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Intelligent Virtual Reality Therapy Systems for Motor and Cognitive Rehabilitation: A Survey based on Clinical Trial Studies

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Abstract

Rehabilitation is the process related to the recovery, maintenance or improvement of physical mental and / or cognitive skills necessary to carry out daily activities. Virtual reality therapy, virtual reality (VR) immersion therapy, simulation therapy or virtual reality exposure therapy is an intervention method of using virtual reality technology for psychological or occupational therapy. The possibility of simulating situations necessary for the treatment, controlling variables and reducing the patient's exposure to risks are popular factors for this tool. Many studies indicate that therapy with the aid of virtual reality brings great benefits to the patient. In this article, we present, through a review of 117 articles, the feasibility of applying VR in treatments with clinical trial methodology, identifying through the "Patient, Intervention, Comparison and Outcomes" the characteristics, population, treatment time, forms of comparison and if the results obtained are effective. The characteristics identified during the process show that virtual reality applied to therapies can be used without negative interference in the treatment. In addition, the results show that VR in rehabilitation treatments are motivating and show better results than traditional treatments.

Keywords

Intelligent systems, Computer-aided design, Virtual reality therapy, Neurorehabilitation.

1. Introduction

Rehabilitation is the process related to the recovery, maintenance or improvement of mental and/or cognitive physical skills required to perform daily activities [1]. Generally, a multidisciplinary team such as physiotherapists, physicians, occupational therapists, psychologists, speech therapists, among others, work together with the patient to achieve this goal. According to WHO [2], around 2.4 billion people currently live with a health problem that benefits from rehabilitation. Several treatment options for rehabilitation that stimulate motor skills and neuropsychological capacity. Physiotherapy sessions,

occupational therapies, hippotherapy, hydrotherapy, music therapy, exposure therapies and virtual reality therapies [3] are examples used by specialists according to the type of disease, age, patient interest and access to treatment. Virtual reality therapy, virtual reality immersion therapy, simulation therapy or virtual reality exposure therapy, is an intervention method of using virtual reality technology for psychological or occupational therapy. The possibility of simulating situations necessary for the treatment, controlling variables and reducing the patient's exposure to risks are popular factors for this tool. Many studies indicate that therapy with the aid of virtual reality brings great benefits to the patient. This type of therapy is possible because virtual reality is an advanced interface for computer applications, in which users can navigate and interact with a computer-generated three-dimensional environment through multisensory devices such as kinect, leap motion and biomedical equipment [32][33][34].

Virtual reality environments combined with treatments for patients with cerebral palsy [7] [8] [9] [10], stroke [11] [12], phobias [13] [14] [15] [16], Autism (Autism Spectrum Disorder) [17] [18] [19] are examples of works that indicate this reality. To verify the effectiveness of virtual reality (VR) in rehabilitation therapies, several techniques are applied, such as comparisons of results of applications on volunteers. Clinical trial is a prospective biomedical or behavioral research study of humans designed to answer specific questions about biomedical or behavioral interventions (vaccines, drugs, treatments, devices, or new ways of using known drugs, treatments, or devices). Clinical trials are used to determine whether new biomedical or behavioral interventions are safe, effective, and efficient [4][6]and can be used to perform this validation. The aim of this study was to review evidence supporting the effectiveness of virtual reality therapies in trial clinics for motor and cognitive rehabilitation helping us to answer the following questions:

1. What are the characteristics that identify the effectiveness of a clinical trial using VR?
2. What is the period of sessions used for clinical trials using VR?
3. What are the evaluation methods of the trial clinic?

In this research, it is possible to view contributions of works related to the theme over the last 5 years, between 2016 and 2021. In total, 117 works were selected, which were classified according to the acceptance criteria defined in the methodology, based on the information collected and classified through the P.I.C.O. (Patient, Intervention, Comparison and Outcomes), which according to the Evidence-Based Practice (EBP), considers that these elements are fundamental to the research question and the construction of the question for the bibliographic search for evidence. The P.I.C.O. can be used to build research questions of different natures, arising from the clinic, the management of human and material resources, the search for instruments for symptom assessment, among others [20].

2. Methodology

Carrying out this research is approached according to the following steps:

1. Develop research terms or keywords related to clinical trial and virtual reality;
2. Search for the most relevant study bases and adapt the keywords and expressions to the search engines referring to each search base;
3. Identify criteria for inclusion and exclusion of articles and classify them by P.I.C.O; and
4. Establish conclusions based on findings related to the topic, as shown in the figure 1.

2.1. Develop search terms and keywords and objective

The objective of identifying the keywords and expressions was to obtain a significant number of results related to research on applications related to clinical trial using Virtual Reality as a complementary tool to the motor rehabilitation of patients with neurological disorders, a topic addressed in our study.The query was defined as: "clinical trial" associated

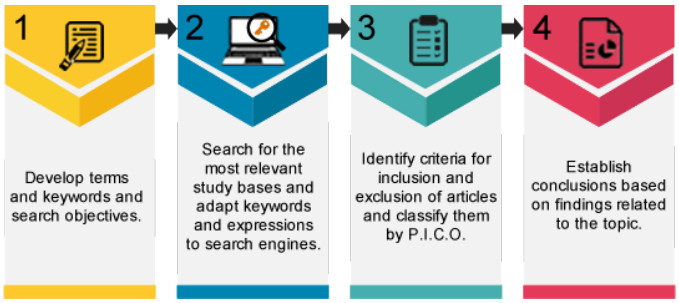

Figure 1. Methodology

with "virtual reality" or "virtual environment" or "artificial environment" in the article title (Publication title), keyword and Abstract applied according to the particularities of the search engines.

2.2. Search for the most relevant study bases and adapt the keywords and expressions to the search engines referring to each search base.

The expressions were adapted to search engines according to the rules defined by each query base and filtering according to:

- Period: 2016-2021
- Idiom: English
- Article Types: Magazines in Digital Format
- Query bases: The selection of studies was made on the bases of IEEEXplore, Springer, Science Direct, SAGE, Nature, PLOS One, MDPI, Wiley, BJS Society, Peerj, ACM Digital Library, Inderscience Online, Hindawi, Frontiers.

2.3. Identify criteria for inclusion and exclusion of articles and classify them by P.I.C.O

The inclusion and exclusion criteria will be responsible for defining the articles that are relevant to the research topic.

As inclusion criteria are being considered:

- Text and title of works in English
- Works related to the use of VR in clinical or experimental trials treatments
- Articles that, although they do not present the keywords in the research, but which have the name of virtual reality tools such as the name of the VR tool or system that is applied to motor and/or cognitive rehabilitation of patients with neurological disorders or dysfunction.

As exclusion criteria we can indicate:

- Title of the article in English but the text of the article in another language.
- Articles found in more than one search will be considered only one.
- Articles whose content does not portray works on rehabilitation in patients.
- Review or Survey articles, as this is not a study that presents a clinical study.
- Abstract type articles in journals, as there may not be enough information about the applied methodology.
- Articles related to simulations or training of clinical practices (simulation of surgeries and procedures).
- Works that do not fit into the topics related to the area.
- Articles that were not possible to view their full content.

After screening according to the inclusion and exclusion criteria of the works found, the P.I.C.O. is applied. The P.I.C.O. define in its acronym for P = Patient/Problem/Population,

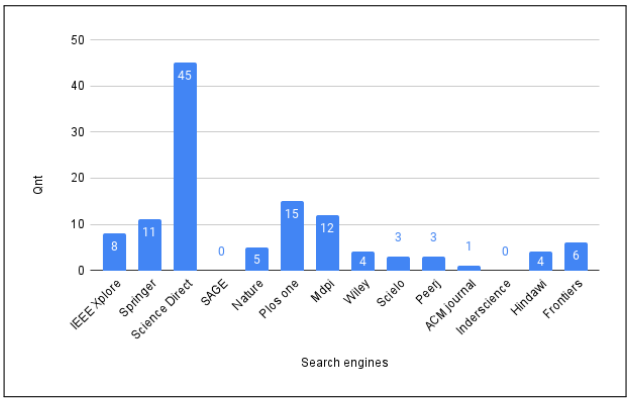

Figure 2. Articles accepted by search engine

that is, who is the target audience in which it is being researched; I = Intervention (or the experimental variable), which is the type of methodology applied during the applications, usually using a control or placebo group that is compared with the group in which the intervention to be evaluated is applied; C = Comparison (or the control variable), where the results are compared and the effectiveness of the applied methodology is verified; and O = Outcome, that is, the result obtained in the study.

The P.I.C.O. is a technique used in evidence-based practice to frame and answer a clinical question in terms of the patient's specific problem that helps clinically relevant evidence in the literature. Defining a clinical question in terms of the patient's specific problem helps the researcher to find clinically relevant evidence in the literature. The P.I.C.O. template is a format to help define the survey question [30] [31].

2.4. Establish conclusions based on findings related to the topic.

Findings were divided according to the type of disease or related problem. As the objective of this study is not limited to the disease, but to the type of method applied, to identify the best results obtained, articles are classified and evaluated by groups according to the similarity of the disease. Finally, a general conclusion obtained analyzing the results of each group will be considered.

2.5. Analysis of Results

Based on the objectives of this work in the search for an understanding of clinical trial applications using virtual reality in rehabilitation therapies, the following keywords were defined: "Clinical trial" and "Virtual reality", "Clinical Trial" and "Virtual environment", " Clinical essay "and "artificial environment" found in the title, abstract and or keyword. The search in the selected databases and using Boolean operators and keywords, resulted in the data. In total, 527 results were found based on the actions performed in step 2.2 where, 26 from IEEEXplore, 22 from Springer, 69 from ScienceDirect, 0 from SAGE, 21 from Nature, 73 from Plos One, 14 from Mdpi, 5 Wiley, 3 Scielo, 49 from Peerj, 11 from AMC Journal, 0 from Inderscience, 4 from Hindaw and 230 from Frontiers. In total, 117 articles were eligible for analysis in this study, the graph below shows the percentage of articles accepted by journal (Fig. 2).

It can be observed in relation to the distribution of annual publications, that within the range consulted, the year 2020 had the period with the highest number of publications, while the year 2016 was the year that was found the lowest number of publications and over the years there is a growing number of research related to the topic (Fig. 3).

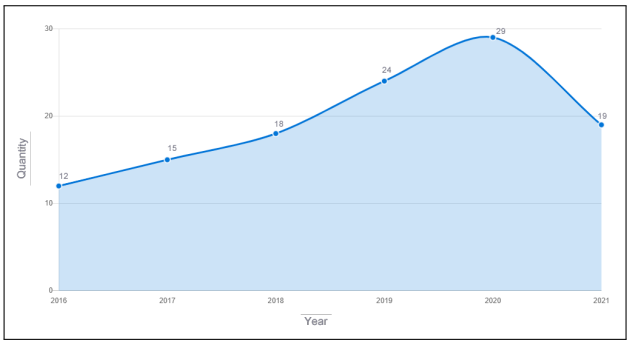

Figure 3. Number of articles per year

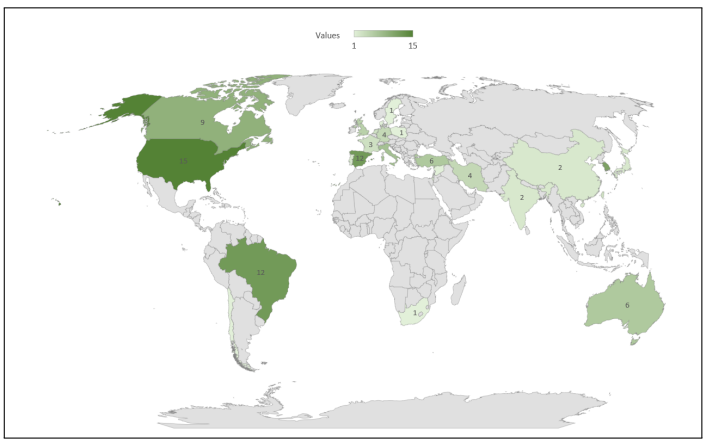

Figure 4. Distributed articles map

During the research, it was observed that the countries that had publications related to the topic between the period 2016 to 2021 are mainly concentrated in the USA, Canada, Brazil and Italy, as shown in the figure 4. According to the surveys, 1.7% China, 5.1% Iran, 3.4% Portugal, 16.9% USA, 5.1% France, 6.8% Spain, 10.2% Spain, 11.9% Brazil, 1.7% The Netherland, 1.7% Chile, 3.4% Turkey, 8.5% South Korea, 13.6% Canada, 5.1% Australia. Two works stand out for carrying out interventions in more than one country, such as Ortiz-Catalan et al. [94] and Hsieh, et al. [121].

Below is the list of accepted articles:

Table 1. Classified articles

Author	Illness	N	Age	Equipment	Own Software	Groups	Session time (min)	Total of Sessions
Al-Nerabieah et al. [73]	Medical procedure	64	6 - 10	Device Mobile	N	2	20	1
Amaral et al. [56]	Autism Spectrum Disorder	15	16 - 38	Computer	Y	1	-	7
Amin, Ashfaq M., et al. [104]	Medical procedure	30	23 - 68	Device Mobile Computer	Y	3	20 - 30	1
Amiri, Paria, et al. [103]	Pregnancy	68	28 - 32	Computer	N	2	60	4
Amritha, N [117]	Balance	30	m 25	Computer	Y	2		4
Arnoni et al. [72]	Cerebral Palsy	35	5 - 14	Game Console	N	2	45	16
Avcil et al. [96]	Cerebral Palsy	30	4 - 11	Game Console Computer	N Y	2	60	24
Barsasellaa et al [125]	Old People	60	60 - 94	Computer	Y	2	15	12

Bentz et al. [141]	Phobia	70	18 - 60	Device Mobile	Y	2	60 (phase 1) 30 (phase 2)	7
Bortone, I [118]	Cerebral Palsy	20	7 - 14 / 8 - 16 / 24- 32	Computer	Y	3	-	-
Huang et al. [83]	Stroke	1	50 - 75		S		30 min	54
Botella [148]	Phobia	63	21 - 70	Computer	Y	2	180	1
Bourque et al. [97]	Amputation	60	> 18	Computer	Y	2	15 - 20	24
Brown et al. [124]	Paranoia	100	> 18	Computer	Y	2	30	1
Buyuk [135]	Medical procedure	78	5 - 10	Device Mobile	Y	2		1
C. P. Amaral et al. [84]	Autism Spectrum Disorder	17	15 - 26	Computer	Y	-	32	3 (try)
Calabrò et al. [100]	Stroke	24	54 - 73	Proprietary solution	Y	2	45	40
Cavalcante Neto et al. [98]	Dispraxia	30	7-10	Game Console	N	2	60	12 - 16
Chan, Evelyn, et al. [102]	Medical procedure	254	4 - 11	Device Mobile	Y	2	30	1
Collado Mateo [169]	Fibromyalgia	76	30 - 75	Computer	Y	2	60	16
De Luca et al. [58]	Traumatic brain injury	100	m 39.9	Proprietary solution	Y	2	60	18
Dehghan, Fateme, et al. [106]	Medical procedure	40	6 - 12	Computer	Y	4	5	1
dela Barrera [156]	Emotional Problems	119	11 - 15	Device Mobile	Y	2	50	-
Dellazizzo et a. [142]	Schizophrenia	74	> 18	Computer	Y	2	-	9
Dellazizzo et al. [68]	Schizophrenia	10	>18	Computer	Y	2		6
Deutsch, Judith, et al. [113]	Stroke	13	30 - 75	Game Console	N	2	60	12
Dimbwadyo-Terrer et al. [57]	Tetraplegia	21	19 - 65	Computer	Y	2	30	15
du Sert et al. [85]	Schizophrenia	19	24 - 62	Device Mobile	Y	2	45	7
Erdogan et al. [133]	Medical procedure	108	7 - 12	Device Mobile	Y	4	application duration	1
Fonseca [166]	HAM / TSP	29	18 - 64	Game Console	N	2	20	20
France and Thomas (2018) [79]	Backache	230	18 - 60	Computer	Y	2	-	18
Gandolfi et al. [59]	Parkinson	76	> 18	Game Console	N	2	50	21
Garca Vravo et al. [159]	Cardiovascular disease	20	m 51.20	Game Console	N	2	60	16
Garrett et al. [71]	Cancer	12	37 -73	Computer	N	2	45	24
Gatica-Rojas et al. [78]	Cerebral Palsy	32	7 - 14	Game Console	N	2	35	18
Gerard Fluet [115]	Stroke	14	3 - 80	Computer	Y	3	60	8
Ghadimi, S., et al. [107]	Medical procedure	28	4 - 5	Computer	N	2	-	2
Gomes et al. [93]	Mobility	30	71 - 92	Game Console	Y	2	50	14
Gülçin et al. [126]	Cancer	42	6 - 17	Device Mobile	Y	2	3 - 5	1
Hamzeheinejad, Negin, et al. [114]	Stroke	21	19 - 35	Computer	Y	2	2	-
Hassett et al. [69]	Mobility	300	18 - 101	Game Console	N	2	30 - 60	60
Hsieh [151]	Development delay	147	3 - 12	Computer	Y	2	30	8
Hsieh, et al. [121]	Multiple sclerosis	144	20 - 65	Computer	Y	2	15 - 45	18

Huang et al. [146]	Medical procedure	50	m 67.5	Device Mobile	Y	2	15 - 45	1
Ikbali Afsar et al. [74]	Stroke	35	m 69.42	Game Console	N	2	60	20
Doraiswamy et al.[**?**]	Alzheimer							
Johnson et al. [137]	Stroke	60	> 18	Proprietary solution	Y	2	45	16
Josiah P [120]	Dyadic motor learning	27	18 - 86	Computer	Y	2		5
Kairy et al. [90]	Stroke	52	> 18	Computer	Y	2	30	24
Cyr et al. [**?**]	Anxiety	54						2
Kakoschke et al. [132]	AAT	24	20 - 45	Device Mobile Computer	Y	3	10	
Keefe et al. [91]	Schizophrenia	323	m 42	Device Mobile	Y	2	75 - 90	2
Kim et al [143]	Stroke	28	m 53.2	Proprietary solution	Y	2	30	20
Kim et al. [140]	Stress	83	19 - 59	Device Mobile	Y	2		
Koo et al. [70]	Total Knee Arthroplasty	60	m 65	Computer	Y	2	20	10
Kutlu et al. [92]	Stroke	10	> 18	Proprietary solution	Y	2	60	17
Lamargue et al. [77]	Multiple Sclerosis	35	18 - 55	Proprietary solution	Y	2	45	50
Le May et al. [164]	Medical procedure	188	7 - 17	Game Console	Y	2	20	1
Lee [158]	Old People	56	m 80.23	Device Mobile	Y	2	50	20
Lee [67]	Stroke	42	> 18	Device Mobile	N	2	120	30
Lee et al. [63]	Stroke	18	> 18	Computer	Y	2	30	18
Liang Peng et Al. [116]	Stroke	24	18 - 70	Computer	Y	2	45	10
Liao et al [172]	Old People	42	> 65	Computer	Y	2	60	36
Lima Reblo et al. [139]	Old People	37	> 18	Computer	Y	2	-	16
Liu, Wang, et al. [109]	Addiction	95	18 - 45	Computer	Y	4	40	2
Machulska et al. [134]	Addiction	96	m 50,3	Computer	Y	2	90	
Maier, M [119]	Stroke	11	45 - 75	Computer	Y	2	30	30
Manuli et al. [88]	Stroke	90	m 43	Proprietary solution	Y	3		40
Maroo Souto et al. [171]	Schizophrenia	61	18 - 50	Computer	Y	2	60	12
Marques Sule et al. [138]	Stroke	29	> 18	Game Console	N	2		8
Marshall [154]	Aphasia	34	m 53.5	Computer	Y	4	20	30
Marshall [150]	Aphasia	20	m 57.8	Computer	Y	2	-	25
Melcer et a. [131]	Medical procedure	60	> 18	Game Console	Y	2	5 - 15	1
Meyns et al. [76]	Cerebral Palsy	41	7 - 14	Game Console	N	2	30	30
Molhemi et al. [128]	Multiple Sclerosis	39	18 - 64	Game Console	N	2	35	18
Montero-Alía et al. [101]	Mobility	380	> 60	Game Console	Y	2	30	24
Garcia-Zapirain, B. [163]	Old People	40	m 83.11	Computer	Y	2	20	9
Mugueta Aguinaga et al. [161]	Old People	46	> 65	Computer	Y	2	20	18
Nasseri [168]	Multiple Sclerosis	38	18 - 60	Device Mobile	Y	2	-	7
Norouzi-Gheidari et al. [66]	Stroke	23	m 42.2 - 57.6	Computer	Y	2	44	8
Norr et al. [87]	Suicidal ideation	162	> 18	Computer	Y	2	90 - 120	10
Norr, et al. [89]	Stress	162	> 18	Computer	Y	2	90 - 120	
Odin et al. [81]	Mobility	20	49 - 65	Computer	Y	2	45	1

Oliveira et al. [170]	Alzheimer	14	> 60	Computer	Y	2	30 - 45	16
Ortiz-Catalan et al. [94]	Amputation	14	26 - 74	Computer	Y	1	2 h	12
Park, Jin-Woo, et al. [112]	Medical procedure	80	4 - 10	Device Mobile	Y	2	4	1
Patrício et al. [95]	HAM / TSP	26	m 49	Game Console	Y	2	20	20
Pazzaglia et al. [82]	Parkinson	51	m 71	Proprietary solution	Y	2	40	18
Pedreira da Fonseca et al. [75]	Stroke	27	18 - 65	Game Console	N	2	60	20
Pericot-Valverde, Irene, et al. [111]	Addiction	102	> 18	Computer	Y	2	90	5
Perin, Alessandro, et al. [105]	Medical procedure	40	18 - 70	Computer	Y	3	30	1
Perry et al. [55]	Amputation	14	20 - 30	Proprietary solution	Y	2	20 - 30	20
Peultier-Celli et al. [99]	symptomatic knee osteoarthritis	236	m 64	Device Mobile	Y	2	25	18
Quero et al. [160]	AjD	57	18 - 54	Computer	Y	2	90	6 - 8
Radder [155]	Old People	91	m 73	Computer	Y	3	180 / per week	21
Ramnath et al. [153]	Old People	45	m 72	Game Console	N	2	60	24
Ramos et al. [149]	Prism shift	20	m 27.1	Computer	Y	3	-	1
Ribeiro et al. [62]	Pregnancy	32	18 - 35	Game Console	N	2	30	12
Ryu et al. [157]	Medical procedure	120	4 - 8	Device Mobile	Y	2	3	1
Ryu, J. H., et al. [108]	Medical procedure	69	4 - 10	Device Mobile	Y	2	4	1
Ryu, Jung-Hee, et al. [110]	Medical procedure	70	4 - 10	Computer	Y	2	5	1
Schuster Amf et al. [145]	Stroke	54	20 - 81	Computer	Y	2	45	16
Sheehy et al. [80]	Stroke	76	> 50	Computer	Y	2	30 - 45	10 - 12
Shimizu [165]	Schizophrenia	8	18 - 64	Game Console	N	2	35	24
Sieluycki [152]	Athletes	24	12 - 28	Computer	Y	2	20	5
Silva et al. [61]	Cardiovascular disease	27	> 45	Game Console	N	2	60	16
Soon Young Lee and Jiyeon Kang [123]	Sleep quality	48	> 18	Device Mobile	Y	2	30	1
Spiegel et al. [147]	Medical procedure	120	> 18	Device Mobile	Y	2	10	1
Sulfikar Alli et al. [136]	Stroke	120	> 18	Proprietary solution	Y	2	30	30
Tejera et al. [65]	Chronic non-specific pain in the neck	44	18 - 65	Device Mobile	N	2	-	8
Tennant et al. [130]	Cancer	90	7 - 19	Device Mobile	Y	2	10	
Thielbar [129]	Stroke	20	-	Computer	Y	2	-	8
Thomas et al. [86]	Backache	52	18 - 50	Computer	Y	2	15	8 - 12
Tuba et al. [122]	Medical procedure	139	4 - 10	Device Mobile	N	3	15	1
Volpi [167]	Hypertensive	49	50 - 69	Device Mobile	Y	2	-	84
Waliño-Paniagua et al. [60]	Multiple sclerosis	26	32 - 62	Computer	Y	2	30	20
Wall [162]	MCI	14	m 82.8	Device Mobile	Y	2	30 - 45	8 - 10

Yang et al. [64]	Autism Spectrum Disorder	17	m 22	Computer	Y	2	10 h	-
Yeo et al.[127]	Mood-related benefits	96	18 - 75	Computer	Y	2	5	1
Zeigelboim [144]	Hereditary spastic paraplegia	40	> 18	Game Console	N	2	30	20

Legend: TSP/HAM - Tropical spastic paraparesis/HTLV-1 associated myelopathy; AjD - Adaptation Disorder ; MCI - Mild cognitive impairment; AAT - Approach Prevention Training;

2.6. Population

The population observed during this study indicates that clinical trials procedures using VR are being widely used in different types of treatment approaches involving Motor Functions, Cognitive Functions, Anxiety, social inclusion, addictions and quality of life analysis. Most of the articles researched were applied to Patients with Stroke, Works with Elderly People, mainly in the care of frailty caused by age (risk of falling, loss of balance and muscle strength), Schizophrenia, Cerebral Palsy, Multiple Sclerosis, Application of medical procedures 5.

The number of people qualified for the interventions was related to the type of methodology applied in the related works. The mean of patients who participated in the interventions was Mean - 63.67 and its Median - 41.5. The age group included a minimum age of 4 years and a maximum of 101 years. All studies elected exclusion criteria and patient classification for intervention. The items considered in the exclusion criteria were patients outside the age group defined in the intervention methodology, not meeting any metrics identified as a result of an examination or previous assessment, sensitivity to light, in addition to having the free will participation of the patient to participate in the intervention. The initial number of patients for the interventions was not considered, only the patients who participated in the entire research proposal.

2.7. Intervention

The articles found during this research, the rehabilitation process is related to the motivation to provide the patient with a life close to normality, either by the psychological aspect in reducing anxiety, phobias, or in the motor recovery process and in the recognition of the body through the movements necessary to regain independence from daily activities. Complementary therapy through virtual reality is presented to all researched works as an

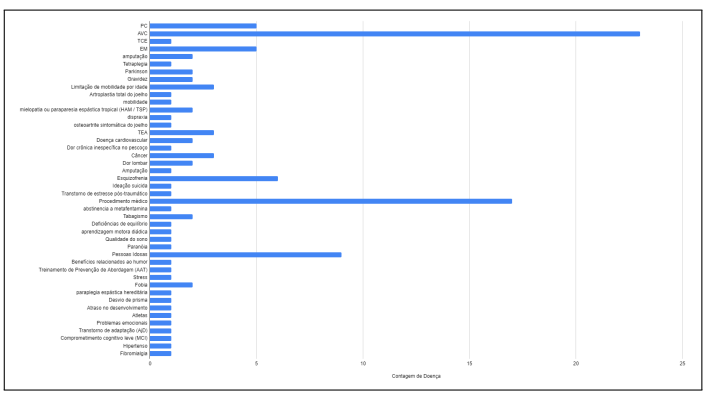

Figure 5. Number of items per illness

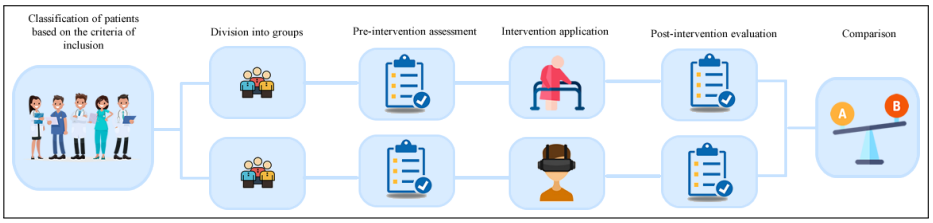

Figure 6. Clinica trial process

Table 2. Classification and domain according to ICF

	Part 1: Functionality and Disability		Part 2: Contextual Factors	
Components Environmental Factors	Body Functions Personal Factors	Structures	Activities	Participation
Body Domain	Functions Body Structures	Vital Areas (tasks, actions)	External influences on functionality and disability	Internal influences on functionality and disability

alternative to a rehabilitation process, with the objective of seeking a speedier treatment or providing a new motivation for the patient to continue in their recovery process.

The process of a clinical trial application consists of a previous classification of patients who will participate, through criteria that indicate the necessary profile and exclusion criteria. These criteria can be indicated as age group, clinical conditions, attendance of treatment, among other aspects. After classification, patients are divided into distinct groups, usually a control group, in which traditional methods are applied and the intervention group applying a new methodology or protocol. Patients are divided blindly, through randomization or random selection systems. After dividing the patients into groups, a prior assessment is applied to compare future results, the assessments are the same for both groups. The intervention is carried out using the methodology indicated by the professionals, the application time, the tools and the duration of the sessions are indicated according to the objective of the treatment. After performing the intervention, an assessment by intervention is performed to compare the pre- and post-assessment, with this the Comparison is performed for each patient and finalizing the analysis and comparison between the groups indicated in the Clinical Trial, as shown in the figure 6.

The articles were classified according to the ICF (International Classification of Functioning, Disability and Health). The ICF is a classification developed by the WHO (World Health Organization) and aims to provide a unified and standardized language and a framework for describing health and health-related status. Your specific goals can be summarized as follows:

- Provide a scientific basis for understanding and studying health determinants, outcomes and health-related conditions;
- Establish a common language for the description of health and health-related conditions, to improve communication between different users, such as health professionals, researchers, policy makers and decision-makers and the public, including people with disabilities;
- Allow comparison of data across countries, across disciplines related to health care, across services, and at different points in time;
- Provide a coding scheme for health information systems.

The ICF was selected for grouping the articles, due to the consideration that one of its applications is intended to be used as a clinical tool assessing needs, matching treatments with specific conditions, evaluating professional skills, rehabilitation and the results [54] (Table 3);

Based on this related classification, we consider the classification of the articles studied as reacting to Part 1: Functionality and Disability, onde 92 foram classificados de como

Tratamentos de Funções e Estruturas do Corpo e 26 como Atividades e Participação.

2.7.1. Group profile

Most of the Clinical Trial groups listed used the methodology generally involving two groups, corresponding to 95.72% of the articles presented, a Control Group (CG) in which they apply traditional treatment procedures and the Intervention Group using Virtual Reality (GRV) with application of Virtual Reality during the treatment sessions. Some studies showed more than two groups such as Marshall [154] that used 6 groups (0.85%), Radder et al. [155], Ramos et al. [149], Kakoschke et al. [132], Tuba et al. [122], Bortone, I [118], Gerard Fluet [115], Perin, Alessandro, et al. [105], Amin, Ashfaq M., et al. [104], Manuli et al. [88], Gerard Fluet [115] conducted their research with 3 groups (7.69%), Erdogan et al. [133], Liu, Wang, et al. [109], Dehghan, Fateme, et al. [106] worked with 4 groups (2.56%) and 2 articles such as Ortiz-Catalan et al. [94], Amaral et al. [56] that used only 1 group (1.70%). Regarding the work by Kim et al. [140] 2 intervention groups divided by age group. The number of groups per study was Average - 2.14 and Median - 2. All groups consider the same method of comparison. There was a concern to divide patients into groups equally and in a blind selection, that is, the patient was randomly assigned to a certain group.

2.7.2. Duration

The duration was presented according to the purpose of the interventions. For anxiety-reducing interventions for medical procedures, such as surgical interventions and invasive procedures such as venipuncture, only one day of application was necessary [102] [104] [105] [106] [108] [110] [112].

- The time of each session varies between 4 to 120 minutes, with an approximate average of 39.02 minutes and a Median of 30 minutes. Some treatments did not report a specific period of sessions as it varied according to the execution of a task or during the application of a procedure.
- The range of sessions 1 to 7 times a week.
- The total amount of sessions ranged from 1 to 60 sessions, with total treatment treatment duration ranging from 1 day to 18 weeks (3 months approximately). Approximate average of 14.19 sessions and Median of 14 sessions.

These items are not considering the evaluation times before and after the intervention period, only the period related to the application of the clinical trial.

2.7.3. Technology of intervention groups in VR

The technologies involved during the application of VR in the rehabilitation process were completed according to the objective of the intervention and the capacity to confirm the aptitude for its use. Exclusion criteria were considered as factors for patient selection, such as light hypersensitivity, movement limitation, age group or risks that could affect the patient's health. In the studies, software intended for entertainment and adapted for rehabilitation treatments were used, representing 22.04% of the studies studied, and 77.96% used software developed specifically for the context of rehabilitation.

Regarding the hardware selected for interventions, 22.89% of the works used Mobile Devices such as Tablets and Smartphones, 48.30% used the Computer, around 20.34% Games consoles on the market for entertainment purposes such as Wii and Xbox and 8.47% of these studies used proprietary solutions with their own hardware development. Some interventions like Tennant et al. [130], Ryu et al. [157], Kakoschke et al. [132], Amin, Ashfaq M., et al. [104], Avcil et al. [96], Hassett et al. [69] used more than one hardware

device to compare which approach among the groups of their clinical trials showed better results during their research.

Virtual reality can be considered as the combination of three basic ideas: immersion, interaction and involvement [35], [36].

According to the type of immersion, VR can be immersive, that is, eliminating noise from real environments from devices that transport the user to a completely virtual environment. Normally, an immersive system is achieved using VR glasses, but there are also immersive systems based in rooms with projections of visions on the walls, ceiling, and floor, where this visual sensation of immersion is directly linked to the three-dimensional presentation of objects, with the sensation of depth, achieved from the stereoscopic visualization [**?**]. And the non-immersive virtual reality, unlike the immersive one, presents experiences through devices that do not provide this immersion but through the feeling of non-inclusion, that is, when the user is, in theory, partially transported to the virtual world, through a window, but it continues to feel predominantly in the real world, but considers three-dimensional projections of this virtual environment in the real world, through image projection devices such as: TV, monitors or projectors and use of output peripherals such as keyboards, joysticks, mouse, for example. Its advantage is to avoid technical limitations and problems arising from the use of glasses and other peripherals, ease of use and cost reduction. Based on this understanding, the use of immersive and non-immersive virtual reality present 49% and 51% of the works respectively.

Iteration with a developed artificial environment is related to the communication between human action and the result of that action processed by the computer, resulting through a response in the virtual environment and the user's involvement when interacting with the virtual system for certain actions. The interaction can be passive, like watching television, in this type of iteration there is no interference from user actions within the virtual environment, or active, when the user has the ability to manipulate objects in a virtual environment.

Engagement, on the other hand, is related to the degree of motivation to engage a user in a given activity. The involvement can be passive, like watching television, or active, like participating in a game with an opponent 14.53% of the works have passive involvement and 85.47% active involvement, this data presents a direct relationship of the iteration on involvement in virtual environments.

2.8. Comparasion

The comparison had a very significant variation in relation to the articles. Each article presented a different method for comparing the results, making it impossible to compare them according to the type of disease. These assessment methods are identified by practitioners to assess through one or more systems for different purposes and, are already used for patient measurements in traditional treatments.

The methods of comparison were related to 3:

None of the articles considered information commonly saved in entertainment games such as time, number of errors and successes to assess the patient's evolution.

2.9. Outcomes

Of the results obtained, most articles had good results related to intervention using VR. 15.38% of the articles revealed that there was no significant difference in outcome between groups, 84.62% indicate that in one or more metrics there were significant improvements in groups that used VR in their intervention. However, it is not clear that the results obtained through the metrics used in comparing the groups remain after the intervention period, demonstrating the need for maturation, increased number of participants and post-intervention evaluation time during patient follow-up. Favorable items presented subjectively during this research, is that the application of VR in rehabilitation treatments increases

Table 3. Evaluations according goals

Classification	Measure
Motor function	ICC; FMA; GMFCS; MMT; WMFT; MAS; MACS; 6MWT; RMT; OLS; FRT; TUG; BBT; FMA-UE; FIM; FMS; FMUE; VADL; VRFCAT; 10MWT;
Anxiety	mYPAS-SF; AES/DES; CAPS; STAI; SCAS; m-YPAS; STAI Y-1; ADIS-IV-L; STAI Y-2; CAM-S; DASS-21;
Fear	CFS; W-DEQ; FPS-R; PedIMMPACT; CAPS; FES-I;
Balance	ABC scale; BBS; CTSIB;
Stress	CSSQ;
Behavior	BAT; W-B faces; ATHQ; VABS; FBRS; OSBD; PBRS; ARI;
Physiological conditions	H.P; METS; SpO2; PPA; EEG;
Paranoia	GPTS-B; AIHQ
Mental disorders	DSM-IV-TR
Pains	PedIMMPACT; SUDs; PI; CPM; PCS; SF29 MPQ
Social	ACSSP;
Depression	BDI-II; DASS-21;
Cancer	TMT - A; TMT - B; TMT - A & B;
Life quality	SF36; Q-LES-Q-SF;
Post-anesthesia recovery	QoR-40;
Protesis	PEQ;
Cognitive	MoCA; FAB;

patients' motivation and interest to remain in the treatment. Furthermore, when using activities that involve immersive VR, it increases the patient's focus and concentration in carrying out the activities. This item is due to a feature of immersive VR in which there is an escape from reality where the sense of reality is more evident, causing the brain to be fooled and take that situation as true.

3. Conclusion

Considering the researched articles, there are common conditions about the problems that virtual reality can solve:

- The diversion of attention, causing procedures. mainly for the control of pain and anxiety can be minimized.
- Motivation, virtual reality has shown that it is effective and brings a new lease of life to rehabilitation treatments.
- No studies reported risks to the patient in the groups that used virtual reality tools as therapy.
- All the works presented considered virtual reality as a complementary treatment, in no article there was a substitution of a traditional treatment.
- It is common agreement that the authors show interest and are optimistic about the use of virtual reality as a therapeutic tool, but further studies are needed to prove its effectiveness.
- The number of sessions per week varies according to the treatment objective, between 1 and 7 times a week. To identify the appropriate duration and application times, it is necessary to understand the objective of the treatment, considering the planning of the rehabilitation specialist as a determinant factor.

The characteristics observed that prove the effectiveness of a clinical trial using virtual reality in rehabilitation treatments vary according to the rehabilitation objective. As factors observed regardless of the purpose of the application is the fact of attraction and motivation. Identifying the patient's profile considering the age group and what he is interested in was taken into account in all studies. It is not necessary to create your own software to work VR in a rehabilitation process, only 20.63% of the researched works used or developed their own software for rehabilitation treatments, while 79.36% of the works used software that

had entertainment as their final purpose. Thus, it was possible to identify that, in order to be effective in the use of these applications, the intervention of the rehabilitation specialist is necessary to plan the activities according to the treatment objective and to select the activities that are suitable for this purpose. Another relevant factor is the need to use some haptic device or support so that the patient can perform the activities properly as found in the authors Lee et al. [63], Kutlu et al. [92], Calabrò et al. [100], Dimbwadyo-Terrer et al. [57], Hassett et al. [69] and France and Thomas [79].

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Conflicts of Interest

We declare that we do not have any conflict of interest regarding the work.

Scronyms

GMFCS - Gross Motor Function Classification System; MACS - Manual Ability Classification System; FMA - The Fugl-Meyer Assessment; WMFT - Wolf Motor Function Test; MAS - Motor Assessment Scale; VAS - Visual Analog Scale; BAT - Behavioral Avoidance Test; FSQ - Fear of Spiders Questionnaire; SBQ - Spider Phobia Beliefs Questionnaire; mYPAS-SF - ofModified Yale Preoperative Anxiety Scale Short Form; H.P - heart pulse rate; W-B faces - Wong-Baker Faces; W-DEQ - Questionnaires of Fear of Childbirth; CSS - Clinician Severity Scale; GPTS-B - Paranoid Thoughts Scale - Part B; PEQ - Prosthetic Evaluation Questionnaire; CFS - childrenś fear scale; Q-LES-Q-SF - Quality of Life Enjoyment and Satisfaction Questionnaire-Short Form; DCDQ - Developmental Coordination Disorder Questionnaire; MABC-2 - Movement ABC-2; FPS-R - Faces Pain Scale-Revised; PedIMMPACT - Pain Assessment in Clinical Trials; MoCA - Montreal Cognitive Assessment; HRS-A - Health Resources and Services Administration; TMT-A - Trail Making Test Part A; TMT-B - Trail Making Test Part B; TMT B-A - Trail Making Test Part A & B; TUG - Timed Up and Go test; FRT - Functional Reach test; FAB - Frontal Assessment Battery; 10MWT - 10-m walk test; MMT - manual muscle test; SUDS - Subjective Units of Distress Scale; BBS - Berg Balance Scale; ICC - induction compliance checklist; POMS - Perfil dos Estados de Humor; ATEC - Autism Treatment Evaluation Checklist; SUDs - Subjective Units of Discomfort; TMS - Transcranial Magnetic Stimulation; WBS - Wong-Baker FACES; PRS - Pain Rating Scale; CFS - Child Fear Scale; FAS - Faces Anxiety Scale; CAM-S - Children's Anxiety Meter-State; FIM - Functional Independence Measure; JAAT - Joint-attention assessment task; QoR-40 - Quality of Recovery Survey; SUS - Slate-Usoh-Steed; SSQ - Simulator Sickness Questionnaire; FMS - Fast Motion sickness Scale; ATHQ - Attitudes Towards Heights Questionnaire; AES/DES - Anxiety and Danger Expectancy scales; SSQ - Simulator Sickness Questionnaire; STAI - State-Trait Anxiety Inventory; MFIS - Modified-Fatigue Impact Scale; ADM - amplitude de movimento ativa do joelho; SFGDS - Short Form Geriatric Depression Scale; NRS - Numerical Rating Scale; CFS - Child Fear Scale; CAPS - Children Anxiety and Pain Scale; MMSE - Mini Exame do Estado Mental; PI - retroactive pain intensity; m-YPAS - Yale Preoperative Anxiety Scale; DTCs - Gait Performance, dual-task costs; TMT - Trail Making Test; SCWT - Stroop Color and Word Test; VABS - Vineland Adaptive Behavior Scales; SF36 - Short-Form Health Survey; FAI - Frenchay Activity Index; ABC scale - Activities-specific Balance Confidence Scale; FBRS - Frankl behaviour rating scale; PANSS - Positive and Negative Symptom Scale; K-BIT -

Kaufman Brief Intelligence Test.

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