

Differential Susceptibility in Early Literacy Instruction Through Computer Games: The Role of the Dopamine D4 Receptor Gene (DRD4)

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ABSTRACT—Not every child seems equally susceptible to the same parental, educational, or environmental influences even if cognitive level is similar. This study is the first randomized controlled trial to apply the differential susceptibility paradigm to education in relation to children's genotype and early literacy skills. A randomized pretest–posttest control group design was used to examine the effects of the Intelligent Tutoring System *Living Letters*. Two intervention groups were created, 1 receiving feedback and 1 completing the program without feedback, and 1 control group. Carriers of the long variant of the dopamine D4 receptor gene (DRD4 7-repeat) profited most from the computer program with positive feedback, whereas they performed at the lowest level of early literacy skills in the absence of such feedback. Our findings suggest that behind modest overall educational intervention effects a strong effect on a subgroup of susceptible children may be hidden.

On average, educational interventions seem to have only modest impact on learning (Bus & Van IJzendoorn, 2004). Not all pupils, however, are equally susceptible to environmental influences even when they do not differ in cognitive potential.

In developmental psychopathology, the concept of “differential susceptibility” has emerged to acknowledge the accumulating evidence that some children with a specific temperamental or genetic make-up seem to suffer most from negative parenting and at the same time appear to profit most from positive parenting (Belsky, Bakermans-Kranenburg, & Van IJzendoorn, 2007; Belsky & Pluess, 2009; Ellis, Boyce, Belsky, Bakermans-Kranenburg, & Van IJzendoorn, 2011). In this study, we present the results of an educational intervention with preschoolers showing that carriers of the long variant of the dopamine D4 receptor gene (DRD4 7-repeat) profit most from positive feedback, whereas they perform at the lowest level of early literacy skills in the absence of such feedback.

Not every child seems equally susceptible to the same parental, educational, or environmental influences. Children with a fearful temperament appear to suffer most from persistent family conflict or low quality of day care but also to benefit most from supportive environments. For example, in a study on children's skin conductance level in response to fear-inducing and neutral film clips, Gilissen, Bakermans-Kranenburg, Van IJzendoorn, and Van der Veer (2008) showed that more fearful children with a less secure attachment relationship showed the highest physiological reactivity to the frightening film clips, whereas comparably fearful children with a more secure relationship showed the lowest reactivity. Similarly, Blair (2002) found that a comprehensive early education program significantly lowered the level of internalizing and externalizing behaviors of 3-year-old children with more negative emotionality but not in children with less negative emotionality. Fearful temperament or temperamental emotionality may not be a

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“risk” but a susceptibility factor. This is the essence of the novel hypothesis of “differential susceptibility.” According to the evolutionary-inspired differential susceptibility model individuals characterized by heightened susceptibility may be more sensitive to *both* negative and positive environments, that is, to both risk-promoting and development-enhancing environmental conditions, for better *and* for worse (Belsky, 2005; Belsky et al., 2007).

Research into differential susceptibility has been mainly restricted to psychology and psychiatry (Bakermans-Kranenburg & Van IJzendoorn, 2006, 2007; Belsky, Hsieh, & Crnic, 1998; Boyce et al., 1995; Sheese, Voelker, Rothbart, & Posner, 2007). Here we present the first educational study on genetic differential susceptibility using a randomized controlled trial to test the differential effects of feedback on early literacy skills in preschoolers. We focus on 4-year-old children who generally engage in a wealth of literacy-related activities at home and in school. As a result most children start to develop early literacy skills before—in first grade—formal reading instruction begins. Especially reading and writing one’s proper name seems to stimulate this development. Most preschoolers learn the proper name through regular exposure to its written form on personal belongings, such as mugs and artwork (Levin, Both-de Vries, Aram, & Bus, 2005). When adults focus children’s attention to letter–sound relations in the proper name, it may become a starting point for the development of code-related knowledge. The current research is based on the premise that interventions effective for some individuals in fostering the development of early literacy skills may simply not be effective for others. Individual differences in receptiveness to instruction apart from general cognitive level have not attracted much attention in the educational sciences. Most work still focuses on instruction that is supposed to apply equally to all children and fails to consider that whether and what kind of instruction influences the child, may depend on children’s neurobiological characteristics.

We advance the proposition that children with the less efficient long variant of DRD4 are more susceptible to both (a) adverse effects of poorly designed programs and (b) beneficial effects of an optimal training. The idea that dopamine-related genetic polymorphisms may play a role in differential susceptibility to the educational environment is not far-fetched (Bakermans-Kranenburg & Van IJzendoorn, 2011). DRD4 has been associated with Attention Deficit and Hyperactivity Disorder (ADHD; Tripp & Wickens, 2008). Low dopaminergic efficiency is associated with decreased attentional and reward mechanisms (Robbins & Everitt, 1999), which may be advantageous or disadvantageous dependent on specific environmental characteristics (Suomi, 1997). The role of dopamine in feedback-based learning has also been tested in a neuroimaging study (Klein et al., 2007). Here we focus on the third exon of the DRD4 7-repeat allele that has been linked to lower dopamine reception efficiency. This polymorphism may

therefore play a role in children’s susceptibility to instructional experiences related to early literacy development. Having the DRD4 7-repeat allele may increase risk for inattention and dependency on feedback provided in the instruction.

In previous studies, a cost-effective, “teacher-free” computer intervention was demonstrated to promote basic literacy skills (Kegel, Van der Kooy-Hofland, & Bus, 2009; Van der Kooy-Hofland, Kegel, & Bus, 2011). In this study, we tested differential effects of a computer-based intervention that has been developed to promote early literacy skills in 4-year-olds. This group may especially benefit from an additional intervention program modeled on activities that seem to stimulate and assist young children in literate homes to acquire early literacy skills. The program is an Intelligent Tutoring System (ITS) that can be personalized or adapted to the performance level of children (Graesser, Conley, & Olney, in press). It provides feedback to inform and to motivate users to increase their efforts and attention (Anderson, Boyle, & Reiser, 1985; Vasilyeva, Puuronen, Pechenizkiy, & Räsänen, 2007). Feedback is supposed to be most effective in maintaining the user’s attention when it is constructive, immediately follows an error (Corbett & Anderson, 2001), and is adapted to characteristics of the user or to the user’s interaction with the system (Vasilyeva, 2007). A lack of feedback may interfere with learning because it may not encourage children to reflect on computer assignments and stimulate an erratic response style and random interactions with the computer program (Meyer et al., 2010). Children with a DRD4 7-repeat polymorphism may be more dependent on constructive feedback than the carriers of the short variants of this allele, and they may in fact perform worse when interacting with a computer program without feedback loops.

In a randomized controlled trial, the Dutch ITS *Living Letters*, developed to promote early literacy skills, was presented to children with and without feedback. Feedback in the program is modeled on early practices in literate homes, where parents tutor reading and writing of the proper name and other names (Levin & Aram, 2004). By calling children’s attention to letter units in the written name and how these units sound in their names (e.g., “It’s /pi/ of Peter”) children’s attention is focused on relevant features and they thus receive a substantial amount of direct instruction about letters as symbols for sounds in the name (Molfese, Beswick, Molnar, & Jacobi-Vessels, 2006). In *Living Letters*, feedback directly follows an assignment, is presented orally, and is adjusted to the learner’s response: The program offers more feedback (more cues for solving the task) when a child fails the task and help is reduced when the learner is more competent and solves problems at the first attempt.

The effects of the computer program are tested in a sample of 182 4-year-olds from 15 junior kindergarten classrooms. The first question is whether intervention effects are moderated by DRD4. Children with the 7-repeat allele are expected to show the largest increase in understanding the combination of how

a name sounds and looks when they participate in the *Living Letters* feedback condition. The second question is whether carriers of the 7-repeat alleles are also more susceptible to negative effects caused by the absence of feedback in the computer program that may lead to erratic interactions with the computer program.

METHOD

Sample

Participants were recruited from a longitudinal study on 15 Dutch schools. Of the initial sample of 312 children, 182 parents (58%) gave informed written consent to participate in the genetic part of the study and to have their children contribute buccal swab samples. The children (59% male) were 48 to 63 months old ($M = 52.9$, $SD = 3.2$). Children of mothers with lower educational level were over-represented. On a 6-point scale ranging from primary education to university the mean score was $M = 3.14$ ($SD = 1.31$).

The subsample participating in the genetic part of the study did not significantly differ from the total sample on age, gender, and educational level of the mother. Furthermore, the interaction between nonresponse versus response and intervention group on our central outcome measure for early literacy skills was not significant ($p = .38$), suggesting that the intervention effect did not differ between the subjects who refused to participate in the genetic part of the study and those who did cooperate.

Study Design

A randomized pretest–posttest control group design was used to examine the effects of the ITS *Living Letters*. Two *Living Letters* intervention groups were created, one receiving feedback (LL-Feedback) and one completing the program without feedback (LL-NoFeedback). Control subjects were assigned to another computer program not focusing on early literacy skills (*Clever Together*). Eligible pupils were randomly assigned to a condition with the restriction that the percentage of boys, number of children per classroom, and children's level of regulatory skills as assessed by the knock and tap test (e.g., Klenberg, Korkman, & Lahti-Nuuttila, 2001) on a pretest were distributed about equally across the conditions (Table 1).

Intervention Program

Living Letters

The ITS *Living Letters*, designed by a team of computer experts, designers, and experts in the field of education, and available for schools and parents via subscription (www.Bereslim.nl), is aimed at training basic literacy skills. The child's name or another familiar word such as "mama" [mom] (Levin, Shatil-Carmon, & Asif-Rave, 2006) is used to draw attention to

Table 1

Descriptives of Treatment (*Living Letters* With and Without Feedback) and Control Groups

	LL-NoFeedback (n = 43)		Control group (n = 93)		LL-Feedback (n = 46)	
Background						
Gender (boys)	28 (65%)		54 (58%)		25 (54%)	
DRD4 7+	18 (42%)		39 (42%)		17 (37%)	
	M	SD	M	SD	M	SD
Maternal education	3.30	1.36	3.11	1.30	3.04	1.30
Peabody Picture Vocabulary Test	66.33	12.36	67.45	11.80	66.72	11.26
Regulatory skills (knock and tap)	13.84	3.64	13.88	2.94	12.89	3.91
Pretest						
Age	55.95	3.07	56.90	3.30	57.07	3.73
Early literacy skills ^a	.04	.78	.04	1.07	.08	1.05
Posttest						
Age	60.47	2.93	61.69	3.31	61.96	3.58
Early literacy skills ^a	-.09	1.00	-.10	1.00	.27	1.06

^az score.

phonemes in spoken words (Bus & Van IJzendoorn, 1999; Ehri et al., 2001). As the proper name is often the first word that young children can read and write, children received the program version with the proper name unless the name's spelling was inconsistent with Dutch orthography (e.g., Chris or Joey). In those cases, the program used "mama," another well-known word, as target word (Both-de Vries & Bus, 2008, 2010).

The computer program starts with 20 games in which children practice finding the proper name and "mama" between other signs and words (Figure 1a and b), followed by 10 games targeting the sound of the first letter of the proper name or mama (e.g., "Which one of the letters [e.g., a, t, s, m, j] is the /m/ of mama?"; Figure 1c), and 10 games in which children are given the task to identify pictures that start with or contain the first letter of the child's name or "mama" (e.g., "which picture starts with the first letter of your name: tiger, duck, or bear?"; Figure 1d). All sessions start with an attractive animation in which preschoolers Sim and Sanne explain the upcoming game.

In the LL-Feedback condition, children received increasingly supportive oral feedback on responses. Unlike most computer games, the program *Living Letters* gives adult-like feedback that goes beyond "great" or "not quite right, try again." After the first error in an assignment, the instruction is repeated and children are encouraged "to listen carefully" to promote more thoughtful responses. After the second error, the program provides cues to solve the task correctly (e.g.,



Fig. 1. The screenshots have been derived from four different games: Selecting the proper name among three alternatives (a), selecting “mama” among five alternatives (b), selecting the first letter of the name among five alternatives (c), and selecting the painting that starts with the letter of the child’s own first name (e.g., Tom—tiger) among three alternatives (d). When the mouse skims a picture, as in d, the computer pronounces the picture’s name.

“Do you remember how the teacher writes your name?”), thus enabling engagement in other, similar tasks independently. A third error is followed by the correct solution with an explanation (e.g., “Listen; in that word you can hear the /p/ of peter”). All feedback was given by Sim’s teddy bear (the tutor), as can be seen in Figure 1b.

In the LL-NoFeedback condition, children were exposed to the same instruction at the start of the session. Assignments were similar as well but without feedback, whereas the number of repetitions was similar to the feedback condition. After each error, the assignment was given again but without any comments of the computer tutor.

After a maximum of three trials per assignment, in both conditions, Sim, Sanne, and the teddy bear started dancing to mark the end of an assignment, whether or not the child had given the correct answer, after which the next game started. When the child had made an error in an assignment, the game was repeated in the next session with a maximum of two

repetitions per game which implied that children received a variable number of sessions.

Clever Together

The control group played with another Web-based program: *Clever Together* (www.Samenslim.nl). Sim and Sanne, the same characters as in *Living Letters*, play hide and seek games. In 40 games of different levels of difficulty, the child had to help Sim by finding Sanne behind objects displayed on screen (“Find Sanne behind something red”).

Measures

Genotyping

DNA Isolation. Buccal swabs collected from individuals were incubated in lysis buffer (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).

Polymerase Chain Reaction (PCR) Amplification. Typical PCR reactions contained between 10 and 100 ng genomic template DNA, 10 pmol of forward and reverse primers, 100 μ M dNTP, 7.5% DMSO, 10 \times buffer supplied with the enzyme, 0.5 Biotherm AB polymerase (5U/ μ l) in a total volume of 30 μ l. For amplification of the exon 3 fragment, primers 5'-GCGACTACGTGGTCTACTCG-3' (5' labeled with FAM) and 5'-AGGACCCTCATGGCCTTG-3' were used. The fragment was amplified by an initial denaturation step of 10 min at 95 $^{\circ}$ C, followed by 39 cycles of 30 s at 95 $^{\circ}$ C, 30 s at 60 $^{\circ}$ C, 1 min at 72 $^{\circ}$ C, and a final extension step of 10 min at 72 $^{\circ}$ C.

Analysis of PCR Products for Repeat Number. The number of repeats for each sample was determined by size fractionating the exon 3 PCR products on an ABI-3100 automated sequencer and fragment data was analyzed using GeneMarker software. On the basis of the length of the amplified fragments, the difference from two to 10 repeats was readily visible with a resolution of ± 5 base pairs. Children were grouped in subgroups with at least one DRD4 7-repeat versus subjects with both alleles shorter than DRD4 7-repeat. These two main DRD4 genotypes (short vs. long) were in Hardy-Weinberg equilibrium, χ^2 ($df = 1$, $N = 182$) = .68, $p = .41$. Thirty-six percent of the children were carriers of at least one DRD4 7-repeat allele.

Children's Intelligence and Regulatory Skills

To test verbal intelligence, we used the Dutch version of the *Peabody Picture Vocabulary Test* (PPVT; Schlichting, 2005). Regulatory skills at pretest were measured with the Knock and Tap Test in which the child had to knock on the table when the experimenter tapped, and vice versa (e.g., Klenberg et al., 2001). The internal consistency of this 16-item test was high ($\alpha = .92$).

Early Literacy Skills

Emergent Writing. Five dictated words (i.e., *papa* [daddy], *Sim* (name of a character of the computer games), *been* [leg], *jurk* [dress], and a word starting with the first name-letter of the child or mama) were assigned one of the following codes (Levin & Bus, 2003): (0) drawing-like scribble; (1) writing-like scribbles, but not similar to conventional symbols; (2) conventional symbols not representing sounds in the word; (3) one phonetic letter; (4) two or more phonetic letters; (5) invented spelling (readable but not spelled correctly); (6) conventional spelling. Kappa values for all double-coded words were high (κ 's between .88 and .97).

Name-Letter Knowledge. After the child had identified the first letter of the own name in a series of five letters, the child had to name it. One point was awarded for a correct response.

Phonemic Sensitivity. In the phonemic sensitivity task, children had to point to the picture of a word that started with or contained the same sound as their name (or mama; for children with an irregular first name letter). The computer named the three optional pictures. A total score of six was possible, one for each correct item.

Early Literacy Skills. Principal component analysis on the three measures mentioned above revealed one component with high loadings (.70 to .77) that explained 55% of the variance. This component was labeled as "Early Literacy Skills" and used as dependent variable.

RESULTS

To examine whether randomization had been successful, we applied ANOVAs with experimental group (LL-NoFeedback; CT; LL-Feedback) as factor to test whether they were similar on intelligence and regulatory skills ($p > .30$), as well as on percentage of DRD4 7-repeat (37–42%).

Because the subjects were recruited from a limited number of schools ($N = 15$), we used the Huber-White estimates to correct for clustering of the measures. We included the estimates in the Complex Sample General Linear Model (CSGLM, SPSS 17) with posttest early literacy skills as dependent variable, experimental group (LL-NoFeedback; CT; LL-Feedback) as factor, and pretest early literacy skills, maternal educational level, children's PPVT score, and DRD4 as covariates (total $N = 174$ children in 15 schools). The explained variance of the model equaled 62%. Pretest early literacy skills, $F(1, 14) = 164.50$, $p < .001$, and PPVT, $F(1, 14) = 4.70$, $p = .048$ were significant covariates, whereas maternal educational level was a nonsignificant one, $F(1, 14) = 0.06$, $p = .81$. Experimental group, $F(2, 13) = 0.67$, $p = .53$, and DRD4, $F(1, 14) = 0.27$, $p = .61$ did not show significant main effects on early literacy skills. The interaction between experimental group and DRD4, however, was significant, $F(2, 13) = 4.81$, $p = .027$.

To examine this interaction between intervention and genotype, we repeated the CSGLM in the long DRD4 and the short DRD4 groups separately (without genotype as a factor). We found a significant effect of experimental group in the DRD4 7-repeat subsample, $F(2, 13) = 7.47$, $p = .007$; $n = 61$, where children in the LL-Feedback group outperformed the other two groups ($p < .01$, $d = .83$). However, there was no significant effect of experimental group in the short DRD4 subsample, $F(2, 13) = 1.99$, $p = .18$; $n = 113$; none of the groups significantly differed from each other ($p > .1$).

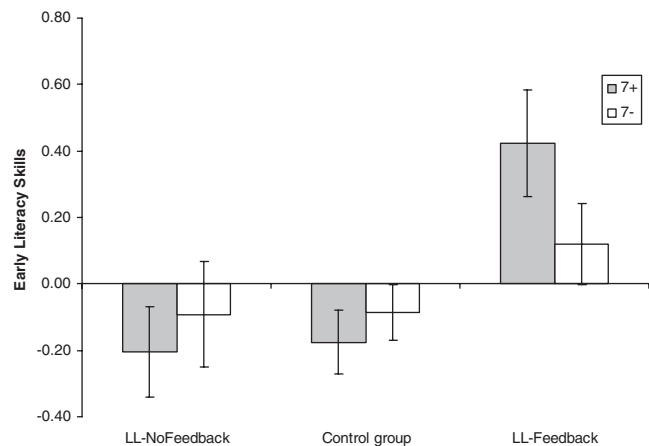


Fig. 2. Estimated means and standard errors for early literacy skills of children with (7+) and without (7-) the Dopamine D4 allele in two intervention groups and in the control group ($N = 182$).

In Figure 2, the interaction between experimental group and DRD4 is presented. The scores on early literacy skills have been residualized with the three covariates, pretest early literacy skills, maternal educational level, and children's PPVT before computing means and standard errors per subgroup. The carriers of DRD4 7-repeats showed the highest score on posttest early literacy skills after the LL-Feedback intervention, and the lowest scores after the LL-NoFeedback intervention. The carriers of the long DRD4 variants seemed to profit most from the feedback condition, and to learn least in the no-feedback condition although this latter effect was nonsignificant.

DISCUSSION

This is the first randomized controlled trial to apply the differential susceptibility paradigm to education in relation to children's genotype. The results support kindergartners' differential susceptibility to computer-based instruction of early literacy skills. Children with the long variant of the DRD4 allele appeared to be more susceptible to the positive variant of the educational intervention program *Living Letters* (with feedback), a computer training for preschoolers that promotes understanding of the combination of letters in words with sounds in their spoken counterparts. Children with the long variant of the allele scored lowest after the negative version of the computer program (without feedback), although they did not differ significantly from the control group. The carriers of two short DRD4 alleles were less influenced by the two kinds of instruction, with or without constructive feedback. To the best of our knowledge, this is not only the first experimental test of genetic differential susceptibility in education but also the first experiment ever including in one design the contrasting effects of a negative and positive

variation of an intervention. In their exhaustive review of the literature on differential susceptibility across all behavioral and medical disciplines, Ellis et al. (2011) deplore the lack of such two-pronged experimental studies.

This study of course does not provide conclusive evidence for genetic differential susceptibility in education but constitutes an illustrative proof of principle that this model may have potential applicability in the educational sciences and practices. We found that about one third of the participants who carried the long and less efficient variant of the DRD4 polymorphism seem most susceptible to the input of the computer program even when we controlled for differences in cognitive level. The susceptible group responded positively to computerized training targeting core early literacy skills, that is, understanding the combination of how words sound and look. The susceptible children learnt most from the computer program when the design was rather optimal and included constructive feedback. In contrast, they seemed to fall back behind peers with the short variant of the DRD4 allele in terms of early literacy skills when they did not receive an intervention program or when the program lacked vital feedback components modeled after efficient scaffolding by parents or caregivers. The no-feedback version of the program included similar instruction and assignments but failed to provide corrective feedback and suggestions for solving problems when children made errors. The finding that a version of the program without feedback did not promote learning in both genetic groups demonstrates the need to equip an ITS with personalized feedback (Graesser et al., in press).

The carriers of two short DRD4 alleles did not profit from the *Living Letters* instruction with feedback, but they also did not seem to experience a setback in their early literacy development during the 15-week training period because of the no-feedback or control condition. In the carriers of the short DRD4 alleles, training with feedback does not have additional advantages for early literacy skills compared to experiences at home or in school as are experienced by the control group. Also, they did not experience a setback when they were involved in the no-feedback program. In fact, they just seem not really susceptible to these educational manipulations of their environment. The flat learning profile of the carriers of the short alleles in this study on early literacy interventions is comparable to the rather indifferent developmental responses of this group to interventions in the socio-emotional domain (Ellis et al., 2011). The finding that about two third of the pupils does not profit from our educational intervention may explain why previous studies revealed rather modest main effects of this and similar interventions (Kegel et al., 2009; Van der Kooy et al., 2011).

That carriers of the long variant of DRD4 profit most from instruction with adequate feedback, whereas they also seem to experience some delay in the development of early literacy

skills when the environment is less ideal, fits well into the pattern of previous findings on gene by environment interactions using dopamine-system related genes as moderators. Through their influence on attention and reward mechanisms, dopamine-related “risk” alleles may make children vulnerable to negative environmental input and at the same time may turn out to be susceptibility genes that in supportive educational environments promote optimal development. The dopaminergic system is engaged in attentional, motivational, and reward mechanisms (Robbins & Everitt, 1999). Lower dopaminergic signaling impedes negative feedback-based learning (Klein et al., 2007) and is related to stronger dependence on immediate positive feedback (Tripp & Wickens, 2008). In a neurobiological model of altered reinforcement mechanisms in ADHD, Tripp and Wickens (2008) suggest that children with ADHD show diminished anticipatory dopamine cell firing. Under conditions of delayed or partial reinforcement learning would be slower or even fail to occur. The weak anticipatory dopamine signal renders these children more sensitive to immediate positive feedback (Bakermans-Kranenburg & Van IJzendoorn, 2011). That may explain why our instruction with immediate positive feedback proved to be most effective for children with the DRD4 7-repeat allele.

This study is of course not without limitations. The first is that children were randomly assigned to the three conditions but we did not stratify for genotype. About the same distribution emerged across the three intervention groups in our study and one third of the individuals in each condition appeared to be carrier of the 7-repeat. As a result, the power to find positive or negative intervention effects may have varied between the two DRD4 groups. In our case, this would run counter our hypothesis. Another limitation is that we did demonstrate the moderating influence of genotype on learning from instruction with or without feedback, but the biochemical as well as behavioral mechanisms responsible for the differential effectiveness remained a black box. Finally, single genes never can be the exclusive cause of protein and neurotransmitter production leading to learning behavior and development. We consider DRD4 as an index to the dopamine-system related genetic pathway comprising several genes working together to regulate dopamine levels in the brain. The rather large number of studies on this *pars pro toto* with confirming evidence for the differential susceptibility paradigm suggest its usefulness (Bakermans-Kranenburg & Van IJzendoorn, 2011).

Conclusions

Differential susceptibility differs rather strongly from received child characteristic by environment models in developmental psychopathology (“diathesis-stress,” Ellis et al., 2011) or in the educational sciences (“aptitude treatment interaction,” ATI; Cronbach & Snow, 1977). From the perspective of

differential susceptibility, the latter class of interactions is so-called contrastive and differs radically from the type of cross-over interaction illustrative of differential susceptibility (Belsky et al., 2007). ATI models assume that all children are susceptible to instruction but that not all children benefit from similar forms of instruction and thus that differentiation of instruction is required. Differential susceptibility implies that only susceptible children (the “orchids” to use a metaphor of Boyce, see Dobbs, 2009) are strongly dependent on the quality of instruction as they suffer more from bad instruction and profit more from optimal teaching—controlling for cognitive level. The less susceptible children (the “dandelions” according to the same metaphor) will adapt to most learning environments without performing too well or too bad. We conclude that children differ in susceptibility to the quality of feedback and support provided in an early reading program and that this susceptibility is associated with a genetic predisposition to dopamine-regulated reward- and attention-related mechanisms, independent of cognitive ability.

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REFERENCES

- Anderson, J. R., Boyle, C. F., & Reiser, B. J. (1985). Intelligent tutoring systems. *Science*, 228, 456–462. DOI: 10.1126/science.228.4698.456
- Bakermans-Kranenburg, M. J., & Van IJzendoorn, M. H. (2006). Gene-environment interaction of the dopamine D4 receptor (DRD4) and observed maternal insensitivity predicting externalizing behavior in preschoolers. *Developmental Psychobiology*, 48, 406–409. DOI: 10.1002/dev.20152
- Bakermans-Kranenburg, M. J., & Van IJzendoorn, M. H. (2007). Research review: Genetic vulnerability or differential susceptibility in child development: The case of attachment. *Journal of Child Psychology and Psychiatry*, 48, 1160–1173. DOI: 10.1111/j.1469-7610.2007.01801.x
- Bakermans-Kranenburg, M. J., & Van IJzendoorn, M. H. (2011). Differential susceptibility to rearing environment depending on dopamine-related genes: New evidence and a meta-analysis. *Development and Psychopathology*, 23, 39–52.
- Belsky, J. (2005). Differential susceptibility to rearing influence: An evolutionary hypothesis and some evidence. In B. Ellis & D. Bjorkland (Eds.), *Origins of the social mind: Evolutionary psychology and child development* (pp. 139–163). New York: Guilford Press.
- Belsky, J., Bakermans-Kranenburg, M. J., & Van IJzendoorn, M. H. (2007). For better and for worse. Differential susceptibility to environmental influences. *Current Directions in Psychological Science*, 16, 300–304. DOI: 10.1111/j.1467-8721.2007.00525.x
- Belsky, J., Hsieh, K. H., & Crnic, K. (1998). Mothering, fathering, and infant negativity as antecedents of boys’ externalizing problems and inhibition at age 3 years: Differential susceptibility to rearing experience? *Development and Psychopathology*, 10, 301–319. DOI: 10.1017/S095457949800162X

- Belsky, J., & Pluess, M. (2009). Beyond diathesis stress: Differential susceptibility to environmental influences. *Psychological Bulletin*, 135, 885–908. DOI: 10.1037/a0017376
- Blair, C. (2002). Early interventions for low birth weight, preterm infants: The role of negative emotionality in the specification of effects. *Development and Psychopathology*, 14, 311–332. DOI: 10.1017/S0954579402002079
- Both-de Vries, A., & Bus, A. G. (2008). Name writing: A first step to phonetic writing? Does the name have a special role in understanding the symbolic function of writing? *Literacy Teaching and Learning*, 12, 37–55.
- Both-de Vries, A., & Bus, A. G. (2010). The proper name as starting point for basic reading skills. *Reading and Writing*, 23, 173–187. DOI: 10.1007/s11145-008-9158-2
- Boyce, W. T., Chesney, M., Alkon, A., Tschann, J. M., Adams, S., Chesterman, B., et al. (1995). Psychobiologic reactivity to stress and childhood respiratory illnesses: Results of two prospective studies. *Psychosomatic Medicine*, 57, 411–422.
- Bus, A. G., & Van IJzendoorn, M. H. (1999). Phonological awareness and early reading: A meta-analysis of experimental training studies. *Journal of Educational Psychology*, 91, 403–414.
- Bus, A. G., & Van IJzendoorn, M. H. (2004). Meta-analysis in reading research. In N. Duke & M. Mallette (Eds.), *Literacy research methods* (pp. 227–252). New York: Guilford.
- Corbett, A. T., & Anderson, J. R. (2001). Locus of feedback control in computer-based tutoring: Impact on learning rate, achievement and attitudes. In J. Jacko, A. Sears, M. Beaudouin-Lafon, & R. Jacob (Eds.), *Proc. ACM CHI'2001 Conference on human factors in computing systems*, pp. 245–252. New York: ACM Press.
- Cronbach, L., & Snow, R. (1977). *Aptitudes and instructional methods: A handbook for research on interactions*. New York: Irvington.
- Dobbs, D. (2009). Orchid children. *The Atlantic Monthly*, pp 60–68. December 2009.
- Ehri, L. C., Nunes, S. R., Willows, D. M., Schuster, B., Yaghoubzadeh, Z., & Shanahan, T. (2001). Phonemic awareness instruction helps children learn to read: Evidence from the National Reading Panel's meta-analysis. *Reading Research Quarterly*, 36, 250–287.
- Ellis, B. J., Boyce, W. T., Belsky, J., Bakermans-Kranenburg, M. J., & Van IJzendoorn, M. H. (2011). Differential susceptibility to the environment: An evolutionary-neurodevelopmental theory. *Development and Psychopathology*, 23, 7–28.
- Gilissen, R., Bakermans-Kranenburg, J. J., Van IJzendoorn, M. H., & Van der Veer, R. (2008). Parent-child relationships, temperament, and physiological reactions to fear-inducing film clips: Further evidence for differential susceptibility. *Journal of Experimental Child Psychology*, 99, 182–195. DOI: 10.1016/j.jecp.2007.06.004
- Graesser, A. C., Conley, M. W., & Olney, A. (in press). Intelligent tutoring systems. In S. Graham & K. Harris (Eds.), *APA handbook of educational psychology*. Washington, DC: American Psychological Association.
- Kegel, C. A. T., Van der Kooy-Hofland, V. A. C., & Bus, A. G. (2009). Improving early phoneme skills with a computer program: Differential effects of regulatory skills. *Learning and Individual Differences*, 19, 549–554. DOI: 10.1016/j.lindif.2009.07.002
- Klein, T. A., Neumann, J., Reuter, M., Hennig, J., Von Cramon, D. Y., & Ullsperger, M. (2007). Genetically determined learning from errors. *Science*, 318, 1642–1645. DOI: 10.1126/science.1145044
- Klenberg, L., Korkman, M., & Lahti-Nuutila, P. (2001). Differential development of attention and executive functions in 3- to 12-year-old Finnish children. *Developmental Neuropsychology*, 20, 407–428.
- Levin, I., & Aram, D. (2004). Children's names contribute to early literacy: A linguistic and social perspective. In D. Ravid & H. Bat-Zeev Shyldkort (Eds.), *Perspectives on language and language development* (pp. 219–239). Dordrecht, The Netherlands: Kluwer.
- Levin, I., Both-de Vries, A. C., Aram, D., & Bus, A. G. (2005). Writing starts with own name writing: From scribbling to conventional spelling in Israeli and Dutch children. *Applied Psycholinguistics*, 26, 463–477. DOI: 10.1017/S0142716405050253
- Levin, I., & Bus, A. G. (2003). How is emergent writing based on drawing? Analyses of children's products and their sorting by children and mothers. *Developmental Psychology*, 39, 891–905.
- Levin, I., Shatil-Carmon, S., & Asif-Rave, O. (2006). Learning of letter names and sounds and their contribution to word recognition. *Journal of Experimental Child Psychology*, 93, 139–165. DOI: 10.1016/j.jecp.2005.08.002
- Meyer, B. J. F., Wijekumar, K., Middlemiss, W., Higley, K., Lei, P. W., Meier, C., et al. (2010). Web-based tutoring of the structure strategy with or without elaborated feedback or choice for fifth- and seventh-grade readers. *Reading Research Quarterly*, 45, 62–92. DOI: 10.1598/RRQ.45.1.4
- Molfese, V. J., Beswick, J., Molnar, A., & Jacobi-Vessels, J. (2006). Alphabetic skills in preschool: A preliminary study of letter naming and letter writing. *Developmental Neuropsychology*, 29, 5–19. DOI: 10.1207/s15326942dn2901_2
- Robbins, T. W., & Everitt, B. J. (1999). Drug addiction: Bad habits add up. *Nature*, 398, 567–570. DOI: 10.1038/19208
- Schlichting, L. (2005). *Peabody Picture Vocabulary Test-III NL*. Amsterdam, The Netherlands: Harcourt Test Publisher.
- Sheese, B. E., Voelker, P. M., Rothbart, M. K., & Posner, M. I. (2007). Parenting quality interacts with genetic variation in dopamine receptor D4 to influence temperament in early childhood. *Development and Psychopathology*, 19, 1039–1046. DOI: 10.1017/S0954579407000521
- Suomi, S. J. (1997). Early determinants of behaviour: Evidence from primate studies. *British Medical Bulletin*, 53, 170–184.
- Tripp, G., & Wickens, J. R. (2008). Research review: Dopamine transfer deficit: A neurobiological theory of altered reinforcement mechanisms in ADHD. *The Journal of Child Psychology and Psychiatry*, 49, 691–704. DOI: 10.1111/j.1469-7610.2007.01851.x
- Van der Kooy-Hofland, V. A. C., Kegel, C. A. T., & Bus, A. G. (2011). Evidence-based computer interventions targeting phonological awareness to prevent reading problems in at-risk young students. In S. B. Neuman, & D. K. Dickinson (Eds.), *Handbook of early literacy research*, (Vol. 3, pp. 214–227). New York: Guilford.
- Vasilyeva, E. (2007). Towards personalized feedback in educational computer games for children: Review of recent research. In *Proceedings of IASTED WBE'2007 Conference*, pp. 597–602, Chamonix, France.
- Vasilyeva, E., Puuronen, S., Pechenizkiy, M., & Räsänen, P. (2007). Feedback adaptation in Web-based learning systems. *International Journal of Continuing Engineering Education and Life Long Learning*, 17, 337–357.