How do genes get outside the skin? Mechanisms underlying Gene×Environment interactions in child externalizing problems

Weeland, J.

Publication date
2016

Document Version
Final published version

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: https://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
6. Does The Incredible Years reduce Child Externalizing Problems through Improved Parenting? The Role of Child 5-HTTLPR Genotype and Negative Affectivity

Abstract

In a randomized controlled trial (the Observational Randomized controlled trial of Childhood Differential Susceptibility (ORCHIDS) study) we tested whether observed parental affect and observed and reported parenting behavior are mechanisms of change underlying the effects of the behavioral parent training (BPT) program The Incredible Years (IY). Furthermore, we tested whether some children are more susceptible to these change mechanisms because of their temperamental negative affectivity and/or 5-HTTLPR genotype. Participants were 387 Dutch children between 4 and 8 years of age (Mage = 6.31, SD = 1.33; 55.3% boys) and their parents. Results showed that although IY was successful in improving parenting behavior and increasing parental positive affect, these effects did not explain the significant decreases in child externalizing problems. We therefore found no evidence for changes in parental behavior or affect being the putative mechanisms of IY effectiveness. Furthermore, intervention effects on child externalizing behavior were not moderated by child 5-HTTLPR genotype or child negative affectivity. However, child 5-HTTLPR genotype did moderate intervention effects on negative parenting behavior. In BPT programs, it might therefore not only be important to focus on what works for which children, but also on what works for which parents.
Parenting behavior, such as parenting strategies and parental affect, is one of the most robust predictors of early externalizing problems (for meta-analyses see Karremman et al., 2006; Rothbaum & Weisz, 1994) and has therefore been targeted in prevention and intervention programs such as behavioral parent training (BPT) (McCart et al., 2006). Although BPT is an effective method for decreasing children’s externalizing problems, mean effect sizes are moderate (McCart et al., 2006; Menting et al., 2013). This might be explained by two things. First, we have limited insight about which specific mechanisms of change are responsible for the intervention effects (“what works”) of BPT programs (for a review see Forehand, Lafko, Parent, & Burt, 2014). Secondly, what these specific mechanisms are may vary considerably between participating families (“what works for whom”) (Leijten et al., 2013; Menting et al., 2013; Scott & O’Connor, 2012). Gaining insight into what works for whom might help us tailor BPT programs by indicating, for specific children or families, what is the needed clinical focus, duration, and intensity, increasing their effectiveness (Chorpita, Becker, & Daleiden, 2007).

Because BPT programs consist of multiple components it is often unclear how specific mechanisms of change contribute to the intervention effects (for a review, see Forehand et al., 2014). Besides changes in the use of adequate parenting techniques, increases in parental positive affect (i.e., happiness and warmth) and decreases in parental negative affect (i.e., anger and harshness) may be important change mechanisms underlying the effectiveness of BPT programs (Coplan, Hastings, Lagacé-Séguin, & Moulton, 2002; Duncombe et al., 2012; Martin, Clements, & Crnic, 2009). Furthermore, due to temperamental or genetic predispositions, these putative mechanisms of change might have a larger impact in some children than in others. Changes in parental affect might be particularly important change mechanisms for children who show heightened arousability and behavioral responses to others emotions (i.e., heightened emotional reactivity). Specifically, temperamental negative affectivity and the 5-HTTLPR polymorphism have been previously related to such individual differences in emotional reactivity and might be related constructs (Auerbach et al., 1999; Belsky & Pluess, 2009; Weeland et al., 2015, Chapter 2). The current study tested whether intervention-induced changes in observed parental affect as well as observed and reported positive and negative parenting behavior mediated the effects of the BPT program The Incredible Years (IY) on parent reported child externalizing problems. Also, we tested whether some children are more susceptible to intervention-induced changes in parental affect and behavior because of their temperamental negative affectivity and/or 5-HTTLPR genotype.
What Works: Parental Affect and Behavior as Mechanisms of Change

BPT teaches parents to use effective parenting behaviors, such as monitoring and giving specific praise, in order to reduce child problem behaviors. Although the idea that BPT programs are effective in reducing child externalizing problems through parenting is strongly grounded in theory, studies testing parenting as a mediator of BPT effectiveness have yielded mixed results (Forehand et al., 2014; Gardner, Burton, & Klimes, 2006; Hanisch, Hautmann, Plück, Eichelberger, & Döpfner, 2014). In fact, a review of 16 intervention studies showed that, depending on the specific parenting behavior assessed, between 11% and 48% of tested mediators were significant (Forehand et al., 2014). Therefore, there has been a call for more research on the putative mediators of effective interventions (Forehand et al., 2014; Kazdin, 2007). Besides actual changes in parenting behavior, BPT encourages parents to increase in warmth and positivity during interactions with their children. Thus, both changes in parenting behavior and changes in parental affect might be important explanatory mechanisms underlying BPT intervention effects on child externalizing problems (for a review and meta-analysis see Kaminski, Valle, Filene, & Boyle, 2008; Sandler et al., 2011, but see also Hanisch et al., 2014). Previous longitudinal research even suggests that parental emotions are stronger predictors of child outcomes than actual parenting behavior itself (Duncombe et al., 2012; Isley, O’Neil, Clatfelter, & Parke, 1996; Rudy & Grusec, 2006). For example, the detrimental effect of authoritarian parenting on children’s self-esteem has been found to be explained by maternal negative emotions (Rudy & Grusec, 2006). Changing parental affect seems to be a key mechanism in promoting desirable child behavior, preventing escalation of parental irritability, anger, and aggression, and breaking coercive interaction patterns within families in which children have high levels of externalizing problems (Isley et al., 1999; Rudy & Grusec, 2006).

Most studies on mechanisms of change in BPT programs only took into account the use of parenting behaviors such as monitoring, limit setting, and disciplinary techniques. Equally as important as what parents do (i.e., parenting behavior) might be how they do it (i.e., expressed affect during parent-child interaction) (Crandall, Deater-Deckard, & Riley, 2015; Dix, 1991; Gardner et al., 2006; Rueger, Katz, Risser, & Lovejoy, 2011). BPT programs might indirectly decrease children’s externalizing problems, through increasing positive parental affect during parent-child interactions, and preventing coercive cycles set off by parental negative affect. In addition to the fact that studies on mechanisms of change mostly look at a limited set of potential mediators, they also have important methodological limitations. First, they mostly rely on parent reports of assessed mediators (parent behavior or affect) and outcomes (child behavior), which are likely to be biased as well as codependent. Second, BPT research often examines mediation by studying associations between an improvement in parenting behavior and a decrease in child externalizing problems at the same time point. These studies are therefore unable to conclude that change in parenting behavior indeed
preceded change in child externalizing problems. Failure to take into account the timeline of change in the mediator and the outcome is seen as “the Achilles’ heel of treatment studies” (Kazdin, 2007, p. 5). Therefore, in the current study we tested whether changes in, specifically observed, parental affect and behavior at six-month post-test mediated the intervention effect of IY on parent-reported externalizing problems at ten-month follow-up.

**What Works for Whom: Differential Effects by Child Temperament and Genotype**

Changes in parental affect and behavior might not be equally important change mechanisms for all children. Children might differ in how strongly they react to other’s emotions due to temperamental and genetic predispositions (Belsky & Pluess, 2009; Weeland, Overbeek, et al., 2015, Chapter 2). There is some evidence these temperamental and genetic predispositions are related constructs (see Auerbach et al., 1999; Belsky & Pluess, 2009, but see Dragan & Oniszczenko, 2005; Auerbach, Faroy, Ebstein, Kahana, & Levine, 2001; Weeland, Slagt, et al., 2015, Chapter 7). For example, both relate to individual differences in amygdala activity after exposure to expressed emotion (Kret, Denollet, Grèzes, & de Gelder, 2011; Murphy et al., 2013). On the one hand, this might suggest that both temperamental and genetic differences in emotional reactivity are able to explain children’s differential reactions to parenting and parenting interventions (i.e., emotional reactivity hypothesis). On the other hand, considering the mixed findings on their relatedness, as well as differences in how proximal they are to actual child behavior, it might be that one or the other moderates the impact of parenting and parenting interventions. The current study assessed whether the effects of changes in observed positive and negative parental affect and observed and reported parenting behavior on parent-reported child externalizing problems are moderated by child negative affectivity and/or 5-HTTLPR genotype.

Children who show heightened emotional reactivity might become more aroused than less emotionally reactive children by others’ emotions, might more easily alter their own mood, and experience difficulties in regulating these emotions and their behavioral response (e.g., Auerbach et al., 1999; Davies & Cicchetti, 2013; Gyurak et al., 2013; Hankin et al., 2011; Murphy et al., 2013; but see Weeland, Slagt, et al., 2015, Chapter 7). Thus, they may be more susceptible to (changes in) positive and negative emotions in the context of intervention (Scott & O’Connor, 2012). At a behavioral level, such differences in emotional reactivity may be indexed by temperamental negative affectivity, defined as children’s tendency to respond with high levels of negative affect such as anger or irritability to their environment (Derryberry & Rothbart, 1988). Children’s negative affectivity has been found to moderate the effects of parenting on child adjustment (Belsky, Hsieh, & Crnic, 1998; Bradley & Corwyn, 2008; Lipscomb et al., 2012; Morris et al., 2002; Ramos, Guerin, Gottfried, Bathurst, & Oliver, 2005), as well as the effects of parenting interventions (Gallitto, 2015;...
Scott & O’Connor, 2012; Van Zeijl et al., 2007). For example, maternal hostility has been found to predict child externalizing problems for children high on negative affectivity, but not for children low on this trait (Morris et al., 2002).

At a genetic level, emotional reactivity may be indexed by a polymorphism in the promoter region of the serotonin transporter gene (i.e., 5-HTTLPR). The 5-HTTLPR polymorphism, which has a high activity long (L) allele and a low activity short (S) allele, regulates serotonin availability, which is an important modulator of neural circuitry controlling behavioral and physiological processes including mood. Children’s 5-HTTLPR genotype has been found to moderate the effects of parenting on child adjustment (i.e., G×E interactions; Van IJzendoorn et al., 2012), as well as the effects of parenting programs (i.e., G×I interactions; Albert et al., 2015; Bakermans-Kranenburg et al., 2008; Van den Hoofdakker et al., 2012). For example, Hankin and colleagues (2011) found that children who carried a 5-HTTLPR S-allele (SS and SL-genotypes) showed more positive affect when their parents were supportive and positive (observed, as well as measured by parent- and child-report), but less positive affect when their parents were non-supportive and negative, compared to children carrying two L-alleles (LL-genotypes). Temperamental and genetic differences in emotional reactivity might thus explain children’s differential reactions to parenting and parenting interventions (emotional reactivity hypothesis). The current study assessed whether the effects of changes in observed positive and negative parental affect and observed and reported parenting behavior on parent reported child externalizing problems are moderated by child negative affectivity and/or 5-HTTLPR genotype.

The Current Study
The current study features a randomized controlled trial (i.e., pre-test, post-test, follow-up) of IY among 387 parents and their children aged 4 to 8 years. We examined (1) whether changes in observed parental affect and observed and reported parenting behavior explained the effects of IY on decreases in parent reported children’s externalizing problems, and (2) whether some children were more susceptible to changes in parental affect and parenting behaviors based on their temperamental negative affectivity and/or 5-HTTLPR genotype. Specifically, we hypothesized that observed parental affect at post-test would mediate the effect of IY on decreasing parent reported child externalizing problems at follow-up. In addition, based on an emotional reactivity hypothesis, we expected that these change processes would be more strongly associated with reductions in externalizing problems in children high on negative affectivity or carrying one or two 5-HTTLPR S-alleles. Specifically, these children were hypothesized to be more susceptible to intervention-induced changes in parental affect and parenting behavior and consequently show stronger decreases in externalizing problems after the intervention than children without these susceptibility characteristics.
Methods and Materials

Participants
Participating parent-child dyads (N = 387) were part of the longitudinal Observational Randomized controlled trial of CHildhood Differential Susceptibility (i.e., ORCHIDS study, for details on design, recruitment and sample see Chhangur & Weeland et al., 2012; Chapter 2; Weeland & Chhangur et al., submitted for publication; Chapter 4). Children were between 4 and 8 years of age at the start of the study (Mage = 6.31, SD = 1.33), mostly born in the Netherlands (97.4%), and 55.3% male. Parents (91% were mothers) were between 23 and 51 years of age (Mage = 38.10, SD = 4.84), over 80% born in the Netherlands, and about half of them (47.8%) were higher educated (i.e., completed higher vocational training or university).

Procedure
Parent-child dyads were recruited in two cohorts through two regional health care organizations. All families with children between the ages of 4 and 8 years living in the targeted municipalities received a personalized invitation letter including the questionnaire used for screening (i.e., Eyberg Child Behavior Inventory; Eyberg, & Pincus, 1999). Families with children scoring at or above the 75th percentile of their respective cohort were invited for further participation. Parents signed written informed consent for participation of both themselves and their child. Participation in the randomized controlled trial (RCT) consisted of three measurement waves (i.e., pre-test, post-test after 6 months and follow-up after 10 months). During all measurement waves families were asked to fill out online questionnaires on parent and child behavior. Also, families were visited at home by one of the researchers or a trained research assistant to conduct an observation during a structured play situation, which was videotaped for later coding. During the first home visit saliva swabs were collected from children. After the first home visits participants were randomly assigned to either the control group or the intervention group (50/50). The intervention group received the IY parent training between the pre-test and post-test. The control group did not receive any intervention through the RCT, but was free to seek other (mental) health care during the study (i.e., “care as usual”). Approval for this study was received from the Institutional Review Board in Utrecht, The Netherlands (METC UMC Utrecht, protocol number 11-320/K). For more information on the procedure see Chhangur & Weeland and colleagues (2012, Chapter 3).

Intervention: The Incredible Years BASIC program
IY (Webster-Stratton, 2008) aims to prevent and intervene in the development of child externalizing problems by reducing harsh and unresponsive parenting and increasing positive and warm parenting. The program has been studied intensely and has been found effective in reducing child externalizing problems across settings and target populations.
Chapter 6

(Menting et al., 2013). The program starts with a focus on positive parenting behavior such as play, praise and incentives before discussing effective limit setting, ignoring unwanted behavior and using time out strategies (Webster-Stratton, 2008). Discussion of these topics includes a focus on parent behavior as well as child and parent thoughts and emotions. IY is a group behavioral parent training consisting of 15 sessions (i.e., 14 weekly 2-hour sessions and a “booster” session). Every group was led by two group leaders with a background in clinical child psychology. The main leader was officially certified as a group leader by conducting at least two complete sets of the program and sending in at least one DVD session for review by a certified IY Trainer (though The Incredible Years Inc.). To ensure and monitor implementation fidelity, all leaders completed a weekly session-specific checklist. These checklists showed that, on average, 70.4% of session activities (e.g., vignettes, brainstorms and role-plays) were executed by trainers. It has been argued that positive intervention effects are obtained when the level of program integrity exceeds 60% (Durlak & DuPre, 2008). Participating parents attended 8.6 sessions on average. Of all parents randomized to the intervention condition, 44 did not attend any sessions. These parents did not differ from parents that did attend sessions (see Chhangur & Weeland et al., submitted for publication, Chapter 4).

Observation Measures

Parent and child were videotaped for 20 minutes at pre-test, post-test and follow-up. The observation procedure consisted of four five-minute periods in which parents and children played with a fixed set of toys: 1) free play (i.e., to get used to being videotaped); 2) child directed play (i.e., child picked a toy and directed the session); 3) parent directed play (i.e., parent picked a toy and directed the session); and 4) clean up (i.e., parent had to make the child clean up the toys). The observations were coded by trained research assistants who were not involved in the study and who were blind to condition and measurement wave. Monthly calibration meetings were held to prevent observer drift. To provide estimates of interrater reliability (intraclass correlation (ICCs)), using SPSS 22.0, a random 20% of the observations were independently coded by two coders. Coders were unaware of which observations were used to assess observer agreement.

Parental Positive and Negative Affect

For each period parental positive and negative affect was coded on a 5-point scale (1 = not all positive/negative to 5 = very positive/negative) (based on the System for coding interactions in parent-child dyads (SCIPD), Lindahl & Malik, 1996). Interrater reliability of the parental affect measure was good at all measurement waves: α > .76 for negative parental affect and α > .80 for positive parental affect (see Table 6.1 for descriptive statistics).
**Observed Positive and Negative Parenting Behavior**

The Dyadic Parent–Child Interaction Coding System (DPICS) was used to code positive and negative parenting behavior during parent–child interactions (Robinson & Eyberg, 1981; Webster-Stratton, 1989). The scale positive parenting behavior consisted of 7 items (i.e., acknowledgement, descriptive question, descriptive comment/encouragement, unlabeled praise, labeled praise, positive affect, and physical positive). The negative parenting behavior scale comprised 6 items (i.e., physical intrusive, physical negative, critical statement, negative command, indirect command without opportunity, direct command without opportunity). Interrater reliability was excellent at all measurement waves; ICCs >.96 for positive parenting behavior and > .85 for negative parenting behavior. The reliability of the parenting scales was acceptable α > .60 for positive parenting and α > .67 for negative parenting (see Table 6.1 for descriptive statistics).

**Questionnaire Measures**

**Child Externalizing problems**

The Eyberg Child Behavior Inventory (ECBI) assesses the occurrence of conduct problems in children aged 2 to 16 years (Eyberg, & Pincus, 1999). The ECBI intensity scale consists of 36 items (e.g., ‘Acts defiant when told to do something’). Parents report how often their child currently engages in each behavior rated on frequency by parents on a 7-point scale (1= never to 7= always). Reliability of the scale was good for all three waves (α > .84) (see Table 6.1 for descriptive statistics).

**Negative Affectivity**

The Children’s Behavior Questionnaire Very Short Form (CBQ-VSF; Putnam & Rothbart, 2006) assesses primary characteristics of temperament in young children of 3 to 8 years of age. We used the scale negative affectivity as an emotional reactivity measure. The scale consists of 12 items (e.g., ‘Gets quite frustrated when prevented from doing something s/he wants to do’) which can be answered using a 7-point Likert scale (1= extremely untrue for my child to 7 = extremely true for my child) or with “not applicable”. Reliability of the scale was satisfactory (α = .69) (see Table 6.1 for descriptive statistics). For analyses, child negative affectivity was coded into three groups: low (0: 1SD below the mean, n = 64), medium (1: mean +/- 1 SD, n = 258) and high (2: 1SD above the mean, n = 64).

**Reported Positive and Negative Parenting Behavior**

The Parenting Practice Inventory (PPI) measures parenting skills and discipline styles of parents with children 6-12 years (Webster-Stratton, 2001). The PPI consists of 15 sections; each containing multiple items, which are answered using different scales (e.g., ‘How likely is it that you respond to this behavior in one of the following ways’). In total, four
summary scales were extracted from this questionnaire; harsh and inconsistent discipline (15 items, e.g., ‘Threatening but not punishing’, α > .76), positive verbal discipline (9 items e.g., ‘Discussing the problem with the child’, α > .71), physical punishment (6 items, e.g., ‘Slapping or hitting when misbehavior occurs’, α > .81), and praise and incentives (11 items, e.g., ‘Giving a hug or compliment’, α > .65). Statements about parenting (e.g., ‘Sometimes one must get very angry with his/her children to teach them a lesson’) were excluded, because we were interested in the actual behavior of parents. Positive parenting behavior was assessed by a combination of the dimensions positive verbal discipline and praise and incentives (r = .29, p = < .001). Negative parenting behavior was assessed by a combination of the scales harsh and inconsistent discipline and physical punishment (r = .29, p = < .001). Reliability for both scales was satisfactory on all measurements (Positive parenting behavior α > .70; Negative parenting behavior α > .78) (see Table 6.1 for descriptive statistics).

**Genotyping**

5-HTTLPR. Buccal swabs were collected in lysisbuffer (100 mM NaCl, 10 mM EDTA, 10 mM Tris pH 8, 0.1 mg/ml proteinase K and 0.5% w/v SDS) until further processing. Genomic DNA was isolated from the samples using the Chemagic buccal swab kit on a Chemagen Module I workstation (Chemagen Biopolymer-Technologie AG, Baesweiler, Germany). Within the ORCHIDS study six genes were analysed (i.e., MAOA, COMT, DRD2, DRD4, DAT1, and 5-HTTLPR). All analyses were automatically performed using specialized genotyping software, after which output of the analysis of each plate was checked by a lab-worker. Analyses showing notable deviations or multiple failings were repeated. The output of all analyses was checked by a second lab-worker. Each 96 well plate consisted of one blank; analyses were only continued if this blank showed a negative result. To further test reliability of the genotype procedure duplicates samples of 9 children were collected to test the replicability of the results: Of the 56 replication genotyping procedures (9 times 6 genotypes) 53 (95%) were successfully replicated. For one duplicate sample, it was not possible to genotype the MAOA polymorphism. The current paper focuses specifically on the 5-HTTLPR because this polymorphism has been associated with individual differences in emotional reactivity (Hankin et al., 2011; Murphy et al., 2013; Pezawas et al., 2005). Results of the ORCHIDS study with a dopaminergic polygenic score were reported elsewhere (see Chhangur et al., in press).

The region of interest from the target gene 5-HTT was amplified by PCR using the following primers: a FAM-labelled primer 5'-TGGGGTGCAGGGGAGATCCTG-3’, and a reverse primer 5'-TCCTCCGCTTTGGCGCCTCTTCC-3’. Typical PCR reactions contained between 10 and 100 ng genomic DNA template and 10 pmol of forward and reverse primer. PCR was carried out in the presence of 5% DMSO, 5x buffer supplied with the enzyme and with 1.25U of LongAmp Taq DNA Polymerase (NEB) in a total volume of 30 µl using the
following cycling conditions: initial denaturation step of 10 min at 95°C, followed by 26 cycles of 30 sec 95°C, 30 sec 60°C, 60 sec 65°C and a final extension step of 10 min 65°C. After PCR 10 µl of the sample was subjected to restriction digestion with the enzyme HpaII in a total volume of 20 µl. Restriction was incubated for 2 hours at 37°C and inactivated by incubating for 20 min. at 80°C. One microliter of PCR product before and after restriction was mixed separately with 0.3 µl LIZ-500 size standard (Applied Biosystems) and 11.7 µl formamide (Applied Biosystems) and run on an AB 3730 genetic analyser set up for fragment analyses with 50 cm capillaries. Results were analysed using GeneMarker software (Softgenetics). The genotype distribution was 32.5% LL genotype, 50.8% SL genotype, and 16.8% SS genotype, and did not differ between participants of the control and the intervention condition ($\chi^2 = 5.80; df = 2; p = .06$). Hardy-Weinberg equilibrium (HWE) proportions were estimated, and no deviations from these proportions were found ($\chi^2 = .65; df = 2; p = .72$) (Rodriguez et al., 2009). For analyses, 5-HTTLPR genotype was coded into three groups, assuming an additive model (i.e., 0 = LL, 1 = SL, 2 = SS).

**Analyses**

We used Cross-Lagged Structural Equation Models (i.e., CLSEM; Cole & Maxwell, 2003; Keijsers, 2015) (see Figure 6.1) in Mplus. We used full-intention-to treat, which means that 44 families in the intervention condition who did not attend any sessions were still included in the analyses. Because the Shapiro-Wilk tests showed that both reported and observed parenting scales were skewed (positively for the negative and negatively for the positive parenting scales), we reported Maximum Likelihood Robust (MLR) model fit indexes. Model fit was assessed using the Root Mean Square Error of Approximation (RMSEA) (model fit satisfactory when $< .08$) and the Confirmatory Fit Index (CFI) and the Tucker-Lewis Index (TLI) (model fit satisfactory when $> .90$) (Hu & Bentler, 1999). The analyses were conducted in two steps. First, in order to assess possible mediation of the intervention effect by parental affect and behavior we used a three wave CLSEM. We included concurrent (within-time) correlations between the variables, the stability effects for variables (auto-regression effects), and longitudinal cross-lagged effects of child behavior and parenting affect or behavior (and vice versa over pre-test (T1), post-test (T2) and follow-up (T3)). In this model we tested whether the intervention had a significant effect on child externalizing problems at T3 (path a, Figure 6.1), on parental affect or behavior at T2 (path b, Figure 6.1), and whether parental affect or behavior at T2 predicted child externalizing problems at T3 (path c, Figure 6.1). For the sake of completeness we reported all separate paths as part of the mediation model. However, significance of all these paths is no requisite for mediation to occur (Zhao, Lynch, & Chen, 2010). As a formal test of mediation, we included an indirect effect to the model of intervention on child externalizing problems at follow-up via parental affect or behavior at T2 (pathway bc, Figure 6.1). As recommended by Selig and Preacher
(2009), a bootstrapping procedure (5000 bootstrap samples) was used to estimate 95% confidence intervals (CI) of the indirect effects. Second, in order to test possible moderation by child temperamental negative affectivity and 5-HTTLPR genotype, we repeated the CLSEM with a multi-group approach (SS, SL, and LL genotype; low, average, and high emotionality reactivity).

To test whether the mediation models were significantly different across groups, we used the chi-square difference test ($\Delta \chi^2$) to compare the models in which all mediation paths were constrained to be equal across groups with the free models in which all mediation paths were estimated freely. Evidence for moderated mediation was found if the constrained model fit significantly worse than the unconstrained model. For the models that indicated significant group differences, we compared the specific path coefficients between the groups, taking into account sample size and standard errors for each group (Cohen et al., 2013; Soper, 2016).

**Results**

**Mechanisms of Change: Parental Affect**

Inspection of the data showed there were no outliers. Descriptive statistics and correlations for all measures are shown in Tables 6.1 and 6.2.

Both positive and negative parental affect CLSEM yielded excellent fit statistics (Figures 6.1 and 6.2). The auto-regressive correlations of the models showed that both child externalizing problems and parental negative affect were predicted by the same variable at an earlier time point, indicating that these behaviors were relatively stable over time (T1 = pre-test; T2 = post-test; T3 = follow-up). Concurrent correlations showed that within-time child externalizing problems and parental negative affect were only weakly correlated. This indicates that within-time parental affect and child externalizing problems were not structurally related.

The main results showed that the intervention was not successful in decreasing child externalizing problems at T3 (path a, Figures 6.1 and 6.2), but was successful in decreasing these problems at T2. Also, the intervention was successful in increasing parental positive affect (but not decreasing parental negative affect) at T2 (path b, Figures 6.1 and 6.2), but not at T3. However, neither parental negative nor positive affect at T2 predicted child externalizing problems at T3 (path c, Figures 6.1 and 6.2), and there was no indirect effect from the intervention to child externalizing problems via parental negative or positive affect (path bc, negative affect: $B = .000; SD = .004; p = .93; 95\% CI - .004 - .009$; positive affect: $B = -.003; SD = .008; p = .72; 95\% CI - .018 - .009$).
Table 6.1 / Descriptives of Parental Affect and Parent and Child Behavior

<table>
<thead>
<tr>
<th></th>
<th>Pre-test</th>
<th></th>
<th></th>
<th>Post-test</th>
<th></th>
<th></th>
<th>Follow-up</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Intervention</td>
<td>Control</td>
<td>Intervention</td>
<td>Control</td>
<td>Intervention</td>
<td>Control</td>
<td>Intervention</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
</tr>
<tr>
<td>Child negative affectivity</td>
<td>4.06</td>
<td>.86</td>
<td>4.21</td>
<td>.92</td>
<td>3.98</td>
<td>.83</td>
<td>4.04</td>
<td>.87</td>
</tr>
<tr>
<td>Child externalizing behavior</td>
<td>3.65</td>
<td>.51</td>
<td>3.75</td>
<td>.55</td>
<td>3.54</td>
<td>.54</td>
<td>3.44</td>
<td>.53</td>
</tr>
<tr>
<td>Negative parental affect</td>
<td>2.05</td>
<td>.70</td>
<td>1.94</td>
<td>.68</td>
<td>2.04</td>
<td>.71</td>
<td>1.94</td>
<td>.64</td>
</tr>
<tr>
<td>Positive parental affect</td>
<td>2.80</td>
<td>.63</td>
<td>2.85</td>
<td>.65</td>
<td>2.82</td>
<td>.66</td>
<td>3.09</td>
<td>.64</td>
</tr>
<tr>
<td>Negative parenting (obs)</td>
<td>1.58</td>
<td>1.07</td>
<td>1.54</td>
<td>1.05</td>
<td>1.54</td>
<td>1.01</td>
<td>1.29</td>
<td>.86</td>
</tr>
<tr>
<td>Positive parenting (obs)</td>
<td>2.32</td>
<td>.87</td>
<td>2.43</td>
<td>.85</td>
<td>2.30</td>
<td>.93</td>
<td>2.79</td>
<td>1.11</td>
</tr>
<tr>
<td>Negative parenting (rep)</td>
<td>2.70</td>
<td>.59</td>
<td>2.80</td>
<td>.62</td>
<td>2.57</td>
<td>.66</td>
<td>2.39</td>
<td>.58</td>
</tr>
<tr>
<td>Positive parenting (rep)</td>
<td>4.67</td>
<td>.62</td>
<td>4.70</td>
<td>.63</td>
<td>4.67</td>
<td>.65</td>
<td>4.88</td>
<td>.64</td>
</tr>
</tbody>
</table>

Note. obs = observed; rep = parent reported

Table 6.2 / Correlations Between Parent and Child Variables at Pre-test.

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Child negative affectivity</td>
<td>-.03</td>
<td>.35***</td>
<td>-.18*</td>
<td>-.03</td>
<td>.05</td>
<td>-.05</td>
<td>.24**</td>
<td>.09</td>
<td></td>
</tr>
<tr>
<td>2. 5-HTTLPR genotype</td>
<td>-</td>
<td>-.06</td>
<td>-.06</td>
<td>-.01</td>
<td>.05</td>
<td>.02</td>
<td>-.06</td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td>3. Externalizing child behavior</td>
<td>-</td>
<td>-.05</td>
<td>-.14**</td>
<td>-.11*</td>
<td>.05</td>
<td>.05</td>
<td>.05</td>
<td>.10</td>
<td></td>
</tr>
<tr>
<td>4. Negative parental affect</td>
<td>-</td>
<td>-.05</td>
<td>-.37***</td>
<td>-.10</td>
<td>-.03</td>
<td>-.09</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Positive parental affect</td>
<td>-</td>
<td>-.19**</td>
<td>.46***</td>
<td>-.16**</td>
<td>-.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Negative parenting (obs)</td>
<td>-</td>
<td>-.05</td>
<td>.11**</td>
<td>.18**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Positive parenting (obs)</td>
<td>-</td>
<td>-.14**</td>
<td>.12**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Negative parenting (rep)</td>
<td>-</td>
<td>-.03</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Positive parenting (rep)</td>
<td>-</td>
<td>-.03</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note. * significant at p < .05; ** significant at p < .01; *** significant at p < .001

Mechanisms of Change: Parenting Behavior
All models regarding parental behavior yielded good model fit statistics (see Figures 3-6). Both child externalizing problems and (negative and positive) parenting behavior were predicted by the same variable at an earlier time point, indicating that these behaviors were stable over time. Child externalizing problems were weakly correlated across all three time-points with both observed and reported negative parenting behavior, but was not significantly correlated with observed and reported positive parenting behavior. This indicates that within-time parenting behavior and child externalizing problems were not structurally related.
The main results showed that the intervention was not successful in decreasing child externalizing problems at T3 (path a, Figures 6.3-6.6), but was successful in decreasing this behavior at T2. Also, the intervention was successful in reducing observed and reported negative parenting behaviors and increasing observed and reported positive parenting behavior at T2 (path b, Figures 6.3-6.6). Moreover, the intervention was successful in decreasing reported (but not observed) negative parenting behavior and increasing observed and reported positive parenting behavior at T3. However, none of the parenting behavior measures at T2 predicted child externalizing problems at T3 (path c, Figures 6.3-6.6), and there was no indirect effect from the intervention to child externalizing problems via parenting behavior (path bc: observed negative parenting: $B = .005; SD = .007; p = .50; 95\% \text{ CI} - .004 - .019$; observed positive parenting: $B = -.013; SD = .009; p = .13; 95\% \text{ CI} - .031 - .001$; reported negative parenting: $B = -.002; SD = .010; p = .88; 95\% \text{ CI} - .019 - .016$; reported positive parenting: $B = -.001; SD = .010; p = .93; 95\% \text{ CI} - .019 -.014$).

**Figure 6.1 / Cross-lagged Panel Model Mediation by Parental Negative Affect.**

*Note. Model fit: $X^2(N = 387, 4) = 7.02, CFI = .99, TLI = .97, \text{RMSEA} = .04.$*
The main results showed that the intervention was not successful in decreasing child externalizing problems at T3 (path a, Figures 6.3-6.6), but was successful in decreasing this behavior at T2. Also, the intervention was successful in reducing observed and reported negative parenting behaviors and increasing observed and reported positive parenting behavior at T2 (path b, Figures 6.3-6.6). Moreover, the intervention was successful in decreasing reported (but not observed) negative parenting behavior and increasing observed and reported positive parenting behavior at T3. However, none of the parenting behavior measures at T2 predicted child externalizing problems at T3 (path c, Figures 6.3-6.6), and there was no indirect effect from the intervention to child externalizing problems via parenting behavior (path bc: observed negative parenting: $B = .005, SD = .007, p = .50, 95\% CI - .004 - .019$; observed positive parenting: $B = -.013, SD = .009, p = .13, 95\% CI - .031 - .001$; reported negative parenting: $B = -.002, SD = .010, p = .88, 95\% CI - .019 - .016$; reported positive parenting: $B = -.001, SD = .010, p = .93, 95\% CI - .019 - .014$).

**Figure 6.1 / Cross-lagged Panel Model Mediation by Parental Negative Affect.**

**Note.** Model fit: $X^2(N = 387, 4) = 7.02, CFI = .99, TLI = .97, RMSEA = .04$.

**Figure 6.2 / Cross-lagged Panel Model Mediation by Parental Positive Affect.**

**Note.** Model fit: $X^2(N = 387, 4) = 7.17, CFI = .99, TLI = .98, RMSEA = .05$.

**Figure 6.3 / Cross-lagged Panel Model Mediation by Observed Negative Parenting Behavior.**

**Note.** Model fit: $X^2(N = 387, 4) = 8.29, CFI = .99, TLI = .96, RMSEA = .05$. 
Chapter 6

Figure 6.4 / Cross-lagged Panel Model Mediation by Observed Positive Parenting Behavior.
Note. Model fit: $X^2(N = 387, 4) = 7.62$, CFI = .99, TLI = 1.00, RMSEA = .05.

Figure 6.5 / Cross-lagged Panel Model Mediation by Reported Negative Parenting Behavior.
Note. Model fit: $X^2(N = 387, 4) = 5.99$, CFI = 1.00, TLI = .99, RMSEA = .04

Post hoc Analysis Mediation
CLSEM have been criticized: It has been shown that when constructs in the model are stable over time, the lagged parameters in CLSEM might not represent within-person relationships between constructs over time, but rather between-person differences (Hamaker, Kuiper, & Grasman, 2015). Therefore, as an additional check of actual within-person relationships between parenting and child externalizing problems, we repeated our analyses using an alternative model that separates the within-person process from stable between-person differences through the inclusion of random intercepts (Hamaker et al., 2015). Overall, these between-person models showed similar results to the “traditional” cross-lagged panel models presented above. One notable difference, however, was that the stability of both parent and child externalizing problems over time was less strong or even absent in some models (supplement B).

What Works for Whom: Moderation by Child Negative Affectivity
Chi-square difference tests of model fit yielded no significant results in any of the mediators (i.e., parent affect or behavior) ($\Delta X^2$ between 22.21 – 28.82, $\Delta df = 18$, $p$s > .05), indicating that the paths in the mediation models were not significantly different between the three temperament groups (i.e., low, mediate, high negative affectivity).
Post hoc Analysis Mediation

CLSEM have been criticized: It has been shown that when constructs in the model are stable over time, the lagged parameters in CLSEM might not represent within-person relationships between constructs over time, but rather between-person differences (Hamaker, Kuiper, & Grasman, 2015). Therefore, as an additional check of actual within-person relationships between parenting and child externalizing problems, we repeated our analyses using an alternative model that separates the within-person process from stable between-person differences through the inclusion of random intercepts (Hamaker et al., 2015). Overall, these between-person models showed similar results to the “traditional” cross-lagged panel models presented above. One notable difference, however, was that the stability of both parent and child externalizing problems over time was less strong or even absent in some models (supplement B).

What Works for Whom: Moderation by Child Negative Affectivity

Chi-square difference tests of model fit yielded no significant results in any of the mediators (i.e., parent affect or behavior) ($\Delta \chi^2$ between 22.21 – 28.82, $\Delta df = 18$, $p$s $> .05$), indicating that the paths in the mediation models were not significantly different between the three temperament groups (i.e., low, mediate, high negative affectivity).
Chapter 6

What Works for Whom: Moderation by 5-HTTLPR

**Negative and Positive Parental Affect**

A chi-square difference test of model fit yielded a nonsignificant results for the model regarding parental negative affect ($\Delta \chi^2 = 27.52, \Delta df = 18, p = .07$), indicating that the paths in the mediation model were not significantly different between the three genotype groups (i.e., LL, SL, SS-genotypes). However, we did find a significant chi-square difference for the model regarding parental positive affect ($\Delta \chi^2 = 31.48, \Delta df = 18, p = .03$). Results showed that the intervention did not have a significant effect on child externalizing problems at T3 in any of the genotype groups (path a, Table 6.3). The intervention was only successful in increasing positive parental affect at T2 (path b, Table 6.3) for parents of children with the SL-genotypes (but not the homozygous groups). However, comparison of the coefficients showed this effect was not significantly larger than for the other groups ($ps > .59$). Thus, children’s 5-HTTLPR genotype did not significantly moderate the intervention effects on child externalizing problems or parental affect. Moreover, parental positive affect did not predict child externalizing problems in any of the groups (path c, Table 6.3), and there was no indirect effect (path bc, Table 6.3).

**Negative and Positive Parenting Behavior**

Chi-square difference tests of model fit yielded a significant result for all parenting behavior models, indicating that the mediation paths were significantly different between the three genotype groups ($\Delta \chi^2$ between 31.48 – 38.28, $\Delta df = 18, ps < .03$).

The results showed that the intervention did not have a significant effect on child externalizing problems at T3 in any of the groups (path a, Tables 6.4 and 6.5). The results did show that the intervention was successful in decreasing *observed* negative parenting and increasing *observed* positive parenting at T2, but only for parents of S-allele carriers (path b, Table 6.4). Comparison of the coefficients showed that the effect on observed negative parenting was indeed significantly larger for parents of children with the SS-genotype than parents of children with the LL-genotype ($p = .04$, but not significantly larger than parents of children with the SL-genotype). However, comparison of the coefficients of observed positive parenting showed that coefficients were not significantly different between the three groups ($ps > .52$). Thus, children’s 5-HTTLPR genotype did significantly moderate the intervention effects on observed negative parenting, but not observed positive parenting. Another interesting finding is that observed positive parenting at T2 predicted child externalizing problems at T3, but only in the SS group (path c, see Table 6.4). For children homozygous for the L-allele there was no significant relation between positive parenting and externalizing problems, whereas for children carrying a S-allele this was a significant, but small, negative relation (significant difference between parents of children homozygous for the S-allele and homozygous for the L-allele: $p < .05$). Thus, only for children homozygous
for the S-allele higher levels of positive parenting at T2 were related to lower levels of child externalizing problems at T3. There was however no indirect effect, for any of the genotype groups (path bc, Table 6.4).

In contrast to the effects on observed parenting behavior, the results showed that the intervention was only successful in decreasing reported negative and increasing reported positive parenting behavior at T2 in parents of L-allele carriers (path b, Table 6.5). Comparison of the coefficients of reported negative parenting showed that this effect was significantly larger for parents of children homozygous for the L-allele compared to parents of children homozygous for the S-allele ($p = .04$) but not compared to parents of heterozygous children). Comparison of the coefficients of reported positive parenting showed that the effect for parents was not significantly larger than in the other groups ($p > .14$). Thus, children’s 5-HTTLPR genotype did significantly moderate the intervention effects on reported negative parenting, but not reported positive parenting. However, reported parenting behavior did not predict child externalizing problems (path c, Table 6.5) and there was no indirect effect, for any of the genotype groups (path bc, Table 6.5).
Table 6.3 / Results Moderated Mediation pathways Observed Parental Negative and Positive Affect by 5-HTTLPR Genotype.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Outcome</th>
<th>Path</th>
<th>B</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Negative parental affect</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group: Intervention</td>
<td>Child externalizing problems T3</td>
<td>a</td>
<td>.01 (.08)</td>
<td>.93</td>
<td></td>
</tr>
<tr>
<td>LL Intervention</td>
<td>Parental negative affect T2</td>
<td>b</td>
<td>-.02 (.12)</td>
<td>.87</td>
<td></td>
</tr>
<tr>
<td>Parental negative affect T2</td>
<td>Child externalizing problems T3</td>
<td>c</td>
<td>-.05 (.06)</td>
<td>.39</td>
<td></td>
</tr>
<tr>
<td>Intervention via Parental negative affect T2</td>
<td>Child externalizing problems T3</td>
<td>bc</td>
<td>.00 (.01)</td>
<td>.92</td>
<td>.00</td>
</tr>
<tr>
<td>Group: Intervention</td>
<td>Child externalizing problems T3</td>
<td>a</td>
<td>-.02 (.06)</td>
<td>.77</td>
<td></td>
</tr>
<tr>
<td>SL Intervention</td>
<td>Parental negative affect T2</td>
<td>b</td>
<td>-.01 (.11)</td>
<td>.91</td>
<td></td>
</tr>
<tr>
<td>Parental negative affect T2</td>
<td>Child externalizing problems T3</td>
<td>c</td>
<td>-.03 (.05)</td>
<td>.53</td>
<td></td>
</tr>
<tr>
<td>Intervention via Parental negative affect T2</td>
<td>Child externalizing problems T3</td>
<td>bc</td>
<td>.00 (.01)</td>
<td>.95</td>
<td>.00</td>
</tr>
<tr>
<td>Group: Intervention</td>
<td>Child externalizing problems T3</td>
<td>a</td>
<td>.17 (.10)</td>
<td>.09</td>
<td></td>
</tr>
<tr>
<td>SS Intervention</td>
<td>Parental negative affect T2</td>
<td>b</td>
<td>.15 (.07)</td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td>Parental negative affect T2</td>
<td>Child externalizing problems T3</td>
<td>c</td>
<td>-.38 (.16)</td>
<td>.03</td>
<td></td>
</tr>
<tr>
<td>Intervention via Parental negative affect T2</td>
<td>Child externalizing problems T3</td>
<td>bc</td>
<td>-.06 (.04)</td>
<td>.17</td>
<td></td>
</tr>
<tr>
<td><strong>Positive parental affect</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group: Intervention</td>
<td>Child externalizing problems T3</td>
<td>a</td>
<td>-.01 (.08)</td>
<td>.91</td>
<td></td>
</tr>
<tr>
<td>LL Intervention</td>
<td>Parental positive affect T2</td>
<td>b</td>
<td>.18 (.11)</td>
<td>.11</td>
<td></td>
</tr>
<tr>
<td>Parental positive affect T2</td>
<td>Child externalizing problems T3</td>
<td>c</td>
<td>.10 (.06)</td>
<td>.08</td>
<td></td>
</tr>
<tr>
<td>Intervention via parental positive affect T2</td>
<td>Child externalizing problems T3</td>
<td>bc</td>
<td>.02 (.02)</td>
<td>.29</td>
<td></td>
</tr>
<tr>
<td>Group: Intervention</td>
<td>Child externalizing problems T3</td>
<td>a</td>
<td>-.01 (.07)</td>
<td>.90</td>
<td></td>
</tr>
<tr>
<td>SL Intervention</td>
<td>Parental positive affect T2</td>
<td>b</td>
<td>.24 (.09)</td>
<td>.01</td>
<td></td>
</tr>
<tr>
<td>Parental positive affect T2</td>
<td>Child externalizing problems T3</td>
<td>c</td>
<td>-.03 (.05)</td>
<td>.52</td>
<td></td>
</tr>
<tr>
<td>Intervention via parental positive affect T2</td>
<td>Child externalizing problems T3</td>
<td>bc</td>
<td>-.01 (.01)</td>
<td>.55</td>
<td></td>
</tr>
<tr>
<td>Group: Intervention</td>
<td>Child externalizing problems T3</td>
<td>a</td>
<td>.15 (.12)</td>
<td>.18</td>
<td></td>
</tr>
<tr>
<td>SS Intervention</td>
<td>Parental positive affect T2</td>
<td>b</td>
<td>.28 (.15)</td>
<td>.06</td>
<td></td>
</tr>
<tr>
<td>Parental positive affect T2</td>
<td>Child externalizing problems T3</td>
<td>c</td>
<td>-.18 (.12)</td>
<td>.16</td>
<td></td>
</tr>
<tr>
<td>Intervention via parental positive affect T2</td>
<td>Child externalizing problems T3</td>
<td>bc</td>
<td>-.05 (.05)</td>
<td>.37</td>
<td></td>
</tr>
</tbody>
</table>

Note. Model fit: Observed negative affect: \( \chi^2(N = 387, 12) = 11.37, \) CFI = 1.00, TLI = 1.00, RMSEA = .00, \( p = .50; \) Observed positive affect: \( \chi^2(N = 387, 12) = 25.33 \) CFI = .98, TLI = .89, RMSEA = .09.
### Table 6.4 / Results Moderated Mediation Pathways Observed Negative and Positive Parenting by 5-HTTLPR Genotype.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Outcome</th>
<th>Path</th>
<th>( B )</th>
<th>95% CI</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Negative parenting behavior (obs)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group: Intervention</td>
<td>Child externalizing problems T3</td>
<td>a</td>
<td>.01 (.08)</td>
<td></td>
<td>.92</td>
</tr>
<tr>
<td>LL</td>
<td>Intervention</td>
<td>Negative parenting T2</td>
<td>b</td>
<td>-.06 (.14)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Negative parenting T2</td>
<td>Child externalizing problems T3</td>
<td>c</td>
<td>.02 (.05)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intervention via Negative parenting T2</td>
<td>Child externalizing problems T3</td>
<td>bc</td>
<td>.00 (.01)</td>
<td></td>
</tr>
<tr>
<td>Group: Intervention</td>
<td>Child externalizing problems T3</td>
<td>a</td>
<td>-.02 (.06)</td>
<td></td>
<td>.75</td>
</tr>
<tr>
<td>SL</td>
<td>Intervention</td>
<td>Negative parenting T2</td>
<td>b</td>
<td>-.26 (.15)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Negative parenting T2</td>
<td>Child externalizing problems T3</td>
<td>c</td>
<td>-.02 (.04)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intervention via Negative parenting T2</td>
<td>Child externalizing problems T3</td>
<td>bc</td>
<td>.00 (.01)</td>
<td></td>
</tr>
<tr>
<td>Group: Intervention</td>
<td>Child externalizing problems T3</td>
<td>a</td>
<td>.09 (.12)</td>
<td></td>
<td>.44</td>
</tr>
<tr>
<td>SS</td>
<td>Intervention</td>
<td>Negative parenting T2</td>
<td>b</td>
<td>-.59 (.26)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Negative parenting T2</td>
<td>Child externalizing problems T3</td>
<td>c</td>
<td>-.02 (.04)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intervention via Negative parenting T2</td>
<td>Child externalizing problems T3</td>
<td>bc</td>
<td>.02 (.05)</td>
<td></td>
</tr>
<tr>
<td><strong>Positive parenting behavior (obs)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group: Intervention</td>
<td>Child externalizing problems T3</td>
<td>a</td>
<td>-.00 (.08)</td>
<td></td>
<td>.98</td>
</tr>
<tr>
<td>LL</td>
<td>Intervention</td>
<td>Positive parenting T2</td>
<td>b</td>
<td>.31 (.16)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Positive parenting T2</td>
<td>Child externalizing problems T3</td>
<td>c</td>
<td>.02 (.03)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intervention via Positive parenting T2</td>
<td>Child externalizing problems T3</td>
<td>bc</td>
<td>.01 (.01)</td>
<td></td>
</tr>
<tr>
<td>Group: Intervention</td>
<td>Child externalizing problems T3</td>
<td>a</td>
<td>.00 (.06)</td>
<td></td>
<td>.95</td>
</tr>
<tr>
<td>SL</td>
<td>Intervention</td>
<td>Positive parenting T2</td>
<td>b</td>
<td>.44 (.13)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Positive parenting T2</td>
<td>Child externalizing problems T3</td>
<td>c</td>
<td>-.04 (.04)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intervention via Positive parenting T2</td>
<td>Child externalizing problems T3</td>
<td>bc</td>
<td>-.02 (.02)</td>
<td></td>
</tr>
<tr>
<td>Group: Intervention</td>
<td>Child externalizing problems T3</td>
<td>a</td>
<td>.14 (.10)</td>
<td></td>
<td>.16</td>
</tr>
<tr>
<td>SS</td>
<td>Intervention</td>
<td>Positive parenting T2</td>
<td>b</td>
<td>.49 (.24)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Positive parenting T2</td>
<td>Child externalizing problems T3</td>
<td>c</td>
<td>-.08 (.04)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intervention via Positive parenting T2</td>
<td>Child externalizing problems T3</td>
<td>bc</td>
<td>-.04 (.03)</td>
<td></td>
</tr>
</tbody>
</table>

Note. Model fit: observed negative parenting: \( X^2(\text{N} = 387, 12) = 12.57, \text{CFI} = 1.00, \text{TLI} = 1.00, \text{RMSEA} = .02 \); observed positive parenting: \( X^2(\text{N} = 387, 12) = 12.19, \text{CFI} = 1.00, \text{TLI} = 1.00, \text{RMSEA} = .01 \).
## Table 6.5 / Results Moderated Mediation Pathways Reported Negative and Positive Parenting by 5-HTTLPR Genotype.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Outcome</th>
<th>Path</th>
<th>B</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Negative parenting behavior (rep)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group: Intervention</td>
<td>Child externalizing problems T3</td>
<td>a</td>
<td>-.01 (.08)</td>
<td></td>
<td>.88</td>
</tr>
<tr>
<td>LL</td>
<td>Intervention</td>
<td>Negative parenting T2</td>
<td>b</td>
<td>-.46 (.09)</td>
<td></td>
</tr>
<tr>
<td>Negative parenting T2</td>
<td>Child externalizing problems T3</td>
<td>c</td>
<td>-.05 (.07)</td>
<td></td>
<td>.44</td>
</tr>
<tr>
<td>Intervention via Negative parenting T2</td>
<td>Child externalizing problems T3</td>
<td>bc</td>
<td>.02 (.03)</td>
<td>-.03 -.02</td>
<td></td>
</tr>
<tr>
<td>Group: Intervention</td>
<td>Child externalizing problems T3</td>
<td>a</td>
<td>-.02 (.06)</td>
<td></td>
<td>.79</td>
</tr>
<tr>
<td>SL</td>
<td>Intervention</td>
<td>Negative parenting T2</td>
<td>b</td>
<td>-.18 (.08)</td>
<td></td>
</tr>
<tr>
<td>Negative parenting T2</td>
<td>Child externalizing problems T3</td>
<td>c</td>
<td>.01 (.06)</td>
<td></td>
<td>.89</td>
</tr>
<tr>
<td>Intervention via Negative parenting T2</td>
<td>Child externalizing problems T3</td>
<td>bc</td>
<td>-.00 (.01)</td>
<td>-.03 -.00</td>
<td></td>
</tr>
<tr>
<td>Group: Intervention</td>
<td>Child externalizing problems T3</td>
<td>a</td>
<td>.13 (.10)</td>
<td></td>
<td>.21</td>
</tr>
<tr>
<td>SS</td>
<td>Intervention</td>
<td>Negative parenting T2</td>
<td>b</td>
<td>-.06 (.13)</td>
<td></td>
</tr>
<tr>
<td>Negative parenting T2</td>
<td>Child externalizing problems T3</td>
<td>c</td>
<td>.14 (.10)</td>
<td></td>
<td>.17</td>
</tr>
<tr>
<td>Intervention via Negative parenting T2</td>
<td>Child externalizing problems T3</td>
<td>bc</td>
<td>-.01 (.02)</td>
<td>-.09 -.01</td>
<td></td>
</tr>
<tr>
<td><strong>Positive parenting behavior (rep)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group: Intervention</td>
<td>Child externalizing problems T3</td>
<td>a</td>
<td>-.00 (.08)</td>
<td></td>
<td>.96</td>
</tr>
<tr>
<td>LL</td>
<td>Intervention</td>
<td>Positive parenting T2</td>
<td>b</td>
<td>.34 (.10)</td>
<td></td>
</tr>
<tr>
<td>Positive parenting T2</td>
<td>Child externalizing problems T3</td>
<td>c</td>
<td>.02 (.06)</td>
<td></td>
<td>.68</td>
</tr>
<tr>
<td>Intervention via Positive parenting T2</td>
<td>Child externalizing problems T3</td>
<td>bc</td>
<td>.01 (.01)</td>
<td>-.02 -.04</td>
<td></td>
</tr>
<tr>
<td>Group: Intervention</td>
<td>Child externalizing problems T3</td>
<td>a</td>
<td>-.03 (.06)</td>
<td></td>
<td>.62</td>
</tr>
<tr>
<td>SL</td>
<td>Intervention</td>
<td>Positive parenting T2</td>
<td>b</td>
<td>.30 (.07)</td>
<td></td>
</tr>
<tr>
<td>Positive parenting T2</td>
<td>Child externalizing problems T3</td>
<td>c</td>
<td>.04 (.04)</td>
<td></td>
<td>.38</td>
</tr>
<tr>
<td>Intervention via Positive parenting T2</td>
<td>Child externalizing problems T3</td>
<td>bc</td>
<td>.01 (.02)</td>
<td>-.01 -.03</td>
<td></td>
</tr>
<tr>
<td>Group: Intervention</td>
<td>Child externalizing problems T3</td>
<td>a</td>
<td>.13 (.10)</td>
<td></td>
<td>.21</td>
</tr>
<tr>
<td>SS</td>
<td>Intervention</td>
<td>Positive parenting T2</td>
<td>b</td>
<td>.11 (.13)</td>
<td></td>
</tr>
<tr>
<td>Positive parenting T2</td>
<td>Child externalizing problems T3</td>
<td>c</td>
<td>-.16 (.12)</td>
<td></td>
<td>.18</td>
</tr>
<tr>
<td>Intervention via Positive parenting T2</td>
<td>Child externalizing problems T3</td>
<td>bc</td>
<td>-.02 (.03)</td>
<td>-.07 -.03</td>
<td></td>
</tr>
</tbody>
</table>

Note. Model fit: reported negative parenting behavior: \(X^2(N = 387, 12) = 13.51, \text{CFI} = 1.00, \text{TLI} = .99, \text{RMSEA} = .03\); reported positive parenting behavior: \(X^2(N = 387, 12) = 8.57, \text{CFI} = 1.00, \text{TLI} = 1.00, \text{RMSEA} = .00, p = .74\)
## Conclusion and Discussion

In a randomized controlled trial ($N = 387$) we tested whether the intervention effects of the behavioral parent training The Incredible Years (IY) on child externalizing problems were explained by changes in parental affect and behavior. Furthermore, we tested whether these mechanisms of change were more important for some families than in others due to children’s temperamental negative affectivity or 5-HTTLPR genotype. Our results showed that IY was effective in decreasing parent reported child externalizing problems at post-test, but not at 10-month follow-up. In addition, the IY intervention was effective in increasing observed parental positive affect (but not in reducing negative affect), reported and observed positive parenting, and reducing observed and reported negative parenting behavior at post-test. Furthermore, the intervention was successful in reducing reported negative parenting, and increasing reported and observed positive parenting behavior at 10-month follow-up. Our findings on intervention effects are in line with many previous study showing effectiveness of IY (for meta-analyses see Leijten et al., 2013; Menting et al., 2013).

Interestingly, the results made clear that the intervention effects on child externalizing problems on the one hand and effects on parental affect and parenting behavior on the other hand, were unrelated. Although this finding contrasted our expectations, lack of support for parenting as mechanism of change underlying BPT effects on child externalizing problems is not unique (Forehand et al., 2014). In fact, the majority of mediation tests in BPT studies have yielded nonsignificant results (i.e., 55% of tests discussed by Forehand and colleagues, 2014). Our findings add to the claim that, to date, we seemingly cannot provide an empirically-supported explanation for how even our most effective and well-studied interventions produce change (Forehand et al., 2014, Kazdin, 2007). Differences in findings between previous studies that did report significant mediation by parenting of BPT effects on child externalizing behavior and our study might also be partly explained by methodological differences. Specifically, unlike many previous studies we employed a highly stringent test, using different informants (i.e., parent-reports and observational data) at different time points (i.e., immediate post-test and follow-up), for the mediator (i.e., parenting) and outcome (i.e., child externalizing problems). Some of the earlier significant findings on parenting as mediator of BPT might be explained by codependency of the mediator and outcome measures.

The fact that the IY intervention produced significant effects on parenting and child behavior that were unrelated indicates that the changes in parenting and child behavior are parallel, but independent processes (see also Weeland & Chhangur et al., submitted for publication). Perhaps, this phenomenon can be explained by a third –unmeasured– factor. Indeed, it has been found that BPT programs have “beneficial side-effects”, for example

### Table 6.5

<table>
<thead>
<tr>
<th>Predictor Outcome Path</th>
<th>B</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative parenting T2</td>
<td>-0.46</td>
<td>(-0.09)</td>
<td>.00</td>
</tr>
<tr>
<td>Child externalizing problems T3</td>
<td>.02</td>
<td>(-.03)</td>
<td>.02</td>
</tr>
<tr>
<td>Negative parenting T2</td>
<td>.01</td>
<td>(-0.06)</td>
<td>.89</td>
</tr>
<tr>
<td>Child externalizing problems T3</td>
<td>-0.00</td>
<td>(-.03)</td>
<td>.90</td>
</tr>
<tr>
<td>Negative parenting T2</td>
<td>-.06</td>
<td>(-.13)</td>
<td>.64</td>
</tr>
<tr>
<td>Child externalizing problems T3</td>
<td>.14</td>
<td>(-.06)</td>
<td>.17</td>
</tr>
<tr>
<td>Negative parenting T2</td>
<td>-.01</td>
<td>(-.02)</td>
<td>.71</td>
</tr>
<tr>
<td>Child externalizing problems T3</td>
<td>-.00</td>
<td>(-.09)</td>
<td>.96</td>
</tr>
</tbody>
</table>

---

**Note:**

Model fit: reported negative parenting behavior:

- $X^2(N) = 1.00$, $CFI = 1.00$, $TLI = 1.00$, $RMSEA = .00$, $p = .74$
by decreasing parent and family distress, and increasing quality of life, and perceived self-efficacy in parents (Feldman & Werner, 2002). This might be specifically the case for interventions such as IY because they use a collaborative approach specifically aiming to empower parents. The group meetings might cause parents to relabel oppositional behavior as common and less problematic, and to feel empowered by sharing experiences and being handed tools for dealing with this behavior.

We did not find that parental affect or parenting behavior were more important mechanisms of change in explaining the effectiveness of IY for some children than others, due to their negative affectivity or 5-HTTLPR genotype. Although theoretically these two markers could be related, our study showed neither a correlation, nor similar moderation patterns, between child negative affectivity and 5-HTTLPR genotype. This contrasts earlier findings from Auerbach and colleagues (1999) who demonstrated that infants homozygous for the 5-HTTLPR S-allele scored higher on negative emotionality than infants carrying the L-allele. However, to our knowledge this finding has not been replicated in school-aged children. Moreover, studies using related constructs such as fear and anger responses, as well as temperamental and observed emotional reactivity, found no associations with the 5-HTTLPR genotype (Dragan & Oniszczenko, 2005; Auerbach et al., 2001; Weeland, Slagt et al., 2015)

Another major finding of the present study is that children’s 5-HTTLPR genotype significantly moderated intervention effectiveness on parenting behavior, as well as the relation between observed positive parenting and child externalizing problems. Intervention effects on observed and reported negative parenting behavior, but not on parental affect or positive parenting behavior, were significantly moderated by children’s 5-HTTLPR genotype. This might indicate that some parents are more susceptible to the IY program than others, due to their children’s genotype. Possibly, due to heritability parents and children might share the same susceptibility characteristics. However, different moderation patterns were found for observed and reported parental behavior outcomes. On the one hand, this might indicate that this gene-based moderation of intervention effects is not highly robust and replicable. On the other hand, this might show that moderation effects are very specific and differ between outcomes using different reporters or instruments. Findings on the role of the 5-HTTLPR in externalizing problems have been mixed, in that both S and L-allele carriers have been shown to be more susceptible to environmental predictors of these problems (for a review see Weeland, Overbeek et al., 2015. Chapter 2). These heterogeneous findings might partly be explained by differences between studies in conceptualization and measurement of the outcome variable (Heininga, Oldehinkel, Veenstra, & Nederhof, 2015; Weeland, Overbeek et al., 2015, chapter 7).

Results indicated that parents of children homozygous for the L-allele reported the largest decrease in negative parenting at post-test. However, compared to parents of S-allele
carriers, these parents showed lower observed decreases in negative parenting during the parent-child interactions at post-test. This might indicate that parents of children carrying two L-alleles are more prone to report improvements, whereas they show less actual changes in their behavior, compared to parents of children carrying two S-alleles. These findings might suggest that actual changes in parenting behavior after intervention are not merely formed during the intervention sessions, but are also informed and shaped over time by the reciprocal influences between parent and child behavior (Sameroff, 2000). Children’s different reactions to intervention-induced changes in parenting behavior might serve as a feedback mechanism for further changes in parenting behavior. For example, when parents see that the use of certain parenting techniques works really well on their children they might further increase the use of these techniques, whether they might stop using techniques that initially evoke resistance. Different families possibly need different clinical approaches when it comes to intervening in the development of externalizing problems, due to children’s 5-HTTLPR genotype.

This relates to another interesting finding of our study: In both the intervention and control groups, observed positive parenting was only a significant predictor of child externalizing problems for SS-genotypes. This effect was very small and was not replicated in any of the other parenting outcome measures. Nevertheless, this might indicate that children carrying the L-allele are less susceptible to –specifically positive– parenting behavior than children homozygous for the S-allele (see also Hankin et al., 2011). Due to this possible decreased sensitivity to specific parenting strategies (in our study positive parenting techniques) children carrying the L-allele might act less responsive to (changes in) this parenting behavior; leading to parental frustration; and in turn escalating cycles of negativity and punishment. It might be that, although families of children with the LL-genotype experience the biggest relief in parenting stress although directly after the intervention (and therefore report a larger decrease in negative parenting after the intervention compared to families of children carrying the S-allele), these families are also the first to fall back in old patterns of negative parent-child interactions, due to certain child characteristics (and therefore show a smaller decrease in negative parenting behavior compared to families of children carrying the S-allele). However, negative parenting strategies might be a specifically ineffective strategies for these children since the 5-HTTLPR L-allele has been related to decreased punishment sensitivity due to impairments in avoidance learning, and overall lower fear and stress responses, compared to S-carriers (Brocke et al., 2006; Finger et al., 2006). In sum, the behavior of children carrying the L-allele might therefore be specifically hard to change.

Our results have to be interpreted in light of some limitations. First of all, we focused on the 5-HTTLPR polymorphism as a candidate for genetic moderation because it has been related to differences in negative affect and reactivity to emotional stimuli. This relation
might however be explained by individual differences in serotonin availability, which
does not only depend on variation in expression of the 5-HTTLPR, but also on variation
in synthesis, reuptake and degradation. Future research could take into account multiple
genetic markers, for example by assessing a serotonergic genetic pathway (e.g., Bralten et
al., 2013). Another important limitation of this study is the modest sample size in relation
to the complexity of the statistical models tested. Although our sample is relatively large for
a BPT RCT (a recent meta-analysis on IY showed an average sample size of 95, see Menting
et al., 2013), the tested models of mediation and moderation contained many parameter
estimations. Perhaps this explains that in our moderation results several “trend findings”
occurred, findings that just fail to reach significance, which might indicate lack of power to
find similar effects in the groups with a smaller n. Therefore, testing these models within a
larger sample might have yielded different results. Furthermore, as with most intervention
studies, our recruitment procedure resulted a select sample of Dutch, relatively high SES
families, and our results might not be generalizable to the general population or other
countries.

Notwithstanding these limitations, our study contributes to the current literature
in a number of important ways. First, testing a specific theory-driven hypothesis on
mediation and moderation has enabled us to specify our research strategies accordingly.
This specificity not only increases replicability of the study, it also prevents a “black box
effect”: Knowing what goes in and what comes out, but not knowing the process in between.
Using specific hypotheses enabled us to confirm or reject specific assumptions on mediation
and moderation, increasing our understanding of the specific processes involved. Second,
using an RCT to test this theory enabled us to draw conclusions about causal effects of
the intervention and change mechanisms on child externalizing problems and to rule out
alternative explanations for moderation effects, such as correlations between environment
and child characteristics. As such, it is a robust approach for testing possible G×E in
externalizing problems. Third, we used observed and reported measures of parenting
behavior. This is important since most previous mediation analyses relied on parent report
of both parenting and child externalizing problems, possibly causing inflated observed
associations due to shared informant variance. Our analyses showed that reported and
observed parenting were only weakly related, indicating they measure different things. We
indeed found different moderation effects using observed and reported parenting behavior.
Furthermore, by measuring the mediator at post-test and outcome at follow-up we were
able to take into account the timeline of mediation processes (Kazdin, 2007).

Taking into account mediators (i.e., what works) and moderators (i.e., for whom)
of intervention effects is of both scientific and clinical importance. From a scientific
perspective, insight into differential effects of specific mechanisms of change can help us
gain insight into differential causal pathways leading to externalizing problems (Tolan,
Dodge, & Rutter, 2013). It will not only teach us which children might be more susceptible to their environment or changes therein, but also to what specific environmental factors they are more susceptible. From a clinical perspective, information on what works for whom might be used to tailor interventions (Chorpita et al., 2005). However, it is unclear if and how information on genetic moderation should be implemented in clinical practice. Using genetic information to identify children who might be more or less susceptible for a certain intervention is costly, invasive and yields ethical concerns (Ross et al., 2013). Genetic screening may have negative side effects, such as alterations in self-image and expectations by self and others or changes in parental perception of the child (e.g., false deterministic claims about child externalizing problems). As a less problematic alternative, knowledge of behavioral (rather than genetic) markers may help us identifying with greater ease those children for whom a specific intervention is suitable, and for whom different or additional care may be more effective (see also Gardner et al, 2006). In our study, temperamental negative affectivity was not a significant moderator of intervention effectiveness. Future research may explore other behavioral markers, such as emotion regulation skills or reward and punishment sensitivity.

In conclusion, our study showed that IY was successful in reducing both observed and reported negative parenting behavior and increasing parental positive affect as well as observed and reported positive parenting behavior at post-test. Importantly, these effects did not explain the IY intervention effects on child externalizing problems. This calls for future intervention studies to take into account alternative mechanisms of change such as decreases in parenting stress and improved quality of life or perceived parental self-efficacy. Furthermore, our results show that effects of BPT programs may depend on child genotype, in our case the 5-HTTLPR genotype was identified as a moderator of intervention effects on negative parenting behavior. Overall, these finding might indicate that in BPT it is not only important to focus on what works for which children, but also on what works for which parents.