Differential Susceptibility in Education

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Cover design *Living Letters* by Carienke Kegel & colleagues (inspired by Keith Haring)
Printed by Mostert & Van Onderen

Differential Susceptibility in Education

Interaction between Genes, Regulatory Skills, and Computer Games

Proefschrift

ter verkrijging van
de graad van Doctor aan de Universiteit Leiden,
op gezag van Rector Magnificus prof. mr. P. F. van der Heijden,
volgens besluit van het College voor Promoties
te verdedigen op woensdag 19 oktober 2011
klokke 16.15 uur

door

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geboren te Mijnsheerenland
in 1984

Promotiecommissie

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This research was supported by a grant from the Dutch organization *Kennisnet/ ICT op School* to Adriana G. Bus.

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1 General Introduction

Parts of this chapter were based on:
Bus, A. G., & Kegel, C. A. T. (in press). Effects of an adaptive game on early literacy skills in at risk populations. In O. Korat & A. Shamir (Eds.), *Literacy, technology, and at risk populations.*

Early literacy development

Before formal reading education begins most children acquire knowledge about code-related skills through activities such as parent-child book sharing (Bus, Van IJzendoorn, & Pellegrini, 1995; Mol & Bus, 2011) and joint writing activities (Levin & Aram, 2004). Especially reading and writing one's name seems to stimulate the development of code-related skills. Most preschoolers learn their own name through regular exposure to its written form on personal belongings, such as mugs and artwork (Levin, Both-de Vries, Aram, & Bus, 2005). Unfortunately this is not the case for all children. Literacy experiences in families with a low socioeconomic status (SES) are often sparse and children from these families may enter school with less well-developed code-related skills compared to peers from middle- to high-SES families (Shonkoff & Phillips, 2000; Stipek & Ryan, 1997). Consequently they may be less successful in the first grades of primary education (Byrne, Fielding-Barnsley, & Ashley, 2000; Silva & Alves-Martins, 2002; Snider, 1995).

Early interventions to prevent reading problems address concerns that an unacceptably large number of children are already, by 4 years of age, lacking in competencies fundamental to their school success. These children are at serious risk to lag behind in the coming years as their capacity to benefit from formal reading instruction may be compromised which may explain why early interventions are especially beneficial (Heckman, 2006). Research based curriculum-level interventions targeting understanding that letters refer to sounds in spoken words can narrow in noticeable ways the skills gap at school entry (Bus & van IJzendoorn, 1999; Ehri, Nunes, Willows, Schuster, Yaghoub-Zadeh, & Shanahan, 2001) but they involve a considerable investment of resources. Moreover, curriculum-level interventions are adapted to the class and not to the individual level although it is only a sub-sample that is in need of an additional or more intensive whole class program in preparation to reading instruction in primary education.

It is however a remarkable phenomenon that effect sizes of special programs to promote code-related knowledge were moderate at the most (e.g., Bus & van IJzendoorn, 1999; Ehri et al., 2001). Computer-aided instruction may hold particular promise for children disadvantaged by learning difficulties or SES, especially when the programs' content and rate are adaptive (Wilson, Dehaene, Duboi, & Fayol, 2009). The challenge for education is to build programs that enhance learning but prevent that children mainly focus on the fun part of the games (Brodova & Leong, 2006). Inconsiderate responses may explain why practicing with computer programs does not improve children's achievements substantially (d = .19) according to a meta-analysis of 50 different experimental studies (Blok, Oostdam, Otter, & Overmaat, 2002). Intelligent Tutoring Systems (ITS), however, may hold more promise since they can provide individualized feedback by responding consistently and adaptively to children's answers thus alerting them to the vital elements of the computer tasks.

Living Letters: An intelligent tutoring system

The program *Living Letters*, modeled after spontaneous activities of young children who grow up in a literate environment, may be a useful tool in support of the preschool and kindergarten curriculum (Van der Kooy-Hofland, Bus, & Roskos, 2011; Van der Kooy-Hofland, Kegel, & Bus, 2011). Although a variety of skills resort under early literacy skills, most researchers and educationalists would agree on the importance of understanding that letters relate to sounds. Instead of simply practicing these skills, *Living Letters* was modeled on how children from literate families acquire the alphabetic understanding. The program takes children's own name as starting point for developing a basic understanding of code-related knowledge. From developmental research in preschool age appears that the very first thing children learn is that letters in the name relate to sounds in its spoken counterpart. Close inspection of children's emerging letter name knowledge, phonemic awareness, and invented spellings supports the hypothesis that the initial letter of the name serves as an early decoder illuminating how sounds relate to letters (Levin et al., 2005; Levin & Bus, 2003). Most children can name the initial letter of their own name or 'mama' earlier than other letters; most can locate the sound of the first letter in other words preceding other sounds (Tom, for instance, will recognize /t/ in 'tiger' prior to /p/ in 'pat'); and most children can use the first letter of the own name first of all in their invented spellings (Both-de Vries & Bus, 2008, 2010).

Familiarity with the written form of the name is an incentive for new activities that stimulate the development of code-related knowledge: Children start talking about letters in the name ("that's my letter"), they play games with the sound of the first letter of their name ("he has the same letter as I have"), and adults target children's attention to letter-sound relations in the name ("the word begins with the same sound as your name"). The program *Living Letters* imitates this kind of natural activities with the own name that take place in literate homes from a very early age and that make young children pay attention to print as an object of investigation (Levin & Aram, 2004). The tasks include identifying the written form of the name (see Appendix a and b) or 'mama' (Appendix c) among other writings, identifying the first letter of the name among other letters (Appendix d), and identifying words that include the sound of the first letter of the name (Appendix e and f).

Tutor. *Living Letters* includes attractive animations to explain the upcoming games; for instance, two characters, Sim and Sanne, discover that their names have the same initial sound. Apart from explaining the games, the program includes an online tutor (Sim's teddy bear, see Appendix c) who offers hints and corrections, and focuses the child's attention on the target problem ("listen carefully, which letter is yours?") and on solving the problems by offering cues ("remember how the teacher writes your name") and explanations ("indeed, 'tent' starts just as Tom"). Because of the tutoring bear, the program may be categorized as an ITS (Anderson, Boyle, & Reiser, 1985; Graesser, Conley, & Olney, in press). According to the research, tutoring is most effective when it immediately follows a response (Corbett & Anderson, 2001) and is personalized, meaning that help is adjusted to characteristics of the user or to the user's interaction with the system (Vasilyeva, 2007). The system's adaptive power is graded up by providing more clues as more errors are made in an assignment: (1) after the first error in an assignment the oral instruction is repeated and children are encouraged "to listen carefully" to promote more thoughtful responses; (2) after the second error the program provides oral cues to solve the task correctly (e.g., "How does your teacher write your name?"), thus enabling solution of the task and engagement in other, similar tasks independently; (3) a third error is followed by the correct solution with an oral explanation (e.g., "Listen; in 'pat' you can hear the /p/ of Peter"). The program thus provides not only feedback to the accuracy of answers but it also offers adaptive, oral cues to correct and optimize children's responses (Fisch, 2005; Vasilyeva, Puuronen, Pechenizkiy, & Räsänen, 2007; Wild, 2009). A lack of tutoring may interfere with learning because it may encourage an erratic response style and random interactions with the computer program (Meyer et al., 2010), especially when children are easily distracted.

Regulatory skills

Feedback may be vital in particular for children who are easily distracted by irrelevant stimuli as is typical for children with low regulatory skills (or executive functions). These children often fail to concentrate on a task and have problems to stay focused, especially when their behavior is not continuously corrected. In general, these children are less proficient in planning, organizing, and applying rules (Meltzer, 2007), are easily distracted and impulsive (Hughes, 2002), and have problems dealing with changing tasks (Moffitt, 1993). They score low on tests when they have to suppress spontaneous reactions and impulses that interfere with carrying out a task. *Working memory*, one component of regulatory skills, may be less vital for benefiting from the target program because the relatively short and simple games of *Living Letters* do not strongly appeal to retention and manipulation of information (Diamond, Barnett, Thomas, & Munro, 2007). *Inhibitory control*, on the other hand, which involves withholding or restraining a motor response in favor of a potentially less dominant, but more adaptive response, may be necessary to stay on task and follow the rules of the computer games (Brock, Rimm-Kaufman, Nathanson, & Grimm, 2009; Diamond et al., 2007; Lonigan, Bloomfield, Anthony, Bacon, Philips, & Samwel, 1999).

It seems not too far-fetched to expect that in particular children with underdeveloped regulatory skills are more dependent on adaptive feedback from a tutor to stay on task and benefit from computer-aided instruction. They may only succeed when the program continuously corrects random choices and keeps reminding children of knowledge and procedures for solving the computer assignments. Built-in computer tutoring may therefore be especially profitable when children fail to regulate their own learning and when they are easily distracted by details or environmental influences.

Differential susceptibility

Effects of *Living Letters* of about half a standard deviation (e.g., Van der Kooy-Hofland, Bus, et al., 2011; Van der Kooy-Hofland, Kegel, et al., 2011) may indicate moderate effect sizes even though the program target foundational literacy skills and present individualized instruction. Another option is that the program causes differential effects; it may have substantial effects in susceptible sub-groups as a priori defined while mainstream children hardly benefit from the intervention. There are a few seminal studies in the domains of temperament, genetics, and physiological development supporting the idea of differential susceptibility (Belsky, 1997; Belsky, Bakermans-Kranenburg, & Van IJzendoorn, 2007; Ellis, Boyce, Belsky, Bakermans-Kranenburg, & Van IJzendoorn, 2011). For instance, 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 a supportive family environment. Blair (2002) found that a comprehensive early education program significantly lowered the level of internalizing and externalizing behaviors of three-year-old children characterized by negative emotionality but not in children with less negative emotionality. In other words, a risk group made improvements as a result of an intervention while the rest did not. The authors derived from such findings that fearful temperament or temperamental emotionality may be a 'risk' under less supportive conditions but a susceptibility factor in a supportive environment. This, actually, is the essence of the novel hypothesis of 'differential susceptibility': Some children may be more susceptible for the environment, learn more from instruction, and benefit more from cognitive interventions than others.

In studies of genetic differential susceptibility dopamine genes were moderators of intervention effects (see Bakermans-Kranenburg & Van IJzendoorn 2011 for an overview). Lower dopaminergic efficiency is associated with decreased attention and typical for children with attention deficits

(Robbins & Everitt, 1999). The long variant of the dopamine D4 receptor gene (DRD4 7-repeat) on the third axon has been linked to lower dopamine reception efficiency which has consequences for learning. Children with this long allele show diminished anticipatory cell firing and because of that they feel less reinforced by the anticipation of a successful outcome during the learning process. This dopamine-related genetic polymorphism may thus play a role in children's susceptibility to experiences related to early literacy development. Having the 7-repeat allele may increase risk for inattention and dependency on feedback provided during instruction (Tripp & Wickens, 2008).

Children from low SES backgrounds with the short variant of the DRD4 allele might benefit from their natural environment in developing alphabetic knowledge. Children's natural environments at home as well as the school curriculum offer many opportunities that can promote learning and development of pre-reading skills. For development enhancement, a special program may not be more assistive than other daily life opportunities. If, however, children are less expert in anticipating successes as is the case for those with the long variant of DRD4, continuous feedback is needed to foster their attention on focal tasks. They might not practice name writing spontaneously and elicit adult comments because they do not anticipate upcoming rewards and therefore fail to concentrate on activities. As a result, children might become dependent on a program that trains code-related skills and offers abundant practice and personalized feedback. The mainstream classroom environment is an obviously unsatisfactory environment for such children. Overcrowded early literacy settings are likely to challenge at-risk students, who need abundant repetition for acquiring code-related skills. Regular education may fail to provide the kinds of intensive, closely monitored, and individualized practice that children at-risk need to attain pre-reading skills.

In other words, children with the DRD4 7-repeat allele are expected to benefit most from an intensive individual-orientated learning environment and show the largest increase in understanding the combination of how a name sounds and looks in *Living Letters*. Carriers of the 7-repeat alleles are expected to lag further behind when the instruction is less optimal caused by the absence of a tutor built in the computer program.

Attention as mediator between DRD4 and reading

If the learn-to-read process is linked to the DRD4 gene we may expect to find a link between the gene and reading achievement. If the link is mediated by attention, as we assumed in the differential susceptibility study, reading and attention may share a genetic base (Ebejer, Coventry, Byrne, Willcutt, Olson, Colrey, & Samuelsson, 2010; Willcutt et al., 2007). There is some evidence in the literature that DRD4 is related with Attention Deficit Hyperactivity Disorder (ADHD, Faraone, Doyle, Mick, & Biederman, 2001; Maher, Marazita, Ferrell, & Vanyukov, 2002) and that ADHD is linked with dyslexia (Tripp & Wickens, 2008; Willcutt & Pennington, 2000). There is however only spare evidence supporting the hypothesis that DRD4 is a candidate gene for reading as well as attention problems. It seems plausible to assume that due to diminished anticipatory dopamine cell firing, people with the DRD4 7-repeat allele may feel less reinforced by the anticipation of a successful outcome of the learning process. Because they are less eager learning to read they often do not succeed to control attention which heightens the risk for developing reading problems. The expected link between reading development and DRD4 may therefore be an indirect one mediated by executive attention.

Aims and outline thesis

Living Letters is an analogous adaptive game designed to improve code-related skills that are required at school entry. The benefits of *Living Letters* were scrutinized in junior kindergarten children (four years) with compromised reading entry skills. A randomized controlled trial (RCT) was carried out with a threefold purpose:

1. Can *Living Letters* stimulate the development of early literacy skills?
2. Who benefits from the remedial computer program?
3. Which features of the program are vital to boost development and school-entry skills?

In **chapter 2** the short-term effects of *Living Letters* are tested in a sample of five-year-old children who are delayed in code-related skills. We tested differential effects of regulatory skills and the relation between regulatory skills and computer behavior during the computer games.

The RCT presented in **chapter 3**, focused on the importance of the tutoring component in *Living Letters*. In this study, four-year-olds from low SES backgrounds participated and we tested whether children with less developed inhibitory control are more susceptible to the presence of an online tutor than the rest.

The main aim of **chapter 4** was to test whether effects of *Living Letters* are moderated by the dopamine receptor gene D4. It is one of the first studies in which the differential susceptibility paradigm is examined in an educational setting (see also Van der Kooy-Hofland, 2011) and the first study that tests genetic differential susceptibility in education. We hypothesized that children with the long variant of the gene (DRD4 7-repeat) would be more susceptible for the tutoring component of *Living Letters* and would perform at the lowest level of early literacy skills in the absence of such feedback.

In **chapter 5** the expected link between DRD4, executive attention, and reading skills is tested. We hypothesized that diminished anticipatory dopamine cell firing as is typical for some DRD4 and DRD2 alleles is linked up with reading skills and that the link subsists when variation in executive attention is removed.

In **chapter 6** the results of the previously mentioned studies are integrated and discussed and implications for future research and educational practice are presented.

2 Improving Early Phoneme Skills with a Computer Program: Differential Effects of Regulatory Skills

Abstract

Research findings: The study focused on 90 five-year-olds from fifteen Dutch schools. The children scored among the 30% lowest on literacy tests. Half were randomly assigned to a phonological skills program on the computer, the other half to a book program. Both programs consisted of 15 ten-minute sessions. During the phonological skills program children's mouse behavior was registered every tenth of a second. Intelligence, phoneme skills, and regulatory skills were tested. Children scoring average on regulatory skills benefited from teacher-free encounters with the phonological skills program, children scoring low or high did not. Typically, the lowest-scoring children showed more meaningless mouse activity and more random clicking. *Practice or policy:* Computer programs can be used to stimulate early phoneme skills of poorly performing kindergarten children, but not for all children. Children with poor regulatory skills did not benefit from the intervention program.

Published as:

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.

Introduction

Dutch kindergarten children generally engage in literacy-related activities at home and in school. As a result most children develop some understanding of letter-sound relationships before formal reading instruction starts in first grade. However, not all children benefit equally from natural stimuli in their environments, partly as a consequence of poor regulatory skills (Bracken & Fischel, 2006; Gioia, Isquith, & Guy, 2001; Spira, Bracken, & Fischel, 2005).

Core regulatory skills are inhibitory control, working memory, and cognitive flexibility (Diamond, Barnett, Thomas, & Munro, 2007). Children with poor regulatory skills are less proficient in planning, organizing, and applying rules (Meltzer, 2007), are easily distracted and impulsive (Hughes, 2002), and have problems dealing with changing tasks (Moffitt, 1993). Whatever the causes – immaturity, neurological deficits, or child-rearing practices (Oh & Lewis, 2008; Ponitz, McClelland, Jewkes, Connor, Farris, & Morrison, 2008) – we expected poor regulatory skills to interfere with the development of entry-level reading skills (Blair & Razza, 2007; Dally, 2006), and thought that regulatory skills would be better predictors of literacy skills than verbal or nonverbal intelligence (Diamond et al., 2007; Spira et al., 2005).

Knowing that computer programs can promote basic phoneme skills (Reitsma & Wesseling, 1998), we wanted the present study to test whether a cost-effective, 'teacher-free' computer intervention can provide purposive, additional practice in learning that phonemes in spoken words relate to letters in written words (e.g., Borstrom & Elbro, 1997; Byrne, 1998). We also studied differential effects of regulatory skills. Exposure to an individual training program on the computer might make too strong an appeal to regulatory skills, especially when these are comparatively poor in a child.

Five-year-olds with rather strong regulatory skills may not need an extra training program, but will achieve a ceiling in their performance as a result of a challenging daily environment that stimulates name writing, exposure to environmental print, and word games. However, we expected kindergarten children with intermediate to poor regulatory skills to be less able to benefit from incentives in their "natural" environment at home and in school, because they are less successful in inhibiting impulsive reactions and have more problems in planning and choosing the right steps to solve tasks (Diamond et al., 2007). Young children with poor regulatory skills need early interventions, but may profit less from interventions compared to same-aged children with intermediate regulatory skills.

Five-year-old participants eligible for treatment of phoneme skills played computer games once a week over a four-month period, 'teacher-free', i.e., without support from a teacher, peer, or other adult. By recording the position of the mouse on the screen every tenth of a second and also recording where the child clicked or hovered, we tested whether children with poor regulatory skills had more problems in planning and choosing the right steps to solve tasks. From recordings of mouse behavior we were able to derive how much time it took to solve the problems, whether random clicking and unnecessary mouse movements occurred, and how often the children resorted to the support and help functions of the computer program (Bippes et al., 2003).

The study addressed the following questions:

1. Is a computer program intended to fix attention on how written words relate to spoken words effective for children performing poorly on early literacy tests?
2. Do regulatory skills explain differential effects of the computer intervention program beyond verbal and nonverbal intelligence?
3. Are children's regulatory skills related to their computer behavior during the computer games?

Method

Participants

We selected 90 children out of 404 children from 15 schools. All selected children (a) spoke Dutch as their first language, (b) were 60 to 72 months old, and (c) were among the 30% with the lowest scores on screening tests for early literacy: a letter test, a rhyming test, name writing, and a word dictation test. Eligible pupils were randomly assigned by the main researcher to a condition, with the restriction that boys and girls, and children from the same school, were distributed about equally across the two conditions. Intervention and control groups were similar in age, gender, verbal (*Peabody Picture Vocabulary Test*; Schlichting, 2005), and nonverbal intelligence (*Raven's Coloured Progressive Matrices*; Van Bon, 1986). Groups differed marginally in parental education, t (88) = −1.94, p < .056 (Table 2.1). Children were very capable of using a mouse to operate the educational software, because computers were in use in the participating kindergarten classes.

Table 2.1
Descriptives of Treatment (Living Letters) and Control Group

	Living Letters (n = 45)		Control Group (n = 45)	
Gender Male /Female	27/18		25/20	
	M	*SD*	*M*	*SD*
Age in Months	64.67	3.25	64.58	3.33
Parental education (max = 8)	5.41	2.15	4.52	2.21
PPVT[a] (raw scores)	81.36	12.75	77.53	11.16
RCPM[b] (raw scores)	16.09	3.45	17.27	3.79
Screening				
Letter knowledge (max = 10)	3.53	1.36	3.42	1.42
Rhyming (max = 12)	9.98	2.19	9.29	3.15
Writing *mama* (max = 6)	2.30	.93	2.39	1.11
Writing words (max = 6)	2.24	.81	2.15	.75

Notes. [a]PPVT = Peabody Picture Vocabulary Test. [b]RCPM = Raven's Coloured Progressive Matrices.

Programs

Living Letters. The Internet program *Living Letters*, recently made available for schools and parents via subscription (www.Bereslim.nl), is aimed at practicing phoneme skills. The program uses the spelling of a familiar word like the child's name (Levin, Shatil-Carmon, & Asif-Rave, 2006) to draw attention to phonemes in spoken words (Bus & Van IJzendoorn, 1999; Ehri et al., 2001). The program uses the child's proper name unless the spelling is inconsistent with Dutch orthography (e.g., Chris or Joey). The program then switches to 'mama', another high frequency name (Both-de Vries & Bus, 2008, 2010).

The first 20 games practicing the proper name (e.g., find your narme, Appendix a and b) and 'mama' (Appendix c) are followed by 10 games on the sound of the first letter (eg., "Which one is the /m/ of mama?"; Appendix d), and 10 games to identify pictures that start or end with the first letter of the child's name or 'mama' (Appendix e and f). Each of the last 20 games is played twice in two consecutive sessions, thus constituting two-thirds of the program. All 15 sessions start with an attractive animation using two characters who explain the upcoming games; for instance, the two characters, Sim and Sanne, discover that their names start with the same sound. Errors when solving the games are followed by increasingly supportive feedback. First the task is repeated, next a clue is given ("How does your teacher write your name?"), and lastly the correct solution is demonstrated.

Living Books. The control group was given the Internet program *Living Books* (www.Bereslim.nl), made up of five age-appropriate picture storybooks on the computer. As text is orally available, children can "read" individually. Per session, the children "read" one book followed by questions. Each book was repeated three times.

Procedure

Fifteen sessions of approximately 10 min took place during morning hours at school over a four-month period (February–May). Children sat alone at the computer screen in their classroom or the computer room, with a headset on. Researchers logged children in on the Internet site and made sure they completed all fifteen sessions. A helpdesk was available for emergencies. After entering the child's name, the correct games appeared automatically and the session was discontinued after four games. When a child received all available feedback a game took at most 90 seconds extra. Mouse behavior was written to the data store of the provider and saved.

With written consent from parents three assessments took place: a pretest, a mid-test (for testing regulatory skills) after about 8 weeks, and a posttest immediately after the intervention. Each session took approximately 25 minutes. Testing took place in a room where only the child and examiner were present. In most cases the four Master's students who did the testing were blind to group allocation. The order of the tests was always the same, except for regulatory skills: Computer and paper tests were counterbalanced, as were the tests within the two clusters. All sessions were videotaped and afterwards scored by Master's students blind for group allocation.

Measures

Parental education. Parents ticked their highest level of education on a scale ranging from primary education to university (1–8).

Intelligence. To test verbal and nonverbal intelligence we used Dutch versions of the *Peabody Picture Vocabulary Test* (PPVT; Schlichting, 2005) and *Raven's Coloured Progressive Matrices* (RCPM; Van Bon, 1986).

Phoneme skills.

Word dictation. Five dictated words (i.e., papa [daddy], Sim (boy's name), been [leg], jurk [dress], duim [thumb]) 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. The intraclass correlation coefficients for all double-coded words were high (r's > .99). The scores on the words were averaged (α's > .84) for pre- and posttest.

Phoneme identification. Children identified the first sounds of five CVC or CVCC words, the last sounds of five CVC or CCVC words, and named all three or four phonemes of five CVC, CCVC, or CVCC words. Cronbach's alphas for pre- and posttest equaled .93 and .92, respectively.

Aggregate measure. Principal component analysis (PCA) resulted in one component explaining 63% and 73% of pre- and posttest, respectively. Component loadings ranged from .79 to .86. The distributions of the variables were normal. A higher score indicates better phoneme skills.

Regulatory skills.

Stroop-like task (dogs). Following the Stroop paradigm, children had to switch rules by responding with an opposite, i.e., saying "blue" to a red dog and "red" to a blue dog (Beveridge, Jarrold, & Pettit, 2002). The task consisted of 96 trials distributed over four conditions, in which demands on working memory (remembering the name of one or two dogs) and inhibition of the most obvious response (e.g., saying "blue" to a red dog) varied. Incorrect naming and corrections were both scored as errors.

Stroop-like task (opposites). Children had to respond with the opposite to contrasting pairs of pictures (e.g., saying "fat" to thin) (based on Berlin & Bohlin, 2002). Incorrect naming and corrections were both scored as errors. This test measured working memory (memorising the names of the pictures) and inhibition.

Same tapping. The child copied the experimenter's hammer taps on cubes (Leidse Diagnostische Test; Schroots & Van Alphen de Veer, 1976). Each correct imitation in this working memory task was awarded one point with a maximum score of 12.

Peg tapping. The child tapped twice with a pencil after one tap by the experimenter, and vice versa (Diamond & Taylor, 1996). The task measures the ability to inhibit a natural tendency to mimic. The total score was the number of correct responses to 16 items. Intraclass correlation coefficients between two independent coders were high for all four tasks (r > .97).

Aggregate measure. PCA revealed one component with high loadings (.61–.76) explaining 49% of the variance. Because square root and log transformations failed to normalize the measure, children were classified in three groups using quartiles (1 = first quartile, 2 = second and third quartile, 3 = fourth quartile). The distribution of this new variable was normal for both the treatment and the control group.

Computer behavior. From mouse behavior, registered and stored every tenth of a second, we derived the time between the question and the child's answer, the total time spent on mouse manipulation, number of mouse clicks, and type and number of support needed to solve the tasks. PCA on these four behaviors resulted in one component that explained 78% of the variance and in component loadings beyond .72. The higher the scores on this component, the more children showed problematic computer behavior, i.e., more mouse clicks, mouse movements and mistakes, and longer response time.

Data analyses. We conducted an ANCOVA with regression techniques to examine the effect of *Living Letters* on phoneme skills (Cohen, Cohen, West, & Aiken, 2003). Effect-coded *Living Letters* was entered in the model, after controlling for age, gender, parental education, PPVT, RCPM, and pretest score on phoneme skills. We hypothesized that treatment effects may be strong among children with average regulatory skills but, due to problems with planning and choosing the right steps, treatment may have a reduced impact in groups with poor regulatory skills and, due to ceiling effects, also in groups with high regulatory skills. Therefore, three categories were created: children scoring among the lowest 25% on regulatory skills (n = 23), children scoring around average (n = 45), and children scoring among the highest 25% (n = 22). The categories were effect-coded by assigning a value of −1 for the base group (here, the 25% highest-scoring). Each of the other categories was assigned a value of 1 for one code variable and 0 for the other (Cohen et al., 2003). Subjects at each level of regulatory skills were appropriately divided to control and treatment groups. By cross-multiplying the coded level of regulatory skills with the coded variable of the treatment program we tested whether the three levels of regulatory skills responded alike or differently to the treatment.

To examine the effects of regulatory skills on computer behavior in the group of 45 children playing the *Living Letters* games we used a one-way ANCOVA model. Because relatively poor literacy skills may increase the need for feedback, we adjusted the computer behavior for differences on the pretest for phoneme skills.

Missing values. Incidental computer registrations that were lost due to technical problems were imputed by using mean scores within a set. One child was excluded due to too many missing data.

Results

Impact of Living Letters

Table 2.2 shows the means and standard deviations for phoneme skills and regulatory skills for treatment and control group. The correlations between predictors were mostly low and moderate at most, as shown in Table 2.3. The final results of an ANCOVA model to test main and interaction effects of *Living Letters* and regulatory skills on phoneme skills are presented in Table 2.4. There were no serious problems of multicollinearity (tolerance values > .10). Gender, age, parental education, PPVT, RCPM, and pretest score on phoneme skills were entered as centered continuous variables or effect-coded category (gender) at step 1. The explained variance equaled 35% (F (6, 76) = 6.91, p < .001). By entering effect-coded treatment and regulatory skills in step 2, the increment to R^2 was 10%, F (3, 73) = 4.19, p < .01, and by entering the interactions between treatment and regulatory skills in step 3, the increment to R^2 was 5%, F (2, 71) = 3.82, p < .028.

Table 2.2
Means and Standard Deviations for Phoneme Skills at Pre- and Posttest, and Regulatory Skills at Mid-test; Grouped According to Treatment or Control Group

	Living Letters		Control Group	
	M	*SD*	*M*	*SD*
Phoneme skills (pre- and posttest)				
Word dictation (pre) (max = 6)	2.45	.67	2.21	.80
Word dictation (post) (max = 6)	3.39	.80	2.87	.61
Phoneme recognition (pre) (max = 15)	5.13	4.86	3.84	4.70
Phoneme recognition (post) (max = 15)	9.40	5.00	8.16	5.34
Aggregate measure (pre)	.20	.94	-.20	1.03
Aggregate measure (post)	.27	1.07	-.27	.85
Regulatory skills (mid-test)				
Stroop task dogs (max = 96)	83.84	9.28	82.00	9.78
Stroop task opposites (max = 48)	30.04	8.02	29.44	7.55
Same tapping (max = 12)	6.64	2.40	6.67	2.06
Peg-tapping (max = 16)	13.29	2.36	12.33	3.24
Aggregate measure	-.00	.92	-.23	1.01
Transformed (1-3)	2.07	.65	1.94	.78

Note. Cell sizes vary from 43 to 45 Pupils.

Table 2.3
Correlations for all Variables

	1.	2.	3.	4.	5.	6.	7.	8.	9.
1. Gender[a]	1.00								
2. Age	.19	1.00							
3. Parental education	-.22*	-.09	1.00						
4. PPVT[b]	-.07	.17	.19	1.00					
5. RCPM[c]	.18	.14	-.09	.09	1.00				
6. Pretest[d]	-.22*	.02	.10	.39**	-.04	1.00			
7. Posttest[e]	-.24*	-.01	.12	.25*	-.10	.57**	1.00		
8. Regulatory skills	-.03	-.14	-.02	.22*	.03	.12	.21	1.00	
9. Computer behavior	.12	.16	.13	-.11	.20	-.42**	-.51**	-.38**	1.00

Notes. For correlations with computer behavior n = 45 and for other correlations n = 90.
[a] Gender (-1= girl, 1=boy), [b] PPVT = Peabody Picture Vocabulary Test, [c] RCPM = Raven's Coloured Progressive Matrices, [d] Pretest = pretest scores of phoneme skills, [e] Posttest = posttest scores of phoneme skills.
* Correlation is significant at the .05 level (2-tailed); ** Correlation is significant at the .01 level (2-tailed).

Table 2.4

Final Model of Hierarchical Multiple Regression Analysis of Phoneme Skills (Y) (N = 90)

	B	*SE*	Tolerance	*t*	*p*
Intercept	-1.81	1.87			
Background					
Gender (Male)	-.10	.10	.82	-1.02	NS
Age	.03	.03	.84	.94	NS
Parental education	.08	.11	.86	.71	NS
Peabody Picture Vocabulary Test	-.01	.01	.68	-1.02	NS
Raven's Coloured Progressive Matrices	.00	.03	.80	.01	NS
Pretest (phoneme skills)	.54	.10	.75	5.62	<.001
Main effects					
RS^1 (low regulatory skill vs. mean)	-.33	.14	.67	-2.28	<.05
RS^2 (intermediate regulatory skill vs. mean)	.24	.12	.71	2.01	<.05
Z (Treatment)	.13	.10	.79	1.32	NS
Interaction					
RS^1*Z	-.15	.15	.65	-.97	NS
RS^2*Z	.33	.12	.69	2.74	<.01

*Note***.** The results represent the final model with all variables included.

One *SD* higher on the pretest meant .54 *SD* higher on the posttest (see Table 2.4). The group lowest on regulatory skills scored below the grand mean (.33 *SD*), the intermediate group scored beyond (.24 *SD*), and the highest group about average (.09 *SD* higher). The lowest regulatory skills level (RS^1) ($t = -2.28$, $p < .05$) and the intermediate level (RS^2) ($t = 2.01$, $p < .05$) differed significantly from the grand mean. The *Living Letters* group did not score beyond the grand mean ($t = 1.32$, ns). The significant interaction (RS^2*Z) indicates that the *Living Letters* group outperformed the control group when children scored around average on regulatory skills, as is shown by the predicted values in Figure 2.1. The group lowest on regulatory skills scored at a relatively low level at pretest, and their score did not improve as a result of the computer treatment. The group highest on regulatory skills scored just above the grand mean on phoneme skills at pretest, but showed no additional increase as a result of the treatment.

Computer behavior

Regarding computer behavior we expected especially children scoring lowest on regulatory skills to differ from children scoring in the normal or highest ranges. A planned contrast between the lowest scores and the rest, after controlling for phoneme skills (F (1, 41) = 7.89, $p < .01$, partial η^2 = .16), was significant (F (1, 41) = 11.83, $p < .01$, partial η^2 = .23 with 95% confidence limits from .11 to .81). Aggregate scores for children low, intermediate, and high on regulatory skills were 1.17, −.14, and −.19, respectively, with high scores indicating more problematic computer behavior.

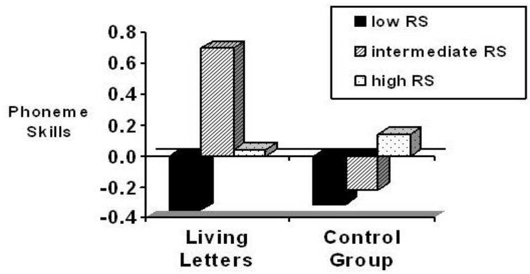

Figure 2.1. The bars in this figure represent the predicted values in treatment and control groups as a function of Regulatory Skills (RS). The scores have been derived by substituting the regression coefficients in Table 2.4 and the effect codes in the regression equation (Cohen et al., 2003). For instance, for the middle-regulatory skills intervention group the outcome was derived as follows: $\hat{Y} = (-1.81 + (.24 *1)) + (.13 + (.33 *1)) = -1.11$. The grand mean was set to zero to give a better interpretable view of the differences between the groups (-1.11 + 1.81 = .70).

Discussion

In general, children with poor early literacy skills did not benefit from *Living Letters*, but as expected there were differential effects of regulatory skills. Children scoring in the normal range on regulatory skills did benefit from *Living Letters*. After treatment this sub-group scored on average more than half a standard deviation (.70 *SD*) beyond the grand mean on phoneme skills, a striking result considering the fact that the tests were rather distal from the program, i.e., requiring children to spell new words and identify letters in spoken words that had not been practiced yet.

Children with equally poor literacy skills but scoring among the lowest 25 percent on regulatory skills were less likely to benefit from the treatment program, probably because the regulatory demands of the program may have outstripped these children's regulatory skills. The group scoring lowest on regulatory skills needed more time to respond, clicked more often, spent more time manipulating the mouse, and made more mistakes (cf. Bippes et al., 2003). It seemed that the feedback loops built into *Living Letters* (e.g., providing cues to find the correct answer) were insufficient to counterbalance problems in planning and choosing the right steps.

Likewise, among children with high regulatory skills the computer treatment was no incentive for phoneme skills. They had relatively high scores on the pretest (approximately .53 *SD* above the grand mean), which may have made *Living Letters* less challenging to this group. However, given the fact that these children scored among the lowest 30 percent despite relatively strong regulatory skills, we can also suppose that relatively more subjects in this group are most at risk for reading problems due to a phonological deficit (Snowling, 2000). This becomes even more plausible when we take into account that this group showed the same computer behavior as the middle-regulatory skills group. In future reports we hope to expand the picture to include follow-up tests in grades 1 and 2.

Our results seem to refute the criticism that regulatory-skills tasks are not informative about learning problems because they do not relate to behavior in complex real-world situations (Brown, 1999). Lower scores on regulatory-skills tests typically coincide with problematic computer behavior. The alternative to this explanation is that poor literacy skills cause a need for more feedback, and more time and mouse clicks to solve the games. However, the present findings refute this hypothesis because after controlling for pretested phoneme skills the relation between computer behavior and regulatory skills still exists.

Another interesting result is that regulatory skills are predictors of school success beyond verbal or nonverbal intelligence. It is also worth mentioning that the results fail to support the hypothesis that gender explains differences in behavioral regulation, as suggested in the literature (e.g., Ponitz et al., 2008).

Future directions and limitations

As the program uses the child's own name, treatments are somewhat different for most children. This may have an impact on generalizability. In so far as we could test differential effects by contrasting effects of the proper name (n = 36) with effects of mama (n = 9), there was no evidence for different outcomes.

Further experiments should consolidate the differential effects of the program by testing regulatory skills prior to the experiment and by assigning equal numbers of children with low, intermediate, and high levels of regulatory skills to treatment and control groups.

The feedback and help options in the present program anticipated problematic regulatory skills, but were evidently insufficient to scaffold learning behavior and to correct for uncontrolled mouse behavior and distraction from the task. Given that the children with poor regulatory skills did not benefit from the intervention, there clearly is a need to individualize games by adapting content (e.g., more games practicing the same) and providing appropriate feedback (e.g., after one or more errors starting each new task with a reminder of relevant steps).

Implications

Computer programs can be used to stimulate early phoneme skills of poorly performing kindergarten children, although our current results also point to the weaknesses of computer programs. Children with poor regulatory skills did not benefit from the computer intervention, probably due to their failure to ignore distracters and to choose an adequate problem-solving strategy.

The program can also be used as a diagnostic tool to detect poor regulatory skills as a barrier to learning, thus also making it a valuable teaching aid.

3 Online Tutoring as a Pivotal Quality of Web-Based Early Literacy Programs

Abstract

In this randomized-controlled trial 312 low-SES children (*M* = 52.9, *SD* = 3.2 months) from 15 Dutch schools participated. Children in the intervention condition played early literacy games via the Intelligent Tutoring System (ITS) *Living Letters.* Control children played a non-literacy computer game. At the beginning of each intervention session, children received instruction from computer characters about how to play the game. While playing the game, half of the children in the intervention group received individualized feedback which included oral corrections and cues from a computer tutor. The other half of the children received no individualized feedback. On average the intervention comprised 11 sessions (approximately 110 minutes). A main finding was that children's code-related skills increased as a result of the *Living Letters* program, but only when the program included a computer tutor who gave oral feedback to children's correct responses and errors. Children with underdeveloped inhibitory control scored disproportionately low in a computer environment without tutoring.

To be published as:
Kegel, C. A. T., & Bus, A. G. (in press). Online tutoring as a pivotal quality of web-based early literacy programs. *Journal of Educational Psychology*.

Introduction

Before formal reading education begins children acquire knowledge about code-related skills through activities such as parent-child book sharing (Bus, Van IJzendoorn, & Pellegrini, 1995; Mol & Bus, 2011) and joint writing activities (Levin & Aram, 2004). Because literacy experiences in low-SES families are often sparse, children from these families may enter school with less well-developed code-related skills compared to peers from middle- to high-SES families (Shonkoff & Phillips, 2000; Stipek & Ryan, 1997), and consequently may be less successful in the first grades (Byrne, Fielding-Barnsley, & Ashley, 2000; Silva & Alves-Martins, 2002; Snider, 1995).

Attempts have been made to level initial differences in entry-level reading skills by exposing young children to special programs that promote code-related knowledge resulting in moderate effect sizes (e.g., Bus & van IJzendoorn, 1999; Ehri, Nunes, Willows, Schuster, Yaghoub-Zadeh, & Shanahan, 2001). It is studied whether computer interventions can provide similar instruction and practice, but overall efficacy of Computer-Assisted Instruction (CAI) appears to be low (d = .19) according to a meta-analysis of 50 different experimental studies (Blok, Oostdam, Otter, & Overmaat, 2002). It is possible that tutoring in computer programs is not present to the same extent as it is in teacher-lead interventions. We therefore hypothesize that computer programs might be more effective when they not only provide feedback about the correctness of the response — as most programs in the Blok et al. study do — but also provide explanations and suggestions to help children improve their responses. In this study we compare a program that provides only rudimentary feedback about the correctness of the response with a program that provides explanations and suggestions modeled on human tutors (Anderson, Boyle, & Reiser, 1985; Graesser, Conley, & Olney, in press; Van der Kooy-Hofland, Kegel, & Bus, 2011). We present the results of a randomized controlled trial of an educational computer treatment with and without availability of a built-in computer tutor who confirms correct responses and explains why the responses are correct, or supplies suggestions to improve the child's responses.

As the number of computers in schools is now about 1 computer per 5 children (Kennisnet, 2010), the availability of educational software for young children has improved. Programs designed to teach core skills are also more available, although they are not yet used on a regular basis in classroom settings. Programs such as *Number Race* (Wilson, Dehaene, Dubois, & Fayol, 2009), *Daisy Quest* (Lonigan, Driscoll, Phillips, Cantor, Anthony, & Goldstein, 2003), and *GraphoGame* (Saine, Lerkkanen, Ahonen, Tolvanen, & Lyytinen, 2011) are CAI programs focused on the teaching of basis numerical or phonological skills in a game-like setting with only rudimentary feedback on the correctness of responses. In *GraphoGame*, for example, balloons showing correct answers color green after they are chosen with clicks. However, in none of these programs an explanation is provided to children regarding why their answers are correct, or how they might be improved, as is common practice in Intelligent Tutoring Systems (ITSs).

What adults expect from children while playing computer games can be very different from what children actually do (L. Labbo, personal communication, October 11, 2004). The challenge for education is, therefore, to build programs that enhance learning but prevent that children mainly focus on the fun part of the games and respond without reflection (Brodova & Leong, 2006). In the Dutch ITS *Living Letters*, an online tutor offers hints and corrections, which are intended to focus the student on target problems and aid them in solving those (Anderson et al., 1985; Graesser et al., in press). The research literature indicates that tutoring is most effective when it immediately follows a response (Corbett & Anderson, 2001) and is personalized, meaning that help is adjusted to characteristics of the user or to the user's interaction with the system (Vasilyeva, 2007). *Living*

Letters builds on these general principles by providing three sorts of responses immediately following children's reply: (1) repeating instruction when children, on their first attempt to solve the game, just pick out an incorrect answer; (2) cues from the tutor if they fail the same task once more; and (3) verbalizing the correct answer; at the end of each game, after they found the correct solution themselves or after the online tutor modeled the answer, the program verbalizes how the correct solution can be found next time they encounter similar problems. The program thus provides not only feedback to the accuracy of answers but it also offers oral cues to correct and optimize children's responses (Fisch, 2005; Vasilyeva, Puuronen, Pechenizkiy, & Räsänen, 2007; Wild, 2009). We examined whether the tutor element in *Living Letters* increases the beneficial effects of the program and is worthwhile to consider when designing new games.

The original program *Living Letters* consists of a series of games designed for young children not yet demonstrating an awareness of the letter-sound relationship in an alphabetic language and aims at stimulating children to combine their understanding of how a familiar word, for example their name, looks with knowledge of how it sounds (Both-de Vries & Bus, 2008, 2010; Molfese, Beswick, Molnar, & Jacobi-Vessels, 2006). The program draws on surface perceptual knowledge of the child's name. Most young children develop this knowledge naturally when they encounter their name on personal belongings such as mugs and artwork (Levin, Both-de Vries, Aram, & Bus, 2005; Levin & Bus, 2003). The program stimulates the basic, but indispensable, understanding that letters in the name can be heard in its spoken counterpart. The program's instructional framework is modeled on how caregivers promote the development of letter-sound knowledge with the name as a starting point (Levin & Aram, 2004; Molfese et al., 2006). Analogous to children's activities in daily life the program emphasizes three successive skill areas: (1) recognizing their name in print; (2) associating the initial name letter with its sound; and (3) identifying the sound of the initial name letter in other words (Both-de Vries & Bus, 2010). A previous study of *Living Letters* revealed both short- and long-term effects of the program for a sample of low achievers in kindergarten-age (Van der Kooy-Hofland, Kegel et al., 2011). Children in the *Living Letters* group outperformed control children on early literacy tests administered directly after the program, as well as on word reading tests at the end of second grade.

In the current study we focused specifically on the importance of the tutoring component of the *Living Letters* program. We therefore created a version of *Living Letters* without tutor (revised program) in addition to the original program with tutor. In both versions of the program, games and instructions were the same and children received an identical number of trials and repetitions. The two programs differed only on the presence of an online tutor to provide oral feedback to children's responses.

A second aim of this study was to test whether a sub-sample of children, with less developed inhibitory control, is more susceptible to the presence of an online tutor than the rest. Previous research has demonstrated that children with regulatory skills in the normal range benefit more from a literate environment (e.g., Davidse, De Jong, Bus, Huijbregts, & Swaab, 2011) including computer games (Kegel, Van der Kooy-Hofland, & Bus, 2009). *Working memory*, one aspect of regulatory skills, may be less vital for learning of our computer intervention because the relatively short and simple games do not strongly appeal to retention and manipulation of information (Diamond, Barnett, Thomas, & Munro, 2007). *Inhibitory control*, another component of self regulation which involves withholding or restraining a motor response in favor of a potentially less dominant, but more adaptive response, may be necessary to stay on task and follow the rules of the computer games (Brock, Rimm-Kaufman, Nathanson, & Grimm, 2009; Diamond et al., 2007; Lonigan et al., 1999).

In particular children with poor inhibitory control may be disadvantaged by a program that lacks an online tutor. These children are easily distracted and, without a program that orally corrects and confirms responses and offers suggestions for improvement of problem solutions, they may react randomly to computer assignments, which may in turn result in low achievement. Poor inhibitory control combined with a less supportive environment may thus create a 'dual risk' for widening the knowledge gap (Belsky, Bakermans-Kranenburg, & Van IJzendoorn, 2007). Children scoring in the normal range, however, may suffer less when a program lacks an online tutor. These children may be less dependent on program qualities, because their inhibitory control may compensate for a less optimal environment. It seems reasonable, therefore, to hypothesize that children with low inhibitory control may be adversely affected by a computer environment that lacks oral support designed to aid the student in problem solving. Poor inhibitory control may not hinder learning in a "positive" environment but may do so in a "negative" environment (Bierman, Nix, Greenberg, Blair, & Domitrovich, 2008; Blair & Razza, 2007; McClelland et al., 2007).

This study

If a tutor offering oral feedback, hints, and explanations is important in computer assisted learning (Vasilyeva, 2007), then *Living Letters* may not be as effective without online tutoring, even if the assignments, instructions, and number of task repetitions remain the same (Meyer et al., 2010). In particular children with low inhibitory control may be at dual risk when a computer program does not provide online tutoring. When a program neither corrects impulsive responses nor offers suggestions for finding the correct solutions after errors, it may reward impulsive reactions and enhance a tendency to respond without reflection. Children are at double risk not to benefit from the program when the environment does not reinforce their regulatory skills. An earlier study (Kegel et al., 2009) supported the hypothesis that weak regulatory skills elicit random computer behavior, thus limiting learning from the ITS *Living Letters*. However, studies so far have not examined whether regulatory skills moderate the effects of computer instruction, especially when the program fails to offer personalized, oral support.

The study addressed the following research questions:

1. Can an Intelligent Tutoring System promote young (low-SES) children's foundational code-related knowledge?
   Living Letters, a computer program for preschoolers with delays in school-entry skills, may foster the development of code-related knowledge.
2. Is an online tutor that provides immediate, personalized oral feedback, explanations, and hints a vital component of a computer program designed to promote preschoolers' foundational code-related knowledge?
   The ITS *Living Letters* with a built-in computer tutor may be more effective than a CAI program that includes the same assignments, instructions, and number of task repetitions but provides only subtle feedback on correctness of the answer.
3. Does a tutor providing immediate, personalized oral feedback, explanations, and hints affect the quality of children's responses and does the children's computer behavior predict gains?
   An online tutor may stimulate children to respond more thoughtfully, which may result in fewer errors in assignments and better posttest scores.
4. Do children's regulatory skills moderate program effects?
   Working memory may not moderate program effects because the tasks are simple; however underdeveloped inhibitory control may level the efficacy of computer activities especially when there is no tutor to correct behavior. As a result, children may be at dual risk especially when poor inhibitory control is not leveled by a compensatory computer environment.

Method

Participants

Participants were 312 kindergartners (60 percent male) from 15 Dutch schools in Rotterdam, Leiden, and the surrounding areas. Schools were selected for inclusion if they served large numbers of low-SES families and agreed to participate. For 70 percent of the mothers in our sample was their highest level of education senior secondary vocational education (about 13 years of education, excluding preK). Children who were about four years old (*M* = 52.9 months, *SD* = 3.2) at the beginning of the year in which the intervention was carried out, and who spoke Dutch as their first language, qualified for participation in the experiment. Parental consent was obtained with a positive response rate of 91 percent. Each school received 1000 Euro for participation in the experiment.

Study design

A randomized controlled trial design was used to examine the effects of the ITS *Living Letters*. Two *Living Letters* intervention conditions were created, one with tutor (LL-Tutor) and one without online tutoring (LL-NoTutor). The first program is the original program examined in earlier studies (Kegel et al., 2009; Van der Kooy-Hofland, Kegel, et al., 2011). Two control groups were assigned to another computer program (*Clever Together*). In this study these two control groups were reported as one condition because there were no between-group differences in pre- and posttest scores on outcome measures. Eligible pupils were randomly assigned by the main researcher to a condition stratified for school, gender, and children's level of regulatory skills (knock and tap) on a pretest (Table 3.1).

Programs

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), aims at training foundational code-related skills. The child's name or another familiar name, i.e., 'mama' [mom] (Levin, Shatil-Carmon, & Asif-Rave, 2006) is used to draw attention to the relationship between letters in a name's visual form and phonemes in the spoken name. Because the name is usually the first word that young children can read and write, children received the program version with their name unless the name's spelling was inconsistent with Dutch orthography (e.g., Chris or Joey). In those cases (22% of the sample), the program used 'mama' as target word (Both-de Vries & Bus, 2008, 2010).

The computer program begins with 20 games in which children practice finding their name or 'mama' between other signs and words (Appendix a, b, and c), followed by 10 games targeting the sound of the first letter of their name or mama (Appendix d), 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: snake, bear, or duck?"; Appendix f). All sessions start with an attractive animation in which preschoolers Sim and Sanne explain the upcoming game; for instance, Sim and Sanne discover that their names start with the same sound.

Table 3.1
Descriptives of Treatment (Living Letters with and without Tutor) and Control Groups

	LL-NoTutor				Control Group				LL-Tutor			
	M	*SD*	Range	*n*	*M*	*SD*	Range	*n*	*M*	*SD*	Range	*n*
Background												
Gender (1 = female)	.37	.49	0 - 1	78	.40	.49	0 - 1	155	.41	.49	0 - 1	79
Age in Months (Fall)	52.40	3.25	48 - 59	78	53.16	3.25	47 - 63	155	53.01	3.36	48 - 59	79
Maternal education (highest)	3.16	1.31	1 - 6	64	3.16	1.31	1 - 6	134	3.30	1.34	1 - 6	67
SON[a] mosaic (raw scores, Winter)	8.16	2.00	3.5 - 15.0	74	8.10	1.71	3.3 - 13.0	148	7.89	1.86	3.4 - 15.0	79
SON[a] mosaic (norm scores, Winter)	10.19	3.32	3 - 19	74	9.74	3.08	1 - 17	148	9.34	3.18	2 - 19	79
PPVT[b] (raw scores, Winter)	67.11	12.26	37 - 104	75	67.95	11.53	40 - 100	150	65.91	11.00	42 - 91	79
PPVT[b] (norm scores, Winter)	101.96	15.38	64 - 145	75	101.85	14.29	67 - 140	150	99.41	12.52	71 - 131	79
Regulatory skills												
Knock and Tap (Fall)	13.14	4.33	0 - 16	78	13.15	4.14	1 - 16	154	12.99	4.01	0 - 16	78
Working Memory (WM; Spring)												
Digit span (words)	5.24	3.39	0 - 10	75	5.07	2.28	0 - 10	148	5.01	2.28	0 - 10	78
Backward digit span	1.80	2.17	0 - 7	75	2.07	2.14	0 - 8	147	1.95	2.01	0 - 8	77
Stroop-like task (dogs, WM errors)	10.13	12.85	0 - 58	75	10.68	11.43	0 - 55	148	10.10	11.43	0 - 44	77
Aggregate Measure WM[c]	-.01	1.03	-3.62 - 1.78	75	.00	.99	-3.40 - 1.71	147	.00	1.00	-2.21 - 1.90	76
Inhibitory Control (IC; Spring)												
Stroop-like task (opposites)	8.31	4.58	0 - 17	75	8.52	5.45	0 - 17	148	8.22	5.88	0 - 18	78
Stroop-like task (dogs, IC errors)	10.63	5.44	3 - 25	75	11.36	6.13	1 - 29	148	11.22	6.79	1 - 34	77
Aggregate Measure IC[c]	.03	.81	-2.17 - 1.53	75	.00	1.04	-2.72 - 2.39	147	-.03	1.10	-3.13 - 1.62	76
Code-related skills												
Developmental spelling (Winter)	2.16	1.03	.20 - 4.60	75	2.17	1.06	0 - 5.60	149	2.21	1.09	.20 - 5.40	79
Developmental spelling (Spring)	2.50	.99	0 - 5.80	75	2.54	.91	0 - 5.80	145	2.75	1.10	.20 - 5.60	77
Name-letter knowledge (Winter)	.53	.50	0 - 1	75	.57	.48	0 -1	150	.48	.50	0 - 1	79
Name-letter knowledge (Spring)	.60	.49	0 - 1	75	.66	.48	0 - 1	148	.74	.44	0 - 1	77
Phonemic sensitivity (Winter)	2.39	1.25	0 - 6	75	2.48	1.51	0 - 6	151	2.51	1.25	0 - 6	79
Phonemic sensitivity (Spring)	2.61	1.41	0 - 6	75	2.68	1.49	0 - 6	149	3.16	1.68	0 - 6	77
Aggregate measure (Winter)[d]	-.02	.88	-1.76 - 2.28	74	.03	1.04	-1.95 - 3.02	148	-.07	.99	-1.57 - 2.93	79
Aggregate measure (Spring)[d]	-.13	1.00	-1.87 - 2.47	75	-.06	.96	-2.15 - 2.75	144	.23	.98	-2.24 - 2.56	77

Notes. Fall = screening; Winter = pretest; Spring = posttest. [a] SON = Snijders-Oomen Niet-verbale intelligentie toets (Snijders-Oomen Non-verbal intelligence test); [b] PPVT = Peabody Picture Vocabulary Test; [c] PCA applied to the stroop-like and digit span tasks revealed two components: *working memory* (high loadings of digit span tasks and of working memory errors in dogs) and *inhibitory control* (high loadings of opposites and of inhibitory control errors in dogs). [d] PCA of developmental spelling, name-letter knowledge, and phonemic sensitivity revealed one component for retests (Winter) and posttests (Spring).

Tutor. In the tutor condition (LL-Tutor), children received increasingly supportive oral feedback from the tutor to their responses. Unlike most computer games, the program *Living Letters* gives adult-like feedback that goes beyond indicating which responses are correct and which ones are not. The computer tutor explains why a response is correct (e.g., "Listen, in 'snake' your can hear the /s/ of Sam"). Furthermore, help from the tutor includes more clues as more errors are made in an assignment: (1) after the first error in an assignment the oral instruction is repeated and children are encouraged "to listen carefully" to promote more thoughtful responses. (2) After the second error the program provides oral cues to solve the task correctly (e.g., "Do you remember how the teacher writes your name?"), thus enabling solution of the task and engagement in other, similar tasks independently. (3) A third error is followed by the correct solution with an oral explanation (e.g., "Listen; in that word you can hear the /p/ of Peter"). All tutoring was provided by Sim's teddy bear (the tutor), as can be seen in Appendix c.

In the non-tutoring condition (LL-NoTutor) children were exposed to *Living Letters* without an online tutor. Instructions and assignments, as well as number of repetitions, were the same as in the condition with tutor. Similar to the LL-Tutor condition an assignment was repeated once or twice after one or two errors, however, without any comments from a computer tutor. In the LL-NoTutor condition the game was repeated after an error. In this way children could be aware of their correct responses and errors.

After a maximum of three trials, 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 and the next game started. When the child had made an error in an assignment, the game was not only repeated in the same session, but also in the next session, with a maximum of two repetitions per game. Thus children received a variable number of sessions. The total number of sessions, each including six games, ranged from 7 to 17, with a mean number of 11.2 sessions (SD = 1.88), each lasting about 10 minutes. Children in LL-Tutor and LL-NoTutor conditions participated in an equal number of sessions (t (150) = 1.1, p = .29).

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 difficulty level, the child had to help Sim by finding Sanne behind objects. For instance, the child was told by the computer voice that Sanne would hide behind a red object. The total number of 10-minute sessions ranged from 7 to 13. The mean number of 8.01 sessions (SD = 1.01) was somewhat lower than the 11.2 sessions in the intervention group (t (299) = 17.4, p < .01).

Procedure

Most computer sessions (67%) occurred during morning hours at school. With few exceptions children had one session per week spread over a four-month period (February-May). Children sat alone at the computer screen in their classroom with a headset on and were logged in by their teachers on the Internet site. After entering the child's name, the correct games appeared. The session was automatically discontinued after six games. Pre- and posttesting data were collected in sessions of approximately 20 minutes in a quiet room in the school. Only child and examiner were present. The testing was carried out by trained Master students who were blind to group allocation. The order of the tests was always the same, except for the testing of regulatory skills, which were tested in counterbalanced order. Regulatory skills sessions were videotaped and scored afterwards by Master students who were blind to group allocation.

Measures

Maternal education. Mothers reported their highest level of education on a six-points-scale ranging from primary education to university.

Intelligence. To test verbal and non-verbal intelligence Dutch versions of the *Peabody Picture Vocabulary Test* (PPVT; Schlichting, 2005) and the subtest mosaic of a standardized non-verbal intelligence test (*Snijders Oomen Niet-verbale Intelligentie toets*; Tellegen, Winkel, Wijnberg, & Laros, 1998) were used.

Code-related skills.

Developmental spelling. Children had to write five dictated words (i.e., *papa* [daddy], *Sim* (name of one of the characters in the computer games), *been* [leg], *jurk* [dress], and a word starting with the first name-letter of the child or mama) that afterwards 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. All words were double-coded with high Kappa's (ranging from .88 to .97). Disagreements were solved by discussion. For pre- and posttest, scores on 5 words were averaged resulting in a 0-6 scale (α's > .84).

Name-letter knowledge. Children had to first point to the first letter of their name among five other letters. With few exceptions, all children were able to complete this task successfully. Children then had to name or provide the sound for the first letter of their name. One point was awarded for naming or sounding the correct letter.

Phonemic sensitivity. In the phonemic sensitivity task, children were asked 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 (α = .62).

Aggregate measure. Principal Component Analyses (PCA) of developmental spelling, name-letter knowledge, and phonemic sensitivity revealed one component for pretests and posttests explaining 53% and 55% and of the variance, respectively, with high loadings ranging from .62 for name-letter knowledge to .80 for developmental spelling. The aggregate measure for pretest scores was used as covariate and for posttest scores as dependent variable.

Regulatory skills.

Knock and tap. Regulatory skills at screening 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, Korkman, & Lahti-Nuuttila, 2001). Similar to the 'Head-to-Toes Task' (Ponitz et al., 2008), this test is an easy to administer measure of behavioral regulation that can be used with very young children. It requires children to pay attention, use their working memory, and inhibit a natural tendency to mimic the experimenter. The internal consistency of this 16-items test was high (α = .92).

Stroop-like task (opposites). Children had to respond with the opposite to three contrasting pairs of pictures (e.g., saying "fat" to thin) in a mixed set of 18 pictures (based on Berlin & Bohlin, 2002). Incorrect naming and corrections were both scored as errors in this inhibitory control test with a maximum score of 18 (α = .91).

Stroop-like task (dogs). Following the Stroop paradigm, children had to switch rules by responding with an opposite, i.e., saying "blue" to a red dog and "red" to a blue dog (based on Beveridge, Jarrold, & Pettit, 2002). The task consisted of 96 trials distributed over four conditions, in which demands on working memory (remembering the name of one or two dogs) and inhibitory control of the most obvious response varied. In the first two conditions the child had to name one or respectively two dogs ('tim' and 'jet') different in color (yellow and green). In the third and fourth condition the paradigm was the same, however the colors of the dogs were incompatible with their names (a red dog was named 'blue' and a blue dog 'red'). Incorrect naming or no response were considered as working memory errors while corrections were scored as inhibitory control errors. Each error was coded as working memory *or* inhibitory control error resulting in maximum scores of 96 for both. Internal consistencies for scales were high (α's equaled .80 to .94).

Digit span (words). In the forward digit span test (*Leidse Diagnostische Test*; Schroots & Van Alphen de Veer, 1976), the children had to repeat a list of unrelated words that was read aloud by the computer. Practice trials were two-word lists. In the test-trials, the word lists increased from two to a maximum of five, and ended when a child failed to succeed three series in succession. The total number of correct responses (max. 12) was the score for this verbal working memory task.

Backward digit span. In the backward digit span test (WISC-III; Wechsler, 1992), the child had to repeat a string of digits in reverse order. During four practice trials with strings of two to four digits, the experimenter corrected the child when needed. The test started with two digits and gradually increased in number of digits. In each trial, there were two strings of digits and at least one of these strings had to be repeated correctly in order to proceed to the next trial. The total score for this working memory task was composed of the total number of correct responses in the practice and test-trials (max. 14).

Intraclass correlation coefficients between two independent coders were high for all tasks (*r's* > .97).

Aggregate measures. PCA applied to the stroop-like and digit span tasks revealed two components for regulatory skills in spring with high loadings (.63 - .86) explaining 34% and 28% of the variance, respectively. The two components can be labeled as *working memory* (high loadings of digit span tasks and of working memory errors in dogs) and *inhibitory control* (high loadings of opposites and of inhibitory control errors in dogs).

Number of trials. Based on automatic computer registration and storage of mouse behavior during each session, the number of trials each child needed within the games to give a correct answer was determined. More trials indicated more errors in completing the computer tasks.

Data analyses

Because participants were recruited from different schools (*N* = 15) we used Huber-White estimates of standard errors to correct for clustering of the scores of children from the same schools (cf. Hatcher et al., 2006; Knafo, Israel, & Ebstein, 2011). We included the corrected standard errors in the Complex Sample General Linear Model (CSGLM, SPSS 17) with the posttest score on the aggregate measure (a compound of code-related skills) as dependent variable, experimental condition (LL-NoTutor; control group; LL-Tutor) as factor, and age, pretest compound of code-related skills, maternal education, PPVT, SON, inhibitory control, and working memory as covariates. We further examined interactions between experimental condition and regulatory skills.

Results

Attrition

Nine children moved during the school year. In the remaining group (N = 303) one child assigned to the LL-Tutor condition refused to play the games of *Living Letters* after three sessions. This child was excluded from the final analyses.

Intervention effects

Table 3.1 presents descriptive statistics for intervention and control conditions on all measures. The three groups were similar in age, maternal education, regulatory skills, and verbal (*Peabody Picture Vocabulary Test*; Schlichting, 2005) and nonverbal intelligence (*Snijders-Oomen Niet-verbale intelligentie toets* [Snijders-Oomen Non-verbal intelligence test]; Tellegen et al., 1998). Correlations between predictors were low to moderate, as is shown in Table 3.2.

Table 3.2
Correlations Between all Included Variables

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
1. Gender[a]	1.00										
2. Age	-.04	1.00									
3. Maternal education	-.11	-.03	1.00								
4. SON mosaic[b]	-.05	.25**	.34**	1.00							
5. PPVT[c]	-.11*	.30**	.27**	.39**	1.00						
6. Pre code-related skills[d]	.15*	.36**	.12	.36**	.45**	1.00					
7. Post code-related skills[d]	.11	.26**	.15*	.34**	.40**	.72**	1.00				
8. Knock and tap	.07	.10	.06	.16**	.20**	.19**	.13*	1.00			
9. Working memory[d]	-.03	.25**	.16**	.38**	.43**	.50**	.46**	.19**	1.00		
10. Inhibitory control[d]	.05	.20**	.07	.27**	.29**	.25**	.28**	.18**	.00	1.00	
11. Trials (computer game)	-.05	-.08	-.10	-.14*	-.06	-.18**	-.22**	-.07	-.14*	-.22**	1.00

Notes. N varies between 254 and 312.
[a] Gender (0 = boy, 1 = girl); [b] Snijders Oomen Nonverbale Intelligentie test – subtest mosaic (raw scores); [c] PPVT = Peabody Picture Vocabulary Test (raw scores); [d] Aggregate measures.
* Correlation is significant at the .05 level (2-tailed), ** Correlation is significant at the .01 level (2-tailed).

The regression model explained 61% of the variance in code-related skills (Table 3.3). The pretest score (β = .62 [95% CI .48, .76]; t (14) = 9.43, p < .001) was a significant covariate while working memory (β = .17 [95% CI -.00, .35]; t (14) = 2.10, p = .06) and inhibitory control (β = .13 [95% CI -.01, .27]; t (14) = 1.96, p = .07) were marginally significant. The background variables (age, maternal educational level, PPVT, and SON) were non-significant covariates (p's between .29 and .81). Planned contrasts between experimental conditions revealed effects for control group versus LL-Tutor (β = -.38 [95% CI -.59, -.16]; t (14) = -3.75, p = .002) and for LL-NoTutor versus LL-Tutor (β = -.48 [95% CI -.66, -.30]; t (14) = -5.58, p < .001), but not for control group versus LL-NoTutor (β = .10 [95% CI -.10, .31]; t (14) = 1.10, p = .29). After using the Šidák-Bonferroni correction (α = .017) to control for Type 1 error rate (Keppel & Wickens, 2004) both contrasts with LL-Tutor remained significant. Contrasting the target programs with the control program, effect sizes equaled d = .48 with tutor and d = -.14 without. The difference between LL-NoTutor and LL-Tutor equaled .71 standard deviation (see Table 3.3).

Table 3.3
Results (CSGLM) with Posttest Code-related Skills (Aggregate Measure) as Dependent Measure; Age, Maternal Educational Level, Peabody Picture Vocabulary Test (PPVT), Snijders Oomen Nonverbale Intelligentie Test (SON), Pretest Code-related Skills (Aggregate Measure), Inhibitory Control (Aggregate Measure), Working Memory (Aggregate Measure), Intervention, and Interactions between Regulatory Skills and the Intervention as Covariates

Measure	Estimate (*SE*)	95% CI	*t*	*p*-value	Cohen's *d*
Background					
Age	-.02 (.01)	-.05 - .02	-1.10	.29	-.14
Maternal education	.01 (.03)	-.06 - .08	.25	.81	.03
PPVT	.00 (.00)	-.01 - .01	.61	.55	.08
SON	.01 (.03)	-.05 - .07	.36	.73	.05
Pretest code related skills	.62 (.07)	.48 - .76	9.43	.00	1.20
Main effects					
Working memory	.17 (.08)	-.00 - .35	2.10	.06	.27
Inhibitory control	.13 (.07)	-.01 - .27	1.96	.07	.25
C1: LL-NoTutor vs LL-Tutor	-.48 (.09)	-.66 - -.30	-5.58	.00	-.71
C2: Control group vs LL-Tutor	-.38 (.10)	-.59 - -.16	-3.75	.00	-.48
C3: Control group vs LL-NoTutor [a]	.10 (.09)	-.10 - .31	1.10	.29	.14
Interaction effects					
C1* Inhibitory control	.17 (.07)	.02 - .31	2.49	.03	.32
C2* Inhibitory control	-.04 (.08)	-.20 - .13	-.45	.66	-.06
C1* Working memory	.03 (.12)	-.23 - .29	.27	.79	.03
C2* Working memory	-.09 (.11)	-.32 - .14	-.82	.42	-.10

Notes. *N* = 248. For calculating Cohen's *d* we used the formula 2t/√n-2 (Thalheimer & Cook, 2002).
[a] Effect was calculated in a separate analysis.

Did regulatory skills moderate intervention effects? We found a significant interaction between the contrast LL-NoTutor versus LL-Tutor and inhibitory control (β = .17 [95% CI .02, .31]; t (14) = 2.49, p = .03). This indicates that with an online tutor the achievement gap between children with low and high inhibitory control was small (see Figure 3.1) while, without online tutoring, the gap between children with low and high inhibitory control increased. According to separate regression analyses, effect sizes of inhibitory control were d = .49 (p = .07) within the LL-Tutor condition and d = .67 (p = .02) within the LL-NoTutor condition.

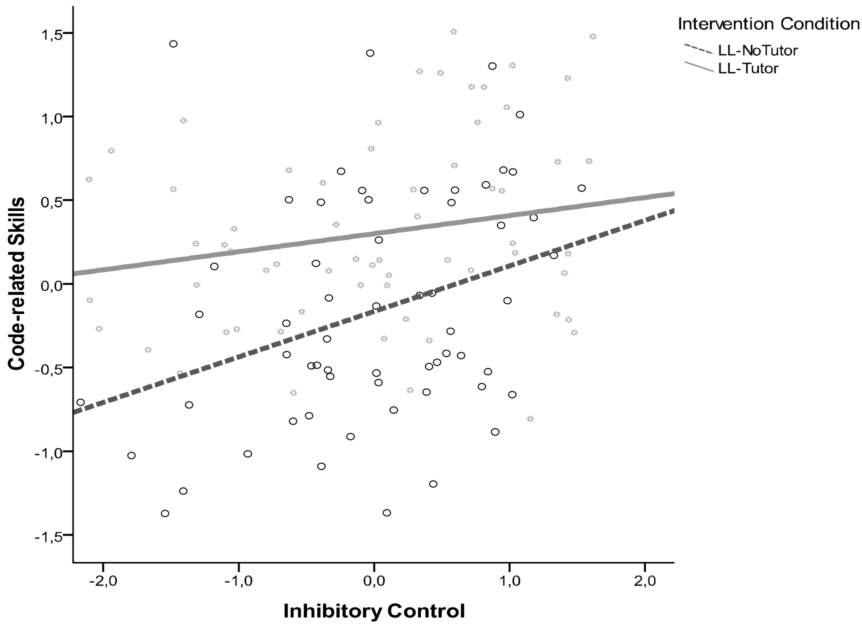

Figure 3.1. Scores on posttest code-related skills (aggregate measure; controlled for pretest code related skills, background variables, and working memory) as a function of inhibitory control for both intervention conditions (LL-NoTutor and LL-Tutor).

Number of trials

There were differences in the average number of trials that children needed to solve the games (further on referred to as 'trials'). Children in the LL-Tutor condition needed fewer trials preceding a correct answer than children in the LL-NoTutor condition (t (158) = 2.0, p = .045), which may indicate that the presence of a tutor discouraged random response behavior and thus errors. In the LL-Tutor and in the LL-NoTutor condition, children needed 1.78 (SD = .40) and 1.92 (SD = .47) trials, respectively. Table 3.2 shows that number of trials was negatively correlated with working memory (r = -.14) and inhibitory control (r = -.22), which may indicate that children with low regulatory skills were more inclined to respond randomly thereby making more errors.

Discussion

An Intelligent Tutoring System, modeled after early literacy activities in literate homes (*Living Letters* with tutor), was shown to improve literacy skills from children of low-educated families. Four-year olds' code-related skills improve substantially when children were exposed to this computer program with minimal supervision by teachers. In this study, more importantly, games were found to be effective only when an online tutor was used to explain how to proceed and why the solution was correct. Consistent with prior research (Azevdo & Bernard, 1995; Meyer et al., 2010; Vasilyeva, 2007), the effects of instructions and assignments are reduced when children do not receive immediate and personalized reactions to their game responses. Children in the tutoring condition outperformed the children in the non-tutoring condition by about three-quarter of a standard deviation supporting the hypothesis that computer programs for young children need built-in tutors (Brodova & Leong, 2006). It was an unexpected result that the intervention group that did not receive immediate and personalized reactions from an online tutor scored lower than the control group. Even though the difference did not reach statistical significance, this result may indicate that *Living Letters* without an online tutor can have negative effects on problem-solving. We hypothesize that a computer program that does not provide tutoring modeled on adult caregivers may reward random responses instead of strengthening thoughtful replies. Without online tutoring, children may be more inclined to guess when they have to solve similar problems during posttest assessments. The on-average higher number of trials to select correct answers in the condition without a tutor corroborates this hypothesis. With online tutors young children may take the computer assignments more seriously and prefer a reflective approach to random clicking and answering.

Our findings are consistent with earlier work showing that regulatory skills are predictors of academic achievements (e.g., Bierman et al., 2008; Blair & Razza, 2007; Davidse et al., 2011; Kegel et al., 2009; McClelland et al., 2007). However, the current results also nuance the importance of regulatory skills. There was no evidence for effects of working memory on code-related skills. Only inhibitory control affected gains in code-related skills. Furthermore, there was no evidence that inhibitory control affects learning across computer environments to the same extent. Inhibitory control had a marginally significant effect on gains in code-related skills in the ITS game where a tutor corrected or confirmed children's responses after each game. In this tutoring condition, inhibitory control explained 6 percent of the posttest differences. In the non-tutoring condition, however, the group high on inhibitory control outperformed the group low on inhibitory control. In this condition, inhibitory control explained 10 percent of the posttest scores. In fact, the outcomes thus evidence a 'dual risk' model (Belsky et al., 2007): Children with some risk (here: low inhibitory control) lagged further behind when they were exposed to a less supportive environment (here: NoTutor), while children with low and high inhibitory control benefited to the same extent from a supportive environment (here: Tutor). The best explanation for the effect of inhibitory control in the condition without tutor seems trial and error behavior. When children are easily distracted by irrelevant cues they may finalize the assignments by clicking randomly without any reflection on questions, which matches our finding that they tend to need more trials preceding the correct solution. It should be noted, however, that differences between children with high and low inhibitory control were rather small, probably because average progress in the condition without online tutor was minor.

Limitations

This study has some limitations. We used the knock and tap test to compose three experimental groups similar in regulatory skills. Attempts to apply more complicated tests of regulatory skills before the intervention failed because they appeared to be too demanding for young children (e.g., Dimensional Change Card Sort Task; Zelazo, 2006). Yet, to test which regulatory skills might affect gains and moderate the effects of the program, another more extensive set of measures of regulatory skills was applied after the intervention, and used in the final analyses to test main and interaction effects of regulatory skills. Scores on the knock and tap test as well as on other measures of regulatory skills were similar across experimental groups. However, some may argue that the intervention may have changed regulatory skills, and that assessment after the intervention is less appropriate to test the effects of regulatory skills on the intervention.

Another limitation is that the current study only provides short-term evidence. Long-term evidence is needed to demonstrate that computer programs targeting early literacy and including an online tutor can be a pre-emptive measure in preschool. Also, because of the moderate effect sizes of the intervention, we may expect that there may be other, not yet considered individual differences that make one group of children more susceptible to interventions than another; a hypothesis to be tested in further research (Belsky et al., 2007).

Implications

Computer instruction seems to be a promising addition to classroom instruction in particular when the programs include an online tutor who corrects children's responses and provides cues. Traditional measures of school readiness focus primarily on pre-academic skills, such as emergent reading and writing, and less on behavioral skills (e.g., Duncan et al., 2007). The present findings are consistent with the earlier work showing that children's regulatory skills are important in addition to cognitive measures (Kegel et al., 2009). The current results evidence that especially children with underdeveloped inhibitory control score disproportionally negative in a less supportive computer environment. Although the reported effects of inhibitory control on learning were rather small, findings make plausible the idea that inhibitory control is an important explanation for outcomes of learning via computers, especially when we consider that a lot of current computer programs lack tutoring.

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

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.

Published as:

Kegel, C. A. T., Bus, A. G., & Van IJzendoorn, M. H. (2011). Differential susceptibility in early literacy instruction through computer games: The role of the Dopamine D4 Receptor gene (DRD4). *Mind, Brain, and Education*, *5*, 71-78.

Introduction

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 three-year-old children with more negative emotionality but not in children with less negative emotionality. Fearful temperament or temperamental emotionality may not be a ‘‘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 four-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 four-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 four-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 4.1).

Table 4.1
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*	.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*	-.09	1.00	-.10	1.00	.27	1.06

Note. * z-score

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 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 (Appendix a, b, and c), 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?''; Appendix d), 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: kite, milk, or tiger ?''; Appendix e). All sessions start with an attractive animation in which preschoolers Sim and Sanne explain the upcoming game.

*Feedback***.** 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., ''How does your teacher write 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 Appendix c.

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 mMNaCl, 10 mMEDTA, 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 µM dNTP, 7.5% DMSO, 10× buffer supplied with the enzyme, 0.5 Biotherm AB polymerase (5U/µl) in a total volume of 30 µl. 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 95ºC, followed by 39 cycles of 30 s at 95º C, 30 s at 60º C, 1 min at 72º C, and a final extension step of 10 min at 72º 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. Based on 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 versus 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-items test was high (α = .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 showed a significant main effect on early literacy skills, $F(2, 13) = 7.33$, $p = .007$, but DRD4 did not $F(1, 14) = 0.27$, $p = .61$. Further, the interaction between experimental group and DRD4 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 ($p > .1$).

In Figure 4.1, 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.

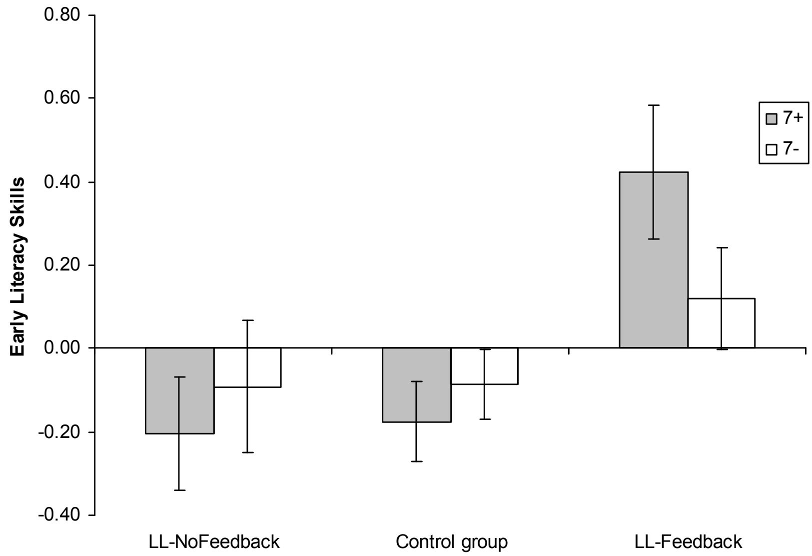

Figure 4.1. Estimated means and standard errors for early literacy skills of children with (7+) and without (7-) the Dopamine D4 allele in two intervention groups (LL = *Living Letters*) and in the control group (N = 182).

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, Kegel, 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.

5 Executive Attention Mediates the Role of the Dopamine D4 Receptor Gene (DRD4) on Reading Acquisition in a Non-Clinical Sample

Abstract

Dopamine genes (e.g., DRD4 and DRD2) have been linked to Attention Deficit Hyperactivity Disorder (ADHD) and dyslexia. In this study we examined whether diminished anticipatory dopamine cell firing as is typical for some DRD4 and DRD2 alleles is related with readings skills and whether these alleles are linked with reading through executive attention. We tested a normative sample of 159 children in both Kindergarten and first grade and found executive attention to be a mediator between DRD4 and reading skills. This is an important finding because it explains why children with ADHD often develop reading problems. It opens a new perspective on early interventions: The findings demonstrate that in many cases early interventions need to target not only reading skills but executive attention as well.

Based on:
Kegel, C. A. T., & Bus, A. G. Executive attention mediates the role of the Dopamine Receptor D4 gene (DRD4) on reading acquisition in a non-clinical sample. *Manuscript submitted for publication*.

Introduction

Family and twin studies have provided accumulating evidence of the hereditary of reading disorders (Grigorenko, 2001; Pennington & Olson, 2005). Consequently, linkage analyses and association studies in families with dyslexia have identified a number of genetics as potential contributors of reading problems (Bates, 2006; Grigorenko, 2005; Scerri & Schulte-Körne, 2010; Schumacher, Hoffmann, Schmäl, Schulte-Körne, & Nöthen, 2007; Williams & O'Donovan, 2006). Dyslexia-susceptibility genes have been labeled as DYX with a number (DYX1-DYX9). One of the suggested genes is the DYX7 on locus 11p15 containing the dopamine receptor D4 (DRD4). D4 receptors are expressed in their highest density in the prefrontal cortex, an area known to be involved in executive attention (Kane & Engle, 2002; Posner & Rothbart, 2007). Because dyslexia is linked with Attention Deficit Hyperactivity Disorder (ADHD, Tripp & Wickens, 2008; Willcutt & Pennington, 2000) and DRD4 with ADHD (Faraone, Doyle, Mick, & Biederman, 2001; Maher, Marazita, Ferrell, & Vanyukov, 2002), a link of DYX7 with dyslexia seems not too far-fetched. Children with the 7-repeat allele of DRD4 (the long/ risk variant in ADHD studies) show diminished anticipatory dopamine cell firing (Tripp & Wickens, 2008), so during the learning process they feel less reinforced by the anticipation of a successful outcome of the learning process and are therefore less attentive. Their inability to control attention gives them a higher risk for reading problems. When reading and attention indeed share a genetic base (Ebejer, Coventry, Byrne, Willcutt, Olson, Colrey, & Samuelsson, 2010; Willcutt et al., 2007), the long variant of the DRD4 gene seems the most plausible option. However the link to reading development may be an indirect one mediated by executive attention as endophenotypical behavior that is most strongly linked to the DRD4 gene.

A study by Hsiung, Kaplan, Petryshen, Lu, and Field (2004) showed a marginally significant link (p = .06) between the DRD4 7-repeat allele and dyslexia. However, the authors did not take account of ADHD within their sample and it is therefore unclear whether the evidence stems from those with dyslexia and ADHD traits or from dyslexia alone (Williams & O'Donovan, 2006). Marino and colleagues (2003) did not find an association between dopamine genes (e.g., DRD4 and DRD2) and dyslexia, irrespective of co morbidity with ADHD. The 7-repeat allele of DRD4 is thus a risk-factor for developing ADHD (Faraone et al., 2001; Maher et al., 2002) and according to Hsiung et al.'s (2004) study for reading problems with poor executive attention as a potential common denominator.

Children with ADHD differ significantly from controls with regard to measures of executive functions (Berlin, Bohlin, Nyberg, & Janols, 2004; Thorell & Wahlstedt, 2006) and executive functions measures are also linked to DRD4 (Froehlich, Lamphear, Dietrich, Cory-Slechta, Wang, & Kahn, 2007; Schmidt, Fox, Perez-Edgar, Hu, & Hamer, 2001), which is probably the underlying gene of both executive functions and ADHD. Executive functions can be split into different domains (e.g., inhibitory control and working memory), however executive attention may be the common factor for all executive functions tasks (Blair, 2006). Executive attention is activated in the lateral prefrontal cortex and modulated by dopamine (Posner & Rothbart, 2007; Rueda, Rothbart, McCandliss, Saccomanno, & Posner, 2005). It is highly related to working memory (Engle, 2002; Gathercole, Alloway, Kirkwood, Elliott, Holmes, & Hilton, 2008) and inattention is a consequence of poor inhibitory control (Barkley, 1997). Therefore executive attention may be a plausible common factor in executive functions as well as ADHD. The acquisition of basic reading skills strongly depends on sustained practice which makes the learning process also vulnerable for executive attention deficits (Shaywitz & Shaywitz, 2008).

In the current study we took into account the possibility that DRD2 is another candidate dopamine gene in affecting reading through executive attention. So far only the study by Marino et al. (2003) examined the relation between the dopamine receptor D2 (*Taq*1) and dyslexia, possibly because only a few studies found evidence for an association between the DRD2 gene and ADHD (Comings et al., 1991; Nyman et al., 2007). It is not too far-fetched to test effects of the DRD2 gene on reading acquisition since there is a link between DRD2 and executive attention in preschool children (Wiebe et al., 2009) and in alcoholic patients (Rodriguez-Jiménez et al., 2006). The risk allele of DRD2 (A1+) is associated with weaker performance on executive function tasks. As a critical test of the hypothesis that dopamine genes affect young children's reading achievement through executive attention the current research targets a normative group of beginning readers and tests whether effects of DRD4 and DRD2 on beginning reading skills are manifest and remain after controlling for executive attention. Actually, this model assumes that children's executive functions can interfere with the process of learning to read.

If this hypothesis applies it may explain why carriers of the long variant of the DRD4 allele were particularly susceptible for a more structured environment with immediate and positive feedback systems as embodied in computer games with a built-in tutor who provides individualized feedback (Kegel, Bus, & Van IJzendoorn, 2011). The theory that children with the risk variant of dopamine genes may take advantage of the computer program offering amply practice of separate skills in support of poor attention while children without the risk variant may show less susceptibility to qualities of instruction was tested in a randomized controlled trial. Children were randomly assigned to a computer intervention with a tutor that provided individualized feedback to all responses (supportive environment) or the same computer program without tutor. The structured learning environment of our educational computer games kept the potentially wandering attention of the carriers of the 7-repeat allele focused on the learning target especially in condition with the many individualized tutoring moments built into the program. In the condition without individualized tutoring children with the long DRD4 variant performed worst whereas qualities of the program did not affect children with the short variant. They performed equally well, with or without tutor, indicating that they could control their attention without external support. In line with the role of executive attention in becoming a reader, this study thus strongly suggests that support of executive attention seems particularly important for children with the long variant of DRD4.

As carriers of the DRD4 7-repeat allele seem to suffer most from less supportive instruction (e.g., no tutor in a computer program) and at the same time appear to profit most from supportive instruction (e.g., a built-in tutor in the computer program), in a "for better *and* for worse" manner (Belsky, 2005; Belsky, Bakermans-Kranenburg, & Van IJzendoorn, 2007), an obvious practical implication of the current finding may be screening of pupils in search of an optimal fit between intervention and individual. However, genotyping of potential intervention participants may not be practically possible or ethically desirable and therefore genotypes may be associated with specific endophenotypes that can serve more easily as a basis for screening (Bakermans-Kranenburg & Van IJzendoorn, 2011). Endophenotypes are internal phenotypes of clinical disorders influenced by one or more of the same genes and more closely related to the biological etiology than the behavioral signs and symptoms of a disorder. An endophenotype should co-occur with the condition of interest, be a trait that can be measured reliably, and show evidence of heritability (Doyle et al., 2005; Gottesman & Shields, 1973; Skuze, 2001). Executive functions are marked as possible endophenotypes of ADHD (Doyle et al., 2005).

This study

In this study we examined the link between the dopamine genes DRD4 (7-repeat) and DRD2 (*Taq*1), executive functions (as possible endophenotype of executive attention), and reading skills in a normative sample in Kindergarten and the same sample in first grade. Although studies have examined the links between the dopamine genes and ADHD or dyslexia, less is known about the influence of these genes on executive attention and reading skills in a non-clinical sample. Therefore, we consider both reading and executive attention as continuous variables and examine their relations in the full range, rather than use categorical diagnoses (Ebejer et al., 2010). We wonder whether diminished anticipatory dopamine cell firing as is typical for some DRD4 and DRD2 alleles is related with reading skills and whether the link still exists after controlling for executive attention. A link between dopamine genes and reading speed seems less likely considering that instruction emphasizes accuracy of reading in the first half year of first grade.

Our research questions are:

1. Is there a link between Dopamine receptors (DRD4 and DRD2) and reading accuracy in a normative sample of beginning readers?
2. Does a similar link exist when the focus is on reading rate?
3. Is there a link between Dopamine receptors (DRD4 and DRD2) and executive attention?
4. Is executive attention a mediator between Dopamine receptors (DRD2 and DRD4) and reading accuracy or rate?

Method

Participants

Participants were recruited from a longitudinal study on 15 Dutch schools. Of the initial sample of 312 children 182 parents (58 percent) gave informed written consent to participate in the genetic part of the study and to have their children contribute buccal swab samples. The children were 60 to 75 months old (M = 65.8, SD = 3.2) at the beginning of the senior Kindergarten year (N = 174). 159 children with consent to participate in the genetic part of the study (59 percent male) still participated in the study in grade 1. The sub-sample 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.

Study design

After three months of education in the senior Kindergarten year (Time 1: T1) we administered children's verbal intelligence (with the *Peabody Picture Vocabulary Test*) and early reading skills. Halfway this school year (Time 2: T2) we tested executive functions extensively. After three months of education in grade 1 (Time 3: T3) we measured (speed) of reading skills and executive functions.

Part of the children in this study was exposed to a literacy intervention in the junior kindergarten year (Kegel & Bus, in press) which may affect links between executive functions, reading, and DRD4. We therefore conducted analyses in the control group that was not exposed to the intervention. At the beginning of the senior Kindergarten year, however, there were no longer differences between intervention and control groups in reading. In the current study we therefore also tested effects of dopamine genes and executive functions on reading skills in the complete sample (see Table 5.1).

Table 5.1
Descriptives of Total Group and Control Group only

	Total Group			Control Group		
N (T1)	174			91		
N (T3)	159			86		
Background						
Gender (boys)	94 (59%)			50 (58%)		
DRD4 7+	64 (37%)			38 (42%)		
DRD2 A1+	71 (41%)			38 (42%)		
	M	*SD*	Range	*M*	*SD*	Range
Age in Months (T1)	65.79	3.21	60 - 75	66.05	3.21	61 - 75
PPVT[a] (raw scores, T1)	78.92	12.80	36 - 120	79.77	13.40	43 - 120
Reading Skills						
Writing (T1)	2.94	.99	0 - 5.80	2.96	.91	.40 - 5.60
Writing (T3)	4.95	.78	2.60 - 6.00	4.92	.79	2.60 - 6.00
Letter knowledge (T1)	8.67	6.01	0 - 22	8.43	5.74	0 - 22
Letter knowledge (T3)	21.43	2.90	12 - 26	21.30	2.92	12 - 26
Word recognition (T1)	18.03	4.71	9 - 29	18.40	4.38	9 - 29
Phoneme deletion (T3)	.46	.22	0 - 1	.44	.22	.08 - 1
Aggregate measure (T1)[b]	-.07	.98	-1.93 - 2.68	-.05	.92	-1.83 - 2.54
Aggregate measure (T3)[c]	-.06	1.04	-2.77 - 2.22	-.12	1.04	-2.75 - 2.22
Time Reading Skills (T3)						
Rapid Automatic Naming (sec.)	53.09	30.30	14 - 252	50.45	23.57	14 - 171
Three Minute Test	13.09	12.70	0 - 82	13.20	13.08	0 - 82
Aggregate measure[d]	.09	1.01	-2.39 - 3.26	.04	.94	-2.28 - 2.53
Executive Functions						
Digit span (words) (T2)	6.42	2.08	0 - 11	6.45	2.03	1 - 11
Backward digit span (T2)	4.11	2.35	0 - 13	4.22	2.31	0 - 13
Stroop-like task (WM[e] errors, T2)	90.35	7.81	58 - 96	89.93	8.87	58 - 96
Stroop-like task (IC[f] errors, T2)	90.72	3.74	76 - 96	90.37	3.93	76 - 96
Head-Toes-Knees-Shoulder Task (T3)	16.81	3.23	0 - 20	16.51	3.86	0 - 20
Aggregate measure Executive Functions[g]	.03	1.06	-4.15 - 1.82	-.02	1.10	-4.10 - 1.83

Notes. T1 = November 2009; T2 = May 2010 (Kindergarten); T3 = November 2010 (Grade 1); [a] PPVT = Peabody Picture Vocabulary Test; [b] PCA of writing, letter knowledge, and word recognition revealed one component; [c] PCA of writing, letter knowledge, and phoneme deletion revealed one component. [d] PCA of RAN speed and TMT revealed one component. [e] WM = working memory. [f] IC = Inhibitory control. [g] PCA applied to the executive functioning tasks revealed one component.

Procedure

Data were collected in sessions of approximately 20 minutes in a quiet room in the school. Only child and examiner were present. The testing was carried out by trained Bachelor and Master Students who were blind for genetic results. The order of the tests was always the same, except for the executive functions, that were tested in counterbalanced order. Assessment of executive functions was videotaped and scored afterwards by students.

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 for DRD4 contained between 10 and 100ng genomic template DNA, 10 pmol of forward and reverse primers, 100 uM dNTP, 7,5% DMSO, 10x buffer supplied with the enzyme, 0.5 Biotherm AB polymerase (5U/µl) in a total volume of 30 ul. 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°C, followed by 39 cycles of 30 sec 95°C, 30 sec 60°C, 1 min 72°C, and a final extension step of 10 min 72°C.

The DRD2/Taq1 region was amplified by PCR using the following primers: a forward primer (5'-CCGTCGACGGCTGGCCAAGTTGTCTA-3') and a reverse primer (5'-CCGTCGACCCTTCCTGAGTGTCATCA-3'). Typical PCR reactions contained between 10 and 100 ng genomic DNA template, 10 pmol of forward and reverse primers. PCR was carried out in the presence of 3,33% DMSO with 0.5 ul of Biotherm AB polymerase (in a total volume of 30 µl) using the following cycling conditions: initial denaturation step of 5 min at 95°C, followed by 35 cycles of 30 sec 94°C, 30 sec 55°C, 30 sec 72°C and a final extension step of 5 min 72°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. Based on 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 main DRD4 genotypes were in Hardy- Weinberg equilibrium, χ^2 (df = 1, N = 174) = .77, p = .38. Thirty-seven percent of the children were carriers of at least one DRD4 7-repeat allele.

To determine the Taq1 polymorphism, PCR fragments were sequenced using the forward primer (5'-CCGTCGACGGCTGGCCAAGTTGTCTA-3') and dye terminator chemistry (BigDye v3.1, Applied Biosystems). Sequence reactions were run on a ABI-3730 automated sequencer and sequence data were analysed using SeqScape software. Children were grouped in subgroups with at least one A1 allele (A1+) versus subjects with no A1 alleles (A1-). These main DRD2 genotypes were in Hardy- Weinberg equilibrium, χ^2 (df = 1, N = 174) = .17, p = .68. Forty-one percent of the participants were carriers of at least one DRD2 A1+ allele.

Intelligence. To test verbal intelligence a Dutch version of the *Peabody Picture Vocabulary Test* (PPVT; Schlichting, 2005) was used.

Reading and writing tasks.

Kindergarten

Writing. Children had to write five dictated words (i.e., *papa* [daddy], *Sim* (name of a character), *been* [leg], *jurk* [dress], and a word starting with the first name-letter of the child or mama) that afterwards 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. All words were double-coded with high Kappa's (ranging from .88 to .97). Disagreements were solved by discussion. Scores on 5 words were averaged resulting in a 0-6 scale (α = .92).

Letter knowledge. Children had to name all letters of the alphabet, except from c, q, x, and y. The total number of correct responses (max. 22) was the score for letter knowledge (α = .92).

*Word recognition***.** Children were asked to identify the depicted target word among four printed words. The (incorrect) alternatives differed in 1, 2, or all letters from the target word. For instance, distracters for *boot* [boat] were *beet* [bite], *bok* [goat], and *vier* [four]. Correct responses were rewarded with 3 points (*boot*); a match of the first and last letter with 2 points (*beet*); a match of the first letter only with 1 point (*bok*); and no match with 0 (*vier*). The total score was the average score on the 10 items (α = .74).

Aggregate measure. A principal Component Analysis (PCA) of writing, letter knowledge, and word recognition revealed one component explaining 74% of the variance, with high loadings ranging from .83 for word recognition to .87 for writing.

Grade 1

Writing. Children had to write five dictated words (i.e., *steen* [stone], *jurk* [dress], *zoom* [hem], *bril* [glasses], and *post* [post] that afterwards were assigned to the same codes as Kindergarten writing scores. Scores on 5 words were averaged resulting in a 0-6 scale (α = .79).

*Letter knowledge***.** Children had to name all letters of the alphabet. The total number of correct responses (max. 26) was the score for letter knowledge (α = .72).

*Phoneme deletion***.** The phoneme deletion test consisted of three trial and 12 computerized test items (Van den Bos, Lutje-Spelberg, & De Groot, 2010). The child had to repeat the stimulus word and was then asked to delete a particular sound. The test started with a three-syllable word of which the child had to remove one syllable (e.g., *kruiwagen* [wheelbarrow] without *krui*). The other items were one-syllable words of which the child had to delete the initial (4 times), final (4 times), or middle (2 times) sound. The alpha of this 12-item test equaled .71.

*Rapid Automatized Naming speed***.** Rapid naming was assessed through the administration of a Rapid Automatized Naming (RAN) test for letters (Van den Bos, Lutje-Spelberg, Scheepstra, & De Vries, 2004). The test consisted of high frequency lowercase letters (e, p, s, r, m, i, and v) randomly distributed over five rows of 10 symbols. The child was asked to name the letters as quickly as possible. The critical measure was the rate in which all letters were named. Because this variable was skewed to the right (S = 3.62, SE = .15), we used a log-transformation (Tabachnick & Fidell, 1996) to pull in disparate values toward the center of the distribution, to correct this substantial skewness, and to satisfy the assumption of normality (S = .96, SE = .15).

*Three Minutes Test***.** Card 1c of the "Drie Minuten Test" [Three Minutes Test, TMT] was administered to test fluency of word reading (Verhoeven, 1995). The card contained 120 words, ordered in four columns of 30 words. The card had one-syllable CV, VC, and CVC words. The total score was composed of the number of words read correctly in one minute. Because this variable was skewed to the right (S = 3.08, SE = .15), we also applied a log-transformation (S = -.29, SE = .15).

Aggregate measures. PCA of writing, letter knowledge, and phoneme deletion revealed one component explaining 67% of the variance, with high loadings ranging from .79 for letter knowledge and phoneme deletion to .87 for writing. A PCA on timed reading tasks (RAN speed and Three Minutes Test) resulted in one component explaining 77% of the variance. The loadings were .88 for both components. We interpreted scores on this component as indicator of processing time in reading.

Executive functions.

Stroop-like task (dogs). Following the Stroop paradigm, children had to switch rules by responding with an opposite, i.e., saying "blue" to a red dog and "red" to a blue dog (based on Beveridge, Jarrold, & Pettit, 2002). The task consisted of 96 trials distributed over four conditions, in which demands on working memory (remembering the name of one or two dogs) and inhibitory control of the most obvious response varied. In the first two conditions the child had to name one or respectively two dogs ('tim' and 'jet') different in color (yellow and green). In the third and fourth condition the paradigm was the same, however the colors of the dogs were incompatible with their names (a red dog was named 'blue' and a blue dog 'red'). Incorrect naming or no response were considered as working memory errors while corrections were scored as inhibitory control errors. Each error was coded as working memory *or* inhibitory control error resulting in maximum scores of 96 for both. Internal consistencies for both scales were high (α's equaled .80 to .94).

Digit span (words). In the forward digit span test (*Leidse Diagnostische Test*; Schroots & Van Alphen de Veer, 1976), the children had to repeat a list of unrelated words that was read aloud by the computer. Practice trials were two-word lists. In the test-trials, the word lists increased from two to a maximum of five, and ended when a child failed to succeed three series in succession. The total number of correct responses (max. 12) was the score for this verbal memory task.

Backward digit span. In the backward digit span test (WISC-III; Wechsler, 1992), the child had to repeat a string of digits in reverse order. During four practice trials with strings of two to four digits, the experimenter corrected the child when needed. The test started with two digits and the number of digits gradually increased. In each trial, there were two strings of digits and at least one of these strings had to be repeated correctly in order to proceed to the next trial. The total score for this working memory task was composed of the total number of correct responses in the practice and test-trials (max.14).

Head-Toes-Knees-Shoulder-Task. The head-toes-knees-shoulder (HTKS) task included 20 test items to measure behavioral regulation (Ponitz, McCleland, Matthews, & Morrisson, 2009). Children have to pay attention, using working memory to remember rules, and inhibit an automatic response. After habituating to two oral commands (e.g., "touch your head" and "touch your toes"), children were asked to respond in an unnatural way to two types (on the first 10 trials) and then four types (on the second 10 trials) of paired behavioral commands. For example, if the administrator said "Touch your toes," the correct response would be for the child to touch his or her head. Correct responses earned 2 points, incorrect responses 0 points, and 1 point was given if children made any motion to the incorrect response, but self-corrected and ended with the correct action. The second part of the task, with four different commands, was used with scores ranging from 0 to 20 (α = .77). Commands were given in the same order.

Intraclass correlation coefficients between two independent coders were high for all tasks (r's > .97).

Aggregate measure. PCA applied to executive functions tasks revealed one component with medium to high loadings (.51 - .69) and explaining 42% of the variance.

Data analyses

Because participants were recruited from different schools (N = 15) we used Huber-White estimates of standard errors to correct for clustering of scores of children from the same schools (cf. Hatcher et al., 2006; Knafo, Israel, & Ebstein, 2011). We included the corrected standard errors in the Complex Sample General Linear Model (CSGLM, SPSS 17). The risk variants of DRD4 (7+) and DRD2 (A1+) were coded 0 and the other variants (7- and A1-) were coded 1, see Table 5.2 for descriptives.

Table 5.2
Descriptives of Reading Skills and Executive Functions Split by DRD4 and DRD2 Genotypes

	DRD4				DRD2			
	7- (n = 117)		7+ (n = 65)		A1- (n = 103)		A1+ (n = 71)	
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
Reading skills (T1)	.03	1.05	-.25	.84	-.02	1.02	-.14	.93
Reading skills (T3)	.09	1.03	-.31	1.03	-.05	1.08	-.07	1.00
Time reading skills (T3)	.05	1.00	.18	1.03	.01	.94	.22	1.08
Executive functions (T2/T3)	.21	1.01	-.27	1.08	.08	1.08	-.04	1.03

Note. T1 = November 2009; T2 = May 2010 (Kindergarten); T3 = November 2010 (Grade 1).

To test the hypothesized mediating role of executive functions, we assessed the following conditions for mediation (Baron & Kenny, 1986): (1) the independent variable (DRD4 or DRD2) must be related to the dependent variable (reading skills); (2) the independent variable must be related to the mediator (executive functions); (3) the mediator must be related to the dependent variable; (4) the independent variable may not have an effect on the dependent variable when the mediator is held constant (full mediation) or should become significantly smaller (partial mediation); and (5) the indirect effect of the independent variable on the dependent variable, as measured by the Sobel test, must be significant. We controlled for gender, age, and children's PPVT scores.

Results

Correlations

Table 5.3 displays correlations between included variables in analyses. Reading skills at T1 and T3 correlated moderately with each other and with executive functions. Correlations of DRD4 with reading skills in grade 1 and with executive functions were low.

DRD4

To test the mediation models for DRD4 and reading, we controlled for age, gender, and PPVT scores. In all models, PPVT was a significant covariate (p's < .05). Gender was a significant covariate in models that included both reading and executive function scores (p's < .05) and age only accounted for variance in the grade 1 reading models (p's < .05).

Table 5.3
Correlations Between all Included Variables

	1.	2.	3	4.	5.	6.	7.	8.	9.
1. Gender[a]	1.00								
2. Age	-.08	1.00							
3. PPVT[b]	-.04	.38**	1.00						
4. DRD4[c]	-.05	-.02	.02	1.00					
5. DRD2[d]	.06	-.01	.00	-.01	1.00				
6. Reading skills (T1)	.21**	.13	.31**	.14	.06	1.00			
7. Reading skills (T3)	.15	-.04	.29**	.19*	.01	.68**	1.00		
8. Time reading skills (T3)	-.02	.07	-.03	-.07	-.11	-.54**	-.56**	1.00	
9. Executive functions (T2/T3)	.00	.12	.26**	.22**	.06	.53**	.60**	-.33**	1.00

Notes. N varies between 159 (measures of T3) and 174 (measures of T1).
[a] Gender (0 = boy, 1 = girl); [b] PPVT = Peabody Picture Vocabulary Test (raw scores); [c] DRD4 (0 = 7+, 1 = 7-); [d] DRD2 (0 = A1+, 1 = A1-).
*Correlation is significant at the .05 level (2-tailed), **Correlation is significant at the .01 level (2-tailed).

We first analyzed the mean effect of DRD4 on readings skills. Dependent variables in the regressions were the aggregate measure for accurate reading after three months in the senior kindergarten year (T1) and after three months in first grade (T3). DRD4 was a significant covariate of reading skills in Kindergarten (β = .32 [95% CI .06, .57]; t (14) = 2.67, p = .02) and first grade (β = .36 [95% CI .11, .61]; t (14) = 3.09, p = .01), see Table 5.4.

A second set of analyses demonstrated that DRD4 was a significant predictor of executive functions (β = .45 [95% CI .05, .85]; t (14) = 2.43, p = .03).

As a third step, the mean effects of executive functions on reading skills were analyzed. Executive functioning was a significant covariate in kindergarten (β = .45 [95% CI .36, .54]; t (14) = 10.49, p < .001) as well as first grade (β = .56 [95% CI .44, .69]; t (14) = 9.73, p < .001).

Fourth, DRD4 and executive functions were entered simultaneously in the models. DRD4 was no longer a significant predictor of reading skills in kindergarten (β = .12 [95% CI -.14, .37]; t (14) = .99, p = .34) and in grade 1 (β = .11 [95% CI -.08, .30]; t (14) = 1.27, p = .22), whereas executive functions were (T1: β = .44 [95% CI .35, .53]; t (14) = 10.33, p < .001; T3: β = .55 [95% CI .42, .68]; t (14) = 9.39, p < .001). The models had an explained variance of 36% in Kindergarten and of 43% in grade 1.

Table 5.4
Testing Executive Functions as Mediator between DRD4 and Reading Skills, in Kindergarten (T1) and in Grade 1 (T3)

	T1 (N = 159)				T3 (N = 159)			
Testing steps in mediation model	ß	t	p	R^2	ß	t	p	R^2
Step 1								
Outcome: reading skills								
Predictor: DRD4	.32	2.67	.018	.16	.36	3.09	.008	.16
Step 2								
Outcome: executive functions								
Predictor: DRD4	.45	2.43	.029	.11	.45	2.43	.029	.11
Step 3								
Outcome: reading skills								
Predictor: executive functions	.45	10.49	<.001	.36	.56	9.73	<.001	.43
Step 4								
Outcome: reading skills								
Predictor: DRD4	.12	.99	.34		.11	1.27	.22	
Predictor: executive functions	.44	10.33	<.001		.55	9.39	<.001	
Total				.36				.43
Step 5*								
Outcome: reading skills								
Predictor: DRD4 via executive functions		2.32	.02			2.24	.03	

Notes. T1 = November 2009; T3 = November 2010. * Step 5 is a hand calculation of the Sobel test (z-value = $a*b$/SQRT($b^2*s_a^2 + a^2*s_b^2$)), so only t- and p- values are available. The Sobel shows that the indirect effect of the independent variable (DRD4) on the dependent variable (reading skills) through the mediator variable (executive functions) is significant.

Finally, Sobel tests of the indirect relation between DRD4 and reading skills were significant (T1: $t(159) = 2.32$, $p = .02$; T3: $t(159) = 2.24$, $p = .03$). The model suggests executive attention, as measured by executive functions, to be an almost complete mediator of the relation between DRD4 and reading skills (see Figure 5.1).

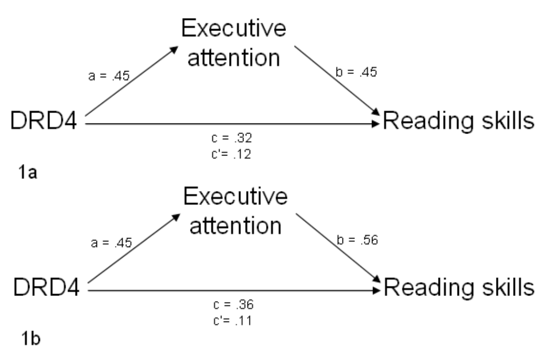

Figure 5.1. Executive attention (as measured with executive functions) as mediator between DRD4 and reading skills in Kindergarten (1a) and Grade 1 (1b). c = direct relationship, c' = indirect relationship.

Results could be replicated in the control group without an intervention in preschool. All effects and levels of significance were about equal for the control group only. The main effects of DRD4 on readings skills were, however, only marginally significance (T1: p = .06; T3: p = .07), probably due to the smaller sample size.

Executive functions predicted timed reading (RAN speed and TMT) in grade 1 (β = -.34 [95% CI -.48, -.20]; t (14) = -5.13, p < .001) but DRD4 did not (β = -.12 [95% CI -.34, .10]; t (14) = -1.21, p = .25) probably because variation in speed between children was low at this early momentum in their reading development.

DRD2

Analyses with DRD2 as predictor revealed no significant effects on reading in Kindergarten (β = .20 [95% CI -.11, .52]; t (14) = 1.39, p = .19) or Grade 1 (β = .02 [95% CI -.31, .35]; t (14) = .14, p = .89), which contradicts a mediation model for reading accuracy. Entering DRD2 instead of DRD4 neither predicted executive functions (β = .14 [95% CI -.22, .50]; t (14) = .85, p = .41) nor timed reading in grade 1 (β = -.21 [95% CI -.50, .08]; t (14) = -1.55, p = .14).

Discussion

So far the relatively new examination of dopamine genes in reading studies revealed mixed results. Hisung et al. (2004), for instance, found some evidence for the DRD4 7-repeat allele to be more frequently transmitted to dyslectic children; however Marino et al. (2003) didn't find an association between the DRD4 7-repeat allele and reading. In our study, with a normal sample of subjects, we found that the DRD4 gene is linked to learning to read and explains about 9% of the differences in reading ability. In other words, genetics predict reading achievement in a normal sample and is not only typical for a small categorical sample diagnosed as dyslexic children (Ebejer et al., 2010). The current findings also support a main role for DRD4 in young children's executive functioning. In line with the study of Schmidt et al. (2001), we found that the 7-repeat allele influences attention processes in a normal sample; apparently, DRD4 contributes to the full spectrum of attentional abilities rather than solely to extreme problems like ADHD. Another important finding is that the dopamine D4 gene affects reading skills in kindergarten and the first half of first grade *through* executive attention. Children's inability to stay attentive during reading practice is apparently one of the reasons for reading failure. The finding that executive attention is a mediator between genetics and reading corroborates the theory of a shared genetic base of reading and attention (Ebejer et al., 2010; Willcutt et al., 2007).

Similar to Marino et al.'s study (2003), we found no evidence for a relation between DRD2 and reading skills. Further, we could not replicate findings of a relation between DRD2 and executive functions. However, evidence for A1+ as a risk allele for executive functions problems is only found in children exposed to prenatal tobacco (Wiebe et al., 2009) or in alcoholic men (Rodriguez-Jiménez et al., 2006), but not in healthy subjects. Thus, expression of this genotype may occur only in adverse environments as the negative outcomes of this study support.

The current findings may explain why children with the DRD4 7-repeat allele often fail to profit from regular exposure to their learning environment, but profit from a structured program as appeared from a computer training of alphabetic skills with a tutor who corrected and confirmed all children's responses (Kegel et al., 2011). The 7-repeat allele shows lower dopamine reception efficiency and in children with this risk allele, dopamine release occurs only in response to actual instances of reinforcement (Tripp & Wickens, 2008). When a built-in computer tutor gives immediate supportive feedback as in the Kegel et al. experiment this may activate dopamine firing and consequently improve attention and thereby enabling the risk group with the long variant of DRD4 to maximally benefit from the computer assignments. In other words, individual, well-structured learning experiences as can some computer programs with built-in tutors offer may be highly profitable for children with the DRD4 7-repeat allele.

Limitations

A limitation of our study is that we examined only two dopamine genes. Single genes never can be the exclusive cause of protein and neurotransmitter production leading to learning behavior and development. We consider DRD4 as an important index to the dopamine-system related genetic pathway comprising several genes working together to regulate dopamine levels in the brain.

Furthermore, in the analyses we distinguished the long from the short variant of the DRD4 allele instead of using a continuum which means that we applied conservative tests of links with DRD4.

Conclusions and practical implications

Especially the finding that the dopamine system, regulated in the prefrontal cortex, can cause problems in the learn-to-read process via poorly developed executive attention has important implications for early interventions. Actually about one third of the children is genetically more at risk for reading problems as a result of their attention problems. To prevent reading failure in this sub-sample of children at-risk for reading problems, programs need to target not only reading skills but regulatory skills as well in contrast to what has become common practice. However, most early interventions are exclusively designed to train elements of literacy. One of the few exceptions is *Tools of the Mind* (Bodrova & Leong, 2007; Diamond, Barnett, Thomas, & Munro, 2007), a literacy program for kindergarten children with built-in instructions and tools to promote that young children stay attentive and focus attention while learning.

6 General Discussion

Parts of this chapter were based on:
Bus, A. G., & Kegel, C. A. T. (in press). Effects of an adaptive game on early literacy skills in at risk populations. In O. Korat & A. Shamir (Eds.), *Literacy, technology, and at risk populations.*

Early interventions to prevent reading problems address concerns that an unacceptably large number of children are already, by four years of age, lacking in competencies fundamental to their school success. These children are at serious risk to fall further behind in the coming years as their capacity to benefit from formal instruction may be compromised. There is therefore an urgent need of effective and efficient intervention programs in support of the kindergarten curriculum targeting precursors of reading. However, studies so far have shown intervention programs with only low to moderate effect sizes (e.g., Bus & van IJzendoorn, 1999; Ehri, Nunes, Willows, Schuster, Yaghoub-Zadeh, & Shanahan, 2001). Using a randomized controlled trial, the studies presented in this thesis examined program features and children's behavioral and genetic characteristics (e.g., regulatory skills and DRD4) that might be of influence on learning effects of an exemplary computer intervention program *Living Letters*.

The studies were carried out with a threefold purpose:

1. Can *Living Letters* stimulate the development of early literacy skills?
2. Who benefits from the remedial computer program?
3. Which features of the program are vital to boost development and school-entry skills?

Efficacy of Living Letters

Although it is well established that early literacy interventions can reduce the risk for developing academic problems in later years (Bus & Van IJzendoorn, 1999; Ehri et al., 2001), there is striking variation in outcomes of experiments (e.g., Al Otaiba & Fuchs, 2002). We compared children who played the *Living Letters* games with children playing another computer game that did not include letters and sounds during a three month period. Similar to previous studies targeting five-year-olds (Van der Kooy-Hofland, Bus, & Roskos, 2011; Van der Kooy-Hofland, Kegel, & Bus, 2011), we found moderate to high effect sizes (*d*'s between .54 and .68) of *Living Letters* in a younger age group on tests analogous to what the program trains. After three months in which the preschoolers played the games once a week, the children that received the target program outperformed the children in the control condition. Although results demonstrated that children can achieve gains as a result of a brief intervention when they receive computer-aided reading instruction, we wondered why effect sizes were only slightly beyond half a standard deviation even though we tested skills that are similar to the assignments in the program. We hypothesized that there is a group of children that hardly profits from the intervention thus reducing the overall effect size. For instance, children with low regulatory skills might benefit less due to responding randomly to computer assignments (Bracken & Fischel, 2006; Gioia, Isquith, & Guy, 2001; Spira, Bracken, & Fischel, 2005).

Regulatory skills

Regulatory skills are behaviors that enable children to stay on target during a task (Diamond, Barnett, Thomas, & Munro, 2007). In the literature they are split into different domains (e.g., inhibitory control and working memory), but executive attention may be the common factor for all regulatory skills tasks (Blair, 2006). Executive attention is highly related to working memory (Engle, 2002; Gathercole, Alloway, Kirkwood, Elliott, Holmes, & Hilton, 2008) and inattention is hypothesized to be a consequence of poor inhibitory control (Barkley, 1997).

In a group of delayed five-year-olds (they scored among the lowest 30% on precursors of reading), we found support for the expectation that children with poor regulatory skills have problems to benefit from a computer intervention. If children's regulatory skills were in the normal range they made more gains after an intervention with *Living Letters* than children with poor regulatory skills. The latter group did not benefit from the program and made more errors during the games, which is in line with the expectation that their learning behavior interfered with benefiting from the program. In direct conflict with our hypothesis, children with the highest regulatory skills benefited less from treatment than children with moderate sores. For them, *Living Letters* was no incentive for alphabetic skills similar to the group with the lowest scores on executive functions. These delayed children - they belonged to the 30 percent weakest performing children in the second year of Kindergarten - did not make progress despite well-developed regulatory skills and a program that responded to their delays. In explanation of this result, we hypothesized that this sub-sample with high regulatory skills but delayed in reading, belong to a group that is most at risk for developing specific reading problems due to a phonological deficit (Snowling, 2000). The current outcomes thus are in line with the hypothesis that, apart from children with specific cognitive deficits, some pupils' regulatory skills enhances the chance that children develop reading problems.

Foundational features of remedial programs for early literacy skills

Even when games provide instructions and practice just as in the regular curriculum, they may coax children into habits of responding that are nonproductive: instead of making purposive attempts to solve the assignments children may just click and enjoy the animations. The *blind eye* of computer-aided instruction can leave children to their own devices, opening the door to *free play* rather than playful engagement with the content, especially when they typically demonstrate poor executive control (De Jong & Bus, 2002). In the same vein, we might expect that a computer program that includes continuous correction or confirmation of the child's responses, modeled on human tutors, would reveal fewer errors in the computer assignments and more growth in target skills irrespective of pupils' level of executive control (Anderson, Boyle, & Reiser, 1985; Graesser, Conley, & Olney, in press; Van der Kooy-Hofland, Kegel, et al., 2011).

As a critical test, we compared the regular version of *Living Letters* with a version cut down to the bone. In the regular version children received adult-like feedback of a computer tutor that becomes more supportive as more errors are made in assignments. The program provided not only positive or negative feedback to the accuracy of answers but it also offered oral cues to correct and optimize children's responses (Wild, 2009). This version of *Living Letters*, with a teddy bear as online tutor, was compared with a version of the target program in which children did not receive continuous feedback to their responses from a tutor. In both versions of the program, computer assignments and instructions that preceded the assignments were exactly the same. Moreover, children received an identical number of trials and repetitions because, similar to the version with tutor, the assignment was 2-3 times repeated conditional upon the number of errors. So the two programs differed exclusively in the presence of an online tutor who provided individualized oral reactions to the child's responses. The tutor group outperformed the group without tutor by far. After correction for background variables and the scores on pretest, children in the tutoring condition scored on average more than one standard deviation higher than children who received instruction and assignments but no feedback. Moreover, when the program did not provide feedback children made more errors in assignments.

Both findings are well aligned with prior research (Azevdo & Bernard, 1995; Meyer et al., 2010; Vasilyeva, 2007) showing that instructions and assignments loose a lot of their impact when children do not receive immediate and personalized feedback to their responses to games. Overall these results suggest that an intelligent tutoring system that not just offers practice but tutors children's behavior while they practice is by far preferable to playing simple games. It seems a vital element of computer-aided instruction that a computer tutor provides immediate corrections of errors and explains after a correct reply to an assignment why the response is correct thereby imitating positive, responsive interactions with the parent or teacher.

To test whether feedback is especially vital when children are easily distracted by irrelevant stimuli, we assigned eligible pupils randomly to experimental conditions stratified for children's level of regulatory skills. The results of this experiment do not corroborate the hypothesis that an online tutor is especially important for children with underdeveloped regulatory skills. Actually, children with low as well as high inhibitory control perform far better in the condition with tutor. However, without tutor, children scoring low on inhibitory control fall behind. Results thus indicate that especially a low inhibitory control group is less able to benefit from computer games without continuous responses from a computer tutor in reply to children's responses to games. The children with low control made significantly more errors in the assignments than high control children. This result corroborates the hypothesis that a program without a tutoring component may reward a tendency to respond randomly instead of strengthening thoughtful replies for children with low inhibitory control. Actually the outcomes evidence the most common model in psychopathology: the 'dual risk' model (Belsky, Bakermans-Kranenburg, & Van IJzendoorn, 2007). That is, an effective program compensates for a child's problems while a negative environment (here: no tutor) combined with problematic learning behavior doubles a child's problems. Children with some risk lag behind as a result of both low inhibitory control as well as less impact of instruction.

Dopamine D4 gene as susceptibility factor

Outcomes are a matter of differential susceptibility when some children benefit from a supportive program and suffer from a less optimal program while other children perform at a similar level under all conditions (Belsky, 1997, 2005). In psychopathology, differential susceptibility is demonstrated for biological or genetic measures (e.g., Belsky et al., 2007; Ellis, Boyce, Belsky, Bakermans-Kranenburg, & Van IJzendoorn, 2011). In the same vein, we designed a study with dopaminergic efficiency (DRD4) as moderator. Children with the 7-repeat allele of DRD4 show diminished anticipatory cell firing and, because of that, they feel less reinforced when they anticipate a successful outcome during the learning process. Those carrying the long variant appeared to be more susceptible to the positive variant of the educational intervention program *Living Letters* (with tutor) than carriers of the short variant. On the other hand, carriers of the long variant scored lowest after being exposed to the negative version of the computer program (without tutor). The carriers of two short DRD4 alleles were less influenced by instruction, with or without constructive feedback of the tutor, indicating that they were rather insensitive for qualities of instruction. As a result, effect sizes of *Living Letters* (with tutor) for the carriers of the long and short allele ranged from strong to rather weak; they equaled .97 and .34, respectively.

In a study with five-year-old kindergartners and first graders we found that the 7-repeat allele influences both attention and reading skills. More importantly, the dopamine D4 gene affected reading skills *through* executive attention. Children with the long variant of DRD4 are at risk to lag behind in reading because they are often inattentive. This result fits our finding that children with the DRD4 7-repeat allele profited less from exposure to their regular learning environment, but did profit from the structured environment of *Living Letters* with continuous feedback of a computer tutor. The 7-repeat allele shows lower dopamine reception efficiency and in children with this risk allele, dopamine release occurs chiefly in response to actual instances of reinforcement (Tripp & Wickens, 2008). Immediate supportive feedback by a built-in computer tutor may activate dopamine firing and, consequently, improve attention thereby enabling the risk group with the long variant of DRD4 to maximally benefit from the computer assignments. In other words, individual, well-structured learning experiences, as some computer programs with built-in tutors offer, may be highly profitable for children with the DRD4 7-repeat allele. The current results are in support of the hypothesis that not the content of a program but the manner to which a program supports and corrects children's learning behavior is of overriding importance for its effects (Bodrova & Leong, 2007).

Further directions and limitations

Although DRD4 is a clear and reliable indicator of susceptibility to *Living Letters*, and probably of other remedial intervention programs, genotyping in search of potential intervention participants may not be practically possible or ethically desirable. In search for endophenotypes that can serve as a basis for screening, executive attention seems a strong candidate. Executive attention appeared to be linked to *Living Letters* but in a different way than DRD4. We need to know more about the specific working of the dopamine gene and the relation with behavioral measures to advice schools and practices on how to recognize children who may be more or less dependent on special programs. Scores on regulatory skills tasks may be less predictive because many young children fail to understand the rather complicated tasks. As long as reliable estimates of program effectiveness cannot be made by practitioners, it seems prudent to expose all children to well-designed early literacy programs, although some do not learn more than in their regular environment.

We extended the theory of differential susceptibility to an educational setting and found evidence for children with the DRD4 7-repeat allele to be more susceptible to a well designed computer environment. In further studies we want to extend these findings to other computer programs, different learning domains, and children of older ages. A better definition of tutoring is required, because, based on the present set of studies, we may expect that programs with a tutoring component give the best opportunities to children with attention problems.

Conclusions

Our conclusions are fairly straightforward and include three major points. First, computer-aided instruction can be a useful tool in early literacy education, even in kindergarten-age. Adaptive computer games designed to behaviorally train a particular aspect of literacy hold particular promise, especially for children disadvantaged by socioeconomic background. The current data show that a computer program is a useful instrument that improves phonological skills of young children from low SES background. The benefit of the software was substantial, considering that children played with the software during a limited number of short sessions. The intervention took place in a normal resource room without additional support of a researcher which demonstrates that this approach is feasible in the school environment.

Second, the finding that a group without computer tutor did not outperform the control group, demonstrates that a computer program without immediate individualized oral feedback is not a stronger stimulus for learning code-related skills than daily experiences with written language, as children in the control condition experienced. Effects of *Living Letters* apparently depend more on the manner to which children's learning behavior is supported than on the program's content. A main element of the program is continuous correction and confirmation in reply to children's responses. The evidence obtained here indicates that delays in reading skills can be neutralized by constantly assessing children's performance and attuning the feedback of a computer tutor to the child's needs.

Third, not all children are susceptible to special programs and benefit from a computer-aided intervention. Only part of the children is strongly dependent on a high-quality computer intervention. These children profit more from teaching that matches their skills level and that provides instruction through positive, responsive interactions; they suffer more from instruction that goes without these vital elements. The less susceptible group seems to benefit from all opportunities for learning without performing too well or too badly. Most surprising is that the susceptible group outperforms the other children when they receive the program probably because their abilities are “freed” in this supportive environment. As a consequence of the continuous feedback, these children start “blooming”. We conclude that children differ in susceptibility to the quality of feedback and support provided in an early reading computer program, and that this susceptibility is associated with a genetic predisposition to dopamine-regulated reward- and attention-related mechanisms, independent of cognitive ability.

Appendix

Note. The screenshots have been derived from four different games: Selecting the proper name among three or five alternatives (a&b), selecting ‘mama’ among five alternatives (c), selecting the first letter of the name among five alternatives (d), and selecting the painting that starts with the letter of the child’s own first name (e.g., Tom – tiger or Sam- Snake) among three alternatives (e&f). When the mouse skims a picture, as in e and f, the computer pronounces the picture’s name.

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Samenvatting (Summary in Dutch)

Letters in Beweging is een interventie ter bevordering van alfabetische kennis: doel is kinderen ervan bewust te maken dat letters samenhangen met klanken. Het programma, dat ontworpen is om leesproblemen tijdig te ondervangen, wordt via de computer aangeboden. Dit heeft als voordeel dat de training niet aangeboden hoeft te worden aan de hele klas maar beperkt kan blijven tot een subgroep. Bovendien kan het materiaal beter dan bij klassikale instructie op individuele behoeften worden afgestemd. In *Letters in Beweging* is dit bijvoorbeeld gerealiseerd door kinderen niet allemaal met dezelfde woorden en letters te laten oefenen maar met de eigen naam omdat die doorgaans het startpunt is van alfabetische kennis (Both-de Vries & Bus, 2008, 2010). Uit een reeks studies is gebleken dat *Letters in Beweging* positieve effecten heeft. Vijfjarigen met een achterstand in alfabetische kennis die door het programma hebben geleerd dat de letters in de naam met klanken samenhangen, profiteren meer van dagelijkse ervaringen thuis en in kleuterklassen en van formele leesinstructie in groep drie en vier dan een vergelijkbare groep kinderen zonder programma (Van der Kooy-Hofland, Kegel, & Bus, 2011). In het onderzoek in dit proefschrift testten we wie vooral profijt hebben van dit remediërende programma op de computer en aan welke voorwaarden het computerprogramma minimaal moet voldoen om in deze jonge leeftijdgroep effect te sorteren.

Effect van Letters in Beweging bij snel afgeleide kleuters

In een eerste studie, beschreven in hoofdstuk 2, participeerden 90 vijfjarigen die tot de laagst scorende 30 procent op tests voor alfabetische kennis behoren. De helft van deze groep speelde met de spelletjes van *Letters in Beweging*, de andere helft speelde met een taalprogramma zonder letters. Kleuters verschillen in afleidbaarheid: sommigen zijn snel afgeleid en hebben veel moeite om geconcentreerd te werken, vooral als er geen volwassene in de buurt is die hen bij de les houdt. Deze kleuters scoren doorgaans laag op taakjes voor aandacht en inhibitiecontrole (het onderdrukken van spontane reacties die de uitvoering van een taak in de weg staan). Daarom testten we naast ontluikende alfabetische kennis en intelligentie ook of kleuters in staat zijn hun gedrag te reguleren. Na drie maanden waarin ze in totaal ongeveer drie uur met het computerprogramma hadden gewerkt, bleken de kinderen met een gemiddelde aandachtspanne en inhibitiecontrole het meest te hebben geprofiteerd van *Letters in Beweging*. Kinderen met zwak ontwikkelde zelfregulatie profiteerden niet en lieten bovendien meer random klikgedrag en doelloze muisactiviteit zien. We vermoeden dat het onvermogen van deze groep kinderen om hun gedrag te reguleren tijdens het uitvoeren van de taakjes interfereert met de mate waarin zij in staat zijn te profiteren van het programma.

Een onverwacht resultaat was dat ook de groep met goed ontwikkelde zelfregulatie, maar zwakke alfabetische kennis, niet profiteerde van *Letters in Beweging*. Ondanks een goede aandachtspanne en inhibitiecontrole waren deze kinderen niet in staat hun achterstanden weg te werken met behulp van het programma. Deze uitkomst kunnen we alleen verklaren als we aannemen dat deze groep, die ondanks adequaat leergedrag achterblijft in alfabetische kennis, een specifiek cognitief probleem heeft. Het zou bijvoorbeeld een risicogroep met een deficit in foneembewustzijn (Snowling, 2000) of identificeren van klankverschillen (Perrachione, Tufo, & Gabrieli, 2011) kunnen zijn.

De online tutor als onmisbaar onderdeel van Letters in Beweging

Aan studie twee, beschreven in hoofdstuk 3, namen 312 vierjarigen deel waarvan het merendeel afkomstig was uit lager opgeleide gezinnen. Kinderen in de interventiegroep speelden met *Letters in Beweging*, de controlegroep kreeg in dezelfde tijd computerspelletje zonder letters en klanken aangeboden. De helft van de interventiegroep kreeg specifieke feedback van een online tutor met aanwijzingen en tips om de spelletjes op te lossen. De andere helft kreeg deze feedback niet. De interventiegroep met tutor presteerde op de nameting direct na de interventie veel beter (meer dan 1 standaarddeviatie) dan de interventiegroep zonder tutor. Zonder gepersonifieerde reacties van een (virtuele) persoon (“goed gedaan”of “nog niet helemaal goed, probeer het nog eens en denk dan aan ..”) benaderen kinderen taken kennelijk anders. Hun computergedrag bevestigt dat ze vaak onnadenkend reageren: ze hebben de neiging om te klikken zonder overwogen keuzes te maken (cf. De Jong & Bus, 2002). Met online tutor maakten kinderen gemiddeld minder fouten per taak dan zonder tutor.

We hadden verwacht dat vooral kinderen met zwakke zelfregulatie zouden profiteren van de online tutor terwijl kinderen met goede zelfregulatie zonder zouden kunnen. Deze hypothese is niet bevestigd. Tegen de verwachting in bleken ook kinderen met een normale aandachtsspanne en inhibitiecontrole beter te presteren met online tutor. Kennelijk is sturing van een tutor onontbeerlijk om kinderen alfabetische kennis te laten exploreren. Wel ondervinden kinderen met gebrekkige zelfregulatie dubbel nadeel van een programma zonder online tutor: als hun gedrag niet voortdurend wordt gecorrigeerd door een tutor die hen bij de les houdt, profiteren ze nog minder van de activiteiten die het programma biedt dan de kinderen die minder problemen hebben met zelfregulatie.

Het meeste profijt bij kinderen met aanleg voor ADHD

In de derde studie, beschreven in hoofdstuk 4, is getest of *Letters in Beweging* voor alle kinderen even cruciaal is. Uit een intrigerende reeks studies binnen het domein van de sociaal-emotionele ontwikkeling blijkt dat genetische en biologische factoren voorspellers kunnen zijn voor “differentiële ontvankelijkheid” voor de omgeving: de omgeving beïnvloedt de sociaal-emotionele ontwikkeling maar niet bij alle kinderen in dezelfde mate (Belsky, Bakermans-Kranenburg, & Van IJzendoorn, 2007). Naar analogie hiervan onderzochten we of sommige kinderen minder gevoelig zijn voor de kwaliteit van instructie en evenveel leren zonder additioneel computerprogramma of met een minder optimale versie van *Letters in Beweging*.

Als kinderen minder geneigd zijn spontaan hun naam te schrijven en door dit en ander gedrag minder instructie bij volwassenen uitlokken, zijn ze afhankelijker van een programma dat niet alleen oefening in alfabetische basiskennis biedt maar ook de aandacht stuurt en voortdurende persoonlijke feedback geeft. Kinderen met een spontane interesse in naamschrijven en daaraan gerelateerde activiteiten leren ook zonder programma en wellicht wordt een systematische training met tutor die hen voortdurend bij de les houdt, daardoor als minder stimulerend ervaren door deze groep. Om deze hypothesen over differentiële ontvankelijkheid voor het computerprogramma *Letters in Beweging* te toetsen selecteerden we een groep kinderen die verschilt van andere kinderen in genetische kenmerken waarvan bekend is dat ze een rol spelen bij taakgericht gedrag. Een geschikte kandidaat leek het dopamine D4-gen (DRD4) dat een centrale rol speelt bij de productie van dopamine. Bij kinderen met de lange variant van het DRD4-allel is sprake van een geringere efficiëntie waarmee dopamine vrijkomt waardoor deze kinderen een kortere aandachtsspanne hebben en meer afhankelijk zijn van sturing en instructie. De lange variant die typerend is voor 30 procent van de populatie, treedt dan ook vaker op bij kinderen met ADHD, ADD en aanverwante problemen (Robbins & Everitt, 1999).

In een onderzoeksgroep met 182 vierjarigen vonden we dat het DRD4-allel de effecten van *Letters in Beweging* modereert en kinderen met de lange variant het meest gevoelig zijn voor een geïndividualiseerde, intensieve computertraining in alfabetische kennis. Kleuters met de lange variant scoren het hoogst na te hebben gespeeld met het programma met online tutor en veruit het laagst in de controle conditie of na te hebben gespeeld met het programma zonder tutor. In de groep kleuters met de korte variant is echter sprake van vergelijkbare groei in de drie condities (met tutor, zonder tutor en controle). Ze maken evenveel vorderingen of ze nu wel of geen programma krijgen. De groep met de lange variant is dus veruit het meest afhankelijk van de kwaliteiten van instructie: ze hebben baat bij geïndividualiseerde adaptieve instructie en presteren in dat geval beter dan de groep met de korte variant terwijl hun prestaties sterk terugvallen als sturing en gerichte hulp ontbreken.

De bevinding dat kinderen met de lange variant het minst leren onder minder gunstige condities sluit aan bij het meest gangbare model van een "double deficit": gevolgen van zwakke aanleg worden verergerd als de omgeving geen houvast biedt om te kunnen profiteren van instructie. Het meest verrassend is dat de groep met de lange DRD4 variant veruit het meest leert onder optimale omstandigheden. Dit valt alleen te verklaren als we aannemen dat het merendeel van de kinderen in deze groep normaliter onderpresteert. Anders dan onder normale instructiecondities worden hun bekwaamheden optimaal geactiveerd door het computerprogramma met online tutor. De groep met de korte variant ervaart het programma in veel mindere mate als impuls voor leren.

Gebrekkige dopamineproductie als oorzaak van leesproblemen

In de laatste studie, beschreven in hoofdstuk 5, onderzochten we de relatie tussen dopamine genen (DRD4 en DRD2), executieve aandacht en beginnend lezen bij 159 kinderen. In de lijn met eerder onderzoek (o.a. Maher, Marazita, Ferrell, & Vanyukov, 2002; Tripp & Wickens, 2008) vonden we dat DRD4 een aanzienlijk deel van de verschillen in leesprestaties (9 procent) in een gezonde steekproef verklaart, maar dat executieve aandacht de relatie tussen DRD4 en leesvaardigheden medieert in zowel groep 2 als groep 3. De dopamine productie, aangestuurd door het dopamine D4-gen, bepaalt hoe goed kinderen erin slagen zich te concentreren op activiteiten binnen het kleutercurriculum en de leesinstructie in groep 3 en hun leesvaardigheden te verbeteren.

Dit resultaat maakt enigermate begrijpelijk waarom een computerprogramma als *Letters in Beweging* met online tutor zo positief uitwerkt bij dragers van de lange variant van het DRD4-gen. De tutor die feedback geeft op alle reacties van het kind, activeert de dopamine productie bij deze kinderen waardoor ze hun aandacht er beter bij kunnen houden en ze veel meer profiteren van de computertaken. In de literatuur over vroege interventies speelt de vraag welke kwaliteiten interventieprogramma's moeten hebben. Deze studie versterkt de hypothese dat het niet alleen belangrijk is welke vaardigheden met een programma worden geoefend, maar dat evenzeer van belang is dat een programma regulatieve vaardigheden ondersteunt en oefent (Bodrova & Leong, 2007).

Conclusies

Dit promotieonderzoek naar *Letters in Beweging* resulteerde in drie belangrijke conclusies. Ten eerste, de studies repliceren de eerdere bevinding dat een kort maar doelgericht computerprogramma in de kleuterleeftijd een nuttig hulpmiddel kan zijn bij preventie van leesproblemen. Een adaptief computerprogramma, dat ontworpen is om een bepaald aspect van geletterdheid te oefenen, is veelbelovend als kinderen thuis te weinig stimulansen krijgen zoals vaak het geval is in laagopgeleide gezinnen. Als we tevens in aanmerking nemen dat kinderen nauwelijks begeleid worden als ze de computerspellen van *Letters in Beweging* spelen, moeten we concluderen dat dit soort computerprogramma's bruikbaar is in de schoolomgeving waar individuele supervisie schaars is en leesproblemen frequent voorkomen. Een leskist voor kleuters met een breed aanbod van remediërende voorbereidende programma's is nog toekomstmuziek. Voor zover programma's beschikbaar en getoetst zijn, bestrijken ze een beperkt terrein (de vroege lees- en rekenontwikkeling) en zijn diverse functies (bijvoorbeeld feedback) nog onderontwikkeld. Maar onze ervaringen met computerprogramma's zijn veelbelovend.

Ten tweede is aangetoond dat computerspelletjes pas effectief zijn als prestaties voortdurend worden gecorrigeerd of bevestigd. Een computerprogramma met exact dezelfde spelletjes en instructie maar zonder algoritmes voor individuele feedback, levert niet meer effect op dan een controleconditie zonder programma. Van computerspelletjes zonder online tutor leren kinderen evenveel als van hun dagelijkse ervaringen met geschreven taal. Het computergedrag tijdens de spelletjes doet vermoeden dat een computerprogramma met exact dezelfde spelletjes en instructie maar zonder tutor willekeurig gedrag uitlokt wat leren blokkeert. Alleen een computerprogramma dat gemodelleerd is naar de interacties tussen ouders en kinderen in geletterde gezinnen en een persoonlijke reactie geeft op goede en foute reacties - "Goed zo, in dat woord hoor je de 't' van Tom" - , is een extra stimulans voor de ontwikkeling van alfabetische kennis. Een ingebouwd algoritme met adaptieve feedback en hulp is essentieel voor jonge kinderen om te leren van een computerprogramma: een computerspel met dezelfde opdrachten en instructies maar zonder hulp- en correctiesysteem werkt niet.

Ten derde blijken niet alle kinderen even gevoelig te zijn voor instructie en niet even sterk te profiteren van interventies. We vonden aanwijzingen voor differentiële ontvankelijkheid voor instructie. Ongeveer 30 procent van de jongste kleuters bleek voor het ontwikkelen van alfabetische kennis afhankelijk te zijn van het interventieprogramma. Deze kinderen profiteren van onderwijs dat aansluit bij hun vaardigheden en van instructie die positieve, responsieve interacties uitlokt, maar blijven achter onder minder gunstige omstandigheden. De andere 70 procent - minder instructiegevoelige kinderen - profiteert weliswaar van stimulansen om alfabetische kennis te exploreren maar hun prestaties zijn minder afhankelijk van geïndividualiseerde hulp en instructie. Ze profiteren evenzeer van andere ervaringen en worden niet in bijzondere mate geprikkeld tot leren door systematische training en de kwaliteit van instructie en feedback. We mogen dus concluderen dat kinderen verschillen in gevoeligheid voor interventies via computerprogramma's en dat deze gevoeligheid kan samenhangen met een genetische predispositie voor dopamine-gereguleerde mechanismen die onafhankelijk zijn van algemene cognitieve vaardigheden.

Samenvattend kan uit dit proefschrift worden geconcludeerd dat – zeker voor kinderen met bepaalde genetische kenmerken die een rol spelen bij taakgericht gedrag – computerprogramma's met geïndividualiseerde feedback van een online tutor een waardevolle bijdrage kunnen leveren om leesproblemen vroegtijdig te ondervangen.

Dankwoord (Acknowledgements)

Een proefschrift schrijven lijkt een eenzaam proces, maar is alleen mogelijk met de hulp van velen. Graag wil ik op deze plek een ieder bedanken die een bijdrage heeft geleverd aan het tot stand komen van dit proefschrift.

Allereerst Stichting Kennisnet die dit onderzoek heeft mogelijk gemaakt door een subsidie toegekend aan mijn promotor Adriana G. Bus. Daarnaast de scholen die drie jaar lang hebben meegewerkt: de Bergse Zonnebloem (Rotterdam), Jonge Wereld (Den Haag), Koningin Emmaschool (Rijnsburg), Maerten van de Velde (Stompwijk), Oranje Nassauschool (Rijnsburg), Pacelli (Leiden), Plevier (Hoogvliet), Roomburg (Leiden), Shalomschool (Rijswijk), Sint Willibrordus (Schiedam), Springplank (Leiden), Triangel (Rotterdam), Volle Leven (Den Haag), Vreewijkschool (Rotterdam) en de Watersnip (Zoetermeer). Groot was de inzet van ouders, leerkrachten en uiteraard de deelnemende kinderen.

Studenten die hebben geholpen met het verzamelen van alle onderzoeksgegevens wil ik bedanken voor hun inzet en nauwkeurigheid. In het bijzonder Danique die veel verzamel- en codeerwerk heeft verricht.

Eens had ik bijles Engels, nu heb ik een Engels boek geschreven. Veel heb ik gehad aan de correcties en leerzame cursussen wetenschappelijk Engels van Ineke Smith en Christine Espin.

Gemotiveerd werken lukt het beste in een motiverende omgeving. Collega's bedankt voor jullie feedback, luisterend oor (zowel op het werk als onderweg ernaar toe), fijne samenwerking en het ontwerpen van mijn cover tijdens één van onze afdelingsuitjes. Jacqueline, een speciaal woordje voor jou als mijn paranimf. Je hulp bij het data verzamelen, betrokkenheid en aanwezigheid als kamergenoot hebben voor mij bijgedragen aan een prettige promotieperiode.

Simon en Josephine, fijn dat jullie – als neefje en nichtje binnen de juiste leeftijdscategorie – bereid waren om mijn taakjes en spelletjes geduldig uit te testen.

Lieve vriend(inn)en uit de Hoeksche Waard (en later daarbuiten), van studie en muziek, oud-huisgenootjes en vrienden via Rudolf: jullie interesse, steun en ontspanning heb ik zeer gewaardeerd. Leuk om met een aantal van jullie de promotie-ervaringen te kunnen delen. Marleen, fijn dat ook jij mijn paranimf wilt zijn, na een gezamenlijke wetenschappelijke carrière van profielwerkstuk, via studeren, tot (?) samen promoveren.

Ten slotte wil ik mijn (schoon)familie bedanken voor het warme thuis dat zij mij bieden. Lieve oma, bedankt voor uw warme interesse. Niels, Reinier en Rogier fijn dat jullie je van tijd tot tijd, naast de verkoop van auto's, ook in de 'executieve functies' van jullie zus hebben verdiept. Lieve pap en mam, bedankt voor het vertrouwen en alle mogelijkheden die jullie mij hebben geboden. Rudolf, bedankt voor je liefde en vertrouwen. Ik kijk ernaar uit om samen binnenkort als kersverse ouders een nieuwe en spannende fase in ons huwelijk in te gaan.

Curriculum Vitae

Cornelia A. T. Kegel (Carienke) was born May 10, 1984 in Mijnsheerenland, the Netherlands. She completed her secondary education (VWO) in 2002 at the Willem van Oranje in Oud-Beijerland. She studied Education and Child studies at Leiden University, specializing in Learning Problems and Impairments (regular master, 2006) and Educational Sciences (research master, cum laude, 2008). During her research master, she was student-assistant of Prof. dr. Adriana Bus (Department of Education and Child studies) and participated in a research project with computer interventions for young children at risk to prevent reading impairments. In January 2008, she started a PhD project under the expert guidance of Adriana Bus. The main aim of her study was to further explore the role of computer interventions for young children, the role of regulatory skills on learning, and genetic components that may influence learning and behavioral processes. Results are described in this doctoral thesis.

Cornelia A.T. Kegel (Carienke) werd geboren op 10 mei 1984 in Mijnsheerenland. In 2002 behaalde zij haar VWO-diploma aan de scholengemeenschap Willem van Oranje te Oud-Beijerland. Ze studeerde Pedagogische Wetenschappen aan de Universiteit Leiden, waar ze zich specialiseerde in Leerproblemen (reguliere master, 2006) en Onderwijs Wetenschappen (onderzoeksmaster, cum laude, 2008). Tijdens haar onderzoeksmaster werkte ze als student-assistent bij Prof. dr. Adriana Bus (vakgroep leerproblemen) en participeerde in het onderzoeksproject naar computer interventies om leesproblemen te voorkomen bij jonge kinderen. In januari 2008 begon ze aan een promotieproject onder leiding van Adriana Bus. Het hoofddoel van haar studie was om de rol van computer interventies voor jonge kinderen nader te onderzoeken en daarnaast te kijken naar de invloed van regulatievaardigheden op leren en de rol van genetische componenten bij leer- en gedragsprocessen. De resultaten van haar onderzoek zijn in dit proefschrift beschreven.

List of Publications

Bus, A. G., & **Kegel, C. A. T.** (in press). Effects of an adaptive game on early literacy skills in at risk populations. In O. Korat & A. Shamir (Eds.), *Literacy, technology, and at risk populations.*

Bus, A. G., **Kegel, C. A. T.**, & Van der Kooy-Hofland, V. A. C. (2011). Interactief leesonderwijs voor kleuters. In P.F. de Jong & H.M.Y. Koomen (Red.), *Interventie bij onderwijsleerproblemen* (pp. 83-93). Apeldoorn: Garant.

Kegel, C. A. T., & Bus, A. G. (in press). Online tutoring as a pivotal quality of web-based early literacy programs. *Journal of Educational Psychology*.

Kegel, C. A. T., & Bus, A. G. (submitted). Executive attention mediates the role of the Dopamine Receptor D4 gene (DRD4) on reading acquisition in a non-clinical sample.

Kegel, C. A. T., Bus, A. G., & Van IJzendoorn, M. H. (2011). Differential susceptibility in early literacy instruction through computer games: The role of the dopamine D4 receptor gene (DRD4). *Mind, Brain, and Education*, *5*, 71-78. doi:10.1111/j.1751-228X.2011.01112.x

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