Will Processing Speed and Intra-Subject Variability be improved in children with ADHD by means of a computerized Executive Function-training with game elements?
Abstract

Most existing therapies for children with Attention Deficit Hyperactivity Disorder (ADHD) focus on mitigating problematic behavior by medication as methylphenidate and adapting the environment (i.e. parents and school) by behavioral therapy. Based on the theory that ADHD stems from executive functions deficits, new treatments are being developed, aimed at improving executive functioning directly. In this study with 61 school children diagnosed with ADHD-combined, it was tested whether a computerized training with gaming elements (Braingame Brian), targeted to improve working memory, cognitive flexibility and response inhibition, would also improve processing speed and intra-subject variability, two known cognitive deficits of children with ADHD. This was not the case, although response inhibition did improve. Considering the potential benefits for children with ADHD, it would potentially be useful to add training exercises for processing speed and intra-subject variability to existing computer training programmes and to test its effects, also using more sophisticated analysis methods.
Introduction

Existing therapies for children with Attention Deficit Hyper-Activity Disorder (ADHD) currently seem to focus on one or more of the following areas: medication (e.g., methylphenidate), psychosocial treatments as behavioral therapy (also in combination with medication, Majewicz-Hefley & Carlson, 2007; MTA study, 1999), self regulation via self-instruction (Hinshaw, 2000; Kendall & Braswell, 1993) and social skills (Abikoff et al., 2004; Pfiffner & McBurnett, 1997). In general, a combination of medication and psychosocial therapy is deemed most effective (Multidisciplinaire Richtlijn ADHD, 2005). Although a fully comprehensive causal theory of ADHD is still lacking, one of the most prominent theories is the model of Barkley (1997; 2006), stating that ADHD is caused by a lack of behavioral inhibition, resulting from several executive functions deficits impacting working memory, response inhibition, cognitive flexibility and interference control (Willcutt, Doyle, Nigg, Faraone & Pennington, 2005).

The above described conventional treatment methods can be characterized as coping strategies to mitigate problematic behavior expressed by children and adults having ADHD. Accepting the executive functions deficit hypothesis as persuasive, new training programmes are being developed that directly target the improvement of executive functions, and thus indirectly aspire to alter problematic behavior.

Klingberg et al. (2005) developed a computerized training of working memory for children with ADHD. This training consisted of a 5-week period wherein children with ADHD performed visuo-spatial working memory tasks (remembering positions in a 4x4 grid) as well as verbal tasks (remembering phonemes, letters or digits) on a computer. The training successfully improved (verbal and visuo-spatial) working memory, response inhibition and reasoning and lead to a decrease of parent-rated inattentive symptoms of ADHD (Klingberg et al., 2005). More recently, also a reduction at behavioral level and executive functioning (measured by the BRIEF, the Behavioral Rating Inventory of Executive Functioning) was found, when the computerized training was provided in a school environment, suggesting effectiveness in real life practice (Steiner, Sheldrick, Gotthelf & Perrin, 2013). Another study showed that it was possible to improve task switching abilities for children with ADHD. The children were trained in switching between two simple cognitive tasks. The ability to flexibly switch improved already after a short intervention of four sessions (Kray, Karbach, Haenig & Freitag, 2012).

Prins, Dovis, Ponsioen, ten Brink and van der Oord (2011) added game elements to a very brief computerized training (three sessions) aimed to train (visuo-spatial) working memory, based upon the notion that children with ADHD would benefit from a training which would specifically motivate and stimulate them. The participants needed to reproduce sequences of randomly lit-up
squares in a 4x4 grid. The gaming elements that were added consisted of an animation, a story line, a goal, rewards and response cost earned or lost in the game, competition and identification with a game character. The gaming elements had greater impact on motivation, training performance and post-training working memory (Prins et al., 2011). The computerized training was then extended to 25 training sessions and expanded to also train cognitive flexibility and response inhibition (“Braingame Brian”) (Prins et al., 2010).

In addition to executive functions deficits as discussed above, children with ADHD also display cognitive weaknesses such as processing speed (Shanahan et al., 2006; McGrath et al., 2011). Shanahan et al. (2006) defined processing speed as the underlying cognitive efficiency at understanding and acting upon external stimuli, thereby integrating low level perceptual, higher level cognitive information and output speed. Accordingly, Jacobson et al. (2011) used three types of tasks to measure processing speed in children with ADHD: i) graphomotor speed (measured by WISC-IV Processing: Speed subtests or Trailmaking tests), ii) naming speed (measured by RAN and Stroop color naming) and iii) reaction time (measured by continuous performance or Go/No go tasks). Children with ADHD differed from controls on graphomotor speed, i.e., involving response selection (similar: Oades & Christiansen, 2008). Processing speed was found to be related to verbal attention/span, verbal working memory and spatial working memory (Jacobson et al., 2011).

Besides a decreased ability to process information as speedily as typically developing children, children with ADHD also react more variably on various neuropsychological tasks whereby reaction time is measured. This inconsistent response style concurs with the variable expression of ADHD symptoms across time and context (Castellanos and Tannock, 2002; Klein, Wendling, Huettner, Ruder & Peper, 2006; Epstein et al., 2011). In research designs, this is operationalised as intra-individual or intra-subject variability (Epstein et al., 2011), measured by assessing coefficients of variation (this is the standard deviation of reaction time divided by the mean reaction time) of different neurocognitive tasks involving a speed component such as the Stop-Signal task. In this task, the children are requested to press left or right in response to a stimulus indicating left or right, but to inhibit this response if a stop signal (visual or auditory) is presented. Higher intra-subject variability on a Stop-Signal task was found by Klein et al. (2006), using coefficients of variation and consecutive variance as indicators, De Zeeuw et al. (2008), using the coefficient of variation, and Epstein et al., using the ex-Gaussian tau as indicator, in line with the meta-analysis of Alderson, Rapport and Koffler (2007). This higher intra-subject variability results from more frequent and exceedingly longer reaction times, reflecting problems of response execution rather than response inhibition (Epstein et al.; Alderson et al.; Van de Voorde, Roeyers, Verté and Wiersema, 2010). A PCA confirmed that intra-response variability consisted of one single factor across various tasks (Klein et al.). Further a positive association with task accuracy and intra-subject variability was established by De Zeeuw et al. and
Epstein et al, (although not by Klein et al.), as well as a positive association with parent ratings of hyperactivity, inattention and executive functions (Gòmez-Guerrero et al., 2011). Together this suggests that the intra-subject variability is detrimental to performance of children with ADHD.

In the intervention programmes of Klingberg et al. (2005) and Prins et al. (2010; 2011) the influence on processing speed and intra-subject variability was not examined. Many executive tasks involve multiple neuro-cognitive processes (Willcutt et al., 2005). In addition, verbal and spatial working memory were found to be associated with processing speed (Jacobson et al., 2011) and working memory was found to be related to intra-subject variability (Klein et al., 2006; Verté, Geurts, Roeyers, Oosterlaan and Sergeant, 2006, visuo-spatial working memory). It therefore seems feasible that a training aimed at improving working memory and other executive functions of children with ADHD will also impact processing speed and intra-subject variability. Illustrative in this respect is that Klingberg et al., (2005) found that their computerized training of spatial-verbal- and visuo-spatial tasks also improved response inhibition and reasoning. Similarly, Thorell, Lindqvist, Bergman Nutley, Bohlin and Klingberg (2009) found that their computerized training of visuo-spatial working memory showed training effects on non-trained tests of spatial and verbal working memory, as well as transfer effects to attention. A study among healthy participants (i.e., not suffering from ADHD) suggested that processing speed can be improved by the training of action games on a computer (Dye, Green & Bavelier, 2009).

As processing speed and intra-subject variability are established to be different in children with ADHD from typically developing children, and are associated with working memory, the general research question is whether it is possible to increase processing speed and decrease intra-subject variability in children with ADHD when training their executive functions (e.g., working memory) in a computerized game training. If such changes in processing speed and intra-subject variability indeed can be established, the second question is whether this will also be associated with a reduction of ADHD symptoms and ADHD related behavior.

This study, in a randomized controlled trial with two conditions\(^1\), with a pre-training and post-training measurement, assessed whether children with ADHD who carried out a computerized training with game elements, aimed at improving working memory, cognitive flexibility and inhibition (Braingame Brian) subsequently demonstrated an increase of processing speed and a decrease of intra-subject variability. If such increase of processing speed and/or a decrease of intra-subject variability would be demonstrated, this study would further assess whether this increase and/or decrease were also associated with a reduction of parent/teacher rated ADHD symptoms and ADHD related behavior.

\(^1\) The training consisted of three training conditions, but as explained below, two groups were analysed together.
The computerized training consisted of three training conditions:

1. a full and adaptive training condition, where both working memory, response inhibition and cognitive flexibility are adaptively trained (Full-adaptive training condition). Adaptive means that the difficulty level of the training is adapted to the performance of the participant;

2. a training condition where response inhibition and cognitive flexibility are adaptively trained and the working memory training is presented non-adaptively and on a low initial training level (Combination-training condition); and

3. a training condition where working memory, response inhibition and cognitive flexibility are presented non-adaptively and on a low initial training level (Non-adaptive training condition).

Both the Combination-training condition and the Non-adaptive training condition train the working memory non-adaptively, and will therefore be considered together and jointly referred to as the Combination and Non-adaptive training condition.

The first hypothesis (H1) was: participants belonging to the Full-adaptive training condition, will show a significant increase of one or more processing speed measures (graphomotor speed, naming speed, and/or output speed) compared to participants in the Combination and Non-adaptive training condition.

The second hypothesis (H2) was: participants belonging to the Full-adaptive training condition will show a significant decrease of intra-subject variability compared to participants in the Combination and Non-adaptive training condition.

The third hypothesis (H3) was: if Hypothesis 1 is confirmed, a negative association can be established between an increase of one or more processing speed measures, and a decrease of parent and/or teacher reported ADHD symptoms.

The fourth hypothesis (H4) was: if Hypothesis 2 is confirmed, a positive association can be established between a decrease of intra-subject variability, and a decrease of parent and/or teacher reported ADHD symptoms.

**Method**

**Participants**

61 children aged 8 to 12 years with a diagnosis of ADHD combined-type participated. The children were approached via five outpatient mental healthcare centers in the Netherlands. The children met the following inclusion criteria: (a) an IQ score ≥80 as measured by the short version of the Dutch Wechsler Intelligence Scale for Children (Wechsler, 1996; Kort et al., 2002). Two WISC-III subtests, Vocabulary and Block Design are administered to estimate Full Scale IQ (FSIQ). This composite score has satisfactory reliability (r = 0.91) and correlates highly with FSIQ (r = 0.86; Sattler, 2001); (b) age between 8 up to and including 12 years old; (c) absence of any neurological disorder or a non-verbal learning disorder (Nigg, 2006); (d) not taking any medication other than methylphenidate; (e) a prior
DSM-IV-TR (American Psychiatric Association, 2000) diagnosis of ADHD combined-type by a child psychologist or psychiatrist; (f) a score within the clinical problem range (95th to 100th percentile) on the ADHD scales of both the parent and teacher version of the Disruptive Behavior Disorder Rating Scale (DBDRS; Pelham, Gnagy, Greenslade, & Milich, 1992; Dutch translation Oosterlaan, Scheres, Antrop, Roeyers, & Sergeant, 2000); (g) meeting the criteria for ADHD combined-type on the ADHD section of the Diagnostic Interview Schedule for Children for DSM-IV, parent version (PDISC-IV; Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000). The PDISC-IV is a structured diagnostic interview based on the DSM-IV, with adequate psychometric properties; (h) absence of Conduct Disorder (CD) based on the CD sections of the PDISC-IV; and (i) absence of a prior DSM-IV-TR diagnosis of any autism spectrum disorder, according to a child psychologist or psychiatrist.

Table 1 provides demographics and characteristics of the children. Children discontinued medication at least 24 hours before each sessions, allowing a wash-out (Greenhill, 1998).

**Table 1**

Means and standard deviations of group characteristics

<table>
<thead>
<tr>
<th>Measure</th>
<th>Group</th>
<th>Full-Adaptive training (n = 21)</th>
<th>Combination and Non-adaptive training (n = 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>M/ratio SD</td>
<td>M/ratio SD F/χ² p</td>
</tr>
<tr>
<td>Gender (M:F)</td>
<td>16:5</td>
<td>32:8</td>
<td>.12 .73</td>
</tr>
<tr>
<td>Medication</td>
<td>19:2</td>
<td>31:8</td>
<td>1.73 .421</td>
</tr>
<tr>
<td>Age (years)</td>
<td>9.8 1.47</td>
<td>9.90 1.2</td>
<td>.62 .435</td>
</tr>
<tr>
<td>FSIQ</td>
<td>102.76 17.09</td>
<td>102.45 15.81</td>
<td>.005 .943</td>
</tr>
<tr>
<td>Gaming</td>
<td>8.97 8.93</td>
<td>10.23 7.34</td>
<td>.34 .564</td>
</tr>
</tbody>
</table>

Note: ADHD = attention-deficit/hyperactivity disorder; FSIQ = full scale IQ; M:F = Male:Female ratio: Gaming = number of hours per week of playing computer games.

**Materials**

Independent variable: The Executive Function training.

The computer game “Braingame Brian” has been developed by a Task Force of clinical child (neuro)psychologists of the University of Amsterdam and Lucertis, a clinic for child and adolescent psychiatry, in close collaboration with a professional multimedia company, Shosho (www.shosho.com). The Executive Functions training is embedded in a fantasy world with a main character with which the player - the child with ADHD - can identify. Throughout the game, the main character may walk through the game world and has to perform various assignments, which are in part fun games and in part Executive Function-training tasks. Play time and training time are
balanced within each training session. The adaptive versions of the training tasks have several levels of difficulty which allow the child to make progress at his own level. In these adaptive tasks the level of difficulty systematically increases with each training session, in a way that is similar for all children. The level of difficulty in a particular session can be adjusted downward or upward, if the child does not reach the minimum set level or performs very well. In the non-adaptive version of the training tasks start at a low difficulty level (for working memory) or practice level (for inhibition and cognitive flexibility) and do not adapt to individual performance during training. Each training task is described into more detail below.

**Executive Function-training tasks.**

Three Executive Function tasks have been developed for the present project: a working memory training, an inhibition training (inhibitory motor control) and a cognitive flexibility training (Dovis, Ponsioen, Geurts, Ten Brink, van der Oord & Prins, 2008a; Dovis, Geurts, Ponsioen, Ten Brink, van der Oord & Prins, 2008b).

**Adaptive Working Memory training**

The visuospatial working memory-training consists of five components: (a) training of short-term memory; (b) training of short-term memory, monitoring and coding and revising incoming information, replacing irrelevant by relevant information (updating, Miyake, Friedman, Emerson, Witzki, & Howeter, 2000; Morris & Jones, 1990), (c) training of short-term memory and manipulation/updating; (d) training of short-term memory and keeping information online during a delay, and (e) training of short-term memory and keeping information online and manipulation of information/updating. These components are each trained for five of the 25 sessions. In the first series of five sessions, squares light up on a 4x4 grid (16 squares), and form a sequence which has to be reproduced by the child. The number of squares progresses adaptively. In the second series of five sessions, squares and one of four vertical bars, placed on the edges of the grid, simultaneously light up. The child needs to reproduce the sequence of the squares and each time after two trials, also the sequence of the bars. In the third series of five sessions, the squares light up in two different colors. The child has to reproduce the sequence of the squares, but now grouped by color, one group after another. In the fourth series of five sessions, first two bars light up, followed by lightening up of the squares. The child has to reproduce the sequence of the squares first, followed by the sequence of the bars. In the fifth series of five sessions, the third and fourth series are combined. First two bars light up, followed by the squares in two different colors. The child has to reproduce the sequence of the squares first, grouped by color, and subsequently the bars, in the right order (Dovis et al, 2008a).

**Low and non-adaptive Working Memory training**

The low and non-adaptive visuospatial working memory-training consists of the first of the five working memory training tasks and is presented on a low difficulty level whereby only two
squares have to be reproduced by the child. The difficulty level of this task does not change during the five week training (is non-adaptive).

**Adaptive inhibition training**

The inhibition training is based on the Stop-Signal task (Logan, 1994) which trains the child to inhibit a behavioral impulse (behavioral inhibition). The Stop-Signal task generates an objective measure of inhibition, the Stop-Signal Reaction Time (SSRT), which is generally lower in children with ADHD than in normal controls (Willcutt et al., 2005). The training aims to improve the SSRT. During the training, the child has to react to a stimulus in 75% of the trials. In the other 25%, just after the stimulus is shown and the child has started his reaction, a stop-signal appears and the child has to inhibit his response. The time interval between stimulus and stop signal gradually shortens as the child progresses in the training, which taxes its inhibitory power.

**Low and non-adaptive inhibition training**

During the low and non-adaptive inhibition training, the child has to react to a Go-stimulus in 100% of the trials while no stop-signal is being presented, which makes the task less difficult. This difficulty level remains the same throughout the whole training.

**Adaptive cognitive flexibility training**

The cognitive flexibility training trains the child to suppress a response and at the same time activates an alternative, more appropriate response (switching). The training is based on the Switch Task (King, Colla, Brass, Heuser, Van Cramon, 2007). ‘Switchcost’ is used to measure the ability to switch between two competing responses (form versus color), and is the extra time it costs to switch between two responses relative to continuing with the same behavior. On every trial during the training the child gets visual feedback on his reaction and reaction times (switches and non-switches). The level of difficulty gradually increases during the training, by shortening the interval to respond, thus aiming to reduce the switchcosts.

**Low and non-adaptive cognitive flexibility training**

The low and non-adaptive cognitive flexibility training trains the child to respond correctly to two stimuli (the child has to press left or right). The child does not have to switch between two sets of stimuli (only non-switch trials are presented). The difficulty level of the low training version of the tasks remains the same throughout the whole training.

Dependent variables

**Processing Speed**

Shanahan et al. (2006) defined Processing Speed as the underlying cognitive efficiency at understanding and acting upon external stimuli, thereby integrating low level perceptual, higher level cognitive information and output speed. This broad, three fold definition is also taken as a basis in
This study and thus the construct Processing Speed is being built up by different aspects of information processing, being perceptual/motor processing, naming speed and output speed. These aspects were measured and analyzed separately.

**Motor speed** of participants to the training was assessed prior to and after the training by means of two tasks of the D-KFES Trail Making Test, (Delis, Kaplan, & Kramer, 2001, Dutch translation, 2007, Pearson). The Trail Making Test is a timed test consisting of five tasks in total, that requires the individual to connect a series of letters and numbers in ascending order, ultimately alternating between numbers and letters. For the purposes of assessing motor speed, the second and third task were used. Task 2, Number Sequencing, requires the children to rapidly draw a continuous line connecting numbers in order and is considered mainly to measure Processing Speed (comparable to Trail A of a former version of the Trail Making Task). Task 3, Letter Sequencing, requires the children to rapidly draw a continuous line connecting letters in order. The internal consistency reliability is intermediate to high, the test-retest reliability is .77 for Task 2 and .57 for Task 3 (age group 8-19) (Delis et al., 2007). There is some evidence for concurrent and criterion related validity, but this was mainly established in other clinical groups (e.g., patients with frontal lesions or with Alzheimer’s disease (Homack, Lee & Riccio, 2005). There is no COTAN assessment available. The completion times on the two tasks were converted into normative scores for various ages, where after an average score was determined.

**Naming speed** of participants was assessed prior to and after the training by measuring the response time of participating children on the color and word naming conditions of the Stroop Test (Golden & Freshwater, 1998, Hammes, 1978) and averaging these scores. This test consists of three tasks. First, children need to rapidly read color words. Secondly, children need to rapidly name the color of ink for coloured rectangles whereby four colors are used. Thirdly, children need to inhibit their natural response to read a word and instead state the color of the ink in which the word was printed. The reliability and construct validity of the Stroop Test were determined as sufficient by the COTAN, the criterion validity was not assessed. The outcome measures were the Stroop color naming score (first task) and the Stroop word naming score (second task).

**Output speed** of participants was assessed prior to and after the training by registration of the performance of participating children on the Go-trials of the Stop-Signal task (Logan, 1997, Morein-Zamir et al., 2008). In the Stop-Signal task the child has to respond to a picture of an arrow appearing on the computer screen as fast as possible by pressing a target key corresponding with the direction of the arrow. When the arrow turns red however, the participant has to inhibit this response. In 25%
of the trials, the arrow turns red. The timing or delay between the go and stop signals will be adjusted by the computer program for every child, using a tracking mechanism. At first the stop signal (the arrow turning red) will appear after 300 ms. Following a successful stop, the delay will be lengthened by 50 ms, making the next stop trial harder to perform. After a failed stop, the delay will be shortened by 50 ms, making the next stop trial easier. Outcome measure for output speed was the mean reaction time on the correctly responded go-trials of participating children on the Stop-Signal task, averaging these scores.

**Intra-subject variability.** To assess intra-subject variability the go-trials of the Stop-Signal task whereby the children correctly responded were used, and the outcome measures were the mean reaction time on these go-trials, the standard deviation of the reaction time and the coefficient of variation (being the standard deviation of the reaction time divided by the mean reaction time) related to these go-trials (De Zeeuw et al., 2008).

**ADHD symptoms and executive functioning** on working memory, cognitive flexibility and inhibition were assessed by means of the following instruments:

- **the Pediatric Quality of Life Inventory Parents** (PedsQL, Pediatrische Vragenlijst Kwaliteit van Leven, Varni, Seid & Kurtin, 2001; Bastiaansen, Koot, Bongers, Varni & Verhulst, 2004). This questionnaire consists of 23 items, scored on a five-point Likert ('never a problem' to 'almost always a problem') and is filled in by parents. The questionnaire is divided in four subscales: physical, emotional, social, and school functioning. Examples of items are: ‘To what extent has your child in the past 2 weeks experienced problems with’: ‘running, be scared or afraid’, ‘getting along with other children’, ‘not being able to do the things other children can’ and ‘difficulty in paying attention in class’. The PedsQL was translated into Dutch using a two-way translation procedure. Internal consistency reliability was found sufficient ($\alpha = .84$ child self-report, $\alpha = .87$ parent proxy-report) and criterion-related validity, convergent and discriminant validity were demonstrated (Bastiaansen et al., 2004). There is no COTAN evaluation available. The outcome measure was the total score and the scores on the four subscales.

- **the Home Situation Questionnaire** (HSQ, Du Paul & Barkley, 1992) is designed to assess the severity and cross-situational pervasiveness of attention problems (e.g., mealtimes, in the car). It consists of 16 items, yes/no answers, and yes answers are scored on a nine-point Likert scale (‘a little serious problem’ to ‘a very serious problem’) and is filled in by parents. Examples of items are: ‘Does the

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3 Notably, processing speed measures frequently include the WISC-IV-I Coding test. The Coding subtest requires children over 8 years to copy symbols associated with numbers based on a key. The task is time-limited with bonuses for speed. It appears however that this subtest not only measures Processing Speed, but also working memory and inhibition. It seems therefore a less suitable measure for determination of processing speed in children with ADHD who are known to have working memory and inhibition deficits, compared to tests like the Trail Making Test and the Stroop test.
situation cause any problems?: ‘when the child plays with other children’, ‘when you are paying a visit to someone’, ‘when the child has to carry out chores’. The English version of the HSQ was found to have adequate levels of internal consistency, test–retest reliability and construct validity (Du Paul & Barkley, 1992). There is no COTAN evaluation available. The outcome measure was the total score.

- the ADHD scales of both the parent and teacher version of the Disruptive Behavior Disorder Rating Scale (DBDRS, Vragenlijst voor Gedragsproblemen bij Kinderen, Pelham, Gnagy, Greenslade, & Milich, 1992; Dutch translation Oosterlaan, Scheres, Antrop, Roeyers, & Sergeant, 2000). The DBDRS assesses DSM-IV disruptive behavior disorder symptoms in children between 6 and 12 years old. It consists of 42 items and four subscales: inattention (nine items), hyperactivity/impulsivity (nine items), oppositional defiant (eight items) and conduct disorder (16 items). The items are scored on a four-point Likert scale, (‘Not at all’, - ‘Very much’). Examples of items are: ‘Has difficulty to maintain attention on task or game’, ‘Fidgets with hand or feet, has trouble to sit still’, ‘Has difficulty to wait on his or her turn’, ‘Is often angry or outraged’, ‘Physically abuses other people’. The reliability of the DBDRS was assessed as sufficient, and the construct validity was assessed as good by the COTAN. The outcome measures were the score on three subscales: inattention, hyperactivity/impulsivity and oppositional defiant behavior, of both the parent and teacher version.

- the Behavior Rating Inventory of Executive Functioning, (BRIEF; Gioia, Isquith, Gy & Kenworthy, 2000, Dutch translation Smidts & Huizinga, 2009). The BRIEF assesses executive functions in children 5–18 years old and contains eight subscales: Inhibition, Flexibility, Emotional Control, Initiate, Working Memory, Plan/Organize, Organization of Materials and Monitoring. The items are scored on a three-point Likert scale (‘Never’, ‘Sometimes’ and ‘Often’). Examples of items are: ‘Has difficulty to limit his/her own behavior’, ‘Gets upset when plans are changed’ and ‘Only remembers the first or last thing when asked to do three things’. The assessment by the COTAN has not been finished yet, but internal consistency and test-retest reliability were considered good (Smidts & Huizinga, 2009). For this purpose of this study, outcome measures were the scores on the subscales Inhibition, Flexibility and Working Memory.

**Procedure**

The study was approved by the Research Ethics Commission of the University of Amsterdam and consisted of six contact moments with the participant and/or his parents.

Parents were initially contacted by their mental-health care center. When they were interested in participating, they received further information about the study and its procedure. Subject to meeting the requirements of the DBDRS for parents and teachers, the child and his parents were invited to the first intake session. This intake session took place at the mental-health care institution. In this session, the parents were interviewed with the PDISC-IV, whilst two subtests of the WISC-III (vocabulary and block design) as a provisional IQ measure were administered to the
child. If the child met the inclusion criteria of the PDISC-IV and the WISC-III, he and his parents were invited to a second intake session and they were invited to take part in the training. In this second intake session parents were asked to fill in the DBDRS, the HSQ, the PedsQL and the BRIEF. The Stop-Signal task, Stroop and the Trail Making Test were administered to the child. Subsequently, parents and children collected the training computer and rewards (e.g., medals to keep children motivated) at the University of Amsterdam and received further detailed training instructions. Children were randomly assigned to one of the three aforementioned training conditions and individual training levels were set (based on their performances on the Stop-Signal task, the Trail Making Test and one other measure, not discussed in the study as administered during the first intake session).

After this session the child started with the training at home. The children performed the training for a duration of 45 minutes each session (10 minutes for each Executive Function training task and 15 minutes for exploring the game world). The total number of training sessions was 25. Children were asked to play the game four to five times a week for a period of five to six successive weeks, until they finished all sessions. They earned small rewards for each completed session (i.e., adhesive stickers with game characters, medallions). The training was embedded in the computer game. During the training period, the parents and child were contacted weekly to see how the training was progressing. The parents and the child were helped to deal with training related problems and encouraged to continue with the training. Finally, it was checked and noted if there were any changes in medication use or in other forms of treatment.

After the training a post-measurement session took place at the mental-health care institution. Parents filled in questionnaires (the DBDRS, the HSQ, the PedsQL and the BRIEF). The Stop-Signal task, Stroop and the Trail Making Test were again administered to the child. Also, the teacher filled in the online DBDRS again.

**Results**

**Analyses**

Baseline differences between the Full-adaptive and Combination and Non-adaptive condition were tested using chi-square tests for categorical and Repeated Measures Analyses of Variance (ANOVAs) for continuous variables. There were no significant differences between the groups with respect to gender, age, use of methylphenidate, number of hours per week of playing computer games (see Table 1). Also, there were no significant differences between treatment conditions on any of the baseline variables, ADHD symptoms and executive functioning as measured by the BRIEF (see Table 2). When carrying out the assumption checks, it turned out that the several dependent variables, were not normally distributed and skewed. Log transformations did not solve this problem. As the distribution was not flattened, which would increase a type-II error, and the sample was larger than 30, violation of this assumption should not influence the reliability of the results and there are
no non-parametric test alternatives available for repeated measures ANOVAs in any instance (Field, 2009).

**Table 2**

*Means and standard deviations of ADHD symptoms as reported by parents and teachers and three executive functions as reported by parents*

<table>
<thead>
<tr>
<th>Measure</th>
<th>Group</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Full-adaptive training</td>
</tr>
<tr>
<td></td>
<td>(n = 21)</td>
</tr>
<tr>
<td></td>
<td>(M)</td>
</tr>
<tr>
<td><strong>DBDRS parent</strong></td>
<td></td>
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<tr>
<td>Inattention</td>
<td>18.05</td>
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<tr>
<td>Hyperactivity/Impulsivity</td>
<td>17.05</td>
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<td>ODD</td>
<td>10.38</td>
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<tr>
<td>CD</td>
<td>1.29</td>
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<tr>
<td><strong>DBDRS teacher</strong></td>
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<tr>
<td>Inattention</td>
<td>14.19</td>
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<tr>
<td>Hyperactivity/Impulsivity</td>
<td>13.62</td>
</tr>
<tr>
<td>ODD</td>
<td>8.24</td>
</tr>
<tr>
<td>CD</td>
<td>1.38</td>
</tr>
<tr>
<td><strong>BRIEF parent</strong></td>
<td></td>
</tr>
<tr>
<td>Inhibition</td>
<td>69.5</td>
</tr>
<tr>
<td>Flexibility</td>
<td>57.9</td>
</tr>
<tr>
<td>WM</td>
<td>69.45</td>
</tr>
</tbody>
</table>

*Note:* ADHD = attention-deficit/hyperactivity disorder; BRIEF parent = Behavior Rating Inventory of Executive Function, parent reported; CD = conduct disorder; DBDRS = Disruptive Behavior Disorder Rating Scale, last two weeks; ODD = oppositional defiant disorder; WM = Working Memory

In order to test whether participants showed significant different training outcomes, factorial ANOVAs were carried out, with time (pre-training, post-training) as within-subjects variable, and type of condition (Full-adaptive, Combination and Non-adaptive) as between-subjects variable. An alpha level of .05 was used for all statistical tests, except for the analyses related to the Stop-Signal Task. For this task, the alpha level was Bonferroni corrected, and an alpha level of .0167 was used to test statistical significance. Effect sizes (Perrson’s correlation coefficient r) are reported for all analyses.
Following Cohen’s guidelines, effect sizes of 0.10 and above were considered small, effect sizes of 0.30 and above were considered medium, and effect sizes of 0.50 and above were considered large. In Table 3 the group means and results of the analyses concerning the interaction effects are set out.
Table 3

Scores at Pretest, Posttest for children in the Full-adaptive training condition (Full adaptive) and the Combination and Non-adaptive training condition (Combination/Non-adaptive)

<table>
<thead>
<tr>
<th></th>
<th>Pretest</th>
<th>Posttest</th>
<th>Time</th>
<th>Effect</th>
<th>Time by group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Full adaptive (n=20)</td>
<td>Combination/Non-adaptive (n=41)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adaptive (n=20)</td>
<td>Combination/Non-adaptive (n=41)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>10.79</td>
<td>10.80</td>
<td>12.12</td>
<td>12.41</td>
<td>(F(1,56) = 29.61^*)</td>
</tr>
<tr>
<td>SE</td>
<td>.54</td>
<td>.41</td>
<td>.48</td>
<td>.36</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(F(1,56) = .26)</td>
<td>(F(1,56) = .00)</td>
<td>(.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroop</td>
<td>72.83</td>
<td>80.34</td>
<td>70.07</td>
<td>75.03</td>
<td>(F(1,59) = 5.77^*)</td>
</tr>
<tr>
<td></td>
<td>4.36</td>
<td>3.16</td>
<td>4.31</td>
<td>3.12</td>
<td></td>
</tr>
<tr>
<td>Stop:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RT</td>
<td>536.38</td>
<td>540.56</td>
<td>456.32</td>
<td>479.88</td>
<td>(F(1,57) = 48.60^{**})</td>
</tr>
<tr>
<td></td>
<td>17.45</td>
<td>14.50</td>
<td>13.87</td>
<td>9.93</td>
<td></td>
</tr>
<tr>
<td>SD of RT</td>
<td>182.91</td>
<td>197.82</td>
<td>165.34</td>
<td>170.83</td>
<td>(F(1,57) = 11.46^{**})</td>
</tr>
<tr>
<td></td>
<td>9.42</td>
<td>6.75</td>
<td>7.78</td>
<td>5.58</td>
<td></td>
</tr>
<tr>
<td>CV</td>
<td>.34</td>
<td>.37</td>
<td>.37</td>
<td>.36</td>
<td>(F(1,57) = .53)</td>
</tr>
<tr>
<td></td>
<td>.013</td>
<td>.009</td>
<td>.016</td>
<td>.012</td>
<td>(F(1,57) = 2.28)</td>
</tr>
</tbody>
</table>

Note: * = significant at level p < .05, ** = significant at level p <.001; a = participants were omitted or data was missing, as discussed below; df = degrees of freedom; r = Pearson’s correlation coefficient; Stop = Stop-Signal Task, CV = Coefficient of Variation (SD/MRT = Standard Deviation of mean Reaction Time in seconds divided by Mean Reaction Time in seconds); SD of mean RT= Standard Deviation of mean Reaction Time measured in seconds, Stroop = average of color and word naming condition scores of the Stroop Test; TMT = average of Number Sequencing and Letter Sequencing condition scores of the Trail Making Test.
**Processing Speed**

Motor speed (Trail Making Test):

The repeated measures ANOVA revealed a significant main effect of time on the Trail Making Test (average of number and letter sequencing task normscores), $F(1, 56) = 29.61, p < .001, r = .58$, and no significant main effect of condition, $F(1, 56) = .48, p = .492, r = .001$. There was no interaction effect between condition and time, $F(1, 56) = .26, p = .613, r = .004$. As illustrated by Figure 1 below, the type of training did not influence the motor speed of the participants, which is not in line with the hypothesis. Two children had problems with the alphabet and one child had problems during the test; the data of these children were not included in the data analysis.

![Figure 1](image.png)

*Figure 1, Average of Number and Letter Sequencing Tasks normscores of Trail Making Test for Full-adaptive versus Combination and Non-adaptive condition at pre (T1) and post-test (T2).*

Naming speed (Stroop task):

The repeated measures ANOVA revealed a significant main effect for time on the Stroop task, $F(1, 59) = 5.77, p = .020, r = .30$, and no significant effect of condition, $F(1, 59) = 1.50, p = .225, r = .16$. There was no significant interaction effect between condition and time, $F(1, 59) = .58, p = .451, r = .10$. As illustrated by Figure 2 below, the type of training did not influence the naming speed, this was not in line with the hypothesis.
Figure 2. Average of color and word tasks of Stroop Task for Full-adaptive versus Combination and Non-adaptive condition at pre- (T1) and posttest (T2).

Output speed (Stop-Signal task):

Applied to the reaction time, the repeated measures ANOVA revealed a significant main effect for time on the Stop-Signal task, $F(1,57) = 48.60, p < .001, r = .68$, and no significant effect for condition, $F(1,57) = .70, p = .406, r = .11$. There was no significant interaction effect between condition and time, $F(1,57) = .92, p = .341, r = .02$. As illustrated by Figure 3 below, the type of training did not influence the output speed of the participants, this was not in line with the hypothesis. The data of two children on the Stop-Signal task were missing, and they were not included in the data analysis.
Figure 3. Mean Reaction Time in seconds of go-trials of Stop-Signal Task for Full-adaptive versus Combination and Non-adaptive condition at pre- (T1) and posttest (T2).

Intra-subject variability:

Applied to the reaction time, now for the purpose of determining intra-subject variability, the repeated measures ANOVA revealed a significant main effect for time on the Stop-Signal task, $F(1,57) = 48.60, p < .001, r = .68$, and no significant effect for condition, $F(1,57) = .70, p = .406, r = .11$. There was no significant interaction effect between condition and time, $F(1,57) = .92, p = .341, r = .02$. As illustrated by Figure 3 above, the type of training did not influence the output speed of the participants, this was not in line with the hypothesis. The data of two children on the Stop-Signal task were missing, and they were not included in the data analysis.

Applied to the standard deviation of the reaction time, the repeated measures ANOVA revealed a significant main effect for time, $F(1,57) = 11.46, p < .001, r = .41$, and no significant main effect for condition, $F(1,57) = 1.49, p = .227, r = .16$. As illustrated by Figure 4 below, there was no significant interaction effect between condition and time, $F(1,57) = .513, p = .477, r = .09$. 
Figure 4. Mean of Standard Deviation of Reaction Time in seconds of go-trials of Stop-Signal Task for Full-adaptive versus Combination and Non-adaptive condition at pre- (T1) and posttest (T2).

Applied to the standard deviation of the reaction time divided by the mean reaction time, the repeated measures ANOVA revealed no significant main effect for time, $F(1,57) = .53, p = .471, r = .10$, nor for condition, $F(1,57) = .13, p = .772, r = .05$. There was no significant interaction effect between condition and time, $F(1,57) = 2.28, p = .137, r = .04$, see Figure 5 below.

The type of training did not influence the intra subject variability, this was not in line with the hypothesis.
Figure 5. Mean of the Coefficient of Variation (=Standard Deviation of Reaction Time in seconds divided by mean Reaction Time) of go-trials of Stop-Signal Task for Full-adaptive versus Combination and non-adaptive condition at pre- (T1) and posttest (T2).

The first hypothesis, participants belonging to the Full-adaptive training condition will show a significant increase of one or more processing speed measures (graphomotor speed, naming speed, and/or output speed) compared to participants in the Combination and Non-adaptive training condition, was thus rejected. The second hypothesis, participants belonging to the Full-adaptive training condition will show a significant decrease of intra-subject variability compared to participants in the Combination and Non-adaptive training condition, was rejected as well. The third hypothesis (if Hypothesis 1 is confirmed, a negative association can be established between an increase of one or more processing speed measures, and a decrease of parent and/or teacher reported ADHD symptoms) and the fourth hypothesis (if Hypothesis 2 is confirmed, a positive association can be established between a decrease of intra-subject variability, and a decrease of parent and/or teacher reported ADHD symptoms) were not tested, since the first two hypotheses were rejected.

Explorative analyses
Processing Speed and Intra-Individual Variability
Exploratively, further analyses were carried out, combining the Full-adaptive training condition (training working memory, cognitive flexibility and response inhibition) with the Combination training condition (training cognitive flexibility and response inhibition), and comparing this against the low-
training condition. On the outcome measures for processing speed (motor speed, i.e. the average of Number and Letter Sequencing Tasks normscores, naming speed (i.e. , Average of color and word tasks of Stroop Task) and output speed (i.e. mean Reaction Time on Go-trials of Stop-Signal Task)) and intra-individual variability (mean reaction time, standard deviation of reaction time and coefficient of variation of Stop-Signal Task), Factorial Repeated Measures ANOVAs did not reveal any significant results for a main effect of condition or the interaction effects between time and condition. Subsequently, explorative analyses were carried out on inhibition and cognitive flexibility, to assess whether these were improved by the training.

Inhibition

A repeated measures ANOVA with the SSRT as a dependent variable revealed a significant main effect for time, \( F(1,57) = 4.85, p = .032, r = .28 \) and no significant effect for condition, \( F(1,57) = 1.28, p = .26, r = .15 \). There was a significant interaction effect of time and condition, \( F(1,57) = 5.44, p = .023, r = .30 \). As illustrated by Figure 6, the SSRT decreased across time more for the participants in the adaptive training condition (\( M = 197.90, SE = 10.40 \) to \( M = 159.73, SE = 7.66 \)), compared to the participants in the non-adaptive training condition (\( M = 193.25, SE = 14.53 \) to \( M = 194.34, SE = 10.70 \)). The change in SSRT was not associated with a change across time of the PedsQL, the HSQ, nor with the DBDRS.
Figure 6. Estimated means of Stop-Signal Reaction Time scores for Full-adaptive condition and Combination-training condition versus the Non-adaptive condition on the Stop-Signal Task at pre- (T1) and posttest (T2).

Cognitive flexibility

A repeated measures ANOVA with the Trail Making Test Number-Switching score as outcome variable, did not reveal any significant main or interaction effects. Similarly, a repeated measures ANOVA with the Stroop Interference score (the outcome variable that measures cognitive flexibility) as dependent variable, revealed no significant main effect for condition, nor a significant interaction effect between time and condition.

Discussion

In this study it was tested for the first time whether a computerized training with game elements, aimed at improving working memory, cognitive flexibility and inhibition (Braingame Brian), was also beneficial to processing speed and intra-subject variability. Processing speed was broken down into three parts: (grapho)motor speed, naming speed and output speed. It turned out that processing speed was not increased, and neither was intra-subject variability decreased, for children that had been trained adaptively on working memory, cognitive flexibility and inhibition, compared to children who were either, adaptively trained on solely cognitive flexibility and inhibition, or non-adaptively trained. Exploratively, it was assessed whether all children that were adaptively trained (on working memory, cognitive flexibility and inhibition or cognitive flexibility and inhibition) improved on processing speed or intra-individual variability, compared to non-adaptively trained children. This was not the case. Subsequently, this was also assessed for cognitive flexibility measures (the Trail Making Test Number-Switching score and the Stroop Interference score), but no differences between the groups could be established. Finally, this was assessed for the inhibition measure, the Stop Signal Task, as well. Here an improvement of the inhibition capacities of the children with a medium effect was found on the Stop Signal Reaction Time (SSRT), indicating that the children who had been adaptively trained, had improved their response inhibition capacities.

How can these findings be interpreted? First, it suggest that the computerized training that was targeted at improving working memory, cognitive flexibility and inhibition, just did that and did not improve other, related, cognitive functions such as processing speed and intra-individual variability. As inhibition, which was intended to be trained, did seem to increase, there is some evidence pointing in this direction. This is in line with some other studies that suggest no transfer to unpracticed skills and narrow transfer of practiced skills (Bergman Nutley et al., 2011). However, based on the notion that processing speed and intra-individual variability have been both associated with working memory (Jacobson et al., 2011; Klein et al., 2006), this is unexpected. Although it has
not been assessed in this study, it is likely that the working memory training is effective based upon research by Klingberg et al. (2005) and Prins et al. (2011).

A further explanation could be that not all children have the same amount of deficits in processing speed, intra-subject variability and inhibition (Solanto et al., 2001). It is also possible that some cognitive functions require more practice than others to be successfully altered. There is some insight on neuropsychological correlates of processing speed and intra-individual variability, but no clear overview has been established yet, and further research is necessary in this area (Bush, Valera & Seidman, 2005; Karalunas & Huang-Pollock, 2012).

Finally, it could be the case that processing speed and intra-individual variability had already been influenced by daily computer games practice. The children that participated in this study spent on average eight to nine hours per week playing computer games on their (game) computer, telephone etc. During the intake procedure parents frequently mentioned that the training raised their attention, specifically because the computer game element appealed to their game playing child. It might be that their practice with other games resulted in a ceiling effect. This is supported by a finding that playing video games optimized executive control skills after 15 hours of training (Strobach, Frensch & Schubert, 2012) and the study mentioned in the introduction section wherein action games improved processing speed (Dye et al., 2009).

It is noted that most measures of processing speed and intra-subject variability in this study showed improvement over time, which suggests a task training effect. It could also suggest that processing speed and intra-subject variability were trained in the computerized game, both in the adaptive as in the non-adaptive condition. In all three types of training the children are trained to respond in a prescribed manner. In the non-adaptive form there is no progressive difficulty, but some practice element is present. In a design with a non-practicing control group this could be checked.

The fact that children progressed on inhibition was contrary to the findings of Thorell et al. (2009). In their inhibition training with tasks based upon the Go/No go, Stop-Signal and the Flanker task (a task requiring responding to the middle arrow in a row of five), significant improvement was made on the Go/No go and Flanker task, but not on the Stop-Signal task.

Several limitations of this study should be mentioned. With respect to intra-variability, it is a known problem that the effects in the Stop-Signal task are very small, which makes it difficult to detect significant differences (Epstein et al., 2011). Ex-Gaussian analyses that determine the mean and standard deviation of the exponential tail of the distribution are better able to detect differences (Epstein et al., 2011; Karalunas, Huang-Pollock & Nigg, 2012). Further, other research (also) utilized a simple Go-No go task (Epstein et al, 2011; Klein et al, 2006). Instead in this study, conforming to other studies such as Gòmez-Guerrero et al (2011), the correct go-trials of the Stop-Signal task were used for the analyses, which limited the number of trials that were available and possibly also caused
for some distraction of the children, anticipating the stop signal. The conditions of the Trail Making Test that are used in this study deviate slightly from the older form of the test that was used in previous research.

In this study the long-term effect of the training, measured after three months, was not assessed for practical reasons. In line with Klingberg et al. (2005), who found training effects on verbal and spatial working memory remained for 90% after three months, it is expected that the results would be approximately be comparable. However, a longer period for assessing the effects seems more suitable for measurement of long term effects (e.g., Holmes, Gathercole, Place, Dunning, Hilton & Elliott, 2009, using a period of six months). Even then it remains the question whether with schoolchildren, wherein so many developments may take place at school or at home, it is possible to validly measure real long term effects.

In this study only children diagnosed with ADHD-combined type (ADHD-C) were included, and the sample did not contain a group diagnosed with ADHD-predominantly inattentive type (ADHD-I) or the ADHD-hyperactive-impulsive subtype. With respect to intra-individual variability either minimal differences were found between children with ADHD-C and ADHD-I (Epstein et al., 2011), or, in case of differences, children diagnosed with ADHD-C displayed the largest variability compared to children diagnosed with ADHD-I (De Zeeuw et al., 2008). It is therefore proposed that including a group diagnosed with ADHD-I would not have altered the results of this study.

As problems with processing speed and intra-subject variability have been demonstrated in children with ADHD, associations with ADHD-symptoms have been demonstrated, and computer assisted training programmes have been found effective with other executive functions, it seems worthwhile to develop and test tasks to improve these cognitive functions. This could be done by adding specific processing speed training tasks such as simple push button-tasks or computerized rapid recognition tasks, as described in Takeuchi and Kawashima (2012), to a computerized training as Braingame Brian or to use various existing computer games as done by Mackey, Hill, Stone and Bunge (2011). Further investigation should be carried out to verify whether this is indeed beneficial to output speed and intra-subject variability, and whether this would correspond with changes at a behavioral level. As traditional reporting measures for parents and teachers are not always consistent (e.g. Klingberg et al., 2005), the use of observational systems like the Restricted Academic Situations Task could also be used in effectiveness research (Green, et al, 2012). Motor speed tasks could presumably better trained by paper and pencil tasks or by physiotherapeutic exercises. For all these (new) tasks, it is necessary to look closely to motivation and rewards, as motivation plays an important role in children with ADHD (Dovis, van der Oord, Wiers & Prins, 2013; Ruthledge, van den Bos, McClure, Schweitzer, 2012). Further developments in this field are important, considering for instance that children with the most severe executive function problems benefit the most of the
training programmes (Diamond & Lee, 2011). Although achieving the same level of competence as typically developing children is perhaps illusory for children with ADHD (Dovis et al., 2013), it remains important to make the developmental gap as small as possible (Diamond & Lee). Further, cognitive treatments are one of the most promising non-pharmaceutical treatments, addressing concerns about presence of side-effects and absence of long-term effects of medication (Ruthledge et al., 2012).
References


