EFFECTS OF DIFFERENT ADDITIONAL INTERVENTIONS: TRANSLATING RESEARCH FINDINGS INTO REHABILITATION PRACTICES FOR CHILDREN WITH CEREBRAL PALSY

Ph.D. Thesis Booklet

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1. INTRODUCTION

1.1. Overview of the topic

1.1.1. What is the topic?

Our primary focus is to assess and implement new additional therapies and interventions in the field of rehabilitation of children with cerebral palsy (CP).

1.1.2. What is the problem to solve?

Progress made in the fields of rehabilitation and special education necessitates the evaluation of the effectiveness of additional innovative therapies and pedagogical approaches.

1.1.3. What is the importance of the topic?

Children with CP require management by a multidisciplinary team. The most common therapeutic interventions are physiotherapy, conductive education, and occupational therapy to improve muscle strength, normalize tone, facilitate normal movement patterns and cognitive functions to increase the quality of life. Various other additional therapies may enhance the efficacy of these interventions.

1.1.4. What would be the impact of our research results?

By assessing the effectiveness of new additional therapies and educational approaches, the quality of life of children with CP can be significantly improved. Evaluating the efficacy of emerging treatments allows healthcare professionals, educators, and caregivers to implement the most suitable additional interventions into daily practice for patients, leading to enhanced outcomes and better overall well-being. Additionally, the implementation of using eye-tracking to objective visual-perception skill monitoring provides caregivers valuable data on the progression and response to cognitive interventions.

2. OBJECTIVES

2.1. Investigating the Effect of Additional Whole-Body Vibration on Musculoskeletal System in Children with Cerebral Palsy

Nowadays, whole-body vibration (WBV) has become increasingly popular as an additional therapy in the intervention of patients with CP. The primary objective of this study is to evaluate the effects of WBV therapy as an additional intervention to conventional physiotherapy (PT) on the musculoskeletal system in children with CP. Specific goals:

- Assessing the impact of WBV on key outcomes such as muscle strength, spasticity, balance, and gait-related functions (e.g., walking speed and step length).
- Investigating differences in WBV effects across varying protocols, including frequency, amplitude, exercise positions, and session durations.
- Exploring subgroup differences based on CP severity levels (GMFCS I–V) to identify potential variations in treatment efficacy.
- Identifying the short- and long-term effects of WBV therapy, including its ability to normalize muscle tone and improve gross motor function.

2.2 Developing Visual Perceptual Skills with Assistive Technology-Supported Application for Children with Cerebral Palsy

Visual perception (VP) allows us to process visual stimuli to identify what we see and, thus, understand the world in which we live. VP ability is one of the many cognitive areas often affected in children with CP. This study aimed to design and evaluate the effectiveness of an educational application tailored to develop visual perceptual skills in children with CP. Specific goals:

- Assessing the application’s impact on visual perceptual skills using the Motor-Free Visual Perception Test (MVPT-4).
- Analyzing changes in gaze patterns and visual attention using screen-based eye-tracking technology.
- Comparing the intervention group’s outcomes with a control group to determine the application’s effectiveness in enhancing visual perceptual sub-skills such as visual discrimination, spatial awareness, and figure-ground perception.
- Highlighting the potential relationship between physical abilities and visual perceptual skills in children with CP.

3. METHODS

3.1. Study I.

Our systematic review and meta-analysis are reported according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 Statement. The Cochrane Handbook's recommendations for Systematic Reviews of Interventions Version 6.1.0 and Cochrane Prognosis Methods Group were followed, and the review protocols were registered on PROSPERO (CRD42021284999).

3.1.2. Literature search and eligibility criteria

Studies published before 1 November 2022 were retrieved from the following databases: MEDLINE (via PubMed), Embase, Cochrane Central Register of Controlled Trials, Scopus, and Web of Science. The following keywords were used for the search: (“cerebral palsy” OR paraplegia OR diplegia OR CP OR hemiparesis OR hemiplegia OR tetraplegia) AND (“whole body vibration” OR “whole-body vibration” OR WBV OR “vibration therapy” OR vibration). No restrictions or filters were applied.

Original articles examined the impact of WBV on the musculoskeletal system or its related aspects in children with CP regardless of subtype and GMFCS level. Primary outcomes were muscle strength and spasticity, gross motor function, bone density, and walking skills: speed, distance, and balance.

The PICO framework was developed to perform an accurate search strategy. The population of children diagnosed with CP was compared, where one group received WBV in combination with conventional physiotherapy (PT). In contrast, the other group received a placebo, sham, or simulated intervention as a control alongside conventional PT. The main outcomes of interest were changes in the musculoskeletal system (mobility, balance, muscle strength, spasticity, muscle function, bone density, gross motor functions, gait speed/walking distance, and motor performance).

3.1.3. Study selection and data collection

Two reviewers independently conducted the study selection process using reference management software (Endnote X9 3.3, Clarivate Analytics). Duplicate records were removed both automatically and manually. The records were selected by title, abstract, and full text according to a set of predetermined rules stated in the data selection and extraction protocol. Disagreements between the two reviewers were resolved through consensus. After each step of the selection procedure, the agreement rate was calculated using the Cohen coefficient.

3.1.4. Quality assessment

The risk of bias was assessed using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2). Two reviewers independently assessed the selected articles for the following domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Inclusion criteria had been established for selecting two independent evaluators: expertise in the field, trained in risk-of-bias assessment, and pilot testing. Consequently, the studies were classified based on their risk of bias as either low, high, or with some concerns. Any disagreement was resolved through the consensus of the authors.

3.1.5. Statistical Analysis

Statistical analyses were conducted using the ‘meta’ package in R, following the recommendations of Harrer et al. The effectiveness of WBV was evaluated by comparing mean changes and standard deviations in outcome measures before and after treatment in both the intervention and control groups. A random-effects meta-analysis was performed using the inverse variance method with a restricted maximum likelihood estimator, incorporating the Hartung–Knapp adjustment due to the limited number of studies.
Heterogeneity was assessed through the I^2 measure and Cochrane Q test, with I^2 values categorized as low (25%), moderate (50%), or high (75%). A positive pooled value indicated greater improvement in the treatment group. When possible, correlations between pre-and post-treatment values were calculated using available raw data or published summaries. Missing standard deviations were estimated from computed averages. Subgroup analyses were planned based on subtype and GMFCS categories.

3.2. Study II.

A matched-pair randomized controlled trial was conducted to investigate the effectiveness of specialized educational software and learning games designed to enhance various sub-skills in preschool and elementary school children with typical and atypical development (e.g., CP).

3.2.1. Intervention enrollment and technical features

The intervention period lasted for a full school year (9 months). During this time, participants in the intervention group were allowed to use the applications for 15 minutes at least three times a week. While some participants used tablets, others utilized an eye-tracking device to interact with the applications. This schedule was developed in collaboration with the conductors in the department to ensure alignment with their daily conductive education program. The control group did not use the applications; instead, they participated exclusively in their regular conductive education program.

The applications run on PCs (web-based) and tablets (iOS, Android). The software collects statistical data about users, enabling the observation of positive changes and identification of problematic areas. It provides real-time feedback to caregivers regarding the children's performance. In addition to its functional software design, usability and ergonomic features were incorporated to evaluate the software's positive effects on cognition, particularly on visual perceptual skills. Another key feature is gamification, which aims to capture and maintain the user's attention and motivation. The user interface is tailored to meet children's needs, featuring a playful and colorful design, varying levels of difficulty, and reward collection opportunities. The intervention targeted specific developmental areas that were chosen based on their relevance to the cognitive, perceptual, and motor skill development of children with typical and atypical development. The following areas were assessed and addressed during the use of the educational software and learning games:

- Visual perception skills: such as visual discrimination, spatial relationships, visual memory, figure-ground, visual closure, perception and recognition of colors and shapes,
- Auditory perception skills: such as auditory closure, auditory conceptualizing, auditory discrimination, auditory memory, and auditory sequential memory,
- Basic mathematical operations (summations, subtractions) and problem-solving skills,
- On tablet: eye-hand coordination, fine manipulation, hand dominance,

- Rule consciousness,
- Decision-making skills,
- Self-awareness.

These areas were systematically addressed through the interactive features of the software, incorporating gamification and adaptive levels of difficulty to meet individual needs.

3.2.2 Participants characteristics

The participants, aged between 4 and 8 years (mean 7.27 ± 1.53), were recruited from the Semmelweis University, András Pető Faculty Kindergarten and Elementary School.
The total sample size was N=18, with equal distribution between the intervention group (N=9) and the control group (N=9).

Participants were matched in pairs based on their age and diagnosis to ensure comparability between groups.
We also conducted the baseline measurement (MVPT-4 test and eye-tracking) with typically developing children (N=12) to analyze and compare this population's visual perceptual skills and gaze patterns.

The exclusion criteria were:

- Children with uncorrectable visual or hearing impairments that would prevent them from using the application.
- Participants unable to comprehend or respond to the MVPT-4 tasks.
- Children with significant behavioral challenges that hinder participation.
- Children with unstable medical conditions or undergoing acute medical treatment that may interfere with participation.
- Cases where informed consent is not provided by parents or legal guardians.

3.2.3.1. Motor-Free Visual Perception Test – 4 (MVPT-4)

The MVPT-4 assesses visual-perceptual abilities in individuals aged 4 to 80+ without requiring a motor response. It evaluates five key areas—visual discrimination, spatial relationships, visual memory, figure-ground, and visual closure—though results are reported as a single standard score. The test consists of black-and-white line drawings in a multiple-choice format. Its motor-free design makes it particularly useful for individuals with severe CP, where motor impairment may hinder traditional assessments.

3.2.3.2. Eye-Tracking

The Tobii Pro X3, a 120 Hz screen-based eye tracker, was used to capture participants' gaze patterns during the MVPT-4 test. This allowed for an analysis of visual attention and cognitive processing without reliance on self-reported data.

For this study, MVPT-4 test sheets were digitalized, enabling computerized test completion. The goal was to examine whether gaze patterns could reveal differences in cognitive processing between children exposed to the application and those who were not throughout the intervention period. We specifically analyzed fixation distribution to identify variations between typically and atypically developing children, focusing on key areas of visual attention.

3.2.4. Research Questions

Research Questions Concerning the MVPT-4:

- What are the differences in MVPT-4 scores between typically developing and atypically developing children?
- How do MVPT-4 scores differ between the intervention group and the control group after the intervention period?
- Are there differences in MVPT-4 scores among children with different CP diagnoses?

Research Questions Concerning Eye-Tracking Data:

- What are the differences in gaze patterns between typically developing and atypically developing children?
- How do gaze patterns and levels of visual attention differ between baseline and re-test measurements?

3.2.5. Data Analysis

Data analysis was conducted using IBM SPSS 26. Due to the small sample size and non-normal distribution, the Wilcoxon signed-rank test was used to compare baseline and re-test values within groups, while the Mann-Whitney U test assessed differences between the intervention and control groups.

For eye-tracking data, Areas of Interest (AOIs) were defined on the digitalized MVPT-4 test sheets, focusing on correct answers. Three variables were analyzed: total fixation duration (TFD), fixation count (FC), and visit count (VC). Normality tests guided the choice of statistical methods: t-tests for normally distributed data and Mann-Whitney U tests for non-parametric comparisons. Repeated measures ANOVA was applied for normally distributed within-group changes, while non-parametric data were analyzed using the Mann-Whitney U test.

4. RESULTS

4.1. Study I.

Our systematic search provided a total of 5,984 potentially relevant records across the databases. After removing 1,890 duplicates, 4094 titles and abstracts were screened, of which 3,976 were excluded for not meeting the eligibility criteria. Out of the remaining 118 studies, 102 were excluded after full-text selection. This was primarily due to the studies not being RCTs, employing inappropriate study designs (e.g., differing comparisons among observed groups), or involving overlapping patient populations. Based on the inclusion and exclusion criteria, 16 articles, encompassing 414 patients, were included in the final analysis.

Of these, 16 studies were deemed eligible for inclusion in the systematic review, and 12 were integrated into the meta-analyses.

The mean age of participants ranged from 19 months to 11.82 years. Regarding the patients' characteristics, some studies exclusively reported data on the Gross Motor Function Classification System (GMFCS) levels of the subjects, ranging from levels I to IV. Other studies specified the type of CP, such as hemiplegia, diplegia, or tetraplegia.

4.1.2. Therapeutic effects

4.1.2.1. Gross motor function

The Gross Motor Function Measure (GMFM) measures the performance of the child in five dimensions, and each dimension can be measured separately or together. However, statistical analysis was feasible only for domains D (standing) and E (gait activities) due to limited overlap in the domains assessed by the individual studies. While most studies reported positive changes in gross motor functions, the pooled effect size was ultimately nonsignificant. For domain D, the mean difference (MD) was 2.80 (95% CI: -4.56, 10.15), and for domain E, the MD was 5.74 (95% CI: -8.38, 19.85). Nonetheless, it is noteworthy that the baseline GMFMD value of the included patients closely resembles that of typically developing children.

4.1.2.2. Muscle strength

Four studies assessed muscle strength as an outcome, three of them measuring knee extensor strength using a dynamometer, reported in Newtons (N). The difference between WBV training and the control group was statistically nonsignificant (MD = 8.77, 95% CI: -12.06, 29.59); however, a positive pooled MD in changes between the treatment groups was observed.

4.1.2.3. Walking performance

The effects of WBV treatment on walking skills were assessed not only with the GMFM E domain but also through various measures, including walking speed, step length, 6-Minute Walk Test (6MWT), and Time Up and Go Test (TUG). Significant changes were observed in these two strongly related outcomes:

- Walking speed (cm/s): (diff. of MD 10.03) (95% CI: 4.22; 15.1583) ($p = 0.02$)
- Step length (cm): (diff. of MD 7.19) (95% CI: -0.15; 14.53) ($p = 0.05$).

4.1.2.4. Spasticity

Five studies assessed spasticity using the Modified Ashworth Scale (MAS), a clinical tool commonly used to measure muscle spasticity in individuals with neurological conditions. For statistical evaluation, MAS scores were assigned numeric values ranging from 0 to 5. Of the five studies, three were included in the statistical analysis due to missing data. While all studies reported increased muscle tone in the lower extremities, the pooled effect size did not reach statistical significance (diff. of MD -0.79) (95% CI: -2.83; 1.25).

4.1.2.5. Overall stability

Studies on WBV and stability report different findings due to varied assessment methods. Some studies found significant post-treatment improvements in balance, with sustained effects in certain cases. Others reported non-significant changes. While different tools, such as the SportKAT 550™ and Pediatric Balance Scale, were used, overall results suggest WBV may enhance stability.

4.1.3. Secondary Outcomes

4.1.3.1. Muscle thickness

Two studies investigated the positive effects of WBV on muscle thickness. Their findings indicated that the experimental group exhibited significantly greater increases in tibialis anterior muscle thickness ($p = 0.001$; 0.48 ± 0.08 mm to 0.63 ± 0.10 mm) and soleus muscle thickness ($p = 0.001$; 0.45 ± 0.04 mm to 0.63 ± 0.12 mm) compared to the control group. However, no significant effect was observed on gastrocnemius muscle thickness. Another study reported significant post-treatment improvements in muscle thickness parameters in favor of the experimental group ($p < 0.05$).

4.1.4. Risk of bias

The included studies were assessed for key domains of bias, including the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. The overall judgments predominantly indicated a "low risk" of bias.

4.2. Study II.

4.2.1. Results of the MVPT-4 Test

The first research question concerning the MVPT-4 test was: What are the differences in MVPT-4 scores between typically developing and atypically developing children? Based on the literature, we hypothesized that the visual-perceptual skills of children with CP are impaired. Our findings supported this hypothesis. The MVPT-4 was used to evaluate whether children with CP demonstrate deficits in visual perception on a motor-free visual perception test. Both baseline and re-test results revealed that children with CP achieved significantly lower mean perceptual quotients compared to typically developing children ($p < 0.001$).

The second research question concerning the MVPT-4 test was: How do MVPT-4 scores differ between the intervention group and the control group after the intervention period? We observed promising trends when comparing the differences in baseline and re-test values between the intervention and control groups. However, these differences were not statistically significant ($p = 0.666$). Within-group comparisons of MVPT-4 test results between the baseline and re-test showed statistically significant differences in both the intervention ($p = 0.008$) and control (p

= 0.002) groups. The data in the intervention group did not follow a normal distribution, whereas the control group data did, so different methods were used to test significance: the Wilcoxon Signed-Rank Test for the intervention group and the Paired Sample T-Test for the control group.

The third research question concerning the MVPT-4 test was: Are there differences in MVPT-4 scores among children with different CP diagnoses? While the small sample size limited our ability to conduct statistical analyses, dividing the data by CP diagnosis.

4.2.2. Results of the Eye-Tracking Data

The MVPT-4 test sheets were digitized to allow computerized completion and facilitate the capture of participants' gaze patterns. Since the test does not require motor responses, digitization was not expected to influence outcomes. Eye-tracking technology was used to record key gaze parameters, including fixation duration, fixation count, and visit count.

The results showed changes in the gaze patterns of atypically developing children. Compared to their initial performance, these children demonstrated improved visual attention during re-testing, as indicated by more structured gaze patterns and reduced response times. Typically developing children primarily focused on target stimuli and correct response options, whereas atypically developing participants exhibited more scattered gaze patterns across multiple images.

Predefined areas of interest (AOIs) were established within the test sheets to analyze specific aspects of visual attention, categorizing target, correct and incorrect stimuli. A subset of tasks was selected for detailed analysis, with comparisons made between typically and atypically developing participants. Significant differences emerged in certain subtests, particularly in total fixation duration, fixation count, and visit count for correct stimuli. Atypically developing participants tended to fixate longer on these areas, suggesting differences in cognitive processing strategies.

However, in these observations, no significant differences were found between the intervention and control groups. Key eye-tracking variables remained consistent across both groups, indicating that the intervention did not lead to measurable changes in gaze behavior.

5. CONCLUSION

In the systematic review and meta-analysis, we comprehensively examined and aggregated all available CP-related outcomes to evaluate the impact of WBV therapy. Significant improvements were observed in two walking-related outcomes—walking speed and step length—while nonsignificant but clinically meaningful positive changes were noted in several musculoskeletal outcomes. The findings suggest that patients with milder forms of CP (GMFCS I-II) tend to experience more substantial benefits from WBV therapy, as supported by significant results primarily related to walking and balance.

Based on the findings, a clear assessment of the usefulness of this intervention cannot be made; nonetheless, due to the promising results, it would be worthwhile to conduct additional RCTs to enhance the available evidence in this field. Additionally, this review highlights a notable gap in the literature, as very few studies included patients with severe impairments, and none involved GMFCS V-level patients. Investigating the effects of WBV therapy on the most severe CP cases could provide valuable insights and represent an important avenue for future research. Furthermore, future research should focus on investigating the short-term effects of WBV therapy on spasticity, particularly immediately after the intervention, to better understand its immediate benefits.

Our other research highlights the importance of addressing visual perceptual deficits in children with CP and demonstrates the value of integrating technology-supported applications into special education programs. The MVPT-4 assessment results showed that children with CP scored significantly lower on mean perceptual quotients compared to their typically developing peers. This study also aimed to investigate the long-term effects of the educational applications developed on the visual perceptual skills of children with CP. While the effect size was not statistically significant, the observed improvements suggest that such interventions hold promise for enhancing visual perceptual and attention skills. The findings also reaffirm the strong relationship between physical condition and visual perceptual abilities, emphasizing the need for holistic approaches in intervention planning.

The integration of eye-tracking technology provides valuable insights into the visual attention and task comprehension of children with serious forms of CP and communication deficits, highlighting its potential as a supportive tool in future assessments and interventions.

Further research with larger sample sizes and longitudinal designs is necessary to fully understand the potential of technology-supported applications in improving cognitive and visual skills. This study contributes to the growing body of evidence that underscores the role of assistive technology in supporting children with CP.

6. Bibliography of the candidate related to the thesis

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Q2 IF: 1.7