Gross Motor Function in Patients with Cerebral Palsy in Rehabilitation Process with Virtual Reality

Função Motora Grossa em Pacientes com Paralisia Cerebral em Processo de Reabilitação com Realidade Virtual

Función motora gruesa en pacientes con parálisis cerebral en proceso de rehabilitación con realidad virtual

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ABSTRACT

Objective: This study aims to evaluate the effects of the correlation between variables of interventions based on Virtual Reality (VR) and its influence (positive or negative) on gross motor function in patients with Cerebral Palsy (CP).

Methods: A systematic search was conducted within the following data bases: PubMed; Web of Science; Scopus; Scielo and, Google Scholar (up to page 25). Seventeen studies met the inclusion criteria applied. A total of 145 patients were evaluated regarding the variables of analysis. Virtual Reality (VR) tools have been classified as specific or non-specific. Statistical analysis, based on tests of multivariate analysis and correlation coefficients, were conducted to determine variables behavior.

Results: Statistical tests suggest that non-specific hardware for rehabilitation programs have higher positive impact. Also, a significant correlation between the time of sessions used in interventions and improvement of motor function were observed, showing that sessions between 45 and 50 minutes tend to be more efficient.

Conclusions: Type of hardware and time of sessions are significant variables to be consider when planning interventions for children and adolescents with CP.

Keywords: Cerebral palsy; virtual reality; rehabilitation; gross motor function.

RESUMO

Objetivo: Este estudo tem como objetivo avaliar os efeitos da correlação entre variáveis de intervenções baseadas na Realidade Virtual (RV) e sua influência (positiva ou negativa) na função motora grossa em pacientes com Paralisia Cerebral (PC).

Métodos: Foi realizada uma busca sistemática nas seguintes bases de dados: PubMed; Web of Science; Scopus; Scielo e Google Scholar (até a página 25). Dezessete estudos preencheram os critérios de inclusão aplicados. Um total de 145 pacientes foi avaliado quanto às variáveis de análise. As ferramentas de Realidade Virtual foram classificadas como específicas ou não específicas. A análise estatística, baseada em testes de análise multivariada e coeficientes de correlação, foi realizada para determinar o comportamento das variáveis.

Resultados: Testes estatísticos sugerem que hardware não específico para programas de reabilitação tem maior impacto...
positivo. Além disso, foi observada correlação significativa entre o tempo de sessões utilizado nas intervenções e a melhora da função motora, mostrando que sessões entre 45 e 50 minutos tendem a ser mais eficientes. Conclusões: O tipo de hardware e o tempo das sessões são variáveis significativas a serem consideradas no planejamento de intervenções para crianças e adolescentes com PC.

Palavras-chave: Paralisia Cerebral; realidade virtual; reabilitação; função motora grossa.

INTRODUCTION

Cerebral palsy (CP) is a non-progressive and non-evolutionary group of disorders, as result of a lesion on central nervous system. It is generally described as a group of permanent disorders in movement, posture, motor coordination and muscle tone, which occurs in brain development on fetal or infants. CP might be classified concerning the motor impairments, namely: ataxica, spastic, extrapyramidal, hypotonic and, mixed. Regarding body distribution CP is characterized in hemiparesis, diparesis and tetraparesis.

Gross Motor Function Classification System (GMFCS) has been largely used to describe gross motor function in individuals with CP. It is a five-level system, age-related, in which level “V” represents the most restriction and level “I” the least, based on self-initiated movements, particularly sitting and walking. A quantitative scale named Gross Motor Function Measurement (GMFM) was developed to evaluate change in gross motor function in patients with CP. This scale describes levels of gross motor function disregarding the quality of motor performance in order to evaluate and support the treatment focused at improving motor function and quality of life.

Among the rehabilitation therapies used with CP patients, the Virtual Reality (VR) tools stand out for promoting multisensory stimuli that stimulates motor development by challenging postural stability and body alignment. Furthermore, this approach enables a great clinical control, such as activity duration and intensity and offers the possibility of a motivational environment for patients.

Although VR is already being widely used in treatments to promote motor improvements in individuals submitted to it, scientific studies found in the literature usually do not present a robust format, and do not include a control group or randomness of participants. Thus, the aim of this systematic review is to verify significant correlation between variables of the VR intervention presented and whether there is an influence (positive or negative) on gross motor function in patients with CP.

METHODS

This is a systematic review of studies that presents results from therapies based on VR for rehabilitation of individuals with CP.

The search was performed within the following data bases: PubMed; Web of Science; Scopus; Scielo and, Google Scholar (up to page 25). The keywords adopted were: “virtual reality”, “cerebral palsy”, “GMFCS” and “GMFM”, and the corresponding terms in Portuguese “realidade virtual”, “paralisia cerebral”, in addition to the Mesh terms for “cerebral palsy” and “virtual reality”. The search was conducted between April and May 2019.

Inclusion criteria were: articles published from 2007 to 2019; publications in Portuguese and English; studies conducted with people with CP; studies conducted with children and adolescents (2-18 years of age); the use of GMFCS scale; the evaluation of motor development through the GMFM scale during pre and post-intervention periods and; studies using any type of VR tool. Exclusion criteria were: studies published in unindexed journals that did not present the impact factor; review articles and; studies that did not mention GMFCS scale to define CP level and GMFM scale to evaluate the gross motor function.

Statistical analysis

The intervention variables collected for statistical analysis were divided into three groups:

Related to patient: age, gender and level of cerebral palsy according to GMFCS classification.

Related to hardware: type of VR hardware (TH) used in intervention (this variable was divided into three subgroups: Nintendo Wii (NW), Xbox (XB) and specific hardware (SH). By SH was
considered all VR tools used in rehabilitation which were designed specifically for that training or therapy. In the present study, the following SH were identified: GRAIL of Motekforce Link\textsuperscript{11}, Rutgers Ankle CP system\textsuperscript{12}, Biodex Gait Trainer 2\textsuperscript{13} and Pediatric Locomat© System\textsuperscript{14}.

Related to the intervention: period of the intervention (PI) measured in weeks; total number of sessions (NS) performed during the period of each intervention; time of sessions (TS), in minutes; the total time of the intervention (TTI), in minutes, calculated by the product between TS and NS applied and, finally, the mean evolution or regression percentage in GMFM scale (PGS). Only GMFM scale dimensions D and E were considered, which measures motor function on feet and the functions walk, run, and jump respectively. The number considered in GMFM scale was the percentage of the mean value between the difference of dimensions D and E, measured before and after intervention, whenever results were presented individually. For those studies that have demonstrated the outcomes as general for all subjects, the same value was considered for each. This parameter was adopted for age as well.

Initially, statistical analysis was conducted to validate the normality among variables and identify which statistical approach should be used, whether parametric or not. Over a multivariate analysis, using software Rstudio version 1.0.136, the distribution of the sample was analyzed first separately and then combined for its better understanding. For non-categorical variables, Shapiro-Wilk test and an array of scatter plots were chosen for examination. The Spearman’s method was adopted to calculate the correlation coefficients using SPSS 20 and the level of significance adopted was \( p < 0.05 \). The categorical variable type of hardware (TH) correlation was analyzed by boxplot charts and models of linear regression as simple quadratic, logistic regression and generalized regression with binomial family, Poisson and Exponential. Stepwise method was used for all models.

All variables presenting \( p \)-value < 0.05 through Spearman’s test, when compared to the response variable PGS, were submitted to H test (Kruskal-Wallis) using Rstudio, intending to identify whether its values affected PGS differently. Subsequently, a multiple comparison test using Wilcoxon method was performed to compare between groups, to identify whether any value or, group of values, had greater influence on PGS. This test also included the result of Boxplot analysis.

Statistical analysis between the variables period of intervention (PI); number of sessions (XS); time of sessions (TS) and; total time of the intervention (TTI) was dismissed due to level of dependency.

RESULTS

A total of 338 articles were found in the initial search. After applying the selection criteria, 17 articles were elected, as presented in Figure 1.

Figure 1. Flowchart presenting the selection steps of articles evaluated (\( n \) – number of articles).
Considering the selected studies, a total of 145 individuals (ages 4-18 years) with CP diagnosis were evaluated and classified according to the analysis variables chosen, i.e. cerebral palsy level (GMFCS); PI; NS; TS; TTI and PGS. One study has presented different duration between sessions\textsuperscript{13}, so weighted average was calculated to add the numbers in the database. Descriptive data is presented in Table 1.

Table 1. Descriptive statistics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Q1</th>
<th>Medium</th>
<th>Q3</th>
<th>máx</th>
<th>min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>7</td>
<td>10</td>
<td>11</td>
<td>18</td>
<td>4</td>
</tr>
<tr>
<td>GMFCS, level</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>PI, weeks</td>
<td>6</td>
<td>8</td>
<td>9</td>
<td>16</td>
<td>3</td>
</tr>
<tr>
<td>NS n</td>
<td>12</td>
<td>16</td>
<td>24</td>
<td>40</td>
<td>8</td>
</tr>
<tr>
<td>TS minutes</td>
<td>30</td>
<td>40</td>
<td>40</td>
<td>60</td>
<td>30</td>
</tr>
<tr>
<td>TTI minutes</td>
<td>480</td>
<td>640</td>
<td>810</td>
<td>1440</td>
<td>240</td>
</tr>
<tr>
<td>PGS</td>
<td>2.5</td>
<td>3.1</td>
<td>5.8</td>
<td>13</td>
<td>0</td>
</tr>
</tbody>
</table>

Abbreviations: Q1, first quartile; Q3, third quartile; PI, Period of Intervention; NS, Number of Sessions; TS, Time of Sessions; TTI, Total Time of Intervention; PGS – % of GMFM scale

The variable TH, that defines the VR tool used, was classified as NW, XB and SH and presented a frequency distribution of 31%, 32% and 36% respectively considering the number of individuals in the sample. Taking in account TH against number of interventions, the distribution revealed 39%, 16% and 44% respectively showing that SH were the most used among rehabilitation studies.

The outcome of W test, for \( \alpha=0.05 \), revealed a non-Gaussian behavior for the analysis variables. Thus, a non-parametric statistical approach was used for subsequent analyses. Spearman’s test indicated a significant correlation between GMFCS and TS compared to PGS, \( p=0.006 \) and \( p=0.014 \) respectively. The box plot chart (Figure 2) – which uses the median as the second quartile, first quartile with positive asymmetry and third quartile negative asymmetry – displayed a correlation between TH and PGS due to the difference in data concentration for each type of hardware, represented by the asymmetry comparing the rectangles of the chart. None of the regression models tested have showed significant covariates, therefore all were dismissed.
The H test was carried out comparing variables GMFCS; TS and; TH with PGS, to identify differences between groups, as shown in table 2. For the GMFCS level the test presents a significant difference between CP level I and II (value-p=0.01), pointing that level II has a better result in development of motor function. No significant differences were found between levels I - III or I - IV, as well as II - III and II - IV. For TS, H test identified a significant difference when comparing sessions using 30 minutes against those of 45 and 50 minutes, as well as 40 minutes against 45 and 50 minutes. H test also suggests a more efficient result for PGS applying sessions of 45 and 50 minutes. No significant differences were revealed when comparing sessions of 30 against 40, nor 45 against 50 minutes, as well as 60 minutes against all others. For TH, outcome pointed significant discrepancy between SH and NW as well as XB, but no differences established between NW and XB. Results also suggest that NW and XB have higher positive impact on PGS.
### Table 2. Kruskal-Wallis Test for GMFCS, TS and TH

<table>
<thead>
<tr>
<th>GMFCS</th>
<th>c-s</th>
<th>df</th>
<th>p-value 1</th>
<th>TS</th>
<th>c-s</th>
<th>df</th>
<th>p-value 1</th>
<th>TH</th>
<th>c-s</th>
<th>df</th>
<th>p-value 1</th>
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<tbody>
<tr>
<td></td>
<td>13,195</td>
<td>3</td>
<td>0.0042**</td>
<td></td>
<td>55,572</td>
<td>4</td>
<td>2.47E-11**</td>
<td></td>
<td>16,46</td>
<td>2</td>
<td>0.0002**</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Groups</th>
<th>p-value 2</th>
<th>Groups</th>
<th>p-value 2</th>
<th>Groups</th>
<th>p-value 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>II - I</td>
<td>0.01*</td>
<td>40 - 30</td>
<td>0.06494</td>
<td>NW - SH</td>
<td>0.00172*</td>
</tr>
<tr>
<td>III - I</td>
<td>0.59</td>
<td>45 - 30</td>
<td>0.00012*</td>
<td>XB - SH</td>
<td>0.00092*</td>
</tr>
<tr>
<td>III - II</td>
<td>0.18</td>
<td>45 - 40</td>
<td>1.20E-10*</td>
<td>XB - NW</td>
<td>0.74931</td>
</tr>
<tr>
<td>IV - I</td>
<td>0.34</td>
<td>50 - 30</td>
<td>0.00299*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV - II</td>
<td>0.59</td>
<td>50 - 40</td>
<td>0.00146*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV - III</td>
<td>0.18</td>
<td>50 - 45</td>
<td>0.17129</td>
<td>60 - 30</td>
<td>0.20404</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>60 - 40</td>
<td>0.20404</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>60 - 45</td>
<td>0.06857</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>60 - 50</td>
<td>0.11891</td>
</tr>
</tbody>
</table>

Abbreviation: TS, Time of session; TH, Type of hardware; c-s, chi-squared; df, degrees of freedom.
** indicates statistical significance for Kruskal-Wallis test,
* indicates statistical significance for Wilcoxon test.
p-value 1 – value of probability for Kruscal-Wallis test, p-value 2 – value of probability for Wilcoxon test, p-value<0.05 shows difference between groups.

### DISCUSSION

This systematic review aimed to evaluate significant correlation between variables of the VR interventions presented and the influence (positive or negative) on gross motor function in patients with CP. The study compares: age, TH, GMFCS level, TI, NS, TS, TTI and PGS.

Results show that 99% of the individuals analyzed, have exhibited improvements in motor function regardless the hardware used. These results emphasize the importance of VR in the rehabilitation processes of patients with CP. This fact corroborates that VR is a well recommended therapy to promote global changes in motor function of children with CP.

Correlation analysis between GMFCS level and PGS suggests a significant difference in motor function only when comparing levels I and II. However, some studies present that VR can bring improvements to children with CP, regardless the GMFCS classification, suggesting that this system may not be able to predict significant differences in gross motor function and that an intervention according to the level of CP should present a more coherent result.

A recent study, presented by Duran et al. have conducted an observational research reporting that less affected children (GMFCS level I and II) tend to benefit more than children with GMFCS-L evels III-IV, but not significantly. The outcome, on this specific topic, was not able to make a clear statement, since statistics have pointed no differences between level I compared to level III and IV, nor level II compared to level III and IV.

Although this investigation points that TS can influence PGS, since TS of 45 and 50 appeared to have greater favorable impact, further research should be conducted for more clear understanding. Some studies suggest the use of longer sessions when there are no positive functional changes in participants of VR therapies, but in the sample analyzed in this review, 70% of the subjects, who presented PGS above median, were submitted to sessions below 60 minutes. It is noteworthy that the results found indicate that longer sessions are not necessarily more efficient.

A survey published in 2011 stated that after intensive 5 days intervention using VR, applying 90-minute sessions, in 4 adolescents with GMFCS CP level I found no changes in dimension E of the GMFM scale. As a complement, there are studies indicating that longer sessions can bring loss of performance, due to the visual system being in constant attention to complete activities. In addition, the intervention that presented the highest positive impact on GMFM scale, used 30
minute sessions\textsuperscript{14}.

Other studies also suggest the necessity of taking attention on the period of the intervention and frequency to which participants interact with the VR tool, as these factors may affect the development of gross motor function\textsuperscript{19}. It is important to consider that statistical analysis of this systematic review have showed no significant correlation between NS or TTI with the improvement of motor function. The results also indicate that the use of non-specific hardware for therapy or training individuals with CP have greater impact on motor development.

To our knowledge, this is the first study showing this type of comparison. It is implied the hypothesis that SH use games that seek to stimulate the most affected regions of the brain, focusing on motor control, consequently, on the greater development difficulties presented by individuals with CP. Commercial hardware (non-specific hardware) uses games that stimulate other general neural regions, whether injured or not. This could explain non-specific hardware greater efficiency, as well as therapies that use non-specific tools to treat brain injuries\textsuperscript{9}.

The great adaptive capacity of the human nervous system comes from neural plasticity which allows, throughout the ontogenetic development during the process of active interaction of each person with the environment, to structure and modify, in all aspects\textsuperscript{22}. Therefore, environment plays a crucial role in promoting neurological recovery functions having a direct and indirect impact on neural plasticity of the nervous system and, consequently, on the rehabilitation of patients with brain injury\textsuperscript{23}.

Children with CP have their neural plasticity and behavioral changes reinforced when treated with therapeutic methods, or given tasks, that require skills to solve problems\textsuperscript{24}. Moreira et al.\textsuperscript{25} worked with therapies that can act compensatory in the rehabilitation process such as music therapy, thus identifying functions or abilities that are still preserved in the patient and compensating the deficit with these alternative skills. It is also noteworthy that motivation and attention, combined with cognitive engagement are crucial factors and can determine the improvement of motor performance, although within the limitations of clinical standards\textsuperscript{26}. These factors were not statistically evaluated because most studies did not present the data quantitatively on the same basis.

Clinical Implications

Statistical tests have pointed non-specific hardware as more efficient for rehabilitation programs. This result reinforces the greater accessibility on using VR tools on treatments of children and adolescents with CP, since that types of hardware are universally available at affordable prices. It also facilitates all logistics involved considering that sessions might be performed anywhere possible to plug and play those types of non-specific hardware.

Concerning TS, professionals could develop their interventions focusing on sessions of 45 to 50 minutes for a short period, since the duration of sessions has showed no significant influence on the gross motor development, according to the statistical outcomes. This aspect can also encourage the use of VR in rehabilitation process, where children can obtain, and feel, positive results in a short period of time.

Limitations

This systematic review did not analyse the intervention variable “type of game used”, which could have influenced the results. However, this question had its effect minimized using the same dimensions of the GMFM scale (D and E), thus, regardless to the type of game used, the movements evaluated were of the same dimension.

The main factors for validation in clinical trials include the presence of a control group, a random distribution of participants between groups, analysis by treatment intention, blind evaluators and sample, and recruitment of groups with homogeneous characteristics\textsuperscript{27}. There is no evidence the studied interventions in this systematic review met all those criteria.

Thus, for future research, it is suggested an investigation with a greater number of children with more functional classifications, a longer intervention period, use of other games and the inclusion of a control group.
CONCLUSION

In order to find significant correlations, between variables of rehabilitation programs with VR and their impact on motor function in children and adolescents with CP, this systematic review have showed that using non-specific hardware in interventions have promoted better results for gross motor function. Also, TS seems to have influence on GMFM, pointing that sessions between 45 and 50 minutes have a greater positive impact.

The studies included in this systematic review have indicated that VR is an effective method for improving gross motor function, since they demonstrated an enhancement on 99% of the individuals, regardless the hardware used.

The relevance of VR was supported by this review and shows the importance of how a rehabilitation process protocol might impact the outcome of motor function development, regarding the type of technology and time of sessions applied to patients. The more standardized the approaches used in interventions, the more reliable the analyses and results, allowing reach a reference protocol to professional and academic community.

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