, cognitive development) it is a vulnerable period in which many adolescents exhibit some kind of externalizing problem behavior (Reitz, Deković, & Meijer, 2005) Externalizing problem behavior refers to behavior that is directed outwards and victimizes others (e.g., aggression and delinquency) (Achenbach, 1991) and can be split up into two subtypes: aggressive behavior (e.g., hitting someone) and rule-breaking behavior (e.g., breaking the evening curfew) (Achenbach, 1991). Reitz et al. (2005) showed that approximately 60% of the adolescents exhibit some kind of problem behavior during adolescence and for a small portion of this group this will lead to delinquent behavior later in life (Moffit, 1993). These findings stress the need for research on which factors play a role in the development of externalizing problem behavior. Therefore, the present study investigated the role of environmental (i.e., parenting) as well as individual characteristics (i.e., temperament, genetic make-up) in association with externalizing problem behavior (i.e., rule-breaking and aggressive behavior; Achenbach, 1991).

Parenting and Adolescents' Externalizing Problem Behavior: Temperament as a Mediator

The literature on parenting adolescents has provided extensive evidence for the association between parenting practices, such as parental support, psychological control, or parental criticism and several developmental outcomes, such as externalizing problem behavior in adolescence (Hanisch et al., 2014). Parental support refers to the warm and affectionate bond between children and their parents. When children or adolescents feel supported, they will be less likely to show aggressive or rule-breaking behavior (Tuggle, Kerpelman, & Pittman, 2014). In contrast, the levels of aggressive and rule-breaking behavior appear to increase when parents exert negative parenting, such as psychological control (Barber, 1996) or criticism (Narusyte et al., 2011).

The associations between parenting and problem behavior may appear straightforward, but other factors, such as individual differences (e.g., child temperament), also play a role. One temperamental trait that has been investigated is effortful control, that is, the capacity to direct one's attention and to regulate emotions and behaviors (Rothbart & Bates, 2006). Previous studies suggested that effortful control moderates the association between parenting and externalizing problem behavior (de Haan, Prinzie, & Deković, 2010) in that individuals with lower effortful control respond more strongly to parenting practices. However, a recent meta-analysis by Slagt, Dubas, Deković, and van Aken (2016) did not consistently find this moderation by effortful control. These mixed results indicate the need to consider alternatives for the moderating role of temperament.

One possible alternative is a mediation model. Some studies suggested that the association between parenting and externalizing problem behavior is partially mediated by effortful control (Eisenberg et al., 2005).

Specifically, these studies found that effortful control partly explained the association between parental support or the use of corporal punishment, on the one hand, and externalizing problem behavior, on the other hand. For instance, parental support was associated with lower levels of externalizing problem behavior, but when effortful control was taken into account, the associations between support and problem behavior were less pronounced. There is also extensive evidence for this mediation model (i.e., parenting -> effortful control -> problem behavior) from the criminology literature. Specifically, the general theory of crime by Gottfredson and Hirschi (1990) addressed this issue and was supported by numerous (longitudinal) studies (Burt, Simons, & Simons, 2006; Hay, 2006). Therefore, the present study will investigate a possible mediating role of effortful control. In other words, supportive parenting is associated with an increase of the child's capacity for effortful control, which in turn would be associated with a decrease in the child's externalizing problem behavior.

Parenting and Adolescents' Externalizing Problem Behavior: Dopaminergic Genes as a Moderator

In addition to the long-standing interest in temperament, researchers are also exploring gene-by-environment (G x E) interactions in externalizing problem behavior (Weeland et al., 2015). This type of interaction implies that genetic characteristics moderate the association between parenting and externalizing problem behavior. The dopaminergic pathway, that is, the entire set of genes related to the neurotransmitter dopamine is linked to impulsivity and emotion regulation skills and thus, is widely believed to contribute to externalizing problems (Weeland et al., 2015). For instance, Weeland et al. (2015) suggest that individuals with reduced dopamine activity are less reactive to normal, everyday stimulation, which is why they often seek out more extreme thrills with potential negative consequences (e.g., experimenting with drugs). According to Padmanabhan and Luna (2014), an increase in dopamine availability and signaling may foster adaptive novelty seeking. However, when dopamine levels are getting too high, this may increase reward sensitivity and hamper the self-regulation, which, in turn, could lead to more risk-taking behavior. In other words, an individual's genetic make-up can make this individual less or more susceptible to his/her environment, which is the central idea of the differential susceptibility hypothesis (Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2007).

The most researched dopaminergic genes in the context of externalizing problem behavior are DRD4, DRD2, DAT1, and COMT and the systematic review by Weeland et al. (2015) showed these genes act as a moderator in the association between parenting and externalizing problem behavior. The findings by Weeland et al. (2015) were mixed regarding whether these single genes amplified or weakened (i.e., more or less susceptible to the environment) the association between parenting and externalizing problem behavior. It is also important to note that previous studies (Burt & Klump, 2013) indicated differences between rule-breaking and aggressive

behavior regarding genetic and environmental influences. Specifically, Burt and Klump (2013) suggest that genetic characteristics contribute more strongly to aggressive behavior, whereas environmental influences may contribute more strongly to rule-breaking behavior. This finding stresses the importance of investigating these two types of externalizing problem behavior separately in order to get a detailed view on their respective contributing factors (i.e., environmental versus genetic).

Current work on G x E interactions involving the dopaminergic system could be expanded upon in two important ways. First, relying on single genes in so-called candidate gene studies could lead to erratic results. A polygenic score, that is, a combined index of genetic risk across different genes offers a broader representation of the underlying genetic pathway (i.e., the dopaminergic pathway). Using such a score could lead to stronger and more consistent genetic moderation effects. Second, once gene-environment interactions are firmly established, the question remains which possible mechanism underlies these G x E effects.

Toward a Comprehensive Model: Examining the Interplay Among Parenting, Effortful Control, and Genetics

Temperamental traits, such as effortful control, could be linked to G x E interactions and could in fact provide a potential underlying mechanism for them. Theoretically, temperament is supposed to have a biological basis and is related to the dopaminergic system, among other systems (Mervielde, De Clercq, De Fruyt, & Van Leeuwen, 2005). This biological link raises the possibility that parenting, genetics, and temperament jointly affect externalizing problem behaviors in a complex process that can be uncovered using more sophisticated models such as mediated moderation or moderated mediation. One study, for instance, examined a mediated moderation model involving parenting, uninhibited temperament (i.e., the opposite of effortful control), and a dopamine-related gene to predict children's externalizing problem behavior. The genetic factor moderated the association between parenting and externalizing problem behavior and uninhibited temperament partially explained or mediated that moderating effect (Davies et al., 2015).

The present study expands on that earlier work. We do not aim to provide a conclusive and definitive answer to the question how genetics interact with parenting and temperament in the development of externalizing problem behavior. Such an answer is unlikely, because very little is known about the association between genetics and temperament. Some authors (e.g., Robbins, 2018) caution against making conclusive statements about this association, especially because there is little support for a one-on-one relation between genes and temperament from genetic studies (Munafo et al., 2003). They argue that psychological, behavioral, and genetic research in humans should be complemented with research on the neural basis of behavior in animal models. Rather, we aim

to provide support for theoretical frameworks that stress the importance of including multiple levels of analysis, such as environment (i.e., parenting), temperament (i.e., effortful control), and genetics (i.e., dopaminergic system) in the investigation of problem behavior.

One such model that could act as a theoretical framework for the current study is the Biosocial Developmental Model (Beauchaine & Gatzke-Kopp, 2012). The Biosocial Developmental Model stresses the importance of both adolescent characteristics (i.e., impulsivity and emotion regulation skills) and their environment in the development of externalizing problem behavior. Individuals with high impulsivity, which is linked to reduced dopamine reactivity, are more susceptible to the environment (e.g., parenting). More specifically, impulsivity is heritable, but it can be altered by repeated exposure to environmental stimuli. For instance, when parents react to adolescent impulsivity with firm limit setting and de-escalation of the impulsivity, adolescents' emotion regulation skills, such as effortful control, will be reinforced, which in turn leads to less externalizing problem behavior. However, when parents react to adolescent impulsivity with coercive control and negative reinforcement of the impulsivity, adolescents' emotion regulation skills will not develop optimally, leading to more externalizing problem behavior (Beauchaine & Gatzke-Kopp, 2012). This line of reasoning can be summarized by means of a moderated mediation model. The mediation model implies that parenting is associated with effortful control, which in turn predicts externalizing problem behavior. Genetic moderation of this mediation model implies that the extent to which adolescents are susceptible to parenting depends in part on their genetic characteristics (Beauchaine & Gatzke-Kopp, 2012). All three levels of analysis, that is, the environment, temperament, and genetics, are represented in the model.

The Current Studies

In the present article, we examined whether the longitudinal association between parenting and externalizing problem behavior was mediated by adolescents' effortful control, and whether the genes that code for dopaminergic reactivity moderated the direct and indirect association between parenting and externalizing problem behavior. Based on a study by Eisenberg (2005), which found that the associations between externalizing problem behavior and parental support and corporal punishment respectively, became less pronounced when adolescent effortful control was taken into account, we hypothesized that the association between parenting (i.e., both positive and negative) and externalizing problem behavior (i.e., aggressive and rule-breaking behavior) was (partially) mediated by effortful control. Furthermore, concerning the dopaminergic moderation, Weeland et al. (2015) showed that several dopaminergic genes (i.e. DRD4, DRD2, DAT1, and COMT) moderated the adolescent susceptibility to his/her parenting environment, which is in line with the differential susceptibility hypothesis. In

the present studies, we hypothesized that children with lower reactivity (i.e., lower BIMPS) showed stronger associations involving parenting practices (i.e. higher susceptibility; Beauchaine & Gatzke-Kopp, 2012).

Methods Study 1

Participants

Data were collected within the [MASKED] project. Permission for the [MASKED]project was obtained from the institutional review board of [MASKED]. This longitudinal study annually surveyed adolescents and their parents in Flanders, the Dutch-speaking part of Belgium. They were selected through a randomized multistage sampling approach. In a first stage, Flemish secondary schools were invited to take part in the study. Stratification was used to include students from general, technical, and vocational tracks. In the second stage, nine schools participated in the study, from which 121 classes in Grades 7, 8, and 9 were selected. Within these classes, 2,254 students and their parents were invited to participate. The final sample consisted of 1,116 adolescents, 841 mothers, and 724 fathers. Family characteristics were representative for the general population $\chi^2(2) = 2.78$, $p = .25$, with 82% two-parent families, 7% single-parent families, and 11% blended families (Janssens et al., 2017). The educational level (EDU) and employment activity level (ACT) of parents differed for both mothers (EMP: $\chi^2((3) = 30.34$, $p = .00$; ACT: $\chi^2((1) = 15.87$, $p = .00$) and fathers (EMP: $\chi^2 (3) = 34.19$, $p = .00$; ACT: $\chi^2 (1) = 15.13$, $p = .00$) with bachelor degrees and active employees being slightly overrepresented [MASKED]; Research Department of the Flemish Government, 2010, 2011). Despite this small deviation, it can be concluded that participants represented all categories of socioeconomic status. The present study used mother-reported data from Wave 3 (parenting), whereas adolescents reported on effortful control at Wave 4 (effortful control) and on externalizing problem behavior in Wave 5 (externalizing problem behavior) of the [MASKED] project. At Wave 3, adolescents were almost 16 (15.74) years old on average (minimum-maximum= [13.44; 19.09]). The present study included 457 mother-adolescent dyads across the three waves.

Researchers visited the school and invited the adolescents to fill out the questionnaires. In concert with the school, adolescents were provided two hours during classes to complete the questionnaires. When they did not finish the questionnaires within these two hours, they were allowed to finish the questionnaires at home and hand them in later using specially designated boxes. Adolescents who left the school or graduated were invited through e-mail and received an online version of the questionnaires. Parents could either fill out their questionnaires online or on paper. The latter was provided through the adolescents and could also be handed in using the designated boxes.

Measures

Parental practices (Time 1). *Parental Support* (Cronbach's α Wave 3 = .90) was reported by mothers and was measured using three parenting measures (Janssens et al., 2015). The first one was the Positive Parenting subscale (8 items, e.g., "If my child wants to tell something, I take my time to listen to me") from the Parental Behavior Scale- Short Form (PBS-S; Van Leeuwen et al., 2013). The second one was the Responsivity subscale (7 items, e.g., "I can make my child feel better when he/she is feeling upset") from the Louvain Adolescent Perceived Parenting Scale (LAPPS; Delhaye et al., 2012) This is an adaptation of a subscale from the Child Report of Parental Behavior Inventory by Schludermann and Schludermann (CRPBI; Schludermann & Schludermann, 1988). The third and final measure was the Autonomy Support scale (8 items, e.g., "I take into account the opinion of my child on affairs that concern him/her"), which was based on the Perceptions of Parents Scale (POPS; Grolnick, Ryan, & Deci, 1991) and the Research Assessment Package for Schools (RAPS; Institute for Research and Reform in Education, 1998). All 23 items were rated by adolescents on a 5-point scale ranging from 1 = *(almost) never* to 5 = *(almost) always*. An average score of the 23 items was calculated, with a high score referring to more maternal support.

Psychological control (Cronbach's α Wave 3 = .84) was reported on by mothers and used two subscales (Janssens et al., 2015). For the subscale Psychological Control (9 items, e.g., "I do not talk to my child when he/she disappointed me until he/she pleases me again"), 8 items were taken from the translated version of Barber's Psychological Control Scale (Barber, 1996; Soenens et al., 2006) and an additional item from a study by Soenens, Sierens, Vansteenkiste, Dochy, and Goossens (2012). The subscale Hostility (6 items, e.g., "I yell at my child when he/she misbehaves") was based on the Verbal Hostility Scale (Nelson & Crick, 2002), which was developed to assess intrusive parenting alongside corporal punishment. All 15 items were rated by mothers on a 5-point scale ranging from 1 = *(almost) never* to 5 = *(almost) always*. An average score of the 15 items was calculated, with a high score referring to more maternal psychological control.

Effortful control (Time 2). Adolescents reported on their own temperament by filling out a Dutch version of the Adult Temperament Questionnaire (ATQ; Evans & Rothbart, 2007). The present study solely used the dimension effortful control (Cronbach's α Wave 4 = .81), which comprised the subscales Activation Control (7 items, e.g., "I am often late for appointments" (reverse scored)), Attentional Control (5 items, e.g., "I often find it difficult to switch between different tasks" (reverse scored)), and Inhibitory Control (7 items, e.g., "I often find it difficult to resist my urge for drinks and food" (reverse scored)). All 19 items were rated by adolescents on a 7-

point scale ranging from 1= *(almost) never* to 7= *(almost) always*. An average score was calculated with a high score referring to more effortful control.

Externalizing problem behavior (Time 3). Adolescents rated their own externalizing problem behavior by filling out a Dutch version of the Youth Self Report (YSR; Achenbach 1991). Externalizing problem behavior consisted of two subscales, that is Aggressive behavior (17 items, e.g., "I destroy my own belongings"; Cronbach's α Wave 5 = .81) and Rule-breaking behavior (14 items, e.g. ''I skip classes or I play truant''; Cronbach's α Wave 5 = .72). A three-point rating scale was used, ranging from 0 to 2 (0 = *not true*, 1 = *somewhat or sometimes true*, to 2 = *very true or often true*). For both subscales, the mean score was computed. Higher scores indicated more externalizing problem behavior.

Biologically informed multilocus profile score (BIMPS). At Wave 1 of data collection for the [MASKED] project, a saliva sample was collected using Oragene DNA kits (DNA Genotek, Ontario, Canada). The present study only used genetic data for non-related participants. (Out of each of the 63 first- or second-degree relatives pairs one adolescent was randomly selected). Using the approach of Nikolova et al. (2011), a BIMPS was computed for each adolescent based on four dopaminergic polymorphisms. These genetic variants comprised two variable number of tandem repeats (VNTRs), that is, the 40-bp VNTR in the DAT1 gene and the 48-bpVNTR in the DRD4 gene, and two single nucleotide polymorphisms (SNPs), that is, the DRD2 Taq1A polymorphism (rs1800497) and the COMT Val/Met polymorphism (rs4680). Nikolova et al. (2011) also used a fifth polymorphism, the DRD2-141C Ins/Del polymorphism (rs1799732), but this genetic marker was not available in the present dataset.

Nikolova et al. (2011) assigned a score of 1 to genotypes associated with relatively high striatal dopamine signaling and/or reward-related ventral striatum reactivity, a score of 0.5 to intermediate genotypes, and a score of 0 to low genotypes (See Table A1). The BIMPS was computed by summing all the scores, which resulted in a continuous variable ranging from 0 to 4.

Statistical Analyses

Descriptive statistics. Means and standard deviations of all the included variables were computed. Additionally, correlational analyses (i.e., Pearson product-moment correlation) were conducted in order to provide a general description of the study variables and their associations. Little's test of Missing Completely At Random (MCAR; Little, 1988) was used in order to assess whether attrition across waves was completely at random in the present study. The test examines whether the null hypothesis of MCAR can be rejected, but cannot

differentiate between missing at random (MAR) and missing not at random (MNAR). This test is based on a chi square test, and thus, is sensitive to large sample sizes. Specifically, relatively small differences may lead to low p-values (Bergh, 2015). Therefore, we decided to adopt a more conservative alpha level of $\alpha = .01$. This test was done in SPSS, v24 (IBM Corp, 2016).

Moderated mediation model. The present study investigated four mediation models, representing each combination of positive/negative parenting and aggressive behavior/rule-breaking behavior. In each model, adolescent-reported effortful control was included as a mediator, whereas dopaminergic reactivity (i.e., BIMPS) was included as a moderator of the associations involving parenting. Parenting and effortful control were controlled for adolescents' age and gender, whereas externalizing problem behavior was additionally controlled for externalizing problem behavior at the first wave. Furthermore, since previous research indicated a common factor underlying both adolescent problem behavior and parenting behavior (Samek et al., 2015), we controlled for a correlation between parenting behavior and dopaminergic reactivity (i.e., rGE) by including the correlation between the parenting behavior and the BIMPS. The R^2 of the variables was used to assess which proportion of the respective variance was explained in the moderated mediation model. A general representation of the model is represented in Figure 1. All variables were standardized. In order to control for inflated probability of Type I error in the moderation mediation model that tests several parameters simultaneously, we followed the suggestion by Cribbie (2007) and applied the Benjamini-Hochberg correction. Since the moderator, that is the BIMPS, is a continuous variable, significant moderations were further explored using the Johnson-Neyman technique (Johnson & Fay, 1950). All analyses were conducted in MPlus version 7 (Muthén & Muthén, 2012). Missing values were handled with the Full Information Maximum Likelihood (FIML) method. Based on Monte Carlo simulations, Preacher, Rucker, and Hayes (2007) suggest a required sample size of approximately 200 observations in order to have sufficient power (>.80; Cohen, 1988) to detect conditional indirect effects using the aforementioned moderated mediation model, assuming medium effect sizes (d = .30; based on Chang et al., 2011). Given the sample size of 457 observations in the present study, we conclude that Study 1 has sufficient power.

Results Study 1

Descriptive Statistics

Descriptive statistics (i.e., mean and standard deviation) and the results from the correlational analyses in the sample of 457 mother-adolescent dyads are presented in Table 1. The BIMPS representing dopaminergic reactivity did not correlate significantly with other variables. Although rule-breaking behavior and aggressive

behavior were strongly correlated, they explained only approximately 47% of each other variance. This finding supports our decision to investigate the two types of externalizing problem behavior separately rather than a general externalizing problem behavior variable. Little's test (Little, 1988) indicated that the null hypothesis, stating that missing data in the present dataset was missing completely at random, could not be rejected at α of .01 ($\chi^2 = 60.497$, $df = 42$, $p = .032$).

Moderated Mediation Models

Model 1a included the association between parental support (controlled for age and gender) and aggressive behavior (controlled for age, gender, aggressive behavior at first time point), mediated by effortful control (controlled for age and gender) and moderated by BIMPS (See Figure 2). In contrast to our hypotheses, the association between support and aggressive behavior was not significant and was not significantly mediated by effortful control. BIMPS did show a significant positive association with aggressive behavior, suggesting that higher dopaminergic reactivity predicts more aggressive behavior in adolescents. Furthermore, we observed a significant interaction between BIMPS and support in the association with aggressive behavior. A further exploration using the Johnson-Neyman technique (See Figure 3) showed that a positive association between support and aggressive behavior was observed in adolescents with a lower BIMPS, whereas a negative association between support and aggression was observed in adolescents with a higher BIMPS. However, it should be noted that the regions of significance (i.e., the range of BIMPS in which the interaction effect differs significantly from zero) are below -2.25 *SD* (1.2% or *N* = 5) and above +0.45 *SD* (32.6% or *N* = 149) regarding the BIMPS. In other words, adolescents with a more extreme, positive as well as negative, seem to be more susceptible to parental support. Dopaminergic reactivity also seems to moderate the direction of the association. The proportion explained variance of the variables in model 1 is presented in Table 2.

Model 2a included the association between parental support (controlled for age and gender) and rule-breaking behavior (controlled for age, gender, and rule-breaking behavior at first time point), mediated by effortful control (controlled for age and gender) and moderated by BIMPS (See Figure 4). Similar to Model 1, we did not observe a significant association between support and rule-breaking behavior or a mediation by effortful control of this association. Furthermore, there was no significant direct association between BIMPS and rule-breaking behavior, nor was there a significant interaction between support and BIMPS in relation with rule-breaking behavior. The proportion explained variance of the variables in model 1 is presented in Table 2.

Model 3a included the association between parental psychological control (controlled for age and gender) and aggressive behavior (controlled for age, gender, and aggressive behavior at first time point), mediated by

effortful control (controlled for age and gender) and moderated by BIMPS (See Figure 5). In contrast to our hypotheses, there was no significant association between psychological control and aggressive behavior, nor was this association mediated by effortful control. The only significant association in Model 3 is the positive link between BIMPS and aggressive behavior, which is in line with results from Model 1. The proportion explained variance of the variables in model 1 is presented in Table 2.

Model 4a included the association between parental psychological control (controlled for age and gender) and rule-breaking behavior (controlled for age, gender, and rule-breaking behavior at first time point), mediated by effortful control (controlled for age and gender) and moderated by BIMPS (See Figure 6). In line with results from Model 2, there were no significant associations observed. The proportion explained variance of the variables in model 1 is presented in Table 2.

Methods Study 2

Participants

Concerning the [MASKED] project, participants were recruited at two sites, namely the University of Denver (Colorado) and Rutgers University (New Jersey). Families with a child in 3rd, 6th, or 9th grades in the broader Denver and central New Jersey areas were sent a letter to inform and invite them to participate in the study. Of these families, 1108 parents called the laboratory to ask for additional information. It was established that both the parent and the child were fluent in English. Furthermore, it was established that the child did not have an autism spectrum disorder, psychotic disorder, or intellectual disability. Of these 1108 families, 665 (60%) qualified as study participants. The remaining 498 (40%) were not retained for the study for the following reasons: 4 (1%) were excluded because the parents reported that their child had an autism spectrum disorder or low IQ; 13 (3%) were non-English speaking families; 330 (71%) declined after learning about the study's requirements; 113 (25%) did get an appointment but did not show up for assessment. Parents provided informed (written) consent for their child's participation, whereas the child provided written assent. Data were collected over a period of three years with an 18-month interval between successive waves. For more details see Hankin et al. (2015). At Wave 1, the present study included 221 parent-child dyads of which the children (M= 12.84, SD= 4.44) were between 7 and 16 years old at the first measuring point.

Measures

Parenting practices (Time 1). Independent raters coded parental support, responsiveness, conflict, and criticism during the parent-child interaction task at Wave 1. Global codes for each aforementioned parenting

construct were assigned on a scale of 1 to 5 (1 = "*not at all characteristic of the parenting behavior during the interaction"* and 5 = "*highly characteristic of the parenting behavior during the interaction"*). These codes were based on validated parent-child coding systems and reflect theoretically grounded parenting dimensions (Melnick & Hinshaw, 2000; NICHD Early Child Care Research Network, 1999). Parents rated high on parental support were engaged and affirming in their interaction with the child. Examples are providing validating comments (e.g., "I can see that") or praise their child. Parental criticism consisted of behaviors such as expressing disapproval or insulting the child, as well as blaming or inappropriately criticizing the child. Codes are consistent with prior work assessing positive and negative parenting (Davidov & Grusec, 2006). About 20% of observations were videotaped and double coded. Intraclass correlations between the two independent coders ranged from .71 to .85 on all subscales in this study, indicating good interrater reliability.

Effortful control (Time 2). Adolescents reported on their own temperament by filling out an English version of the Adult Temperament Questionnaire (ATQ; Evans & Rothbart, 2007). The subscale of effortful control showed adequate reliability (Cronbach's $\alpha = .78$). The same measure for effortful control was used as in Study 1.

Externalizing problem behavior (Time 3). Adolescents rated their own externalizing problem behavior by filling out an English version of the Youth Self Report (YSR; Achenbach 1991). The subscale of aggressive behavior showed good reliability (Cronbach's $\alpha = .84$), whereas the subscale of rule-breaking behavior showed adequate reliability (Cronbach's $\alpha = .72$). The same measure for externalizing problem behavior was used as in Study 1.

Biologically informed multilocus profile score (BIMPS). The computation of the BIMPS was identical to the one in Study 1.

Statistical Analyses

The analysis plan was identical to the one adopted in Study 1.

Results Study 2

Descriptive Statistics

Descriptive statistics (i.e., mean and standard deviation) and the results from the correlational analyses in the sample of 221 parent-adolescent dyads are presented in Table 3. The BIMPS representing dopaminergic

reactivity did not correlate significantly with other variables. Although rule-breaking behavior and aggressive behavior were strongly correlated, they explained only approximately 37% of each other variance. This finding supports our decision to investigate the two types of externalizing problem behavior separately rather than a general externalizing problem behavior variable. Little's test (Little, 1988) indicated that the null hypothesis, stating that missing data in the present dataset was missing completely at random, could not be rejected at α of .01 ($\chi^2 = 57.552$, $df = 40$, $p = .036$).

Moderated Mediation Models

Model 1b included the association between parental support (controlled for age and gender) and aggressive behavior (controlled for age, gender, aggressive behavior at first time point), mediated by effortful control (controlled for age and gender) and moderated by BIMPS (See Figure 7). In contrast to our hypotheses, there was no significant association between support and aggressive behavior, nor a significant mediation by effortful control. Furthermore, in contrast to Model 1a, there was no significant direct association with aggressive behavior, nor a significant interaction with support in the relation with aggressive behavior. The proportion explained variance of the variables in model 1 is presented in Table 2.

Model 2b included the association between parental support (controlled for age and gender) and rule-breaking behavior (controlled for age, gender, and rule-breaking behavior at first time point), mediated by effortful control (controlled for age and gender) and moderated by BIMPS (See Figure 8). There was no significant association between support and rule-breaking behavior or significant mediation by effortful control. We observed a significant interaction between BIMPS and support in the association with rule-breaking behavior. A further exploration using the Johnson-Neyman technique (See Figure 9) showed that a negative association between support and rule-breaking behavior was observed in adolescents with a lower BIMPS, whereas a positive association between support and rule-breaking was observed in adolescents with a higher BIMPS. This is in contrast to the interaction effect between support and BIMPS observed in Model 1a. It should be noted that the regions of significance (i.e., the range of BIMPS in which the interaction effect differs significantly from zero) are below -0.17 *SD* (43.3 % or $N = 96$) and above +2.08 *SD* (1.8 % or $N = 4$) regarding the BIMPS. In comparison with the interaction effect in Model 1a, there is a larger region of significance at the negative end of BIMPS and a smaller region of significance at the positive end of BIMPS. Dopaminergic reactivity also seems to moderate the direction of the association. The proportion explained variance of the variables in model 1 is presented in Table 2.

Model 3b included the association between parental criticism (controlled for age and gender) and aggressive behavior (controlled for age, gender, and aggressive behavior at first time point), mediated by effortful

control (controlled for age and gender) and moderated by BIMPS (See Figure 10). There was no significant association between criticism and aggressive behavior or a mediation of this association by effortful control, whereas there was a significant negative association between effortful control and aggressive behavior. Furthermore, we did not observe a significant direct or moderating effect of BIMPS in Model 3b. The proportion explained variance of the variables in model 1 is presented in Table 2.

Model 4b included the association between parental psychological control (controlled for age and gender) and rule-breaking behavior (controlled for age, gender, and rule-breaking behavior at first time point), mediated by effortful control (controlled for age and gender) and moderated by BIMPS (See Figure 11). There was no significant association between criticism and rule-breaking behavior or a mediation of this association by effortful control. Furthermore, we did not observe a significant direct or moderating effect of BIMPS in Model 4b. The proportion explained variance of the variables in model 1 is presented in Table 2.

Discussion

Externalizing problem behavior in adolescence is a major problem and for some adolescents this will lead to delinquent behavior in adulthood (Moffit, 1993). Previous research indicated that the link between parenting and adolescent problem behavior is (partially) explained by effortful control (Eisenberg et al., 2005), whereas another line of research indicated that the link between parenting and externalizing problem behavior is moderated by the genetic characteristics of the adolescent (i.e., dopaminergic pathway; Weeland et al., 2015). Despite the fact that effortful control has a biological basis and that mediation and moderation could co-occur in the context of the association between parenting and problem behavior (cfr., Biosocial Developmental Model; Beauchaine & Gatzke-Kopp, 2012) there is very limited research on how these factors act simultaneously. The present article adopted a moderated mediation model to investigate whether the longitudinal association between parenting and externalizing problem behavior was mediated by effortful control, and whether this association was moderated by a polygenic score based on dopaminergic genetic variation. In general, the results in the present article stress the importance of including multiple levels of analysis (i.e., parental environment, adolescent temperament, genetic characteristics) in research on externalizing problem behavior.

The findings did not show significant associations between parenting (at Time 1) and externalizing problem behavior (i.e., rule-breaking or aggressive behavior) (at Time 3). Furthermore, there was no mediation of this association by effortful control (at Time 2). The findings did suggest an interaction between parenting, and more specifically parental support and dopaminergic reactivity in association with externalizing problem behavior.

It is important to note that the interaction differed in direction between aggressive behavior and rule-breaking behavior. This finding may indicate an etiological difference between the two types of externalizing problem behavior, which is in line with previous research (Burt & Klump, 2013). Finally, the findings from the two studies (i.e., questionnaire versus observational data for parenting, different cultures, different languages) yielded some differing results, which indicates the importance of using multiple methods and being attentive to potential differences due to methodological differences.

The Mediating Role of Effortful Control in the Link Between Parenting and Externalizing Problem Behavior

The direct association between parenting and externalizing problem behavior, as well as the mediation of this association by effortful control were found to be non-significant. It is important to note that all the models took into account age and gender of the participants and that the externalizing problem behavior was additionally controlled for externalizing problem behavior at the first time point. It is possible that the expected association were not observed given the stability of externalizing problem behavior in adolescence (Reitz et al., 2005), and thus, the fact that a large proportion of the variance was already explained by including problem behavior at the previous time point. Together with the mixed findings concerning a moderation model in the study by Slagt et al. (2016), it seems that the role of effortful control in the association between parenting and externalizing problem behavior is more complex than just a mediator or just a moderator. It is possible that effortful control functions as a moderator and mediator simultaneously or switches between these two functions. More research is needed on which factors (i.e., individual characteristics or environmental factors) affect the role of effortful control.

The Role of Dopaminergic Reactivity

In the first study, we observed a significant direct positive association between dopaminergic reactivity and aggressive behavior, which indicates that a stronger dopaminergic reactivity leads to more aggressive behavior in adolescents. This is in line with previous research, such as the study by Telzer (2016), that suggested that a heightened reactivity may orient adolescents toward more risky behaviors. This association was not observed in the model including rule-breaking behavior, which is consistent with previous research suggesting that genetic characteristics contribute more strongly to aggressive behavior compared with rule-breaking behavior (Burt & Klump, 2013). However, it has to be noted that the direct association between dopaminergic reactivity and aggressive behavior was not replicated in Study 2, which used the same measures for both dopaminergic reactivity as well as externalizing problem behavior. Future studies should address the potential difference in contribution

from genetics and environment in rule-breaking and aggressive behavior. A more detailed knowledge on the relative contribution to the development of these types of externalizing problem behavior may improve prevention and intervention efforts.

In both studies, we found a significant interaction between parental support and dopaminergic reactivity in the association with externalizing problem behavior (i.e., aggressive behavior in Study 1, rule-breaking behavior in Study 2) and not in association with effortful control. It is important to note that this association was observed after taking into account the correlation between parenting and dopaminergic reactivity. Although there is an imbalance between the low and high end of the BIMPS spectrum, the total proportion of individuals that show an interaction between dopaminergic reactivity and support is considerable (i.e., 34% study 1; 45% study 2). The Biosocial Developmental Model (Beauchaine & Gatzke-Kopp, 2012) suggests numerous pathways that lead to externalizing behavior and one of them is that the interaction of a child's genetic characteristics (e.g., dopaminergic reactivity) and his/her environment (i.e., parenting) is associated with emotion regulation skills (i.e., effortful control), which in turn predicts externalizing problem behavior. Our results do not provide evidence for the role of effortful control and rather suggest a more direct influence of the genetics and environment combination on externalizing problem behavior. The link between genotypes (e.g., dopaminergic reactivity) and phenotypes (e.g., effortful control) is very complex and should be addressed on different levels of analysis in order to not oversimplify it (Robbins, 2018). Therefore, we want to stress that we do not aim to draw definitive conclusions based on the present results.

When we take a closer look at the observed interaction between observed parenting and dopaminergic reactivity (i.e., Study 1), the results suggest that adolescents both at the negative and positive extreme of the spectrum are more susceptible to their parenting environment, which goes beyond our hypotheses stating that we expect a stronger associations involving parenting in adolescents with lower dopamine reactivity (Beauchaine & Gatzke-Kopp, 2012). In Study 2 investigating observed parenting, the finding of susceptibility to the parenting environment in adolescents both at the low and high end of the dopaminergic reactivity spectrum was largely replicated. This finding is consistent with a systematic review by Weeland et al. (2015) regarding the association between dopaminergic genes and susceptibility to parenting. For all the dopaminergic genes included in the present study (i.e., DRD4, D2, DAT1, and COMT), Weeland et al. (2015) found studies showing that both hypo- and hyper reactivity lead to a susceptibility to the parenting environment.

Concerning the direction of the interaction, we found that parental support as reported in questionnaires (i.e., Study 1) predicted less aggressive behavior in adolescents with high dopaminergic reactivity, whereas

parental support predicted more aggressive behavior in adolescents with low dopaminergic reactivity. In contrast, the findings suggest that observed parental support (i.e., Study 2) predicted less rule-breaking behavior in adolescents with low dopaminergic reactivity, whereas parental support predicted more rule-breaking behavior in adolescent with high dopaminergic reactivity. In line with Weeland et al. (2015), our findings were mixed concerning the consistency as well as the direction of this moderation. The use of different measures for parenting and problem behavior across studies as well as a limited number of dopaminergic genes may partially explain the mixed findings in this context. Furthermore, as mentioned in the introduction, although the present study goes beyond the candidate gene approach, it does not allow to make decisive claims about G x E interactions, and more specifically the interplay between parenting, effortful control, and externalizing problem behavior. For instance, other neurotransmitter systems, such as the serotonergic pathway, could also play an important role in this interplay. It is possible that individual differences regarding other neurotransmitters play a role in the direction of the interaction. The present studies do provide some evidence of genetic moderation of the association between parenting and externalizing problem behavior, and moreover stress the need to include multiple levels of analysis in the investigation of externalizing problem behavior. However, more research using alternative methods, such as a genome-wide approach, is needed to get detailed information on these G x E interactions.

Limitations and Future Research

Despite the strengths of the present study (e.g., two independent samples from different cultures with different languages, longitudinal data, and both observational and questionnaire data on parenting), the two studies also have some limitations. First, most of the data were self-report measures, which could lead to social desirability bias. This may especially be the case for sensitive topics, such as problem behavior or parenting practices in Study 1. Second, although power analyses indicated sufficient power, it is possible that the hypothesized effects are smaller than the medium effect sizes used in our power analyses, which would require a larger sample size to have an adequate probability to be detected. Third, the present study used a polygenic index score based on four genes, which is already a more comprehensive approach than a candidate gene approach. However, four genes still provide a relatively limited representation of a genetic pathway. In recent years state-of-the-art GxE techniques such as Genome Wide Analysis (i.e., GWAS) has become popular given the fact that it allows to include an individual's complete genome rather than selecting a number of genes from a specific pathway. This technique has become less expensive and easier to implement. However, this GWAS approach was not as widely available in 2012, the starting period of the present projects, as it is today. Related to this issue, it would be interesting if multiple pathways were included. Genetic pathways other than the dopamine system, and the serotonin pathway

in particular, might also play a role in the interplay between parenting, effortful control, and externalizing problem behavior. Finally, a study by Hay and Forrest (2006) suggests that the association between parenting and effortful control is stronger in the first decade of a child's life. In other words, before the age of 10, parenting behavior may have a stronger impact on the child's self-regulation skills. Given the fact that both our studies used an adolescent sample, it would an interesting future research venue to replicate our findings in a younger sample (<10 years old).

Conclusion

Personal factors (temperament, genetic characteristics) as well as environmental factors (i.e., parenting) are important in the development of externalizing problem behavior in adolescence. However, there is little known about the interplay among these factors. The present article used two adolescent/late childhood samples from two three-wave longitudinal studies and investigated whether effortful control mediated the longitudinal association between parenting and externalizing problem behavior and whether this mediation model was moderated by the dopaminergic pathway. The present studies did not find a mediation of the association between parenting and externalizing problem behavior by effortful control, but did provide some evidence that the association between parental support and externalizing problem behavior was moderated by dopamine reactivity as assessed by a polygenic index score. This genetic moderation was inconsistent, but these findings imply that it is important to take into account the genetic characteristics of an individual when examining externalizing problem behaviors. Moreover, the present article shows that the development of externalizing problem behavior in the adolescence is subject to factors that lie both within the individual, such as genetic characteristics, and in the environment, such as parenting practices. A better understanding of these factors and how they act together is essential in advancing theoretical knowledge as well as the prevention/intervention efforts regarding externalizing problem behavior in adolescence.

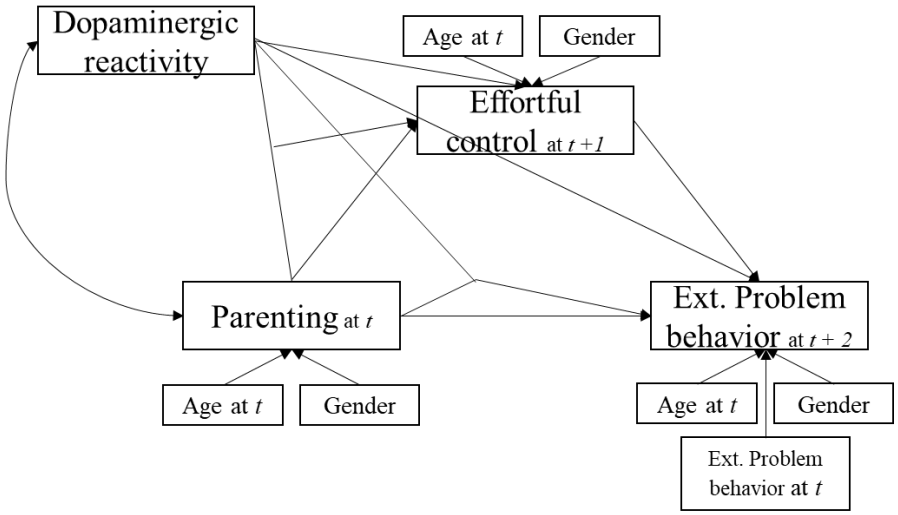

Figure 1. Representation of the moderated mediation model investigated in the present studies.

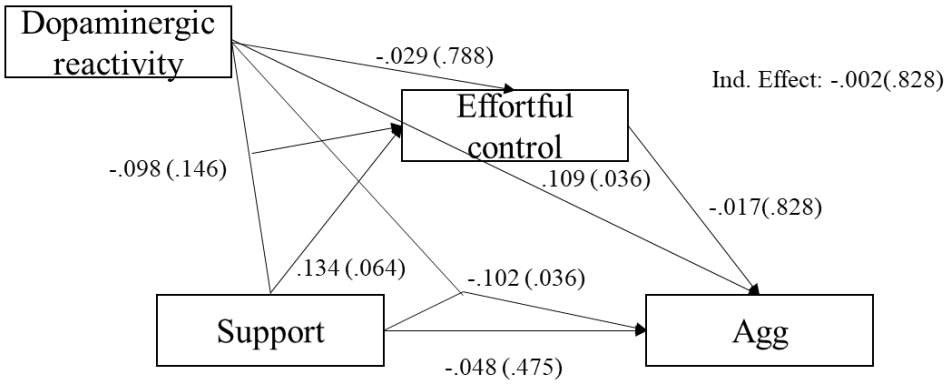

Figure 2. Results of the moderated mediation model including support and aggressive behavior (Agg) (Model 1a; Study 1).
Note. standardized coefficients and *p*-values corrected according the Benjamini-Hochberg method are presented.

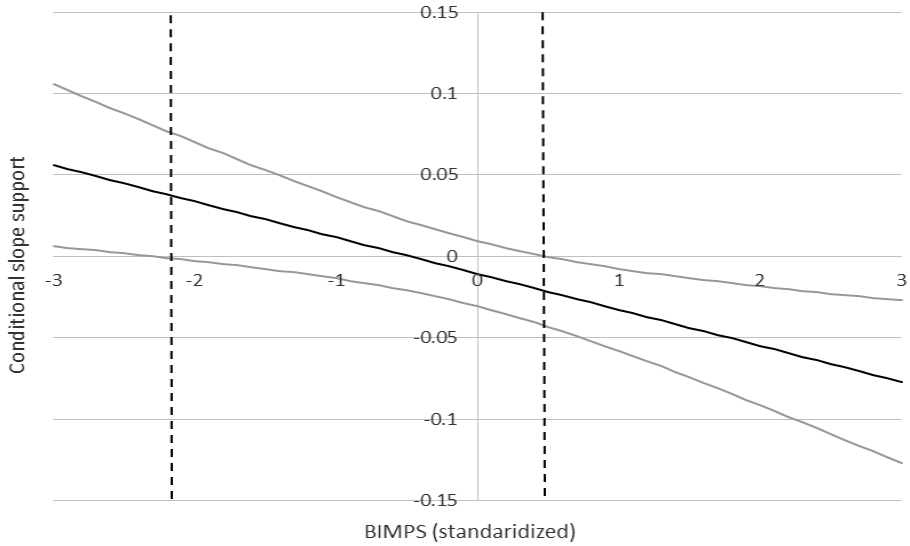

Figure 3 . Johnson-Neyman plot of the regions of significance of the interaction between BIMPS and support in relation with aggressive behavior.

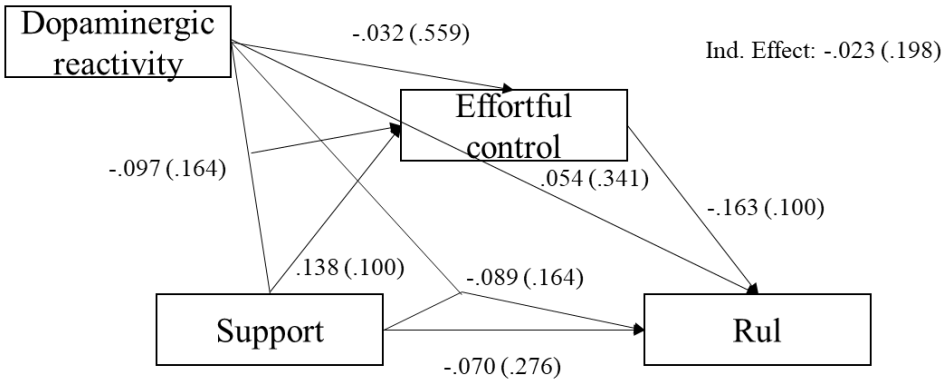

Figure 4. Results of the moderated mediation model including support and rule-breaking behavior (Rul) (Model 2a; Study 1).
Note. standardized coefficients and *p*-values corrected according the Benjamini-Hochberg method are presented.

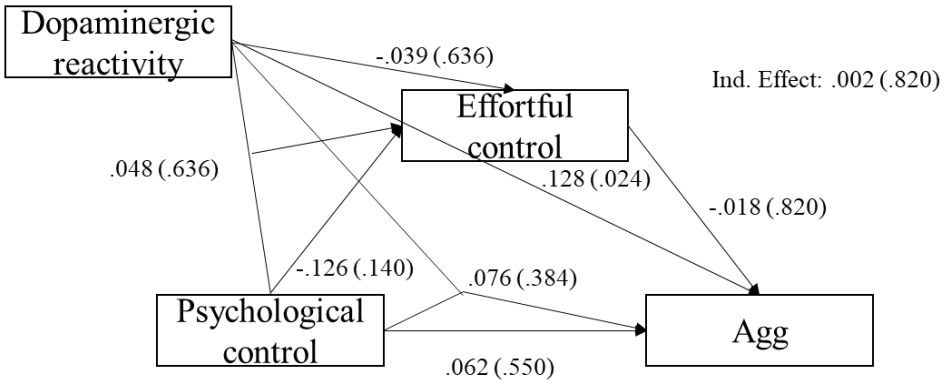

Figure 5. Results of the moderated mediation model including psychological control and aggressive behavior (Agg) (Model 3a; Study 1).
Note. standardized coefficients and *p*-values corrected according the Benjamini-Hochberg method are presented.

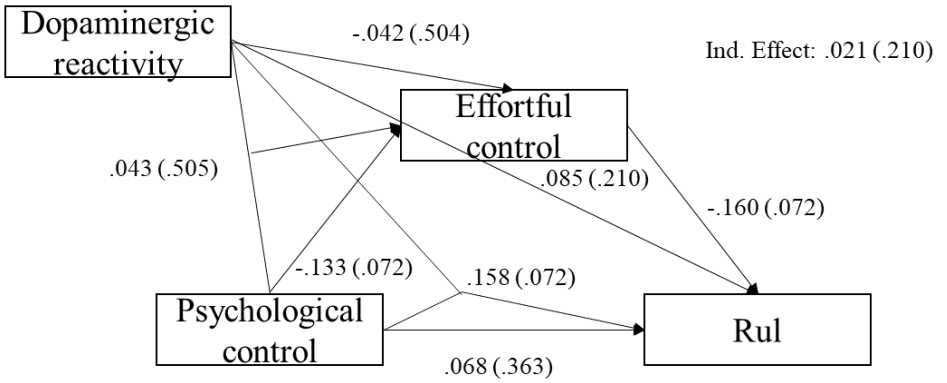

Figure 6. Results of the moderated mediation model including psychological control and rule-breaking behavior (Rul) (Model 4a; Study 1).
Note. standardized coefficients and *p*-values corrected according the Benjamini-Hochberg method are presented.

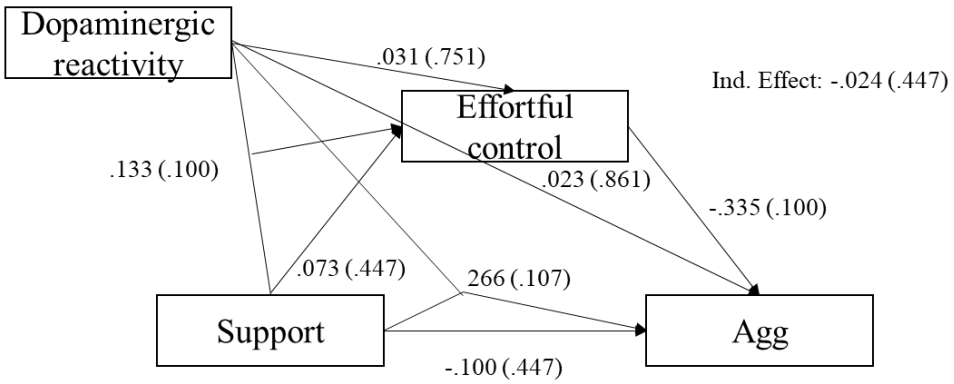

Figure 7 . Results of the moderated mediation model including support and aggressive behavior (Agg) (Model 1b; Study 2).
Note. standardized coefficients and *p*-values corrected according the Benjamini-Hochberg method are presented.

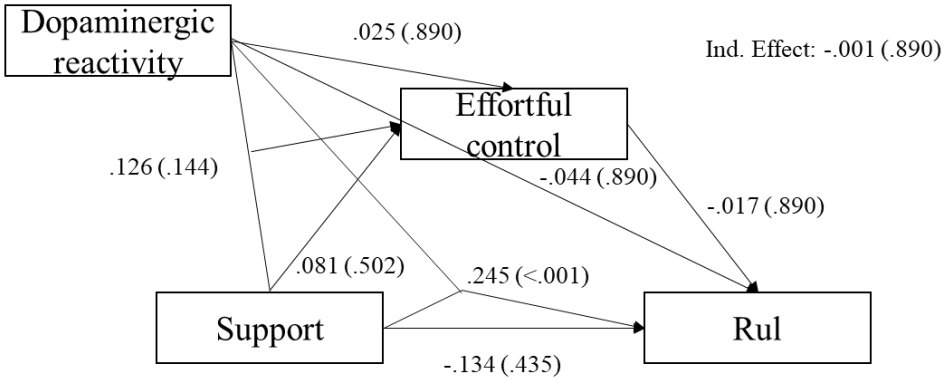

Figure 8 . Results of the moderated mediation model including support and rule-breaking behavior (Rul) (Model 2b; Study 2).
Note. standardized coefficients and *p*-values corrected according the Benjamini-Hochberg method are presented.

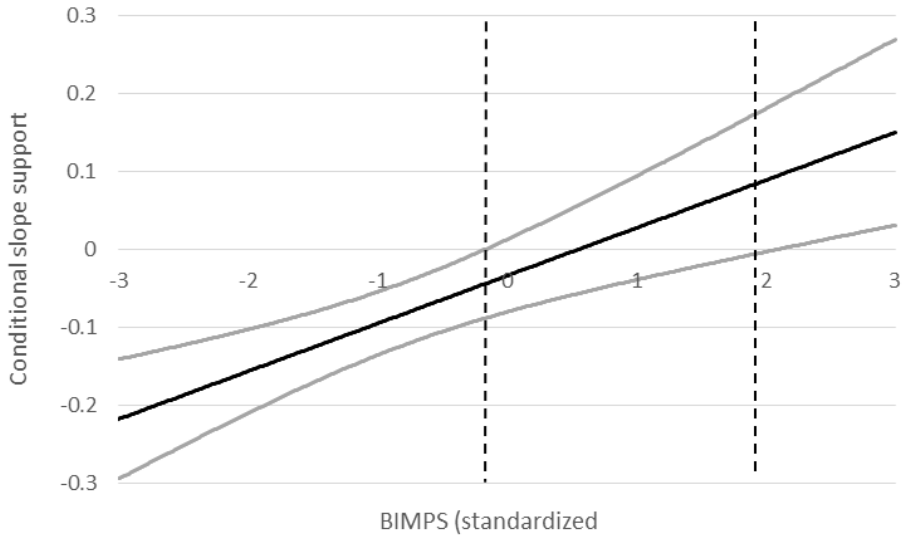

Figure 9. Johnson-Neyman plot of the regions of significance of the interaction between BIMPS and support in relation with rule-breaking behavior.

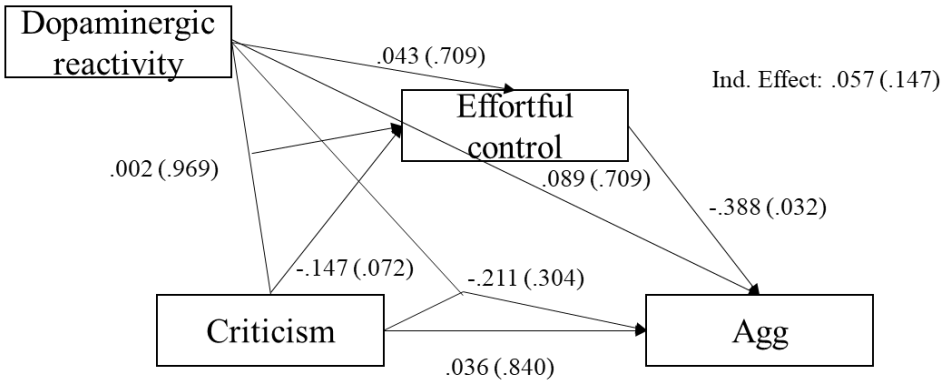

Figure 10 . Results of the moderated mediation model including criticism and aggressive behavior (Agg) (Model 3b; Study 2).
Note. standardized coefficients and *p*-values corrected according the Benjamini-Hochberg method are presented.

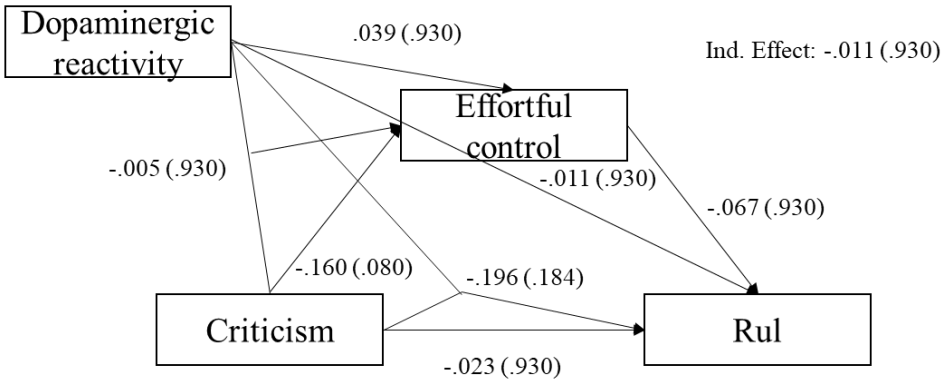

Figure 11 . Results of the moderated mediation model including criticism and rule-breaking behavior (Rul) (Model 4b; Study 2).
Note. standardized coefficients and *p*-values corrected according the Benjamini-Hochberg method are presented.

Table 1.

Descriptive Statistics and Correlational Analyses of Variables in Study 1.

	M (*SD*)	Min - Max	1	2	3	4	5	6
BIMPS (1)	2.14 (.84)	0 - 4	1					
Support (2)	4.27 (.40)	2.83 - 5.00	-.043	1				
Psychological control (3)	1.79 (.48)	1.00 - 4.13	-.034	-.315***	1			
Effortful control (4)	4.31 (.72)	2.37 - 6.37	-.024	.138*	-.171**	1		
Rule-breaking behavior (5)	.21 (.18)	0.00 - 1.21	-.013	-.199**	.205*	-.309***	1	
Aggressive behavior (6)	.25 (.21)	0.00 - 1.42	.030	-.242**	.264**	-.390***	.685***	1

Table 2.

Proportion Explained Variance of the Variables in the Moderated Mediation Model of Study 1 and Study 2.

Model	1a	2a	3a	4a	1b	2b	3b	4b
Effortful control	.033	.034	.024	.026	.093	.095	.091	.098
	(.132)	(.125)	(.174)	(.165)	(.018)	(.011)	(.020)	(.010)
Pos. parenting	.017	.017			.002	.010		
	(.178)	(.178)			(.724)	(.540)		
Neg. parenting			.001	.001			.002	.002
			(.713)	(.713)			(.743)	(.790)
Rule-breaking		.345		.364		.578		.540
behavior		(<.001)		(<.001)		(<.001)		(<.001)
Aggressive	.490		.490		.309		.302	
behavior	(<.001)		(<.001)		(<.001)		(.001)	

Note. Empty cells indicate that the variable was not included in that specific model; Pos. parenting= positive parenting; Neg. parenting= negative parenting

Table 3.

Descriptive Statistics and Correlational Analyses of Variables in Study 2.

	M (*SD*)	Min - Max	1	2	3	4	5	6
BIMPS (1)	1.77 (.75)	0 - 4	1					
Support (2)	2.87 (1.10)	1.00 - 5.00	.028	1				
Criticism (3)	2.00 (1.09)	1.00 - 5.00	.013	-.380***	1			
Effortful control (4)	3.53 (.55)	2.31 - 4.81	-.006	.124*	-.205***	1		
Rule-breaking behavior (5)	.38 (.25)	0.00 - 0.83	-.040	-.123	.092	-.393**	1	
Aggressive behavior (6)	.33 (.25)	0.00 - 0.86	.031	-.216*	.164	-.370***	.612***	1

Appendix

Table A1

Composition and Distribution of Biologically Informed Multilocus Profile Score (BIMPS)

Polymorphism	Genotype	N (%)	Score
DAT1 40-bp VNTR	9R carriers	45.6	High (1)
	10R/10R	54.4	Low (0)
DRD2 Taq1A	A2/A2	62.0	High (1)
	A1/A2	33.8	Intermediate (0.5)
	A1/A1	4.2	Low (0)
DRD4 48-bp VNTR	7R carriers	34.5	High (1)
	7R non-carriers	65.5	Low (0)
COMT Val158Met	Met/Met	26.0	High (1)
	Val/Met	47.8	Intermediate (0.5)
	Val/Val	26.2	Low (0)

Note. The scoring system of Nikolova et al. (2011) is used to compute a biologically informed multilocus profile score (BIMPS) representing four dopamine polymorphism. Genotypes associated with high dopamine signaling received a score of 1, low genotypes a score of 0, and intermediate genotypes a score of 0.5.

Authors' Contributions

LG, HC, WVDN, KV, and KVL were involved in the conceptualization of the STRATEGIES project. BH and JY were involved in the conceptualization of the GEM project. MVH was responsible for data analysis and report writing. PB, LC, HC, BH, WVDN, KV, and KVL provided feedback on the manuscript. All authors read and approved the final manuscript.

Data Sharing Declaration

The datasets generated and/or analyzed during the current study are not publicly available but are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors report no conflict of interests.

Compliance with Ethical Standards

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Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee at the University of Denver, Rutgers University, and at the University of Leuven (ML7972) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

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