Virtual Reality in Rehabilitation of Executive Functions in Children (VREALFUN) – Study Protocols for Randomized Control Trials

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Abstract. Children with attention and executive function disabilities often have a long-lasting need for rehabilitation to support their functional ability. Yet the availability of rehabilitation services is insufficient, regionally unevenly distributed, and unequal in terms of access to rehabilitation. There is a need for easily accessible services. In this paper, we present the VREALFUN project where the major aim is to develop a novel Virtual Reality (VR) rehabilitation method for children with deficits in attention and executive functions. This ongoing Randomized Control Study (RCT) includes two arms, one in children with attention deficit hyperactivity disorder (ADHD) and the other in children with mild to moderate traumatic brain injury (TBI).

Keywords: Virtual Reality · Attention · Executive Functions · Rehabilitation · Child

1 Introduction

Children with attention deficit hyperactivity disorder (ADHD) and traumatic brain injury (TBI) often have deficits in their attention and executive functions causing disability in daily living. Many of these children need long-lasting rehabilitation, and there is a

M. Särestöniemi et al. (Eds.): NCDHWS 2024, CCIS 2084, pp. 117–124, 2024.
https://doi.org/10.1007/978-3-031-59091-7_8

growing demand for effective, cost-efficient, and feasible rehabilitation interventions where the training is targeted to support the everyday life functional ability of these children. Combining metacognitive skills and strategy training with skill practice seems to support everyday performance better [1]. Also, teaching parents to interact with their children more positively seems to promote their children's self-regulating ability [2, 3].

There is accumulating evidence that virtual reality (VR) can be effective in the rehabilitation of cognitive functions in children with ADHD [4, 5]. Also, VR in the rehabilitation of cognitive functions in adult patients with TBI has given some support [6], but in children with TBI the effectiveness of such a treatment method is still poorly understood. VR offers opportunities to build digitalized environments emulating situations where daily life attention and executive function deficits are manifested and to train skills helping to manage such challenging situations. In VR, it is also possible to expose the child to many repetitions in a highly motivating way which boosts learning of new skills.

In this registered (ClinicalTrials.gov, trials 206/2021 and 206/ 2021) randomized control study, the major aim is to develop and assess the feasibility of a novel rehabilitation method for children with deficits in attention, activity control and executive functions by using a virtual environment that corresponds to typical everyday life situations. Head-mounted displays (HMD) are used to present the tasks, and the levels of difficulty are adjusted according to the child's progress. The VREALFUN project consists of two RCT studies related to VR rehabilitation of attention and executive function deficits: S1) one conducted in children with ADHD and; S2) the other in children with mild to moderate TBI. After these two pilot studies, a national multicenter study with larger study groups will be set up.

We expect that; 1. Intensive training improves the attention regulation, activity control skills, and executive functions of the children in the intervention group; 2. Training of executive skills with motivating tasks in a virtual environment that is built to meet challenging everyday life situations transfers to the child‘s everyday life and; 3. The duration of the training effect does not depend on the success of the VR training itself, but on how well the child adopts new strategies that make everyday life easier and how the guardian is able to support the child's positive behavior in everyday life.

2 Subjects and Methods

This is a multidisciplinary project performed in collaboration with three faculties of the University of Oulu (Faculties of Medicine, Education and Psychology, and Information Technology and Electrical Engineering), two clinics of the Oulu University Hospital (Paediatric Neurology and Child Psychiatry Units), and researchers from the University of Helsinki, Helsinki University Hospital and Aalto University.

Two VREALFUN studies on VR rehabilitation in 8–12-years old Finnish-speaking children with ADHD and TBI are initiated in January 2024 and will be completed by the end of 2025. The Northern Ostrobothnia Regional Ethics Committee has approved the project plan on 30th August 2022 (EETTMK: 64/2021). The Wellbeing Services County of North Ostrobothnia has admitted research permission for this study on 23rd June 2023.

2.1 Participants

Eighty-eight children from the pediatric neurology and child psychiatry units of the Oulu University Hospital will be recruited for the ADHD study (S1) based on the informed consent of the guardian and the child, and randomized in three parallel intervention groups A, B, and C, and a treatment-as-usual (TAU) control group D (see below for a detailed description of the groups) with an allocation ratio 1:1:1:1. For the TBI study (S2) 44 children will be recruited, including one intervention group A and a TAU control group D, each of 22 children (an allocation ratio 1:1). Randomization will be performed by sealed envelopes and the randomization code will be released only after a baseline measure. The number of participants is based on sample size calculations for limited efficacy and effectiveness testing, with an expected meaningful training-induced behaviour change of 1 standard deviation mean difference between groups. The mean total score in the Behaviour Rating Inventory of Executive Function, Second Edition (BRIEF 2), is 50 and the standard deviation is 10 [7]. When considering that 10 would be a clinically significant difference in means, with a power of 80% and a statistical significance threshold of 0.05 the estimated sample size was 17 children per group. To consider possible dropouts of 20%, a total of 22 children will be recruited per group.

Patients in the control group are stratified to those in the intervention group for diagnosis (ADHD or TBI), age, sex, and very preterm birth status (< 32 weeks of gestation). Inclusion criteria in the ADHD group are the diagnosis of ADHD (ICD-10 F90.0) and methylphenidate medication; and in the TBI group, mild to moderate traumatic brain injury (ICD-10: S06.0-S06.6 and S06.8-S06.9, and criteria defined in the Current Care Recommendation 2021), and the challenges of attention and executive functions identified in the assessment of a neuropsychologist/experienced psychologist, as well as age 8–12 years and Finnish as a native language in both groups. The exclusion criteria in both groups include sensitivity to flashing light, epilepsy (ICD-10 G40), mental retardation (ICD-10 F70-F79), pervasive developmental disorders (ICD-10 F84), inflammatory diseases of the central nervous system (ICD-10 G00-G09), severe CP syndrome (ICD-10 G80), brain tumour, and twins/triplets, etc. In the ADHD group, TBI is also an exclusion criterion.

2.2 Procedure

The VREALFUN study set-up and methods are presented in Fig. 1 including four research visits: Baseline measure and three follow-up measures at 4–6 weeks, 6 months, and 12 months. The research methods are similar in ADHD and TBI cohort studies of which the ADHD cohort is randomized into four groups. In group A, children play the HMD-EPELI game and guardians get guidance to positive behavioural support and the introduction of a reward system (parental guidance); in group B the intervention is parental guidance only and no HMD-EPELI game is deployed; in group C children play the HMD-EPELI game only and no parental guidance is deployed. These interventions are described in more detail in Sect. 2.3 Intervention. Group D is a control group where children follow their rehabilitation plan drawn up in specialized medical care (treatment-as-usual). The TBI cohort with a smaller number of eligible patients is randomized into two groups (group A: HMD-EPELI game and parental guidance, and

group D: treatment -as usual). In all intervention groups (A, B, C) children may also receive conventional forms of rehabilitation or treatment, as planned in their rehabilitation plan, and no therapy or rehabilitation is discontinued because of the intervention offered in this VREALFUN study.

At the pretest and each follow-up visit, the neuropsychologist conducts the following neuropsychological examinations on children of all groups: The Conners Continuous Performance Test 3rd Edition (Conners CPT3) [8] which is a computerised attention task; n-back-test for working memory, and a virtual Executive Performance in Everyday Living (EPELI) task [9, 10] to measure the effectiveness of executive functions, time management, behaviour, task planning, memorization, and sensitivity to distractions. Furthermore, at each visit, the children in all research groups (A, B, C, D) are requested to fill out questionnaires about the functional ability of the child and the amount of positive feedback given by the guardians to the child (EPELI Questionnaire- child report, drawn up for this research), satisfaction with the assessment, and feelings of nausea and presence after playing the EPELI task using HMD and a hand controller as well as a questionnaire for measuring quality of life (KINDL-R Questionnaire for Measuring Health-Related Quality of Life in Children and Adolescents Revised Version, self-report) [11]. Guardians in groups A, B, C, and D are also requested to fill out the EPELI Questionnaire (parent report) and KINDL-R (parent version). Furthermore, they are asked to fill out questionnaires regarding the child´s executive function (BRIEF 2, parent form [7]) and ADHD symptoms (ADHD-rating scale IV (ADHD-RS), parent report) [12]. After each research visit based on the consent of the guardian the child´s teacher is sent BRIEF 2 (teacher form) and Concentration questionnaire [13] (in Finnish: Keskittymiskysely) which is an assessment of attention and executive function difficulties.

2.3 Intervention

There are three different intervention groups in the ADHD study where either the child plays the HMD-EPELI game (group C), the guardian gets guidance on positive behavioural support and use of a reward system (Group B), or both (Group A). In the TBI study there is one intervention group where the guardian gets parental guidance, and the child plays the HMD-EPELI game (group A) (Fig. 1). During the intervention period, guardians fill out a rehabilitation diary prepared for this study.

During the first research visit guardians in intervention groups A and B get guidance from the neuropsychologist on the use of self-care programs on the Health Village website on children's challenging behaviour, positive behavioural support, and the introduction of a reward system (https://www.mielenterveystalo.fi/fi/omahoito/lasten-haastavan-kaytoksen-omahoito-ohjelma). On this website, there is information on how to support the child‘s positive behaviour and use a reward system as well as rehearsals for the guardians on these topics. The guardians can return to these pages anytime they want to. A rehabilitation diary developed for this study will be introduced including four rehabilitation goals that are the same for all children of intervention groups of ADHD (groups A, B, and C) and TBI (group A) (Fig. 1), as well as two individual rehabilitation goals, which are defined together with the child and the guardian during the first research visit. Guardians fill in the rehabilitation diary daily for the first four weeks, and then once a week for five months, recording the actual activity of the child in accordance

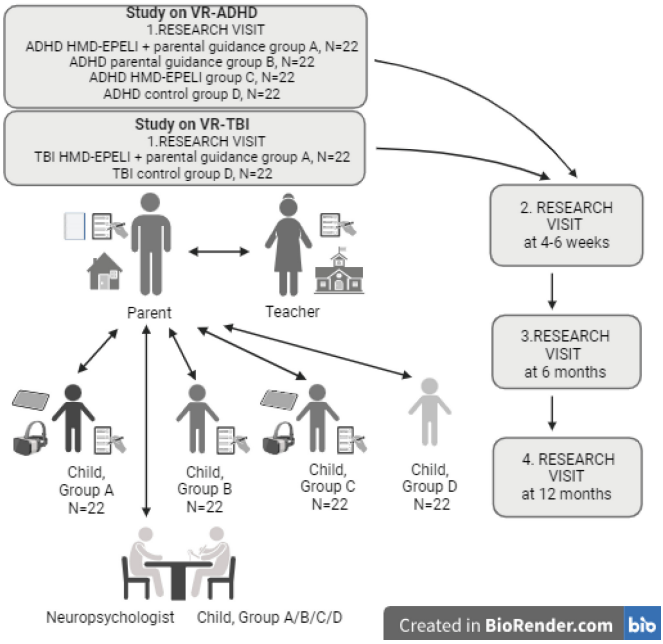

Fig. 1. The VREALFUN study set-up methods

with the rehabilitation goals, the amount of positive feedback given to the child, and the implementation of the rehabilitation plan drawn up in specialized medical care (e.g., occupational therapy sessions and any other rehabilitations, use of medication and possible changes in it). In addition, during the first research visit, the children of intervention groups A and C in the ADHD study and group A in the TBI study will be instructed in the use of the HMD-EPELI game under the supervision of the guardian for four weeks (five days a week, 30 min/day). This game is a VR rehabilitation program where the child rehearsals daily skills like homework and evening tasks in a virtual home environment instructed by a virtual character. After each rehearsal session, the child gets feedback in the form of a scoreboard. According to the child‘s progress, the level of difficulty is adjusted to keep rehearsal motivating. During the intervention period guardians also record in the diary how the gaming succeeded on those days the child has played. Gaming compliance is monitored through the server and guardians are reminded if necessary.

2.4 Research Ethical Considerations

In this study, research ethical principles are followed. Participation is based on voluntariness. The guardian and the child will be informed about the VREALFUN study in written form, and they have the possibility to ask questions concerning this study. Participation is based on informed consent and the participants can withdraw from this study at any time without any reason. Withdrawal does not influence on child‘s treatment. Information collected during research is confidential. This study does not cause any

pain or harm to the child, nor does it disturb their daily life. If the child feels a headache or nausea during the VR rehearsal, the child is instructed to stop playing. In the intervention groups participation in this study requires the guardian's commitment to home rehabilitation and time resources when they are following the child's rehearsal and/or filling the rehabilitation diary. In the intervention groups participation in this study might have some benefit, but not in the control groups during the research period. After the last follow-up visit the guardians in the control groups have a chance to get guidance on the use of self-care programs on the Health Village website about children's challenging behaviour, positive behavioural support, and the introduction of a reward system.

3 Results

As a part of this research project a new HMD-EPELI rehabilitation program has been developed (implemented by Peili Vision Company, which is not a collaborative partner of the research (http://www.peilivision.fi/)) as well as a rehabilitation diary to follow changes in each child´s functional ability during the intervention period. The EPELI diary will later be adapted into a mobile application for a digital care pathway. This is an ongoing study, the recruitment process has been initiated, and the data will be gathered by the end of 2025. Patients in the control group are stratified to those in the intervention group for diagnoses, age, sex, and very preterm birth status (<32 weeks of gestation) to control differences between groups other than the intervention. Other confounding factors (individual rehabilitation and pharmacotherapy) are considered by standardizing their effect in the analyses. The guardians of children in all intervention groups record in the rehabilitation diary daily the time of taking medication to support the child's attention and the individual rehabilitation received by the child (e.g. occupational therapy or neuropsychological rehabilitation). The results of RCT studies on ADHD and TBI cohorts will be published in high-quality international scientific journals.

4 Discussion

The prevalence of ADHD among children and young people in the general population is substantial, with 5–10% worldwide [14, 15]. However, the availability of rehabilitation services is insufficient, regionally unevenly distributed, and unequal in terms of access to rehabilitation. Attention difficulties, activity control and executive functions impair the functional capacity of these children and significantly increase their risk of social exclusion, academic underachievement, substance use, and co-morbidities including psychiatric disorders. A thesis on 200 families with ADHD children [16] revealed that families had unequal opportunities in getting support from educational, social and health sectors, and there was one socially excluded person or someone at risk of social exclusion in every third family. Furthermore, the Ministry of Education in Finland has estimated that every socially excluded young person costs EUR 1.2 million € for society and in Finland there are about 50,000 socially excluded people in the age groups between 15–29 years [17].

This VREALFUN study provides a potential to develop a novel VR-rehabilitation method with lower requirements for wireless communication (merely a wireless

consumer-grade Pico Neo 3 Pro Eye) enabling broader applicability and affordability. This project is linked to the strategic profiling 6 program of the University of Oulu, 6G-Enabling Sustainable Society (https://www.6gflagship.com/6gess/) that is based on 6G Flagship´s technological expertise to develop novel digital solutions for preventive healthcare and evaluate their feasibility, cost-effectiveness and impact on people´s health, lifestyles, and quality of life, and to develop virtual health care services involving digital care pathways, and implementation of novel health-related technologies. Thereby this VREALFUN project will promote long-term sustainability by supporting four of the sustainable development goals (SDGs) and their specified targets set by the United Nations: SDG3, good health and well-being (3B); SDG4, quality education (4.3); SDG5, gender equality; and SDG10, reduced inequalities.

Acknowledgments. This project is supported by the Arvo and Lea Ylppö Foundation, Helsinki, Finland, the Alma and K.A. Snellman Foundation, Oulu, Finland, the Finnish Brain Foundation, Helsinki, Finland, Academy of Finland (grant #352981 to Juha Salmi), Profiling 6 program 6G-Enabling Sustainable Society (6GESS), University of Oulu 6, Finland and FUWIRI (Research Infrastructure for Future Wireless Communication Networks), Academy of Finland.

Disclosure of Interests. The authors have no conflicts of interest relevant to the content of this article.

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