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Original Article

Executive Function Computerized Training in Very Preterm-Born Children: A Pilot Study

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Abstract

Objective: Attention problems are one of the most pronounced and documented consequences of very preterm birth (gestational age ≤32 weeks). However, up to now, there is no research published on suitable interventions at school age aimed to overcome these problems. Research in this population did show that executive functions (EFs) are strongly associated with inattention. BrainGame Brian is a newly developed computerized training, in which, in 25 training sessions, the core EFs, including working memory, impulse control, and cognitive flexibility, are trained. This pilot study aimed to examine the feasibility of studying BrainGame Brian in very preterm-born children with attention problems.
Design: Pilot feasibility intervention study with one baseline and one follow-up assessment.
Materials and Methods: Feasibility was measured by the participation rate, dropout rate, and user experiences with regard to effort, training characteristics, and recommendation to others. From a larger cohort study, 15 very preterm-born children at age 10 years with parent-reported attention problems on the Child Behavior Checklist/6–18 years were invited to participate in this pilot study. BrainGame Brian was performed for a period of 6 weeks. Training outcome measures included visual working memory, impulse control, cognitive flexibility, speed variability, and parent-rated attention, for which pre- and post-training differences were examined at the group level by the Wilcoxon signed-rank test as well as for each individual child separately by the reliable change index.
Results: Twelve of 15 children and their parents agreed to participate and 11 children successfully completed BrainGame Brian in the 6-week period. Parents were positive about training characteristics and lack of interference with schooling, but scored the effort as high. We found clinically significant changes in visual working memory and speed variability in post-training assessments.
Conclusion: BrainGame Brian is a feasible intervention for very preterm-born children with attention problems.

Keywords: Attention, Premature, Neurocognitive, Feasibility

Introduction

Attention problems are one of the most pronounced and documented consequences of very preterm birth (gestational age ≤32 weeks).[1] These attention problems include 0.6 standard deviation (SD) higher problem scores on attention questionnaires[1] as well as a 2.6-fold increase in attention-deficit/hyperactivity disorder [AD(H)D] diagnoses compared with same-aged controls.[2] Studies that investigated which components of attention are specifically impaired after very preterm birth report poor focused attention and high distractibility, as well as frequent lapses of attention.[3,4]

Recent studies have shown that impaired executive function (EF) is strongly related to very preterm-born children's inattention.[4–6] EF refers to inter-related neurocognitive processes, such as working memory, impulse control, and mental flexibility, which control thought and behavior.[7] Poor EF after very preterm birth has been related to disruptions of white matter

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circuits connecting frontal, striatal, and thalamic regions.[8–10] Studies have presented behavioral and neurophysiological evidence that by improving EF, attention problems can be reduced.[11] In particular, for children with AD(H)D, training EFs using adaptive computerized training programs yielded a significant reduction of attention problems.[11–13]

Results on efficacy of such EF computerized training programs in AD(H)D cannot be simply extrapolated to very preterm-born children since the profile of attention deficits differs from that typically observed in term-born children with AD(H)D.[14] Lapses of attention are more pronounced in very preterm-born children than impulse control problems that are more pronounced in attention-deficit/hyperactivity disorder in the general population.[4,14] In addition, attention problems in very preterm-born children are usually part of a set of multidomain problems that result from damage to white matter circuits across the brain.[15] There is some evidence that very preterm-born children may also benefit from computerized EF training.[16,17] However, in the two studies[16,17] conducted on this issue, also unimpaired very preterm children were trained and a training program was used that only focuses on working memory. Recent meta-analyses showed that because of this focus on a single domain, these training programs may yield limited effects.[18] Whether it is possible to improve very preterm children's attention problems by computerized training of a broad set of EFs has not been examined yet.

Recently, we developed a computerized EF training program named BrainGame Brian.[19] In contrast to other EF training programs[11] that solely train working memory, BrainGame Brian focuses on working memory, impulse control, and mental flexibility,[19] and training blocks are built into a game. Computerized neurocognitive training challenges children's motivation because of its time-consuming and intensive nature. Adding game elements to the training is a child-friendly solution to better maintain the child's attention and enhance motivation.[20] BrainGame Brian's main focus is on training of EFs. Game elements have been added to increase a child's motivation, but are not dominant during the training. In BrainGame Brian, the three primary EFs, working memory, cognitive flexibility, and inhibition, are all trained in each training session. In other available training programs (please see for a review, e.g., Rapport et al.[21]), solely one EF is trained or training of EFs is not adaptive or not gamified, thereby not challenging the child and lowering the potential to have an effect. BrainGame Brian is distinctive from commercially available EF or attention training software since it is underpinned by well-validated neurocognitive paradigms. Specific for our study, BrainGame Brian was advantageous since it is in Dutch, which makes it more easily accessible and understandable than other cognitive training programs that use languages not mastered by the participants in our study. BrainGame Brian has been shown to produce beneficial near and far transfer effects on EFs in three randomized trials in children with autism,[22] AD(H)D,[23] and obesity,[24] but has not been studied in very preterm children, in whom EF problems are commonly found.[1,25]

Before a future, randomized controlled trial to examine the efficacy of improving attention difficulties in very preterm-born children by BrainGame Brian, we conducted a pilot study. The aim of this pilot study was to examine the feasibility of BrainGame Brian in very preterm-born children with attention problems. To study feasibility, we evaluated the participation and completion rates, training procedures, and parental and children's opinions about the effort and training characteristics. Training outcome measures included parental ratings of the child's attention as well as neurocognitive measures of EFs and attention. Parental ratings of attention were included as proximal indices of a child's attention before and after the training. Since parents, however, are not blinded and are actively involved in motivating and monitoring of their child, we also administered neurocognitive measures of EFs and attention since these are not biased by expectations.[18,26] Pre- and post-training differences were calculated at the group level as well as at an individual level.[27]

Methods

Participants

Children born with a gestational age ≤ 30 weeks or birth weight ≤ 1000 g in 2002–2004 and admitted to the Neonatal Intensive Care Unit of the Academic Medical Centre, Amsterdam, The Netherlands, and who participated in our prospective cohort study[15,28,29] were sent a Child Behavior Checklist/6–18 years (CBCL/6–18 years) at age 10 years. Children with an attention scale score of 55 or higher on the CBCL/6–18 years were eligible for this pilot study. The cutoff score of 55 was chosen because this score has been shown to efficiently discriminate children at risk for a clinical attention deficit diagnosis.[30] Fifteen parents and children were invited to participate in this pilot study.

The Institutional Review Board of the Amsterdam Medical Centre, Amsterdam, The Netherlands, approved the study protocol. Informed consent was obtained from parents of all participating children.

BrainGame Brian

BrainGame Brian is a computer program suitable for children aged 8–12 years, which can be downloaded at www.gamingandtraining.nl Readers interested in the background of the development of BrainGame Brian are requested to see publications by De Vries et al.,[22] Dovis et al.,[20,23] and Verbeken et al.[24] Parents and children who participated in this pilot study received a username and password to install the training on their home computer. Installation and the first training session were performed with a member of the research team. BrainGame Brian is designed with an internal monitoring feature that provides the research team insight and data about a child's actual performance, progress, and pitfalls.

In BrainGame Brian, the child acts as inventor Brian, the main character in a virtual world. To fabricate inventions and thereby improve a virtual world, EF tasks have to be performed. The 25 sessions (45 minutes each) include 2 training blocks with 3 EF tasks (working memory, impulse control, and flexibility) in each block. The difficulty level of the EF tasks is adapted to the child's level of performance. The first training task is always a working memory task (used for drawing a blueprint of the invention). The second and third tasks, a cognitive flexibility task and an impulse control task, are presented in changing order (used for sorting building materials and electrically charging the invention). Parents and children were instructed to perform all 25 sessions within 6 weeks.

In the working task, five different types of training are involved. These five types are arranged according to difficulty level and include (1) training of short-term memory, (2) training of short-term memory, updating, and keeping information online, (3) training of short-term memory and manipulation/updating, (4) training of short-term memory and keeping information online during a delay, and (5) training of short-term memory and keeping information online and manipulation of information/updating. Each level is trained for 5 of the 25 sessions. The child is presented with a 4×4 grid of equally sized squares that randomly light up in a sequence. The goal for the child is to reproduce this sequence by clicking on the squares as requested in each of the five levels of training. In the first level, the child has to reproduce the sequence forward. In the second level, the child has to reproduce the sequence backward. In the third level, squares light up in two different colors; the child has to reproduce the sequence of squares in one color first, followed by reproduction of the sequence of the other color. In the fourth level, the child has to reproduce the presented sequence forward while keeping in mind which bars surrounding the squares have lit up. In the fifth level, task demands of the third and fourth levels have to be combined.

The impulse control task trains impulse control by reducing the reaction time the child needs to stop his or her response after a stop signal is presented. The task is visually designed as a factory, in which the child has to respond as quickly and accurately as possible to an arrow on a machine (go trials). A target stimulus lights up on the left or right side of the computer screen, indicating that the child has to press the left button or the right button. The child has to respond within a time interval. This interval is presented to the child by a bar turning green between 700 and 1000 milliseconds. Before 700 milliseconds and after 1000 milliseconds, the bar turns red, indicating that the child should not respond. In the stop trials, a stop signal is given (a tone and the stimulus turns red) after presentation of the stimulus. The stop signal is presented 50 milliseconds later if the child successfully inhibited the previous stop trial and is presented 50 milliseconds earlier if the child failed the previous stop trial. Twenty-five percent of the trials are stop trials and 75% are go trials.

The cognitive flexibility training task trains switching ability by reducing the time that the child needs to switch between concepts. The task is also designed as a factory. Circles and triangles painted in blue or red are presented to the child who is asked to sort these objects either according to color or according to shape. A switch is induced by feedback given. As in the impulse control task, the child has a time interval in which his or her response has to be given. A cue is presented 600 milliseconds after presentation of the stimulus whereafter the child has 1300 milliseconds to respond. The interval is shortened by 50 milliseconds after two correct responses and is lengthened by 50 milliseconds after two incorrect responses. Twenty-five percent of the trials are switch trials and 75% of trials are nonswitch trials.

Figure 1 shows screenshots of the working memory training task, impulse control training task, and cognitive flexibility training task, respectively.

Feasibility

Feasibility was studied by evaluating the participation rate and dropout rate and by an interview that assessed experiences of parents and children simultaneously regarding effort, that is, duration and frequency of training sessions, school absence due to the training, the training itself, that is, whether it was tiring/boring and enjoyable/motivating, and recommendation to others. Answers of the evaluation interview were categorized as being positive (+1), negative (−1), or neutral (0) by two independent research psychologists. The inter-rated agreement between the research psychologists was 90%.

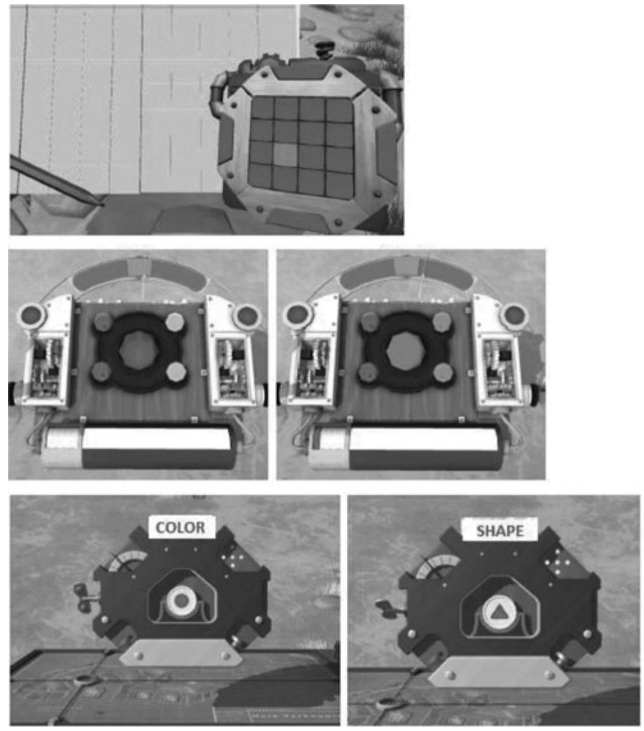

FIG. 1. Screenshots of the working memory training task, impulse control training task, and cognitive flexibility training task, respectively.

Training outcome measures

Training outcome measures included parental ratings of the child's attention as well as neurocognitive measures of EFs and attention. Parents rated their child's inattention at home on the inattention scale of the Dutch version of the Disruptive Behavior Disorders (DBD) rating scale.[31,32]

Neurocognitive measures administered appealed to the three trained EFs, which include visual working memory, impulse control, and cognitive flexibility. Speed variability, which reflects lapses of attention, and parent ratings of attention problems were also assessed.

Visual working memory was measured using an adapted version of a task developed by Nutley et al.[4,33] In this task, children have to reproduce sequences of circles appearing in a 4×4 grid on a touchscreen forward and backward. The difficulty level was increased during the course of the task by increasing span and by manipulation of stimulus position. The dependent variable used was the total span backward.

Impulse control was measured using the stop signal task.[25,34] In this task, children have to respond as quickly and accurately as possible to a go stimulus (cartoon airplane presented for 1000 milliseconds) and to inhibit their response if a stop stimulus (cross presented for 50 milliseconds) is presented. The dependent variable used was the stop signal reaction time,[34] which is an estimate of the time a child needs to stop his or her response defined by mean reaction time (MRT) minus the mean delay.

Cognitive flexibility was assessed with a stimulus response compatibility task.[25] In this task, target stimuli (arrows) differed in color, with a green arrow indicating that the child has to respond with a spatially compatible response (left arrow mapping onto the left response button) and a red arrow indicating that the child has to respond with a spatially incompatible response (left arrow mapping onto the right response button). The dependent variable used was the switching time defined as the MRT on incompatible trials minus MRT on compatible trials.

Speed variability, reflecting lapses of attention, was assessed using the intrasubject variability (ISV) of speed coefficient, which was calculated by dividing the SD of MRT on stop signal task correct go trials by the MRT.[35]

Procedure

All participating very preterm-born children underwent, 2 weeks before the start of BrainGame Brian and 2 weeks after finishing the last training session, a baseline and a post-training assessment, respectively. All tests were administered at the Emma Children's Hospital, Academic Medical Centre, Amsterdam, The Netherlands, and performed by trained research psychologists using standardized instructions. At baseline assessment, information about technical computer requirements and training characteristics was given to the participating children and their parents. The evaluation interview was administered during the post-training assessment.

Statistical analyses

Because of the small number of participants, the data cannot be assumed to be normally distributed, and the nonparametric Wilcoxon signed-rank test was used to examine whether changes between pre- and post-training neurocognitive scores and parent ratings of the child's inattention were significant. We also calculated reliable change indices for each child individually to assess whether changes within each child were clinically significant and not subject to measurement error. The reliable change index (RCI) is defined by the difference between the child's baseline and post-training scores divided by the standard error of the difference.[27] The RCI is to be interpreted as a z-score. An RCI of ≥ 1.65 was considered as clinically significant.[27]

P-values of <0.05 were considered as statistically significant. Analyses were performed using IBM SPSS Statistics 21.0 (IBM Corp., Armonk, NY).

Results

Participants

Of the 15 very preterm children and their parents approached for this study, 12 (80%) agreed to participate. Reasons for nonparticipation were the computerized character of the training that did not appeal to parents ($n=2$) and parents being satisfied with their child's functioning ($n=1$). There were no significant differences between the total cohort ($n=92$) and the children who participated in this pilot study in gestational age ($P=0.92$), birth weight ($P=0.64$), and parental educational level ($P=0.24$). Table 1 presents the participant characteristics.

Table 1. Characteristics of the Sample ($N=12$)

Gender: boys, n (%)	6 (50)
Age[a] (years), mean (SD), range	10.2 (0.5), 9.5–11.0
Gestational age (weeks), mean (SD), range	28.7 (1.5), 26.0–31.4
Birth weight (g), mean (SD), range	1020 (256), 640–1340
Parent educational level (high:medium:low), n (%)	8:2:2 (62:15:15)
IQ,[b] mean (SD), range	105.6 (11.2), 83–123
Child Behavior Checklist/6–18 years Attention Scale T-score, mean (SD)	67.8 (6.2)
AD(H)D medication, n (%)	3 (27)

[a]Calendar age; not corrected for prematurity.
[b]IQ was measured with the Vocabulary and Block Design subtests of the Wechsler Intelligence Scale for Children-III-NL.
AD(H)D, attention-deficit/hyperactivity disorder; IQ, intelligence quotient; SD, standard deviation.

Feasibility

Eleven of the 12 participating children successfully completed BrainGame Brian. One child dropped out because of motivational reasons. While 7/11 parents evaluated the effort to complete BrainGame Brian as high, 8/11 parents were positive about BrainGame Brian, in that it is enjoyable and motivating. All parents also were positive about the fact that performing BrainGame Brian did not interfere with their children's schooling and homework; 6/11 parents would recommend BrainGame Brian to others.

Results for training outcome measures

In Table 2, means and SDs of pre- and post-training test scores are shown for the 11 participating children as a group. Wilcoxon signed-rank tests indicated that at the group level, post-training scores for visual working memory and speed variability were significantly higher than the pretraining scores ($z=-2{,}41$, $P=0.02$; $z=-2.71$, $P=0.007$, respectively).

Table 2. Means and Standard Deviations of the Training Outcome Measures

		Pre-training		*Post-training*	
Measures	N	*Mean*	*SD*	*Mean*	*SD*
Working memory					
Backward span	11	3.9	0.4	5.0	0.4
Impulse control					
Stop signal reaction time, milliseconds	11	273.2	16.3	246.8	15.3
Cognitive flexibility					
Switching time, milliseconds	11	27.5	19.2	75.3	36.1
Speed					
Intrasubject variability	10	0.2	0.0	0.2	0.0
DBD questionnaire					
Inattention score	11	14.3	0.3	14.0	0.4

DBD, Disruptive Behavior Disorders.

Table 3. Reliable Change Index per Child per Measure

	Children										
Measures	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*
Working memory											
Backward span	5.00	1.67	0.00	1.67	5.00	0.00	3.33	0.00	0.00	1.67	1.67
Impulse control											
Stop signal reaction time	1.12	0.84	0.17	0.62	1.72	–0.31	1.01	–0.26	–0.68	–1.89	2.18
Cognitive flexibility											
Switching time	–0.38	–0.59	–1.19	–5.35	–0.05	0.64	–0.21	0.06	0.24	–1.10	0.82
Speed											
Intrasubject variability	2.50	1.67	5.83	8.33	5.83	7.50	5.00	8.33	5.00	–0.83	–1.67
DBD parent-rated											
Inattention scale	0.83	–0.83	–0.83	0.00	0.83	1.67	2.50	0.83	–0.83	–0.83	–0.83

For the parent ratings of inattention and the measures of inhibition and cognitive flexibility, changes between pre-and post-training scores were not significant ($P\text{s} > 0.25$).

Table 3 presents the RCI per child per measure. Seven of the 11 children had a positive reliable change (RCI ≥ 1.65) for visual working memory and 9 of the 11 children for speed variability. One child had a negative reliable change (RCI = –1.67) for speed variability.

Discussion

This pilot study showed that studying the efficacy of BrainGame Brian in improving attention problems in very preterm-born children is feasible. A large majority of approached parents were willing to participate. Only one child dropped out during the training period. The intense training schedule and high frequency of training sessions were an effort for parents and children, but majority of them nevertheless considered BrainGame Brian as enjoyable and motivating. At least half of the parents would recommend the training to others.

With respect to training outcomes, we found, in this small sample, clinically relevant changes after training for working memory and speed. Reliable change indices were calculated in addition to analyses at the group level because of the small sample size and because these are designed to determine whether changes are larger than expected from measurement errors. Because of our lack of a placebo intervention as a control group, we cannot, however, conclude whether observed changes were due to the training, practice effects, or any other circumstances, such as lack of blinding of test administrators.[27]

Working memory and attentional control are related in a bidirectional manner not only in children but also in very preterm-born children.[4,6,36,37] Working memory training helps children to become more attentive in their daily activities.[18] Although as stated above firm conclusions cannot be made given our study design, the variability of responses in our pilot study decreased significantly after BrainGame Brian. Such a decrease in attentional lapses may have facilitated the storage capacity of the working memory system.[38] In addition, the reverse is true, children with well-developed working memory skills are less ready to get off a task and are better able to focus and maintain attention than children with poor working memory skills. Astle and colleagues recently showed using magneto-encephalography that connective brain pathways were strengthened in response to computer working memory training.[39]

Parents did not report better attentional skills at home after the BrainGame Brian training. This finding was somewhat unexpected since parents were not blinded and were actively involved in motivating and monitoring of their child. Such a design, usually, yields the biased result that parents rate their children's attention better after training than at baseline. Placebo training, as opposed to the real intervention, would have enabled us to unravel this issue. We also did not include other measures of EFs or attention, or academic achievement, to examine far transfer effects of the training. This was not done because the primary aim was to assess the feasibility of BrainGame Brian in the very preterm population. Our sample was selected on the basis of parent ratings of inattention and turned out to have an estimated intelligence quotient (IQ) range of 83–123. The sample was too small to relate treatment success to IQ, but this can, however, be addressed in the randomized placebo-controlled trial that was initiated recently.

Conclusion

In conclusion, BrainGame Brian is a feasible intervention for school-aged very preterm-born children with attention problems. Clinically significant changes were observed for the areas of working memory and speed variability, although the lack of a control group and the small sample size attenuate any conclusions based on these promising results.

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Author Disclosure Statement

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