Epilepsy & Behavior 100 (2019) 106521

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Positive outcome of visuospatial deficit rehabilitation in children with epilepsy using computer-based FORAMENRehab program

Marianne Saard [a,*,1], Madis Bachmann [b,1], Kirsi Sepp [c], Lisanna Pertens [d], Kai Kornet [a], Liina Reinart [d,e], Christen Kööp [a], Anneli Kolk [a,d]

[a] University of Tartu, Faculty of Medicine, Tartu, Estonia
[b] Cognitive Psychology Laboratory, Tallinn, Estonia
[c] University of Tartu, Faculty of Social Sciences, Institute of Education, Tartu, Estonia
[d] Tartu University Hospital Children's Clinic, Department of Pediatrics and Neurology, Tartu, Estonia
[e] University of Tartu, Faculty of Social Sciences, Institute of Psychology, Tartu, Estonia

ARTICLE INFO

Article history:
Received 12 May 2019
Revised 24 August 2019
Accepted 24 August 2019
Available online 29 September 2019

Keywords:
Children
Epilepsy
Visuospatial deficits
Cognitive rehabilitation in children
Computer-based rehabilitation
Visuospatial rehabilitation

ABSTRACT

Children with epilepsy often show deficits in attention and visuospatial functions. Still, very few systematically controlled evidence-based pediatric neurorehabilitation methods exist. The aim was to assess the effectiveness of a computer-based rehabilitation program for visuospatial deficit remediation in children with epilepsy.
Fifty-eight children aged 8–12 years participated: 17 children with epilepsy diagnosis in intervention group, 22 patients in waiting-list control group, and 19 healthy age equivalent controls. The intervention group received guided visuospatial functions rehabilitation with FORAMENRehab software twice a week for a 5-week period. Baseline assessments were carried out before and immediately after the intervention period, and as follow-up 1.31 years later. Intervention group showed positive immediate rehabilitation effect in 3 out of 4 visuospatial components: visual organization, visual attention, and visuospatial perception. A long-term rehabilitation effect in the study group was observed in all 4 of the trained components. Also, a positive generalized effect was confirmed by the parents' and children's qualitative feedback with some of the improved skills transferring to children's everyday life. One hundred percent compliance further confirmed the children's motivation to participate and the effectiveness of FORAMENRehab for pediatric neurorehabilitation.

1. Introduction

1.1. Visuospatial functions

The ability of the visual system to process spatial relations between objects or parts of an object is imperative in processing of visual information [1]. Visuospatial functions are an important element of intellectual ability and involve multiple processes [2,3]. Various components of visuospatial functions have been recognized in research (see Table 1).

In the current study, the concept of visuospatial functions includes visual recognition, visual organization, visual attention, and visuospatial perception (see Table 4 for details of tasks).

There are various reasons why the research of visuospatial functions in children is important. Skills as visual-motor abilities, visuospatial organization, visual discrimination, and the ability to integrate perceptual and motor processes are required to learn to count or perform arithmetic calculations [8]. Moreover, visuospatial skills have been found to predict achievements in mathematics [8,9]. Children have presented a strong relationship between academic performance in math, reading, writing, and visual-motor integration, visual perception, hand control, and overall motor proficiency [10]. Visuospatial skills and visuomotor integration were significantly correlated with number line estimation tasks, which have a significant relationship with mathematical achievement [11]. A longitudinal study showed that spatial skills predict achievement in all the science, technology, engineering, and mathematics (STEM) domains [65].

1.2. Visuospatial deficits in children with epilepsy

Deficits in visuospatial functions are often present in children with epilepsy, which has an estimated prevalence rate of 0.5–1% in the general population [12]. The incidence rate of childhood epilepsy in Estonia is up to 86.3/100000 [13].

Children with focal epilepsy (FE) with left side focus had deficits in categorization, verbal long-term memory, and visuospatial analysis [14]. Children with epilepsy, with and without migraine, have presented deficits in visual–spatial analysis and visual attention [15]. In addition, children with newly diagnosed FE, prior to medication, develop deficits in attention,

* Corresponding author at: Lunini 6, Tartu 51014, Estonia.
E-mail address: mariannesaard@gmail.com (M. Saard).
[1] These authors contributed equally.

https://doi.org/10.1016/j.yebeh.2019.106521
1525-5050/

Table 1
Components of visuospatial functions [3–7].

Components	Abilities involved
1. Spatial perception	Determine spatial relationships
2. Mental rotation	Rotate two or three dimensional figures
3. Spatial visualization	Manipulate spatially presented information
4. Visual recognition	Recognize faces/objects/categories
5. Visual organization	See object/picture as sum of parts
6. Visual attention	Process certain areas of visual field
7. Visuospatial perception	Represent physical environment in mind
8. Visual-motor abilities	Integrate perceptual and motor processes

short-term memory, and visuoperceptual functions [16]. Also, deficits in spatial perception and visual-constructive skills in children with Rolandic epilepsy have been reported [17]. Other cognitive deficits in children with epilepsy include impairments in attention [16,18–20], executive functions (EF) [18,20], and social perception [20,21], which may remain stable up to 6 years without evidence of progressive worsening or recovery [19]. It is necessary to rehabilitate the deficits early on, because these increase the clinical burden and impair the patients' quality of life [22].

1.3. Visuospatial deficit rehabilitation

One of the most suitable treatment methods would be cognitive rehabilitation (CR), which refers to systematic therapeutic approaches to improve information processing [23]. The aims of CR are to compensate impaired functions by incorporating individual and context-related demand [22], generalization to other cognitive functions [22], and improving the everyday functioning of the patient [24].

Various studies have concluded that CR has been effective for remediation of visuospatial functions, attention, memory, social skills, and EF after different acquired brain injury (ABI) diagnosis [25–28]. As for epilepsy, various studies have found positive outcome of CR in adult patients [29–33], but for now, relatively few studies have focused on CR in children [33]. Cognitive rehabilitation for deficits in visuospatial functions in adults or children with epilepsy has not been previously carried out.

Modern computer-based CR includes many advantages over traditional paper-and-pencil approaches. These include being personalized, and the difficulties of tasks could be set according to the patients' performance [34]. Computer-based CR has been previously found to be effective in children with various diagnoses, including epilepsy [35–38]. Furthermore, a positive outcome in remediation of attention impairment in children with epilepsy was revealed with our previous studies using the Attention module of the ForamenRehab program. Children's sustained and complex attention components showed significant long-term improvements [35,36]. Also, technology-based trainings are motivating for children with ABI, thus ensuring good compliance [39].

A comprehensive review of the use of computerized treatment for attention and EF has revealed improvements following interventions [40]. Less research could be found on the methods of computer-based CR for visuospatial deficit. Some studies have shown positive effects of programs in patients with stroke [41]. More often, computer-based CR has been used to treat patients with visual neglect [25,42,43].

Many authors have expressed the need for more randomized controlled studies to assess the effectiveness of pediatric CR [12,35,40,44–48]. Taken together, there is a need for modern CR techniques for children with ABI that are individualized, computer-based, therapist-guided, and motivating.

The main aim of the current study was to assess the effectiveness of the Visuospatial module of the computer-based ForamenRehab program in visuospatial deficit rehabilitation in children with epilepsy aged 8–12 years.

The specific aims were as follows:

1. to assess the rehabilitation effect on specific visuospatial components in 8- to 12-year-old children with epilepsy using the ForamenRehab program;
2. to create an individual-based intervention design with optimal difficulty levels and duration of rehabilitation;
3. to measure the long-term rehabilitation effect with follow-up assessments; and
4. to evaluate the generalized effect and provide clinical implications for computer-based visuospatial deficits rehabilitation in children with epilepsy.

2. Methods

2.1. Participants

2.1.1. Study group

The study was conducted in the Department of Neurology and Neurorehabilitation in the Children's Clinic of Tartu University Hospital. Seventeen children aged 8–12 years (M = 9.95, standard deviation (SD)

Table 2
Study group characteristics.

Pt	Age (years)	Sex	Age at FE onset (years)	Duration of FE (years)	Specification (EEG/MRI)	AED medication
P1	10.75	M	8.75	2.00	EEG: focal epilepsy with spike–wave activity CT sin/MRI: N	LEV
P2	11.08	F	10.08	1.00	EEG: focal epilepsy with spike–wave activity T˙C sin/MRI: N	OXC
P3	10.33	F	8.75	1.58	EEG: focal epilepsy with spike–wave activity TC sin/MRI: N	VPA
P4	9.67	M	9.50	0.17[a]	EEG: focal epilepsy to bilateral spike–wave activity, C region/MRI: N	OXC
P5	10.50	M	6.58	3.92	EEG: focal epilepsy with spike–wave activity CT dex/MRI: N	VPA
P6	10.42	F	7.42	3.00	EEG: focal epilepsy with spike–wave activity in sleep T3/MRI: arachnoid cyst (5 mm) in temporal lobe dex	CBZ
P7	9.33	M	6.42	2.91	EEG: focal epilepsy to bilateral spike–wave activity S > T/MRI: N	VPA
P8	11.33	M	7.92	3.41	EEG: focal epilepsy with spike–wave activity CT dex/MRI: N	OXC
P9	9.75	M	6.50	3.25	EEG: focal epilepsy with spike–wave activity in T region/MRI: N	VPA
P10	8.42	M	6.58	1.84	EEG: focal epilepsy with spike–wave activity CT sin/MRI: arachnoid cyst in F–P lobe dex	VPA
P11	11.58	F	11.50	0.08[a]	EEG: focal epilepsy with spike–wave activity in sleep CT sin/MRI: hippocampal malrotation sin	OXC
P12	8.17	M	8.08	0.09[a]	EEG: focal epilepsy to bilateral spike–wave activity, O region/MRI: multifocal white matter and left mesial temporal lobe lesions	OXC
P13	11.08	M	10.92	0.16[a]	EEG: focal epilepsy with spike–wave activity in sleep T > C/MRI: N	OXC
P14	9.33	M	6.67	2.66	EEG: focal epilepsy with spike–wave activity PT > T, slow bioelectrical activity dex/MRI: N	VPA
P15	11.25	F	6.17	5.08	EEG: focal epilepsy with spike–wave activity sin/MRI: N	CBZ, LEV
P16	8.08	M	6.33	1.75	EEG: focal epilepsy with spike–wave activity in PC sin/MRI: N	VPA
P17	8.08	M	5.25	2.83	EEG: focal epilepsy with spike–wave activity in sleep FT sin/MRI: N	VPA

Pt — patient, M — male, F — female, EEG — electroencephalography, MRI — magnetic resonance imaging, N — normal finding, O — occipital, T — temporal, C — central, FT — frontotemporal, CT — centrotemporal, PT — parietotemporal, sin — left, dex — right, AED —antiepileptic drug, OXC — oxcarbazepine, VPA — valproate, LEV — levetiracetam, CBZ — carbamazepine.
[a] Newly diagnosed epilepsy.

= 1.212) with FE and previously diagnosed visuospatial deficits participated in the intervention (see Table 2). Patients in the intervention group received individual trainings with the Visuospatial module of the FORAMENRehab software. The age group was chosen for the reason that the children were required to have sufficient reading and mathematical skills. Also, to keep the children's age range and developmental level comparable.

The following inclusion criteria were used:

1) Previously diagnosed FE (ICD-10 G40.0, G40.1, G40.2), confirmed by child neurologist;
2) Mild to moderate visuospatial impairment confirmed by a certified clinical neuropsychologist on the basis of neuropsychological assessment (included visuospatial subtests from the A Developmental NEuroPSYchological Assessment (NEPSY) test battery);
3) Fluency in Estonian (first spoken language);
4) Age between 8 and 12 years; and
5) Parental written consent and child's verbal agreement for participation.

Exclusion criteria included other documented diseases involving the central nervous system (e.g., stroke, tumors, encephalitis, cerebral palsy), psychiatric comorbidity (e.g., attention deficit hyperactivity disorder (ADHD), anxiety disorder, mental retardation (ICD-10 F70-F79)), and treatment with any psychotropic medication other than antiepileptic drugs during the rehabilitation period. Altogether, the characteristics of the study group included 4 newly diagnosed patients, maximum duration of epilepsy was 5.08 years, 1 patient underwent polytherapy and 16 were on monotherapy. Seizures in all patients were well controlled by antiepileptic drugs.

The study was approved by the Research Ethics Committee of the University of Tartu. The parental informed consent was received prior to the intervention process.

2.1.2. Control groups

Two control groups were included in the study –— waiting-list control group and healthy children's control group.

1. The waiting-list group consisted of 22 children (M = 10.29 years, SD = 1.85) with visuospatial impairment and FE diagnosis, including 15 boys and 7 girls (Table 3). The inclusion and exclusion criteria were the same as for the study group. The two groups did not differ significantly regarding the age at epilepsy onset.

All patients attended regular schools and did not receive special education. Also, they were at first presented with an opportunity to participate in the rehabilitation. Frequently, children from outside Tartu City could not regularly attend the intervention because of difficulties with transportation and were assigned to the waiting-list group.

2. To assess the baseline levels of visuospatial tasks and obtain the results of healthy population, the healthy children's control group was composed of 19 healthy age equivalent children aged 8–12 years (11 boys and 8 girls). The children were recruited from an ordinary school in Tartu and attended 2nd to 5th grades. Children with any known neurologic or psychiatric diagnosis were excluded. The three groups did not differ significantly in terms of age and sex.

2.2. Rehabilitation software

The FORAMENRehab Cognitive Rehabilitation Software® (FORAMENRehab) was used. FORAMENRehab is a tool for CR that was developed in the year 2000 by Koskinen and Sarajuuri [24] in Finland. It was first adapted to Estonian children in our pilot study [36]. In a present study, the Visuospatial module was implemented. Different components of visuospatial function were assessed and trained. The tasks were divided into four categories or components (see Table 4). The exercises were playful and mostly took up to 5 min to complete. The menu structure, toolbar, and icons of the software were illustrative; each task had a clear written instruction as well as a model animation. The parameters of each task were adjustable. The results were given both in numerical tables and graphs. Several outcomes were recorded for every application: solving and/or reaction time, number of correct responses and subcategories of mistakes (omission errors, premature responses,

Table 3
Waiting-list control group characteristics.

Pt	Age (years)	Sex	Age at FE onset (years)	Duration of FE (years)	Specification (EEG/MRI)	AED medication
P1	8.92	M	6.25	2.67	EEG: focal epilepsy with spike–wave activity C > TP sin/MRI: N	Diazepam
P2	9.58	M	9.58	0[a]	EEG: focal epilepsy with spike–wave activity TC sin/MRI: N	LEV
P3	12.99	F	8.58	4.84	EEG: focal epilepsy with spike–wave activity C sin > dex/MRI: bilateral mesial temporal sclerosis (dex > sin)	CBZ
P4	12.50	M	7.00	5.5	EEG: slow bioelectrical activity/MRI: cavernoma in frontal lobe sin	CLZ
P5	12.42	M	12.42	0[a]	EEG: focal epilepsy with spike–wave activity in sleep, C region/MRI: N	VPA
P6	9.17	M	6.75	2.42	EEG: focal epilepsy with spike–wave activity C3/MRI: enlargement of insular cisterns	OXC
P7	12.25	M	7.17	5.08	EEG: no interictal epileptical activity/MRI: N	CBZ
P8	8.83	F	8.83	0[a]	EEG: focal epilepsy with spike–wave activity TO sin/MRI: N	VPA
P9	9.08	M	7.25	1.83	EEG: focal epilepsy with spike–wave activity in sleep O > T/MRI: N	LEV, VPA
P10	8.75	F	8.75	0[a]	EEG: focal epilepsy with spike–wave activity CT sin > dex/MRI: N	VPA
P11	9.50	M	8.25	1.25	EEG: focal epilepsy with spike–wave activity PC > T sin, in sleep bilateral sin > dex/MRI: N	VPA
P12	8.42	M	8.42	0[a]	EEG: focal epilepsy with spike–wave activity CT dex/MRI: N	VPA
P13	7.83	F	7.62	0.21[a]	EEG: focal epilepsy to bilateral spike–wave activity T > 0/MRI: N	OXC
P14	12.08	M	12.06	0.02[a]	EEG: focal epilepsy with spike–wave activity T > P, in sleep T > P, FT/MRI: N	VPA
P15	11.83	M	9.97	1.86	EEG: focal epilepsy with spike–wave activity OT dex > sin/MRI: N	OXC
P16	8.75	F	6.39	2.36	EEG: focal epilepsy to bilateral spike–wave activity CT sin/MRI: N	VPA
P17	12.89	F	7.08	5.81	EEG: focal epilepsy with spike–wave activity CT bilateral dex > sin/MRI: polymicrogyria in parietal lobe dex	VPA
P18	11.12	M	9.51	1.61	EEG: focal epilepsy to bilateral spike–wave activity sin > dex/MRI: N	VPA
P19	12.00	F	11.24	0.76[a]	EEG: focal epilepsy to bilateral spike–wave activity dex > sin/MRI: N	VPA
P20	8.90	M	9.62	0[a]	EEG: focal epilepsy with spike–wave activity T sin/MRI: N	OXC
P21	8.00	M	6.92	1.08	EEG: focal epilepsy with spike–wave activity C dex/MRI: N	VPA
P22	12.81	M	1.75	11.06	EEG: focal epilepsy with spike–wave activity F dex/MRI: N	LEV, VPA

Pt — patient, M — male, F — female, EEG — electroencephalography, MRI — magnetic resonance imaging, N — normal finding, O — occipital, T — temporal, C — central, FT — frontotemporal, CT — centrotemporal, PT — parietotemporal, sin — left, dex — right, AED — antiepileptic drug, OXC — oxcarbazepine, VPA — valproate, LEV — levetiracetam, CBZ — carbamazepine, CLZ — clonazepam.

[a] Newly diagnosed epilepsy.

Table 4
Tasks in four visuospatial components and affected functions.

Task	Description	Affected functions
Visual recognition		
Circle Following	To hold the gaze and maintain the direction of movement of objects	Eye–hand coordination
Line Orientation Judgment	To determine and replicate the inclination of a line inside a circle	Spatial awareness; executive functions
Visual organization		
Geometric Pattern Recognition	Fragment of an object inside a window shown; patient required to recognize and pick the object from a set of different objects	Visual attention, visual memory, visual construction
Visual attention		
Spatial Attention	Dot appears briefly in a matrix; patient required to recognize which row and column the dot appeared in	Reaction time, visual attention, visual field
Visuospatial perception		
Cubes	To count all cubes shown in an image, including the ones not directly visible	Mathematical and visual construction abilities
Construction	To use small blocks of different shapes to recreate a shown pattern	Visual construction, attention, executive functions
Maze	To move through a maze as quickly as possible and make as little navigation errors and collisions (wrong moves) as possible	Visual–spatial relations, planning skills

commission errors, and total number of errors — sum of omission and commission errors).

2.3. Rehabilitation procedure

The rehabilitation of the patients took place over 6 weeks twice a week. Altogether, 13 meetings were conducted: the first baseline assessment, 10 active trainings, and the second assessment with baseline tasks (primary outcome). The final follow-up assessment with baseline tasks as the secondary outcome was carried out 1.31 years (SD = 0.40) after the training period (see Fig. 1). Ten children from the study group and 9 children from the waiting-list group participated in the follow-up.

Trainings occurred in an outpatient setting in the Tartu University Hospital Children's Clinic. The duration for each individual session was about 40 min, and all visuospatial components were covered for each session. At the first meeting, the intervention methods and goals were introduced to the children. Thereafter, the first performance with the baseline tasks was conducted and the training sessions started on the second meeting. The therapist introduced the tasks, and motivated and guided the child individually, in order to help him/her to better cope with complicated situations. Besides training specific skills, the children also learned planning, following a strict protocol, and applying new strategies. This generalized effect of the training process on everyday behavior was assessed in both patient groups with Behavior Rating Inventory of Executive Function (BRIEF). Also, a parents' questionnaire (created for this study) was used, which involved questions about the child's visual performance, behavioral manifestations of concentration, general school-performance, and the rehabilitation. As parents filled the questionnaires at different time points, the change before and after the training could be measured.

2.4. Rehabilitation design

The procedure protocol for the intervention was created. In the baseline assessment, all four components of visuospatial function were tested (see Table 4). For trainings, different tasks under the same components were used, divided into three difficulty levels: easy, medium, and difficult.

The development on difficulty levels was individual-based. If the child made no mistakes on the task, he/she advanced to the next level. If the child's response was incorrect, he/she had to perform the same task level at least 80–90% correctly (depending on the task) for 3 consecutive sessions until advancing to the next level. Thus, the training procedure followed a strict protocol but at the same time considered the children's current capabilities.

2.5. Assessment of the control groups

The patients in the waiting-list control group participated in all three assessments with baseline tasks. During the five-week period between the first and the second assessment, the waiting-list group received no intervention. One-time baseline assessments of the healthy control children were performed.

2.6. Data analysis

Statistical data analysis was performed with the R version 3.1.2. For some of the figures, the Statistical Analysis Software (SAS) data analysis package 9.2 was used. The Kolmogorov–Smirnov test was used for the assessment of normality. Statistical comparisons between non-normally distributed continuous variables were performed with Wilcoxon–Mann–Whitney test. Differences at baseline assessments between study group patients, waiting-list control patients, and healthy

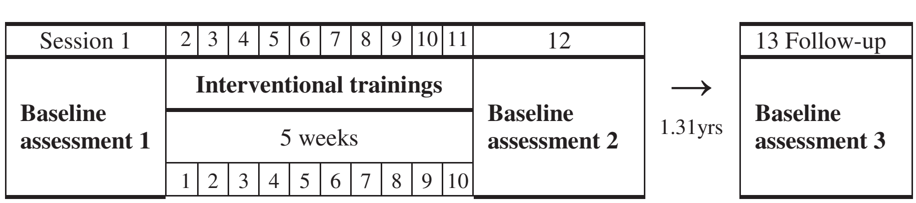

Fig. 1. Design of the intervention.

Table 5
Comparison of results on the first baseline assessment between training group, waiting-list group and healthy controls.

First baseline assessment (B1) Tasks	Training group (T)	Waiting-list group (W)	Healthy controls (H)	T vs W vs H	T vs H	W vs H	T vs W
	Median (lower and upper quartiles)[a]	Median (lower and upper quartiles)[a]	Median (lower and upper quartiles)[a]	*p*	*p*	*p*	*p*
Visual recognition							
Circle Following (%)	30.81 (21.69...57.44)	28.89 (16.18...39.85)	71.58 (50.10…93.07)	0.1061	0.1626	0.0470	0.3958
Line Orientation Judgment (°)	5.83 (4.75...16.92)	8.92 (6.13...21.58)	2.92 (1.67...3.75)	<0.0001	0.0003**	<0.0001**	0.2999
Visual organization							
Geometric Pattern Recognition (nr)	14.35 (13.34...15.36)*	14.60 (13.63...15.57)*	14.06 (12.90...15.22)*	0.7865	0.8473	0.5050	0.6741
Geometric Pattern Recognition (%)	61.54 (53.33…71.43)	64.10 (51.67...73.61)	73.33 (71.43...81.82)	0.0140	0.0101**	0.0134**	0.9029
Visual attention							
Spatial Attention (%)	80.00(50.00...90.00)	70.00 (67.50...81.67)	95.00 (90.00...100.00)	<0.0001	0.0003**	<0.0001**	0.8055
Spatial Attention (s)[b]	8.50 (7.00...14.86)	8.82 (6.74...11.97)	6.15 (5.04...7.47)	0.0015	0.0034**	0.0010**	0.7722
Visuospatial perception							
Cubes (%)	20.00 (0.00...40.00)	20.00 (0.00...50.00)	80.00 (40.00...80.00)	0.0006	0.0007**	0.0011**	0.6585
Cubes (s)[b]	37.43 (30.04...44.81)*	38.67 (31.46...42.87)	48.15 (25.56...61.40)	0.6087	0.4694	0.3370	0.9393
Construction (%)	66.67 (33.33...100.00)	66.67 (33.33...100.00)	100.00 (100.00...100.00)	0.0007	0.0005**	0.0008**	0.6382
Construction (s)[b]	243.17 (148.31...311.24)	221.93 (160.25...321.04)	103.16 (74.00...198.50)	0.0027	0.0030**	0.0030**	0.9878
Maze (nr)	6.00 (4.00...9.00)	6.00 (2.50...16.50)	1.00 (1.00...3.00)	0.0002	0.0002**	0.0008**	0.8306
Maze (%)	32.87 (27.62...36.96)	24.62 (11.98...38.48)	8.53 (0.45...12.11)	<0.0001	<0.0001**	0.0008**	0.2171
Maze (s)[b]	54.83 (46.16...84.60)	63.18 (56.87...75.81)	42.46 (37.37…51.35)	0.0004	0.0047**	0.0001**	0.4929

[a] Median (lower 25%ile and upper 75%ile).
[b] Seconds.
* Mean (95% confidence interval (CI)).
** We controlled the FDR to be lower than 5% by using linear step-up procedure [49] for multiple t-tests.

controls were tested with Kruskal–Wallis test and pairwise comparison with Wilcoxon–Mann–Whitney test. Repeated measures ANOVA was conducted to assess whether longitudinal changes in groups were significantly different. The Wilcoxon signed-rank test was used to compare the baseline performance to primary (immediate intervention effect) and secondary outcomes within study group and waiting-list control group. Continuous outcome variables were log-transformed when necessary to satisfy model assumptions. We controlled the false discovery rate (FDR) to be lower than 5% by using linear step-up procedure [49] for multiple t-tests. Only *p*-values that are below the adjusted FDR significance threshold are therefore significant and marked as such (***) in the tables.

3. Results

3.1. Baseline characteristics of visuospatial components in children with FE and healthy controls

3.1.1. Visual recognition

Significant differences between the training group, waiting-list group, and healthy controls existed in the Line Orientation Judgment task ($p < 0.0001$). Both the training and the waiting-list group performed significantly worse compared with the healthy controls ($p = 0.0003$ and $p < 0.0001$, respectively) (see Table 5 and Fig. 1 in Supplementary material).

3.1.2. Visual organization

No significant differences between the three groups in the number of solved exercises in the Geometric Pattern Recognition task were revealed. Still, there were significant differences between the groups in the percentage of correct responses ($p = 0.0140$). Pairwise comparisons showed differences between healthy children and the training group ($p = 0.0101$) and the waiting-list group ($p = 0.0134$) (Table 5 and Fig. 2 in Sup. material).

3.1.3. Visual attention

Statistically significant differences between the three groups in the percentage of correct responses were seen ($p < 0.0001$). Both patient groups performed significantly worse compared with the healthy children ($p = 0.0003$ and $p < 0.0001$). Significant differences also existed in reaction time ($p = 0.0015$) as healthy children were significantly

Table 6
Mean difficulty levels achieved by the end of intervention and average number of completed sessions before moving from 1st to 2nd difficulty level.

Visuospatial component	Nr of task	Mean level	Mean sessions
		Mean (95% CI)	Mean (95% CI)
Visual recognition	1	1.56 (1.29...1.84)*	4.69 (3.3...6.07)
	2	1.81 (1.33...2.3)	5.06 (3.99...6.14)
	3	2.19 (1.74...2.63)*	2.38 (1.35...3.4)
Visual organization	1	3.25 (2.84...3.66)	1.62 (1.08...2.17)
	2	3.12 (2.55...3.7)	1.5 (1.02...1.98)
Visual attention	1	3.31 (2.89...3.74)	2 (1.25...2.75)
Visuospatial perception	1	1.38 (0.99...1.76)	6.25 (5.35...7.15)
	2	2.12 (1.7...2.55)*	3 (2.13...3.87)
	3	3.31 (2.81...3.82)	1.88 (1.26...2.49)
	4	1.62 (1.3...1.95)*	3.94 (3.04...4.84)
	5	1.25 (1.01...1.49)	3.94 (2.98...4.9)

* Tasks with a maximum difficulty level of 3.

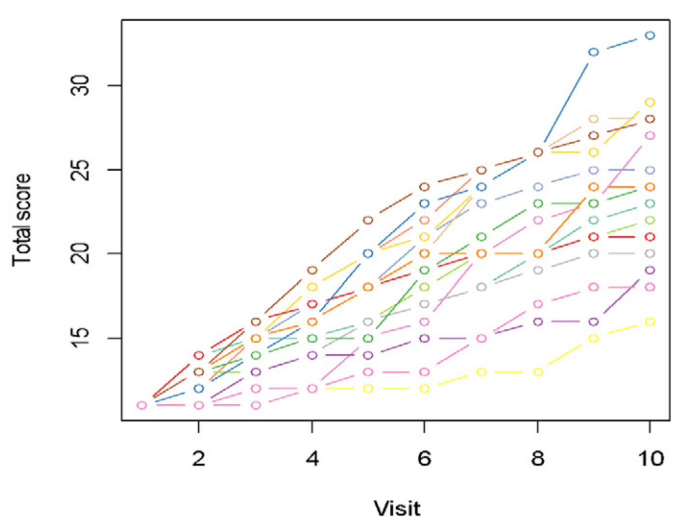

Fig. 2. Each patients' individual progress trajectories for 10 training sessions (total score achieved per visit).

quicker compared with the training ($p = 0.0034$) and the waiting-list control groups ($p = 0.0010$) (Table 5 and Figs. 3–4 in Sup. material).

3.1.4. Visuospatial perception

Significant differences were seen between the three groups in the percentage of correct responses in the Cubes task ($p = 0.0006$). The healthy controls gave significantly more correct responses compared with the training ($p = 0.0007$) and the waiting-list groups ($p = 0.0011$). Also, in the Construction task, the healthy controls gave significantly more correct responses ($p = 0.0005$, $p = 0.0008$) and were significantly quicker ($p = 0.0030$, $p = 0.0030$) (Table 5 and Figs. 5–7 in Sup. material). In the Maze task, differences between the three groups were found in the number of wrong moves ($p = 0.0002$) and the percentage of navigation errors ($p < 0.0001$). Both patient groups performed significantly worse compared with the healthy controls ($p < 0.0001$ and $p = 0.0008$). The healthy children also performed better in solving time ($p = 0.0047$, $p = 0.0001$) (Table 5 and Figs. 8–9 in Sup. material).

3.2. Patients' individual improvement during the rehabilitation

Individual improvement in the training group during the rehabilitation was measured by the mean difficulty levels of tasks achieved by the end of the intervention in each visuospatial component (see Table 6). Furthermore, the progress on reaching higher difficulty levels was also examined by measuring the average number of sessions needed to move from the first to the second difficulty level (Table 6). The tasks had three to four difficulty levels. Slower rehabilitation effect occurred in two visual recognition and two visuospatial perception tasks.

All children in the training group showed positive individual advancement. Still, all the patients had individually different progress trajectories (see Fig. 2). The difference between the difficulty levels reached at the end of the intervention was up to two times higher for children with the quickest improvements compared with the slowest children.

Table 7
Comparison of performances on three assessments within training group and waiting-list group.

Tasks of FORAMENREHAB Visuospatial module		Training group	Waiting-list group	B1 vs B2	B1 vs B3	B2 vs B3
		Mean (95% CI)[b]	Mean (95% CI)	*p*	*p*	*p*
Visual recognition						
Line Orientation Judgment (degree of deviation)	B1[a]	9.38 (4.98...17.65)**	13.26 (6.11...28.78)**	n. s.	T = 0.0007***	n. s.
	B2	3.83(1.67...8.80)**	10.76 (4.90...23.61)**			
	B3	2.67 (1.42...5.0298)**	5.63 (3.02...10.49)**			
Visual organization						
Geometric Pattern Recognition (nr of solved tasks)	B1	14.23 (13.07...15.39)	13.80 (12.34...15.26)	T = 0.0371	n. s.	n. s.
	B2	15.62 (14.61...16.62)	14.00 (11.57...16.43)			
	B3	14.31 (12.97...15.65)	15.10 (13.58...16.62)			
Geometric Pattern Recognition (% of correct answers)	B1	64.29 (56.00...73.33)*	55.83 (50.00...66.67)*	T = 0.0327	T = 0.0002*** W = 0.0020***	n. s.
	B2	76.47 (66.67...85.57)*	60.48 (44.44...78.57)*			
	B3	76.92 (66.67...81.25)*	76.79 (66.67...88.89)*			
Visual attention						
Spatial Attention (% of correct answers)	B1	80.00 (45.00...90.00)*	70.00 (65.00...80.00)*	T = 0.0054***	T = 0.0059*** W = 0.0313	n. s.
	B2	95.00 (85.00...100.00)*	67.50 (60.00...80.00)*			
	B3	97.50 (85.00...100.00)*	90 (65.00...100.00)*			
Spatial Attention (reaction time)	B1	9.38 (7.03...12.51)**	9.76 (7.63...12.49)**	T = 0.0005***	T = 0.0134***	n. s.
	B2	5.67 (4.72...6.80)**	9.11 (7.15...11.60)**			
	B3	6.53 (5.56...7.68)**	7.51 (5.85...9.65)**			
Visuospatial perception						
Cubes (% of correct answers)	B1	24.62 (9.69...39.54)	26.00 (9.41...42.59)	T = 0.0469	n. s.	n. s.
	B2	36.92 (17.28...56.56)	62.00 (39.18...84.82)			
	B3	43.08 (24.07...62.09)	48.00 (29.90...66.10)			
Cubes (reaction time)	B1	33.66 (24.30...39.03)*	41.27 (32.49...41.92)*	n. s.	n. s.	n. s.
	B2	26.86 (23.06...35.72)*	39.85 (30.22...46.05)*			
	B3	26.51 (24.02...35.76)*	36.62 (29.27...47.52)*			
Construction (% of correct answers)	B1	50.00 (0.00...83.34)*	66.67 (66.67...100.00)*	T = 0.0098***	T = 0.0313***	n. s.
	B2	100.00 (83.34...100.00)*	83.34 (33.33...100.00)*			
	B3	83.34 (66.67...100.00)*	100.00 (66.67...100.00)*			
Construction (reaction time)	B1	243.59 (166.21...320.96)	218.95 (153.71...284.19)	W = 0.0234	T = 0.0479	n. s.
	B2	195.58 (126.72...264.45)	193.87 (126.38...261.37)*			
	B3	159.97 (110.52...209.41)	174.06 (116.32...231.79)*			
Maze (nr of wrong moves)	B1	7.04 (4.82...10.26)**	7.85 (2.93...21.01)**	n. s.	n. s.	W = 0.0391
	B2	4.15 (1.54...11.20)**	8.22 (3.83...17.69)**			
	B3	4.25 (1.63...11.07)**	3.29 (1.87...5.79)**			
Maze (% of navigation errors)	B1	30.59 (25.79...36.29)**	23.96 (15.53...36.99)**	n. s.	T = 0.0105***	n. s.
	B2	12.31 (5.61...27.02)**	27.99 (18.74...41.80)**			
	B3	8.62 (3.58...20.80)**	12.62 (5.67...28.07)**			
Maze (solving speed)	B1	61.30 (48.38...77.67)**	72.21 (57.68...90.41)**	n. s.	W = 0.0371	n. s.
	B2	55.92 (43.77...71.45)**	74.46 (57.83...95.87)**			
	B3	52.60 (39.69...69.71)**	52.44 (36.96...74.40)**			

n. s. — not significant.
[a] B1 — first baseline assessment, B2 — primary outcome assessment, B3 — secondary outcome assessment (follow-up), T — training group, W — waiting-list group.
[b] Mean score (95% CI for mean).
* Median (lower 25%ile and upper 75%ile).
** Geometric Mean (95%CI).
*** We controlled the FDR to be lower than 5% by using linear step-up procedure [49] for multiple t-tests.

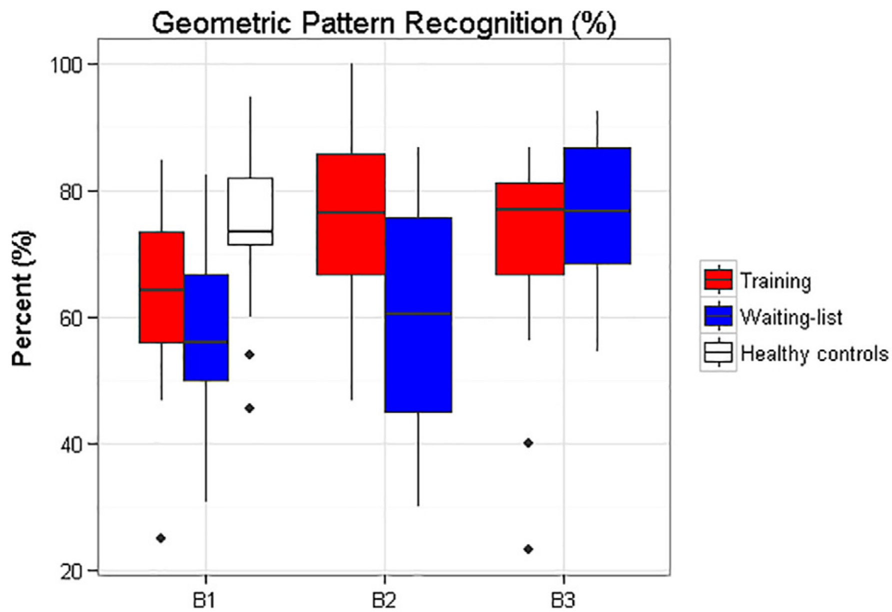

Fig. 3. Longitudinal changes in the percentage of correct responses in visual organization task at three assessment points (B1 — baseline, B2 — primary outcome, B3 — secondary outcome).

3.3. Comparison of performances between training group and waiting-list group

The comparison of performances between the patient groups on the baseline, primary outcome, and secondary outcome (long-term follow-up) was carried out.

3.3.1. Visual recognition

In the follow-up assessment for secondary outcome, the training group showed positive long-term rehabilitation effect ($p = 0.0007$) in Line Orientation Judgment task. The degree of deviation from a given horizontal line in the task was smaller in the secondary outcome compared with the first baseline assessment (see Table 7).

3.3.2. Visual organization

There was a significant positive immediate rehabilitation effect in the training group in the amount of solved exercises in the Geometric Pattern Recognition task ($p = 0.0371$), therefore, the study group had quicker solving time compared with the baseline assessment (see Table 7). The training group also showed positive immediate ($p = 0.0327$) and long-term rehabilitation effects ($p = 0.0002$) in the percentage of correct responses. The waiting-list group had only improved on the secondary outcome ($p = 0.0020$) (see Fig. 3 and Table 7).

3.3.3. Visual attention

Compared with the baseline, the training group had significantly improved their performance in the percentage of correct responses in the

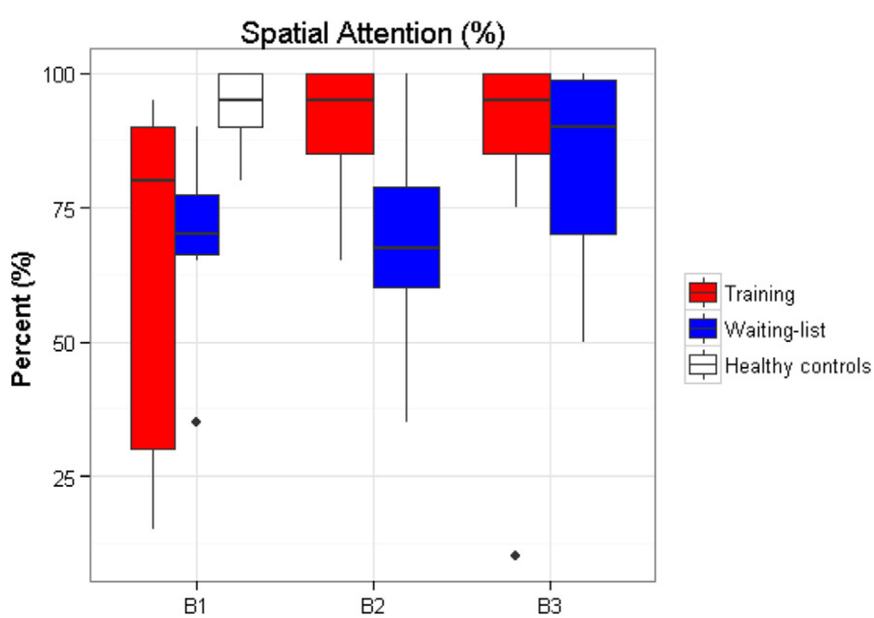

Fig. 4. Longitudinal change in the percentage of correct responses in visual attention task at three assessment points (B1 — baseline, B2 — primary outcome, B3 — secondary outcome).

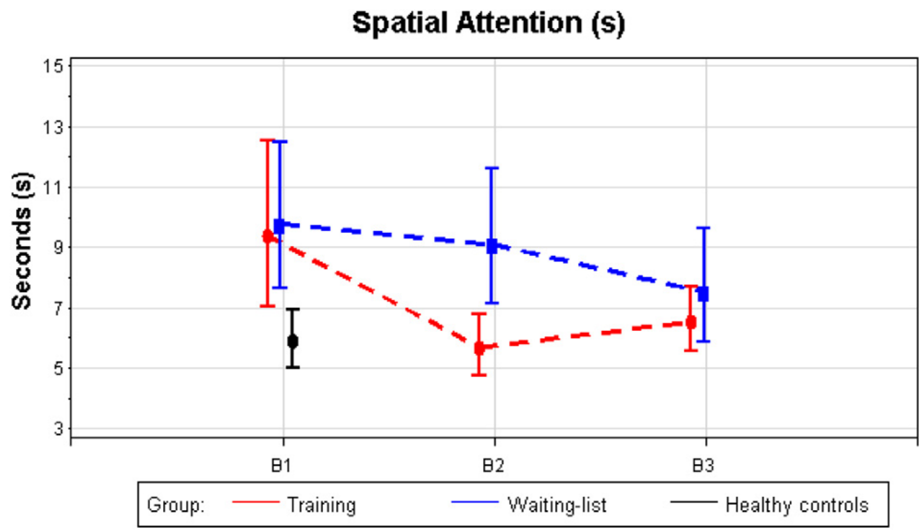

Fig. 5. Longitudinal change in the reaction time of visual attention task at three assessment points (B1 — baseline, B2 — primary outcome, B3 — secondary outcome).

Spatial Attention task on the primary ($p = 0.0054$) and secondary outcome assessments ($p = 0.0059$) (see Fig. 4 and Table 7).

There was a statistically significant longitudinal change in the reaction time in the Spatial Attention task between the two groups ($p = 0.0085$). The training group showed positive immediate ($p = 0.0005$) and long-term rehabilitation effects ($p = 0.0134$) (Fig. 5 and Table 7).

3.3.4. Visuospatial perception

The training group showed a positive immediate effect in the Cubes task ($p = 0.0469$) by giving more correct responses (Table 7). There was also a significant longitudinal change in the percentage of correct responses in the Construction task between the two groups ($p = 0.009$). Compared with the baseline assessment, the training group gave more correct responses in the primary ($p = 0.0098$) and secondary outcome assessments ($p = 0.0313$) (Table 7). The training group children also improved their reaction time in the secondary outcome ($p = 0.0479$) (Table 7). Furthermore, they showed a long-term intervention effect in decreased navigation errors in the Maze task ($p = 0.0105$) (Table 7).

3.4. Generalized effect

Generalized effect of the rehabilitation was measured with subjective measures before and after 1.31 years during the secondary assessment. Parents' feedback showed positive behavioral change after the training: children were less distracted, and their visual performance had improved. Furthermore, the skills in reading, writing, mathematics, and visuomotor functions improved. Children declared better functioning in school tasks and improved concentration skills. Children also reported their preference from the visuospatial perception tasks: the Maze and the Construction tasks were their favorites.

4. Discussion

The main aim of the current study was to test the effectiveness of a computer-based rehabilitation program ForamenRehab for the treatment of visuospatial deficit in children with epilepsy aged 8–12 years.

4.1. Visuospatial function profiles in children with epilepsy

In children with epilepsy, deficits in visual recognition component with additional spatial awareness and EF were observed on baseline level. Previously, lesions in anterior regions of the right temporal lobe in epilepsy have also been found to impair recognition of the identities of familiar faces, as well as the learning of new faces [50]. Deficits in EF in children with epilepsy have also often been reported before [18–20,51]. In visual organization component, the patients gave significantly less correct answers, although the solving time of tasks did not differ from the healthy children. This result could in part show that the patients rushed through the tasks with less concentration and, therefore, making more errors. The tasks in this category also showed that the patients had deficits in visual attention, visuospatial memory, and construction abilities. Our results were in line with Danielsson & Petermann [17] who found deficits in visual-constructive skills in children with Rolandic epilepsy and with Deonna et al. [52] who reported deficits in visuospatial memory and visuospatial organization in children with FE. This adds an important basis for CR as a significant positive association has been demonstrated between visuospatial working memory and mathematical performance [53]. Previously, an alteration of functional connectivity within visuospatial working memory-related brain network in patients with right temporal lobe epilepsy have been found with Functional magnetic resonance imaging (fMRI) [54]. Rehabilitation would help to better the connectivity by training specific functions. Also, the activation of mesiotemporal structures during visuospatial memory retrieval has been found to be asymmetrical in patients with medial temporal lobe epilepsy. The activation of the mesiotemporal structures is usually reduced ipsilateral to the epileptogenic region [55].

Our patients also showed deficits in visual attention, which have been reported before in children with benign epilepsy with centrotemporal spikes (BECTS) and in children with both BECTS and migraine [15]. Newly diagnosed children with BECTS have displayed brain activity alterations in the ventral and dorsal attention networks with fMRI [56], which also impact visual attention. Furthermore, children with epilepsy also showed deficits in the visuospatial perception component. In epilepsy, the right lateral temporal cortex has shown a pattern of inhibition of neuronal activity during short-term visuospatial memory that contrasts with excitation during other functions, particularly figure matching and perception [57].

In children, visuospatial memory predicts mathematics achievement through early adolescence [58], and low visuospatial abilities lead to a decrease in the mental number accuracy [59]. Therefore, visuospatial impairments should be treated early on for these children to not fall behind in school. Also, representations of own and others' body play a crucial role in social interaction [60], which may also be affected in children with visuospatial deficits.

Altogether, before the intervention, children with epilepsy showed significant deficits in all 4 of the visuospatial components. The baseline assessment with the FORAMENRehab successfully distinguished patients from healthy children, which gives an opportunity to use the program for screening visuospatial deficit in the future and distinguish the children needing neurorehabilitation.

4.2. Immediate rehabilitation effect

After the intervention, the training group showed a positive rehabilitation effect in 3 out of the 4 visuospatial components: visual organization, visual attention, and visuospatial perception. The effect was seen in all parameters of visual organization and visual attention. In visuospatial perception, the number of correct responses increased, but no significant improvements in reaction time were observed. This could indicate that the rehabilitation helped the children find better strategies to solve tasks, without quickening in reactions. The results suggest that visual recognition component needs longer rehabilitation. The waiting-list control group improved their performance only on one parameter (reaction time) of one visuospatial perception task.

4.3. Individual improvements during rehabilitation

The slowest advancements were seen in visual recognition and visuospatial perception tasks. This suggests that these components require longer training on easier levels. In contrast, higher difficulty levels were achieved in all visual organization and visual attention tasks. Furthermore, both components also demonstrated a significant improvement in outcome assessments. Results from the individual improvement trajectories point out the need for individualized approach of rehabilitation, which takes each child's progress into consideration.

4.4. Long-term rehabilitation effect

The long-term rehabilitation effect was examined 1.31 years after the intervention. In visual recognition, a positive long-term effect was observed, even though no immediate rehabilitation effect was found. This may suggest that the positive effects were observable not immediately, but more than a year later, since the waiting-list group did not show any improvements. In visual organization, the percentage of correct responses improved also in the secondary outcome. The strategies learned during active training were maintained, but regular training is required to keep up the solving speed. In visual attention and visuospatial perception, the positive effects in most of the parameters had preserved.

To sum up, the training group showed a positive long-term rehabilitation effect in all 4 visuospatial components. In contrast, the waiting-list control group had only improved in few parameters under two components. The normal developmental processes do not explain the immediate and long-term positive rehabilitation effects in the training group, since there was a noticeable difference in performances between the two patient groups.

4.5. Effectiveness of the computer-based intervention

Altogether, we found that the FORAMENRehab computer-based rehabilitation program was suitable for children with epilepsy aged 8–12 years. Children were very motivated, which was evident by the 100% compliance and positive feedback from both the children and their parents, who reported improved functions in everyday life: better outcome in school tasks and positive behavioral change. Amonn and colleagues [61] have stated that cognitive training-programs should focus more strongly on specific neuropsychological deficits. This study confirmed that for an effective rehabilitation, it is important to focus on specific deficits in different visuospatial components. Still, the aim of CR is to improve the everyday functioning of the patient's life [24]. Neurorehabilitation is effective in remediating cognitive deficits, which in turn also leads to improvements in activities of daily living and community integration [62].

4.6. Clinical implications

The children require active guidance from the therapist to more effectively learn the new strategies. Combining metacognition/strategy use and drill-based training has been most promising, as it can lead to improvements in both cognitive and psychosocial functioning [63]. Therefore, the therapist's role is to help the children link the trained skills with everyday life activities. The intervention setting and duration also play a role. Often, the children needed continuous motivation to finish the tasks that required longer sustained attention. Providing frequent and immediate feedback and reinforcement to the child is crucial in computer-based trainings [61]. Furthermore, we found that the children's motivation was also influenced by the parents' motivation, which is why it is necessary to educate the parents about the importance of the rehabilitation. Involving the parents in the process gives them a better comprehension of the used strategies and outcome [64]. Slomine & Locascio [46] have pointed out that educating the parents in CR helps to alleviate the cognitive and behavioral problems of the children. In the current study, personalized feedback for the parents was provided after the baseline assessment to educate them about the child's specific visuospatial deficits. Feedback was also provided after outcome assessments to inform them about the child's progress and give future guidelines.

With this study, a strict rehabilitation protocol and specific baselevels for the rehabilitation of visuospatial functions were created, which could be used in the future for hospitals, outpatient clinics, or rehabilitation centers. Furthermore, the program could be adapted to be used in children with different ABI diagnosis, such as traumatic brain injury (TBI) or stroke.

4.7. Limitations

The patients were not randomized to the intervention. The study group only involved children who lived in or near Tartu City, because of the transportation difficulties from other cities. Children from bigger cities, such as Tartu, may be used to different learning environments and conditions compared with children from smaller cities or villages, which could affect the generalization of the results for the whole population. It would be advised to include children from all over Estonia in the future.

As the rehabilitation process and different assessments are very time-consuming, the other neuropsychological assessment measures were not repeated after the training. This was also due to the fact that our main aims were to discover the children in need of the training at the baseline and to measure the rehabilitation effect with the current program after the intervention, not validating the baseline tasks for separate assessment of visuospatial skills.

5. Conclusions

Visuospatial deficit in children has been under-researched and underdiagnosed, especially in children with epilepsy. Neurorehabilitation with the Visuospatial module of the computer-based FORAMENRehab software was effective for children with FE. Before the intervention, the patients showed cognitive deficits in all four visuospatial components. However, the training group showed positive immediate rehabilitation effect after the intervention in 3 out of 4 visuospatial components: visual organization, visual attention, and visuospatial perception. Furthermore, a positive long-term effect was observed in all 4 visuospatial components. At least 10 intervention sessions were needed to notice significant improvements in visuospatial function. Visual recognition and visuospatial perception components need longer active training periods or retrainings.

In addition, a positive generalized effect of the intervention was confirmed by the parent's and children's feedback by questionnaires with some of the learned skills transferring to everyday life. The 100% compliance and positive objective and subjective results showed that modern neurocognitive rehabilitation is an efficient way to guide children towards their full potential. The individual improvement trajectories point out the need for individualized approach for CR.

Declaration of Competing Interest

We have no conflicts of interest to declare. All authors declare no competing interests.

Acknowledgments

This study was supported by the Estonian Science Foundation (GARLA 9016) and by the Estonian Ministry of Education and Research TARLA 2695.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2019.106521.

References

[1] van der Ham IJ, Borst G. Individual differences in spatial relation processing: effects of strategy, ability, and gender. Brain Cogn. 2011;76(1):184–90.
[2] Uttal DH, Meadow NG, Tipton E, Hand LL, Alden AR, Warren C, et al. The malleability of spatial skills: a meta-analysis of training studies. Psychol Bull. 2013;139(2):352.
[3] Linn MC, Petersen AC. Emergence and characterization of sex differences in spatial ability: a meta-analysis. Child Dev. 1985;1:1479–98.
[4] Kolb B, Whishaw IQ. Fundamentals of human neuropsychology. 5th ed. New York: Worth; 2003.
[5] Mervis CB, Robinson BF, Pani JR. Visuospatial construction. Am J Hum Genet. 1999; 65(5):1222–9.
[6] Cave KR, Bichot NP. Visuospatial attention: beyond a spotlight model. Psychon Bull Rev. 1999;6(2):204–23.
[7] Donnon T, DesCôteaux JG, Violato C. Impact of cognitive imaging and sex differences on the development of laparoscopic suturing skills. Can J Surg. 2005;48(5):387.
[8] Assel MA, Landry SH, Swank P, Smith KE, Steelman LM. Precursors to mathematical skills: examining the roles of visual–spatial skills, executive processes, and parenting factors. Appl Dev Sci. 2003;7(1):27–38.
[9] Carlson AG, Rowe E, Curby TW. Disentangling fine motor skills' relations to academic achievement: the relative contributions of visual-spatial integration and visual-motor coordination. J Genet Psychol. 2013;174(5):514–33.
[10] Pienaar AE, Barhorst R, Twisk JW. Relationships between academic performance, SES school type and perceptual-motor skills in first grade South African learners: NW-CHILD study. Child Care Health Dev. 2014;40(3):370–8.
[11] Simms V, Clayton S, Cragg L, Gilmore C, Johnson S. Explaining the relationship between number line estimation and mathematical achievement: the role of visuomotor integration and visuospatial skills. J Exp Child Psychol. 2016;145:22–33.
[12] Chung YT, Hsieh IC, Lai MC, Huang CW. The potential role of neurocognitive rehabilitation in epilepsy. Int J Neurorehabil. 2014;1:125.
[13] Veri K, Talvik I, Vaher U, Napa A, Ilves P, Uibo O, et al. Incidence of childhood epilepsy in Estonia. J Child Neurol. 2018;33(9):587–92.
[14] Riva D, Saletti V, Nichelli F, Bulgheroni S. Neuropsychologic effects of frontal lobe epilepsy in children. J Child Neurol. 2002;17(9):661–7.
[15] Parisi P, Matricardi S, Tozzi E, Sechi E, Martini C, Verrotti A. Benign epilepsy of childhood with centro-temporal spikes (BECTS) versus migraine: a neuropsychological assessment. Childs Nerv Syst. 2012;28(12):2129–35.
[16] Kolk A, Beilmann A, Tomberg T, Napa A, Talvik T. Neurocognitive development of children with congenital unilateral brain lesion and epilepsy. Brain Dev. 2001;23(2):88–96.
[17] Danielsson J, Petermann F. Cognitive deficits in children with benign rolandic epilepsy of childhood or rolandic discharges: a study of children between 4 and 7 years of age with and without seizures compared with healthy controls. Epilepsy Behav. 2009;16(4):646–51.
[18] Bender HA, Marks BC, Brown ER, Zach L, Zaroff CM. Neuropsychologic performance of children with epilepsy on the NEPSY. Pediatr Neurol. 2007;36(5):312–7.
[19] Rathouz PJ, Zhao Q, Jones JE, Jackson DC, Hsu DA, Stafstrom CE, et al. Cognitive development in children with new onset epilepsy. Dev Med Child Neurol. 2014;56(7): 635–41.
[20] Zilli T, Zanini S, Conte S, Borgatti R, Urgesi C. Neuropsychological assessment of children with epilepsy and average intelligence using NEPSY II. J Clin Exp Neuropsychol. 2015;37(10):1036–51.
[21] Genizi J, Shamay-Tsoory SG, Shahar E, Yaniv S, Aharon-Perez J. Impaired social behavior in children with benign childhood epilepsy with centrotemporal spikes. J Child Neurol. 2012;27(2):156–61.
[22] Farina E, Raglio A, Giovagnoli AR. Cognitive rehabilitation in epilepsy: an evidence-based review. Epilepsy Res. 2015;109:210–8.
[23] Cope DN. The effectiveness of traumatic brain injury rehabilitation: a review. Brain Inj. 1995;9(7):649–70.
[24] Sarajuuri JM, Koskinen SK. Holistic neuropsychological rehabilitation in Finland: the INSURE program—a transcultural outgrowth of perspectives from Israel to Europe via the USA. Int J Psychol. 2006;41(5):362–70.
[25] Cicerone KD, Langenbahn DM, Braden C, Malec JF, Kalmar K, Fraas M, et al. Evidence-based cognitive rehabilitation: updated review of the literature from 2003 through 2008. Arch Phys Med Rehabil. 2011;92(4):519–30.
[26] Hanssen KT, Beiske AG, Landrø NI, Hofoss D, Hessen E. Cognitive rehabilitation in multiple sclerosis: a randomized controlled trial. Acta Neurol Scand. 2016;133(1): 30–40.
[27] Livelli A, Orofino GC, Calcagno A, Farenga M, Penoncelli D, Guastavigna M, et al. Evaluation of a cognitive rehabilitation protocol in HIV patients with associated neurocognitive disorders: efficacy and stability over time. Front Behav Neurosci. 2015;9:306.
[28] Cherrier MM, Anderson K, David D, Higano CS, Gray H, Church A, et al. A randomized trial of cognitive rehabilitation in cancer survivors. Life Sci. 2013;93(17):617–22.
[29] Engelberts NH, Klein M, Adèr HJ, Heimans JJ, Trenité DG, Van der Ploeg HM. The effectiveness of cognitive rehabilitation for attention deficits in focal seizures: a randomized controlled study. Epilepsia. 2002;43(6):587–95.
[30] Helmstaedter C, Kurthen M, Lux S, Reuber M, Elger CE. Chronic epilepsy and cognition: a longitudinal study in temporal lobe epilepsy. Ann Neurol. 2003;54(4):425–32.
[31] Radford K, Lah S, Thayer Z, Miller LA. Effective group-based memory training for patients with epilepsy. Epilepsy Behav. 2011;22(2):272–8.
[32] Koorenhof L, Baxendale S, Smith N, Thompson P. Memory rehabilitation and brain training for surgical temporal lobe epilepsy patients: a preliminary report. Seizure. 2012;21(3):178–82.
[33] Langenbahn DM, Ashman T, Cantor J, Trott C. An evidence-based review of cognitive rehabilitation in medical conditions affecting cognitive function. Arch Phys Med Rehabil. 2013;94(2):271–86.
[34] Witt JA, Alpherts W, Helmstaedter C. Computerized neuropsychological testing in epilepsy: overview of available tools. Seizure. 2013;22(6):416–23.
[35] Saard M, Kaldoja ML, Bachmann M, Pertens L, Kolk A. Neurorehabilitation with FORAMENRehab for attention impairment in children with epilepsy. Epilepsy Behav. 2017;67:111–21.
[36] Kaldoja ML, Saard M, Lange K, Raud T, Teeveer OK, Kolk A. Neuropsychological benefits of computer-assisted cognitive rehabilitation (using FORAMENRehab program) in children with mild traumatic brain injury or partial epilepsy: a pilot study. J Pediatr Rehabil Med. 2015;8(4):271–83.
[37] Boivin MJ, Busman RA, Parikh SM, Bangirana P, Page CF, Opoka RO, et al. A pilot study of the neuropsychological benefits of computerized cognitive rehabilitation in Ugandan children with HIV. Neuropsychology. 2010;24(5):667.
[38] Bangirana P, Giordani B, John CC, Page C, Opoka RO, Boivin MJ. Immediate neuropsychological and behavioral benefits of computerized cognitive rehabilitation in Ugandan pediatric cerebral malaria survivors. J Dev Behav Pediatr. 2009;30(4):310.
[39] Kolk A, Saard M, Pertens L, Kallakas T, Sepp K, Kornet K. Structured model of neurorehab: a pilot study of modern multitouch technology and virtual reality platforms for training sociocognitive deficit in children with acquired brain injury. Appl Neuropsychol Child. 2018;27:1–7.
[40] Bogdanova Y, Yee MK, Ho VT, Cicerone KD. Computerized cognitive rehabilitation of attention and executive function in acquired brain injury: a systematic review. J Head Trauma Rehabil. 2016;31(6):419.
[41] Park IS, Yoon JG. The effect of computer-assisted cognitive rehabilitation and repetitive transcranial magnetic stimulation on cognitive function for stroke patients. J Phys Ther Sci. 2015;27(3):773–6.
[42] Ogourtsova T, Souza Silva W, Archambault PS, Lamontagne A. Virtual reality treatment and assessments for post-stroke unilateral spatial neglect: a systematic literature review. Neuropsychol Rehabil. 2017;27(3):409–54.
[43] Kerkhoff G. Rehabilitation of visuospatial cognition and visual exploration in neglect: a cross-over study. Restor Neurol Neurosci. 1998;12(1):27–40.
[44] Limond J, Leeke R. Practitioner review: cognitive rehabilitation for children with acquired brain injury. J Child Psychol Psychiatry. 2005;46(4):339–52.
[45] Shaw DR. Pediatric cognitive rehabilitation: effective treatments in a school-based environment. NeuroRehabilitation. 2014;34(1):23–8.
[46] Slomine B, Locascio G. Cognitive rehabilitation for children with acquired brain injury. Dev Disabil Res Rev. 2009;15(2):133–43.
[47] Tal G, Tirosh E. Rehabilitation of children with traumatic brain injury: a critical review. Pediatr Neurol. 2013;48(6):424–31.
[48] Laatsch L, Harrington D, Hotz G, Marcantuono J, Mozzoni MP, Walsh V, et al. An evidence-based review of cognitive and behavioral rehabilitation treatment studies in children with acquired brain injury. J Head Trauma Rehabil. 2007;22(4):248–56.
[49] Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J R Stat Soc B Methodol. 1995;57(1):289–300.
[50] Glosser G, Salvucci AE, Chiaravalloti ND. Naming and recognizing famous faces in temporal lobe epilepsy. Neurology. 2003;61(1):81–6.
[51] Riccio CA, Pliego JA, Cohen MJ, Park Y. Executive function performance for children with epilepsy localized to the frontal or temporal lobes. Appl Neuropsychol Child. 2015;4(4):277–84.
[52] Deonna T, Zesiger P, Davidoff V, Maeder M, Mayor C, Roulet E. Benign partial epilepsy of childhood: a longitudinal neuropsychological and EEG study of cognitive function. Dev Med Child Neurol. 2000;42(9):595–603.

[53] Allen K, Higgins S, Adams J. The relationship between visuospatial working memory and mathematical performance in school-aged children: a systematic review. Educ Psychol Rev. 2019;8:1–23.
[54] Lv ZX, Huang DH, Ye W, Chen ZR, Huang WL, Zheng JO. Alteration of functional connectivity within visuospatial working memory-related brain network in patients with right temporal lobe epilepsy: a resting-state fMRI study. Epilepsy Behav. 2014;35:64–71.
[55] Jokeit H, Okujava M, Woermann FG. Memory fMRI lateralizes temporal lobe epilepsy. Neurology. 2001;57:1786–93.
[56] Xiao F, Li L, An D, Lei D, Tang Y, Yang T, et al. Altered attention networks in benign childhood epilepsy with centrotemporal spikes (BECTS): a resting-state fMRI study. Epilepsy Behav. 2015;45:234–41.
[57] Holmes MD, Ojemann GA, Lettich E. Neuronal activity in human right lateral temporal cortex related to visuospatial memory and perception. Brain Res. 1996;711(1–2):44–9.
[58] Li Y, Geary DC. Children's visuospatial memory predicts mathematics achievement through early adolescence. PLoS One. 2017;12(2):e0172046.
[59] Crollen V, Noël MP. Spatial and numerical processing in children with high and low visuospatial abilities. J Exp Child Psychol. 2015;132:84–98.
[60] Corti C, Poggi G, Massimino M, Bardoni A, Borgatti R, Urgesi C. Visual perception and spatial transformation of the body in children and adolescents with brain tumor. Neuropsychologia. 2018;120:124–36.
[61] Amonn F, Frölich J, Breuer D, Banaschewski T, Doepfner M. Evaluation of a computer-based neuropsychological training in children with attention-deficit hyperactivity disorder (ADHD). NeuroRehabilitation. 2013;32(3):555–62.
[62] Kanchan A, Singh AR, Khan NA, Jahan M, Raman R, Rao TS. Impact of neuropsychological rehabilitation on activities of daily living and community reintegration of patients with traumatic brain injury. Indian J Psychiatry. 2018;60(1):38.
[63] Resch C, Rosema S, Hurks P, de Kloet A, van Heugten C. Searching for effective components of cognitive rehabilitation for children and adolescents with acquired brain injury: a systematic review. Brain Inj. 2018;32(6):679–92.
[64] van't Hooft I, Andersson K, Bergman B, Sejersen T, von Wendt L, Bartfai A. Sustained favorable effects of cognitive training in children with acquired brain injuries. NeuroRehabilitation. 2007;22(2):109–16.
[65] Wai J, Lubinski D, Benbow CP. Spatial ability for STEM domains: aligning over 50 years of cumulative psychological knowledge solidifies its importance. J Educ Psychol. 2009;101(4):817.