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Interventions for Cognitive Impairments and Mental Health by the Means of Virtual Reality among Stroke Survivors

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A Systematic Review

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Abstract

Background: Cognitive impairments and poor mental health are prominent adverse effects that patients are often burdened with after suffering from a stroke. Treatment guidelines are not available yet for the two different factors. For that reason, Virtual Reality is explored as a possible intervention as it can take on different modes, be applied in different settings, and hence is quite adjustable to a stroke patient's special needs. The objectives of this review were to examine characteristics of Virtual reality interventions aimed at improving a) cognition and b) mental health in stroke survivors at home and inpatient/outpatient settings and their effectiveness. Further, similarities and differences between the different settings were explored.

Method: The data sources used for this systematic literature review were Scopus, Web of Science, and PubMed. The main eligibility criteria concerned records with stroke-patients, virtual reality interventions, outcomes concerning cognition and/or mental well-being as well as a publication after 2016. Both, qualitative and quantitative data were reviewed.

Results: A total of 1824 records were found, of which 23 were used. During the review process next to the home and inpatient setting, a mixed setting was identified and added. Only a small number of studies made use of fully immersive virtual reality in all settings. Instead of commonly known VR glasses, tablets and computer working stations were mainly used. The most prevalent intervention mode consisted of games. Results on the effectiveness of VR deviated among the records, still it is seen to be beneficial as a complementary treatment component to conventional treatment.

Conclusion: Limitations of this review may lie in its single-rater nature and the variety of research designs included. Implications for future research are to further explore the use of VR for mental health interventions in different settings as well as to explore a possible integration of different settings, to smoothen the transition after discharge, and simultaneously allow a continuation of rehabilitation. Overall, VR seems to be a promising complementary intervention for cognitive impairments and poor mental health among stroke patients.

Content

Introduction

Stroke is seen to be the second leading cause of death and the third major cause of disability across the globe (Feigin et al., 2015). The development of treatments during the acute phase has led to a decrease in mortality among stroke patients. However, many are left behind with physical, cognitive, and psychological impairments. Between the years 1990 and 2010 an increase of 86.7% could be noticed in global years lived with disability (YLDs) among stroke survivors (Vos et al., 2012). Even though many rehabilitation programs have been designed and shown to be successful in the treatment of physical impairments, the same does not hold true for the restoration of cognitive functions. As indicated by Kapoor (2017), about half of stroke survivors, despite rehabilitation, had cognitive impairments two to three years after the onset of the stroke. In terms of mental health, 20-30 percent of stroke survivors suffer from symptoms as for example depression or anxiety post-stroke (Kirkevold et al., 2018).

Cognitive Consequences of Stroke

When a stroke occurs, the arteries leading towards and within the brain, are affected (American Stroke Association, 2020). The blood vessels that supply the brain with oxygen and nutrients may be blocked or ruptured. In such cases, the brain cells of the certain regions die due to the undersupply caused by the affected vessel.

Since a stroke is causing damage to certain areas of the brain it is standing to reason that a patient's cognitive functions are affected as well. Impairments in cognitive functioning might affect only one cognitive area, but as indicated by Kim et al. (2011), they are more likely to affect several areas of cognition at the same time such as ”attention, concentration, memory, spatial processing skills, language, problem-solving skills, and planning skills”. Research has shown that approximately two-thirds of stroke survivors suffer from cognitive impairments 2 and 3 months after the onset of stroke (Nijsse et al., 2017; Blackburn et al., 2012). About 50% of people are still experiencing cognitive restrains 6 months post-stroke and despite rehabilitation even after 2 to 3 years (Nijsse et al., 2017; Kapoor, 2017). As indicated by Cumming et al. (2014), cognitive impairments might be associated with a poorer quality of life post-stroke. Further, poor cognitive functioning, regardless of the physical functioning, increases the likelihood of being dependent on other people's aid after discharge, may it be at home or in nursing facilities (Tatemichi et al., 1994).

Mental Health Consequences of Stroke

Apart from the rather obvious impairments due to stroke, such as physical and cognitive dysfunctions, stroke may also be related to a client's mental health. As indicated by Norrving et al. (2018), "around a third of stroke survivors are disabled, have poor post-stroke cognitive ability and poor mental health". Different factors can be representative of poor mental health among stroke survivors, such as depression, anxiety, general psychological distress, and fatigue, just to name a few (Kirkevold et al., 2018; Norrving et al., 2018). Experiencing such difficulties may influence a patient's long-term functioning, impede the rehabilitation process, and impact one's overall quality of life (Kirkevold et al., 2018). To give some examples with regards to the prevalence of mental health issues post-stroke, as indicated by the authors Kirkevold et al. (2018), about one-third of the patients experience depressive symptoms post-stroke, which might lead to a full depression that may still be present several years post-stroke. When it comes to anxiety, approximately 20% of stroke survivors experienced anxiety within the first months post-stroke.

Interventions

Until today, treatment guidelines of stroke solely focus on the recovery process of physical impairments. To give examples, the European Stroke Association (2008) and the American Stroke and Heart Organization (Powers et al., 2018) mentioned that cognitive functions and mental health can be affected by a stroke but that research data is not sufficient to provide enough evidence for effective treatment. However, due to the high numbers in the prevalence of cognitive impairments and poor mental health one might wonder what kind of interventions, respectively treatments, are available and applied at the moment. For cognitive impairments in general, one can say, that two different forms of cognitive rehabilitation exist in today's clinical application (de Luca et al., 2018). The first being restorative rehabilitation, which facilitates the development of lost functions by the means of cognitive exercises. The latter type is named compensatory rehabilitation, which trains the patient in making use of aids and tools. The progress in the advancement of technologies in the health sector has also made its way into rehabilitation bringing along computer-based interventions. One of those interventions entails the application of Virtual Reality (VR).

Virtual Reality

With the aid of VR, patients can run through both of the aforementioned forms of cognitive rehabilitation in " complex individualized and natural simulated environments"

(Kober et al., 2013). Not only can VR be used for cognitive rehabilitation but the assessment and treatment of mental health as well (Valmaggia et al., 2016). VR can be applied in different forms and since there is an ongoing development in the field of technology, VR does also keep on developing at a rapid pace. VR can be described as a virtual environment that a person can find him- or herself in and can interact with. A difference can be made between immersive, non-immersive and semi-immersive VR. Among immersive technology, “headmounted displays, body movement sensors, real-time graphics, and advanced interface devices (e.g., specialized helmets)” are used (Zeng et al., 2018). The user can turn around 360° within the virtual environment, which can generate a stronger sense of presence within that environment (Ventura et al., 2016) and hence might increase the sensation of reality. Utilizing non-immersive technology, the user rather functions as an observer from the outside, still able to enact with the environment by moving connected devices. The interface of non-immersive VR rather consists of devices such as flat screens “and requires the use of a corresponding keyboard, controller, and/or joystick” (Quian et al., 2020). Overall, one can say, that the degree to which a user feels actually present in the virtual environment decreases with the degree of immersiveness (Zeng et al., 2018).

To name a few more different hardware devices, which are capable nowadays to display virtual environments, those can be tablets, smartphones, computers, or VR glasses. Numerous software exist that run on those hardware devices. Further, those VR modes can take on different forms such as exercises, serious games, or exergames. Serious games comprise of those games that do not solely serve the purpose of entertainment but aim at e.g. educating the player or benefitting one's health. Another game-mode would be exergames which emphasize body movement through for example movement-tracking. To create an impression of what tasks in the virtual environment might look like, they can be designed for the patient to implement things such as grocery shopping at the supermarket or other daily activities.

Additionally, VR is also being tested for its applicability not only in treatment but as an assessment-tool for example for mental health (Bell et al., 2020). Bell et al. (2020) concluded that VR can be beneficial as an assessment tool in a broad range among mental health. The authors stated that “VR elicits similar psychological and physiological reactions to real-world environments, extending the reach of current assessments beyond the lab or clinic” (Bell et al., 2020). According to them, VR could be beneficial in mental health assessment as it comes closer to real-life experiences, which cannot be fully given in laboratories or clinics.

As described by Kim et al. (2011), stroke survivors can work in VR independently of any physical disabilities such as motor-dysfunctions of their limbs or hands, which adds a great advantage to it. This way, cognitive abilities can still be trained, and mental health can be improved, even though patients might not be able to visit outpatient centers or go grocery shopping on their own. VR can establish a safe and guided virtual environment, which might be relocated into the real-life again, as implicated by Chen et al. (2020). Those applications offer a chance for stroke survivors, to rehearse activities not fearing to do something wrong (Chen et al, 2020).

However, one should take a stroke survivors special needs into account as well. Visual impairments as for example a visual field loss, that is common among stroke survivors and other deficits in perception and senses might occur (Wiley et al. 2019), asking for very user-specific characteristics. Since VR mainly runs employing visual stimuli, this tool option might not be fully suitable for stroke patients with visual limitations or it would need to be sufficiently adaptable.

As indicated by Wiley et al. (2019) and Kannan et al. (2019), semi-immersive and non-immersive VR might be more appropriate, due to economical factors. High-quality VR glasses might be found at the upper end of price ranges until this point, whereas tablets, computers, and smartphones are more likely to already be owned by patients. Beyond that, semi-immersive and non-immersive VR devices have a smaller degree of intrusiveness, which might be rather suitable for stroke survivors (Wiley et al. 2019). The authors mention that the glasses that are used are heavy. The heavyweight might be unfavorable for patients as their physical and strength capacities might have been enfeebled by the stroke. Additionally, among longer use, unfavorable side-effects such as eye strains may occur (Wiley et al., 2019). Even among healthy patients, cybersickness can occur, which derives from a visual-vestibular conflict (Kim et al., 2018). This conflict can emerge once the actual movements of a user do not match the movement in the virtual environment. As a consequence, adverse effects such as nausea, dizziness or eye strains can burden the user. Since stroke survivors often suffer from cognitive deficits and especially visual field deficits (Pollock et al., 2011), they might be even more affected by the usage of VR devices.

Several reviews have shown, that VR “can be a promising and effective tool in the recovery of neurological symptoms, including cognitive ones” (Maggio et al., 2019). A review by Moreno et al. (2019) indicated that VR in cognitive rehabilitation among stroke patients might improve memory, dual tasking, and visual attention. Further, VR treatment has shown to be effective among stroke patients especially in the area of visual-spatial functioning, (Dehn et al., 2020) and attention (De Luca et al., 2018).

When it comes to a patient’s mental health, conditions such as post-stroke depression are often neglected in treatment, even though they might have an impact on the physical recovery and a patient's quality of life. As indicated by Paolucci (2008) only a minority of patients receives a diagnosis and gets treated with regards to their depression. According to Kirkevold et al. (2018), many studies have been conducted, aiming to explore potential interventions that prevent or treat post-stroke psychological problems, but the outcomes have not been promising yet. A qualitative study conducted by Chen et al. (2020), however, indicated that VR under the form of telerehabilitation might be beneficial for the improvement of mental wellbeing in stroke patients. Chen et al. (2020) reported that the patients perceived subjective positive effects with regards to their limb functions, cognition, and emotional well-being due to the telerehabilitation. Further, it was mentioned, that an educational module of the intervention helped participants to understand and cope with their misfortune.

Clinical vs. Home Setting

Even though treatment options seem to be available and VR a promising method in the field of rehabilitation after stroke, the numbers of stroke survivors, suffering from cognitive deficits and mental problems still seem to be quite high, especially when taking a look at the prevalence after a couple of years. As indicated by Sheehy et al. (2019), most stroke patients are discharged from inpatient rehabilitation after 8-10 weeks after the stroke. Afterward, for most rehabilitation is still necessary, but not necessarily easy to take part in. This could be explained by the fact that outpatients still might suffer from continuing physical deficits accompanied by dependence and transportation difficulties.

In other areas, especially in the rehabilitation of physical impairments such as upper limbs, a multitude of quantitative research about the application and effectiveness of VR in the home environment has already been conducted and systematically reviewed, demonstrating the possibility of VR as a treatment option in home settings in general (Schröder et al. 2018). Results revealed, that an increase in motivation might be implied by VR training sessions due to the game mode. Similar results were found by Llorens at al. (2016), who reported that a competitive game mode combined with virtual reality can be beneficial for motivation among stroke patients with cognitive deficits. As a consequence, a higher motivation might result in patients engaging in longer training sessions more frequently, which could benefit the overall rehabilitation outcome.

Functional improvements appear to be comparable to the progress in clinical settings, also emphasizing the factor of cost-efficiency. However, for cognitive impairments and mental health, no systematic reviews exist in the home setting. There might lie several advantages in introducing at-home VR-treatment for stroke survivors. Those might be decreasing the necessity of transportation, as the mobility of stroke survivors still might be affected. Among the issue of mobility comes also the factor of dependence, which might be decreased as well, once treatment can be conducted from home. Further, economical aspects come into play as well, that might be counteracted by a simplification of the effort put into treatment by several parties.

Current Study

To summarize, many patients' cognitive functions and mental health are affected by a stroke. Not only do those factors seem to impede the rehabilitation process of physical impairments, but they can affect stroke survivors' quality of life. VR is one way of treating cognitive impairments and mental health problems. However, this kind of intervention is not necessarily kept on after being discharged from clinics or rehabilitation centers. Since cognitive impairments and mental health problems have shown to be still present a couple of years post-stroke it is of great interest to investigate how interventions of applying VR at home might contribute to the improvement of those factors among stroke survivors and hence their overall quality of life. Until today, most research has focused on the application of VR in clinical rather than home settings when it comes to treating cognitive impairments and mental problems among stroke patients. As far as our knowledge goes, no systematic reviews exist yet, exploring the characteristics as well as the effectiveness of VR interventions for stroke survivors in their home environment. The recent systematic reviews focus on physical rehabilitation, but not on cognitive and mental interventions. For that reason, the objectives of this research are as follows:

1) to examine characteristics of Virtual Reality interventions aimed at improving a) cognition and b) mental health in stroke survivors at home and inpatient/outpatient settings

2) to examine the effectiveness of Virtual Reality interventions aimed at improving a) cognition and b) mental health among stroke survivors at home and inpatient/ outpatient settings

3) to examine similarities and differences with regards to characteristics and effectiveness of Virtual Reality interventions between the in-home and inpatient/outpatient settings.

Methods

Search Strategy

The current study followed the guidelines of a systematic literature review in the form of a state-of-the-art review. This type of methodology appears suitable as it covers more temporary matters (Higgins & Green, 2008, as cited in Grant & Booth, 2009). Especially in the field of VR, focussing on more recent findings of the past few years appears adequate, because of the fast development of the technology and its rising prevalence in usage in and outside of research.

Due to the difference in the nature of the objectives of this study, a qualitative, as well as quantitative synthesis, will be conducted. To create a general overview and identify characteristics of possible and/ or available interventions, a qualitative synthesis will be conducted. Possible quantitative results of the former qualitative synthesis will be included to evaluate the effectiveness of the identified interventions.

In this thesis, the literature search was conducted in the electronic databases Scopus, PubMed, and Web of Science. The databases Scopus and Web of Science were chosen due to their multidisciplinary content that could combine the technological, medical as well as psychological aspects of this study. The database PubMed was added due to the medical component of this study. Within the databases, it was searched for published journal articles.

The following search terms were used: stroke AND “virtual reality” AND cognition AND/OR “mental health”. The full search strategy can be found in Appendix A. The search was conducted in April 2020.

Study selection

In line with the guidelines of Higgins & Green (2008 as cited in Grant & Booth, 2009), the articles were selected employing the following steps. First, articles were detected by searching in the database. In the second step, titles and abstracts were examined. In the third step, the full texts of the relevant reports were retrieved. In the next step the full texts were screened and in the final step accepted or rejected based on the inclusion and exclusion criteria.

To be included in this review, the following inclusion criteria had to be met for the qualitative synthesis: 1) the sample included stroke patients, 2) the study included VR as an intervention, 3) publication in English or German language 4) publication in a peer-reviewed journal, 5) published after 2016 for the home setting 6) published after 2018 for the inpatient/outpatient setting. The publication year after 2016 for the home setting was chosen due to the state-of-the-art nature of this review, as it supposes that one should only focus on the last couple of years. Since systematic reviews have been published until 2018 in the inpatient/outpatient setting, it was decided to set the year 2018 as an inclusion criterion to prevent any repetition of former work and instead create novel insights. For reports to be eligible for the quantitative synthesis 7) the study design has to be quantitative. Additionally, 8) the research design of the inpatient-reports had to be either in the form of a literature review or randomized controlled studies due to the multitude of records.

Excluded from the review were reports: 1) not including stroke as a medical condition, 2) where outcomes concerning stroke were not explicitly reported, if other medical conditions were included, 3) published before 2017 for the home setting, 4) published before 2019 for the inpatient/outpatients setting. An explanation for the exclusion criteria of the publication year choice is identical with the inclusion criteria decision.

Data analysis

Quality Assessment

The Mixed Methods Appraisal Tool (MMAT)- Version 2011 (Pluye et al., 2011) was used for the quality assessment. The rationale behind this tool choice can be explained by the broad scope of study designs included in this review. The MMAT allows to include qualitative, quantitative (randomized controlled, non-randomized, descriptive) and mixed-method designs. The tool comprises of different items, which need to be answered. The first two items apply to every study design. In case the first two items are not successfully met, further appraisal should not follow due to insufficient scientificity. The aforementioned two items are followed by four items specific to the studies design, except for the mixed methods design, which uses three follow-up items (See Appendix B for the content of the items). With regard to the scoring metrics, an overall quality score can be calculated. For each criterium, the score is indicated by scores from 1-4. The total score for qualitative and quantitative studies is calculated with the sum of scores divided by four, indicating the number of criteria met (25%-100%) and therefore the quality of the study. Concerning the mixed methods studies, "the overall quality of a combination cannot exceed the quality of its weakest component" (Pluye et al., 2011).

Due to the possible diversity of study designs, an additional appraisal tool will be included for systematic reviews, namely the methodology checklist for systematic reviews and meta-analysis provided by the Scottish Intercollegiate Guidelines Network, Healthcare Improvement Scotland (2019, see Appendix C for the entire checklist). Systematic reviews with or without meta-analysis will be included in this review.

Data Extraction

The following data were extracted from the included articles:

- characteristic of the study design
    - study design
    - randomization/blinding/control groups
- Characteristics of the population
    - country
    - diagnosis
    - sample-size
    - time post-stroke
- characteristics of the intervention
    - setting (home/inpatient/other)
    - treatment objective
    - intervention mode (e.g. game. Exergame, exercise, education)
    - hardware/software
    - delivery mode (number of sessions, duration, assistance available)
    - outcome measurements of interest for this review (primary, secondary outcome, such as cognitive functioning, mental well being in general or indicated by e.g. depression, fatigue, anxiety)
- Outcomes
    - Measurement tools
    - Results
    - Conclusion

Results

Selection of studies

By using the databases PubMed, Scopus, and Web of Science a total of 2807 records were retrieved in the literature search (see Figure 1). The number of duplicates, which were removed, amounted to 983, and 1197 records published before the year 2017 were excluded as well due to the nature of this state-of-the-art study. The remaining 627 records were screened on title and abstract, resulting in the exclusion of further 464 records. A total of 163 full-text articles were screened of which 23 articles remained as eligible for the qualitative synthesis (Objective 1) and 17 for the quantitative synthesis (Objective 2). During the literature review, a third group was identified that appeared to be essential, consisting of studies that combined inpatient/outpatient or in-home rehabilitation.

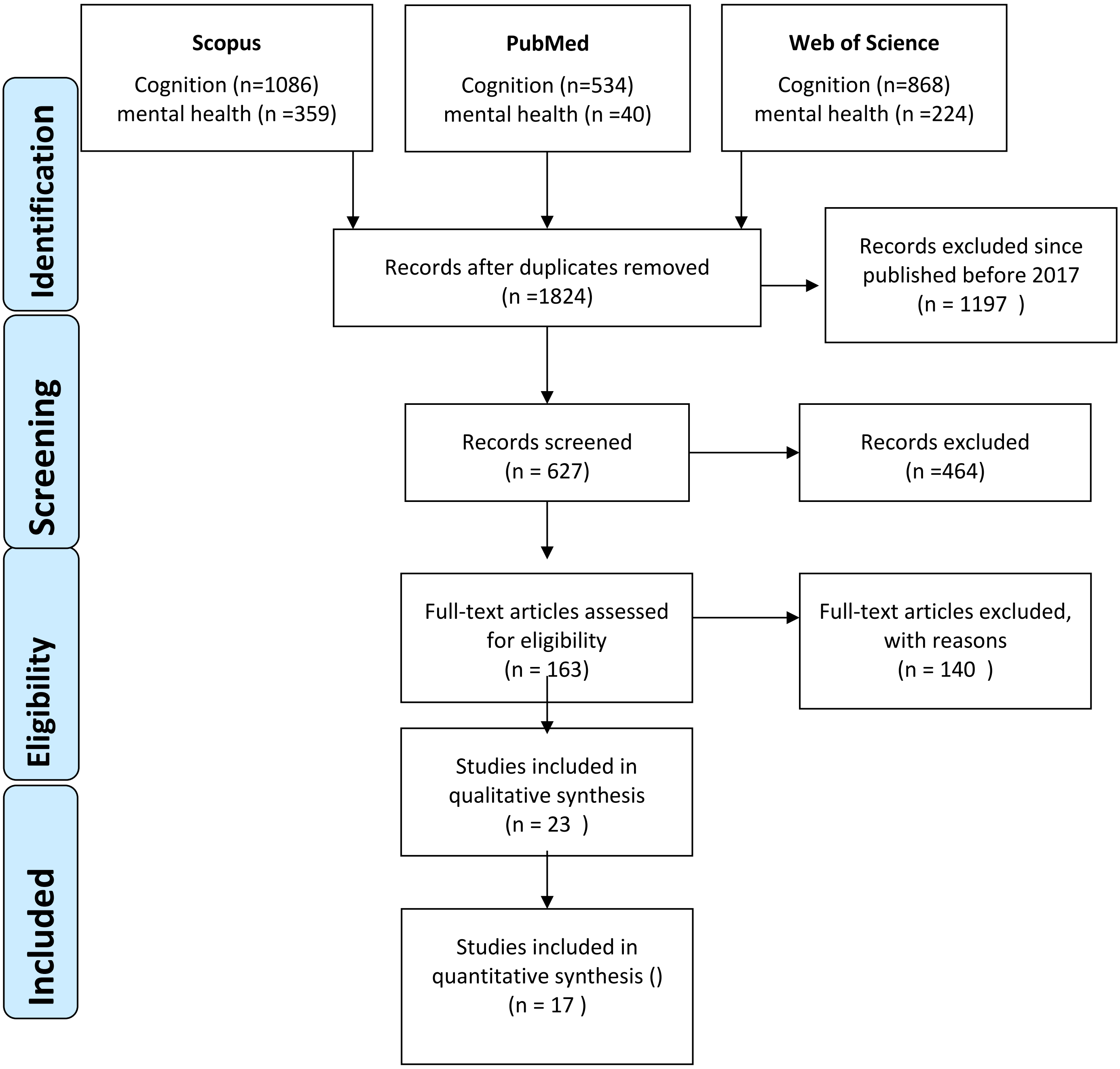

Figure 1- Flowchart of the Literature Search

In the following, the quality of studies, their characteristics with regard to the study population, design, intervention, and outcomes are presented. Findings will be presented organized by the research objective and further divided by the setting it was designed for.

Quality Assessment of studies

The quality of the 21 qualitative and quantitative records were appraised by means of the Mixed Methods Appraisal Tool (MMAT) and the quality of the two literature reviews by Wiley et al. (2019) and Maggio et al. (2019) by means of the Checklist for Systematic Reviews and Meta-analysis provided by the Scottish Intercollegiate Guidelines Network, Healthcare Improvement Scotland (2019) (See Table 1 and 2). The majority of the quality of records was highly satisfying, ranging from 2-4, indicating 75%-100% satisfaction. Four out of 21 studies scored at 2 or less, indicating a less satisfying quality of fulfilling only 50% or less of applicable characteristics. Three Records did not receive a total score due to their nature of being protocols. However, based on the given evaluation points, the quality would appear satisfying as well. With regards to the literature reviews, the review by Wiley et al. (2019) was evaluated to have high quality, whereas the review by Maggio et al. (2019) was rated with low quality (see table 2).

Table 1- Quality Assessment- Qualitative, Quantitative and Mixed-methods

Author.	1	2	.1	.2	.3	.4	Total
Burdea et al., 2019	√	√	2	4	2	-	2
Calabro et al., 2018	√	√	4	3	-	-	-
Cano-Manas et al., 2020	√	√	4	3	3	3	3,25
Chen et al., 2020	√	√	3	4	4	4	3,75
Dodakian et al. 2017	√	√	2	4	3	3	3
Fu et al., 2019	√	√	4	3	4	2	3,25
Kannan et al., 2019	√	√	3	1	2	1	1,75
Kilbride et al., 2018	√	√	3	4	2	-	-
Lee et al., 2020	√	√	4	3	4	4	3,75
Lin et al., 2020	√	√	4	3	4	4	3,75
Maier et al., 2020	√	√	4	2	4	3	3,5
Maresca et al., 2019	√	√	1	1	1	1	1
McKay et al., 2019	√	√	4	4	-	-	-
Mohd et al., 2019	√	√	2	2	3	1	2

Table 1 continued							
Author.	1	2	.1	.2	.3	.4	Total
Oh et al., 2019	√	√	4	3	4	4	3,75
Paulino et al., 2019	√	√	1	3	4	1	2,25
Pugliese et al., 2019	√	√	3	4	3	4	3,5
Rai et al., 2017	√	√	3	3	2	2	2,5
Rivas et al., 2019	√	√	3	3	3	1	2,5
Torrisi et al., 2019	√	√	4	3	1	1	2,25
Wall et al., 2018	√	√	3	3	4	2	3

Column 1 and 2 represent the screening questions for all type with a checkmark √ indicating the item to be answered with yes; Columns with .1,.2,.3,.4, refer to the 4 follow-up items of the different study designs; The last column represents the total score of the paper

Table 2-Quality Assessment literature review

	1.1	*1.2*	*1.3*	*1.4*	*1.5*	*1.6*	*1.7*	*1.8*	*1.9*	*1.10*	*1.11*	*2.1*	*2.2*
Wiley	√	√	√	√	√	*x*	√	√	√	√	*x*	*High quality*	√
Maggio	√	√	*Can´t say*	*Can´t say*	*x*	*x*	√	*x*	*x*	*x*	√	*Low quality*	√

Checkmark √ indicates the item to be met; Cross x indicates the item not to be met

Population and Study Design Characteristics

The entire data of the population characteristics are displayed in Table 3. The studies included in this review emerged all over the world including Europe (Italy, Spain, Portugal, UK), America (USA, Canada, Mexico), Asia (Malaysia, Taiwan, South Korea), and Australia. The number of (expected) participants ranged from 5-152. Nineteen out of the 23 studies focused solely on stroke as a diagnosis, two studies added Traumatic Brain injury and infection and the remaining two focused on either Aphasia post-stroke or Hemiplegia post-stroke. The age of participants reached from 37 to over 90 years with one exception of a study implemented with children aged 4-7. When it comes to the recruitment methods, different approaches could be seen such as convenience sampling, community posters, newsletters, recruitment through therapists/doctors. The time passed after the stroke until the implementation of the intervention would range between 3 days and 10 years.

Table 3- Population Characteristics

Author	Country	Sample Size	Diagnosis	Time post-stroke	Setting
Burdea et al., 2019	USA	N=7; Stroke	Stroke	>9 months	Home
Calabro et al., 2018	Italy	N=80	Stroke (n=40)	<1 year	home
Chen et al., 2020	USA	N=13	Stroke	4-36 weeks	Home
Dodakian et al., 2017	USA	N=12	Stroke	3-24 months	Home
Kilbride et al., 2018	England	N=30	Stroke	>12 weeks	Home
Maier et al., 2020	Spain	N=30	Stroke	6months<x<10years	Home
McKay et al., 2019	Australia	N=80	ABI (TBI, Infection, Stroke)	>6 months	Home
Mohd et al., 2019	Malaysia	N=6	Stroke	-	home
Paulino et al., 2019	Portugal			-	home
Rai et al., 2017	Australia	N=5	Stroke	-	home
Rivas et al., 2019	Mexico	N=5	Stroke	-	home
Cano-Manas et al., 2020	Spain	N=56	Stroke	15days-6monts	Inpatient
Kannan et al., 2019	USA	N=24	Stroke	> 6 months	Inpatient
Lin et al., 2020	Taiwan	N=152	Stroke	24 hours-3 days	Inpatient
Maggio et al., 2019	Italy	N=112 for Stroke;- N=25 for Control	Stroke	-	inpatient
Oh et al., 2019	South Korea	N=31	Stroke	6 months	Inpatient
Wiley et al., 2019	Canada	N=124	Stroke	18.2 ± 11.3 days to 41.1 ± 41.0 months	Inpatient
Fu et al., 2019	USA	N=7	Post-stroke hemiplegia	>6 months	Outpatient & Home
Lee et al., 2020	South Korea	N=36	Stroke	< 6 months	Inpatient, outpatient
Maresca et al., 2019	Italy	N=30	Post-stroke Aphasia	-	Inpatient & home

Table 3 continued

Author	Country	Sample Size	Diagnosis	Time post-stroke	Setting
Pugliese et al., 2019	Canada	N=30	Stroke	4 days	Inpatient & home
Torrisi et al., 2019	Italy	N=40	Stroke	3-6 months	Inpatient & home
Wall et al., 2018	Australia	N=96	Stroke	-	Community-dwelling

With regards to the study design (see Table 4), a total of five Randomized Controlled Trials (RCT), two RCT pilot studies, two RCT study protocols, and two systematic reviews were included. Further five study designs took the form of Intervention Technology design studies, a feasibility study, a feasibility study protocol, a qualitative semi-structured interview, a system performance pilot study, a single group prospective cohort study, and a controlled parallel-group pilot study.

Table 4- Study Design Characteristics

Author	Study Design	Setting
Burdea et al., 2019	Feasibility Study	Home
Calabro et al., 2018	Study protocol of a multicentric observational, rater-blinded, active-controlled, parallel-group pilot study	home
Chen et al., 2020	Qualitative, semi-structured interviews	Home
Dodakian et al., 2017	System performance pilot study	Home
Kilbride et al., 2018	Study protocol about Intervention feasibility nonrandomized trial Semi-structured interviews	Home
Maier et al., 2020	RCT pilot study	Home
McKay et al., 2019	Study protocol of RCT	Home
Mohd et al., 2019	Intervention technology Design & Feasibility study concept	home
Paulino et al., 2019	Intervention technology redesign study	home
Rai et al., 2017	Intervention Technology design study	home
Rivas et al., 2019	Intervention technology development study	home
Cano-Manas et al., 2020	RCT	Inpatient
Kannan et al., 2019	RCT	Inpatient

Table 4 continued		
Author	Study Design	Setting
Lin et al., 2020	RCT	Inpatient
Maggio et al., 2019	Systematic review	inpatient
Oh et al., 2019	RCT	Inpatient
Wiley et al., 2019	Systematic review and Meta-Analysis	Inpatient
Fu et al., 2019	Exploratory case study series	Outpatient & Home
Lee et al., 2020	RCT	Inpatient, outpatient
Maresca et al., 2019	RCT pilot study	Inpatient & home
Pugliese et al., 2019	unblinded, single-group, prospective cohort study	Inpatient & home
Torrisi et al., 2019	Prospective, assessor-blinded, controlled parallel-group pilot study	Inpatient & home
Wall et al., 2018	Intervention Technology design study	Community-dwelling

Intervention characteristics

In the following, the characteristics of the VR interventions aimed at improving a) cognition and b) mental health in the different settings will be presented in line with the first research objective. The characteristics are based on different criteria as displayed in Tables 5 and 6 (for detailed information, see Appendix D).

Technology

Home. From 10 out of the 11 studies focusing on the home setting, only one study applied a fully immersive VR, namely the study conducted by Mohd et al. (2019). In their study, the researchers made use of the HTC Vive virtual reality headset. However, the authors indicated as well, that the intervention is designed to be implementable with other, more affordable devices to maximize consumer-friendliness. The remaining 10 records reported only methods of a non-immersive nature.

The majority of technical devices creating virtual environments consisted of workstations build of Computers and Screens. Apart from that, two studies implied the use of tablets and the study by Rai et al. (2017) the use of any mobile device with a web browser. As aforementioned, only one study made use of VR glasses (Mohd et al. 2019). Further tools, that were utilized, are controller, microphones, speakers, joysticks, an eye tracker, various kinds of hand sensors, and the Kinect sensor (Microsoft Corporation, Redmond, WA, USA), a movement tracker that enables the user to control the software merely by the means of body-movement.

When it comes to the software integrated into the interventions, no identical software could be identified within the 11 records. However, the kinds of software that were made use of, consisted of game design software, telecommunication platforms and commercial video games and the so-called Reh@City software.

Inpatient. In terms of immersiveness, two out of six studies of the inpatient-setting reported the usage of immersive VR. Those were the studies by Lin et al. (2020) and Wiley et al. (2019). Since the study conducted by Wiley et al. (2019) was a literature review, they reported to have included interventions of all modes, meaning immersive, semi-immersive, and non-immersive VR. Due to the immersive nature, those two authors also mentioned VR glasses as in terms of hardware as part of their interventions. The other hardware devices used in the clinical setting, consisted primarily of game consoles such as the Xbox or Wii or PC-workstations with monitors. Additionally, tools such as the Kinect were utilized as well.

Concerning the software, two studies made use of the Joystim, a 3D manipulator, and others used software such as Reh@Task and Reh@City, BTs-Nirvana, and commercial video games.

Mixed. In the mixed setting, only non-immersive VRs were made use of. However, all six of the studies applied Tablets as their main hardware device. One study additionally reported the use of a computer and tools such as hand sensors were used. With regards to the software, the only ones mentioned were the Unity game engine (version 4.6) used for software development and “RecoverNow”.

Table 5- Intervention Technology Characteristics

Criteria	Home	Inpatient	Mixed
Immersive	1	2	-
Hardware			
○ VR-Device (glasses)	1	2	-
○ Screen/monitor	4	1	-
○ PC	6	1	1
○ Tablet/ mobile device	3	-	6
○ Games console (Wii, Xbox)	-	2	-

Table 5 continued

Criteria	Home	Inpatient	Mixed
Additional tools			
○ Controller/ Joystick	4	-	-
○ Kinect	1	2	-
○ Microphone/speakers/webcam	5	-	-
○ Handsensor/Wristbands/smartgloves	4	-	3

Intervention design

Home. Six out of the 11 interventions in the home setting established cognitive rehabilitation as one of their overall intervention goals, followed by five interventions having upper extremity or motor improvement as their primary treatment target and one intervention explicitly mentioning mental well-being as a primary outcome. Additionally, the goal of two studies was not primarily the treatment but the recognition of multimodal affective states (Rivas et al., 2019) to create a system that automatically adjusts the exercises to a patients needs. Dodakian et al. (2017) presented a home-based telerehabilitation system, that can measure depressive symptoms.

The main content mode of the interventions consisted of games, which could take the form of serious games, exergames, videogames, etc. as indicated by all 11 of the home-setting studies. Other modes that were made use of, are an educating approach, exercises such as card sorting or the tower of Hanoi, and telecommunication with practitioners, nurses or therapists. The duration of the interventions would range from 20-70 minutes, 5-7 times a week for 4-12 weeks. Further, different types of assistance were offered by the researcher team such as an initial introduction of the treatment modality and if necessary a caregiver could be included. Only in the study of Calabro et al. (2018), a telecommunication system was integrated to implement videoconferences with the therapist to process and evaluate the progress. The interventions of Calabro et al. (2018), Dodakian et al. (2017), and Rai et al. (2017) included an online platform were both the therapist as well as the patient could monitor the process and the therapist could adjust the tasks.

Inpatient. In the inpatient-setting, three interventions focused on rehabilitation of upper extremities and motor function, two on cognitive rehabilitation, and one on the patients quality of life as their primary target. The modes of content provision were games, education, and exercises. Telecommunication was not needed. The duration of a single session could vary between 15-180 minutes and two to seven sessions were conducted within 1-8 weeks. In this category, it occurred that the VR intervention was implemented in combination with conventional therapy.

Mixed. Three interventions focused on upper extremity/ motor functioning, three emphasized cognitive rehabilitation, one quality of life, and another one operated as an assessment tool as the primary intervention outcome. The authors' Wall et al. (2018) demonstrate preliminary support for the feasibility of an App for cognitive assessment for patients with aphasia, which can be used for in- as well as outpatients.

Content-wise did three studies describe the application of a game mode, three presented exercises, and two mentioned telecommunication. With regards to the duration of the intervention, one session could last between 20-60 minutes, 3-7 times per week in 8-24 weeks. The longitudinal interventions of 24 weeks were part of Torrisi et al. (2019) and Maresca et al. (2019) studies. They introduced a two-phased intervention. The first half consisting of 12 weeks would be implemented as an inpatient/outpatient and the second half could be conducted from home.

In terms of assistance, three of the six mixed setting studies offered an initial introduction to the technology and training and one mentioned to include the caregiver, if necessary. Two studies integrated videoconferences twice a week with a therapist to monitor the process and if necessary adjust the tasks. And one study provided an online platform for the therapist and patient to monitor the progress and adjust the tasks.

Table 6- Intervention Design Characteristics

Criteria	*Home*	*Inpatient*	*Mixed*
Primary Intervention Goal :			
Treatment			
• upper extremity/ motor functioning	6	3	3
• cognition	6	2	3
• well-being	1	-	-
• quality of life	-	1	1
Assessment	1		1
Mode			
• Game (serious game, exergame…)	11	3	3
• Education	2	1	-

Criteria	*Home*	*Inpatient*	*Mixed*
• Exercise	3	3	3
• Telecommunication	3	-	2
Duration			
• Minutes	20-70	15-180	20-60
• Sessions per week	5-7	2-7	3-7
• Weeks	4-12	1-8	8-24
Assistance			
• Initial introduction	4	-	3
• Including caregiver, if necessary	2	-	1
• Video conferencing for process monitoring	1	-	2
• Online platform for process monitoring and task adjustment	3	-	1

Study outcomes

With regards to the second objective of this review, examining the effectiveness of VR interventions aimed at improving a) cognition and b) mental health among stroke survivors in the different settings, 17 out of 23 studies will be used for the quantitative synthesis.

Cognition

Both primary and secondary outcomes were included, measuring a participant's cognitive state. Those measurements would either assess the overall cognitive state or be specific towards e.g. attention, memory, executive function and spatial awareness

Home. When it comes to executive functioning, the authors Burdea et al. (2019) and Fu et al. (2019) could identify significant gains due to their at-home intervention within their data. The authors Chen et al. (2020) described that patients experienced enhanced cognitive skills, as well as memory through playing the games of the intervention. Maier et al. (2020) stated that their at-home Adaptive Conjunctive Cognitive Training (ACCT) might positively influence attention and spatial awareness. Considering the technology that was used in those studies, all of them were using a computer as well as a screen. Further, additional tools operated with the hands were used such as controllers, joysticks, or gloves. All four studies focused on games as their content mode. Other factors such as duration, software or assistance differed.

Inpatient. The authors Kannan et al. (2019) noticed an improvement in balance as well as cognition due to the designed exergame intervention, which might reduce the motor-cognitive interference after stroke. The author Oh et al. (2019) described that a combination of VR with real instruments could be beneficial for cognitive functioning, as the client gets to practice daily activities in a simplified mode. In the meta-analysis by Wiley et al. (2019), outcomes revealed, however, that Virtual therapy would not be more effective than conventional therapies as compared to the control groups when it comes to global cognition. Kannan et al. (2019) and Oh et al. (2019) both described different technology systems, the one being a game console and the other being a workstation with a computer. The latter could also be found in the review conducted by Wiley et al. (2019). All three studies emphasized cognitive rehabilitation as one of their primary treatment goals. However, with regards to the other criteria of intervention characteristics, no overlap could be found

Mixed. The findings of the meta-analysis by Wiley et al. (2019) are in line with the findings of Lee et al. (2020) who suggested that the outcomes of their VR-intervention group did not differ from the control group. In Lee et al.s´ study, the primary outcome was to enhance motor function in outpatients that visited a local rehabilitation unit for their treatment. Contradicting to those outcomes are the findings of Torrisi et al. (2019) who demonstrated the effectiveness of their VRRS treatment for cognitive impairments post-stroke. Torrisi et al.´s intervention comprised, as earlier described, of a 2-phased intervention, including treatment as an inpatient followed by treatment at home, which specifically aimed at improving cognitive functioning. Torrisi et al.´s outcomes refer to the global cognitive level as well. Both, Lee et al. (2020) and Torrisi et al. (2019) made use of technological devices specifically designed for VR. Further, both researchers integrated game-like exercises in their intervention.

Apart from treatment interventions, did Wall et al. (2018) demonstrate preliminary support for the feasibility of an App for cognitive assessment for patients with aphasia, which can be used for in- as well as outpatients.

Mental health

In terms of mental health, the studies mainly included the symptoms of depression and anxiety. One study mentioned the survivor's mental well-being. All of the findings regarding mental health were secondary outcomes.

Home. The studies conducted by Burdea et al. (2019), as well as Maier et al. (2020), provided support for the assumption that VR therapy at home might reduce depression in stroke survivors. The authors Chen et al. (2020) mentioned in their qualitative study that patients “felt more socially connected after using the system”. All three interventions comprised monitors, tools for the hands such as controllers or wristbands and all ran in a game mode.

Regarding assessment tools, Dodakian et al. (2017) presented a home-based telerehabilitation system, that can measure depressive symptoms.

Inpatient. In the inpatient setting, Cano-Manas et al. (2020) indicated that a combination of conventional treatment with a semi-immersive video-game approach might result in a positive effect when it comes to the “perception of pain/discomfort, sensation of anxiety/depression”. Those findings are in line with the research conducted by Lin et al. (2020.) stating that supplementing VR training to early rehabilitation might lead to an improvement in a survivors mood state, which includes depression and anxiety. In both studies the Kinect sensor device was present. Additionally. Mental health was targeted in each study. Another factor prevalent in both studies was the implementation of conventional therapy, to which the VR-therapy was added.

Mixed. The authors Maresca et al. (2019) concluded that the application of their intervention, might reduce depression and promote psychological well-being. They introduced a VR tablet system into their intervention, which started with inpatients, being discharged after 12 weeks but keeping the VR-tablet training for another 12 weeks.

Similarities and differences

The third research objective served to examine similarities and differences with regards to the characteristics and effectiveness of VR interventions between the different settings, which will be presented in the following.

Differences

Several differences between the three location settings could be derived from the records (see Table 7). Concerning the technology, one of the main differences can be seen in the hardware that is used. In the home settings computer-based workstations, in the inpatient setting game consoles, and the mixed setting tablets were most prevalent. Further, additional tools were mentioned more frequently in the home-setting than the other two.

In terms of the overall intervention goal, two Assessment tools, one for depression (Dodakian et al., 2017) and one for affective states (Rivas et al., 2019) were introduced and in the mixed setting one for cognitive assessment (Wall et al. 2018). For the inpatient setting, no such thing is available as indicated by the records.

In the home setting, all four content modes could be identified, games, education, exercise as well as telecommunication. In the inpatient setting, telecommunication was missing, which however might be expected. In the mixed setting, no education mode was found in the records. The minimum and maximum duration of the period, the intervention was offered, differed between the settings as well, with an inpatient setting starting by only one week, followed by the home setting with four weeks and the mixed setting with 8 weeks. The maximum duration differed as well, as a maximum of 8 weeks were given in the inpatient setting, followed by the home setting with 12 weeks and a total of 24 weeks by the mixed setting.

As far as conclusions can be drawn with regards to the effectiveness, in the home setting, studies preliminarily indicated that VR might be beneficial for cognitive rehabilitation. In the inpatient and mixed setting, however, results deviated. Results of the meta-analysis conducted by Wiley et al. (2019) and an RCT by Lee et al. (2020) concluded that VR is not necessarily more effective than conventional therapy, as measured by means of a control group. However, a more recent RCT in the inpatient setting pleads for the more convenient usability of VR for cognitive rehabilitation.

Only in the inpatient setting, assumptions were drawn that VR might be related to an improvement of mental health concerning anxiety. In general, mental health was addressed in all inpatient studies, but only partly in the home-setting. Further, VR was seen as a supplementing factor in the inpatient settings, whereas in the home setting it partly would stand by itself.

Table 7- Differences between the settings

criterium	home	inpatient	mixed
hardware	PC	Game console	Tablet
tools	Used very frequently	Barely used, but if, Kinect	Barely used, but if, Handtools
Overall Intervention goal	assessment	No assessment	assessment
Content mode	All 4 modes	No telecommunication	No education

criterium	home	inpatient	mixed
duration	4-12	1-8 weeks	8-24 weeks
Effectiveness			
cognition	Preliminary effective	Meta-analysis says not more efficient than the control group, but newer RCT pleads for possible positive impact	Not more efficient than control group,
Mental well-being	Positively influence depress	Pos. influences depress/anxiety -VR in early rehabilitation might affect mood including Anx. & depression	Pos. influences Depress.
	Not each study	Mental health targeted in each study	-
	Only VR or additionally	VR as a supplementing factor	

Similarities

A summary of the similarities can be found in Table 8. Similarities about the hardware were computer-based workstations that could be found in each setting, even when they were not the main choice of hardware. Further, in all settings, the overall intervention goal of treating upper extremities/ motor function or cognitive functions could be found. All settings included games or exercises as content modes.

An overlap could be seen in the duration per session, as in each category sessions of 20-60 minutes could be found, and the number of sessions per week could also go up to seven days per week in each setting. Especially with regards to the home and mixed setting, an overlap could be seen in the assistance provided. Both settings checked all four common criteria of an initial introduction, inclusion of the caregiver, videoconferencing and an online platform for process monitoring and task adjustment available for both, therapist and client.

Table 8 - Similarities between the settings

criterium	home	inpatient	mixed
hardware	PC	“	“
Overall intervention goal	- Upper extremities/motor function - cognition	“	“
Content mode	Games, exercises	“	“
Duration	20-70 min	15-60 min	20-180 min

criterium	home	inpatient	mixed
	Up to 7 times per week	“	“
assistance	Initial introduction	-	“
	Inclusion of caregiver	-	“
	Videoconferencing	-	“
	Online platform for process monitoring	-	“

Discussion

In this literature review, interventions for cognitive impairments and poor mental health by the means of VR among stroke survivors were investigated. For this purpose, a state-of-the-art review was performed to explore the characteristics of possible interventions as well as their efficacy. Due to the novelty in the field of VR-interventions especially in the home setting, it was aimed at creating an overview of the differences and similarities regarding the characteristics and effectiveness between the home-setting and the inpatient setting. Along the research process, it became prominent that a third category had to be added, where the setting for the interventions was mixed.

At the start of the systematic search, a total record number of 1824 records were found in the databases Scopus, Web of Science, and PubMed after extraction of duplicates. At the end of the selection process, 23 articles remained to be included in this literature review.

One of the main findings was that fully immersive VR devices such as VR-glasses, which might be more familiar to the average consumer, were only found in three out of the 23 studies. In response to the first research objective, exploring the characteristics of VR interventions aimed at improving cognition and mental health in stroke survivors, the following findings could be deducted from the included records. The criterium of hardware among the characteristics of the technology revealed, that different devices such as screens/monitors, computers, tablets, and game consoles were used among the different settings, with VR glasses not being the main choice.

One might have expected that VR-glasses might be frequently used, especially in the home setting due to their mobile nature. However, the findings of this review might be related to the assumption of Wiley et al. (2019) and Kannan et al. (2019), which reported that non-immersive or semi-immersive VR interventions might be more suitable for stroke populations. Those findings might be explainable by Kim et al. (2018) who described cybersickness already among healthy individuals, and Pollock et al. (2011) who highlighted that visual field deficits are quite prevalent among stroke survivors. Not being exposed to a fully immersive VR might leave space for the stroke patient to feel connected with the real world and avoid a visual-vestibular conflict resulting in adverse effects such as nausea or dizziness. Due to the special needs of stroke survivors and possible restrainments, typical VR glasses hence might not be suitable. Therefore, the authors' findings might contribute to an explanation of why the number of fully immersive devices used is rather limited. Additionally, those indications might explain the preferred use of computer-based workstations with screens in the home setting or tablet screens in the mixed settings, as they are less immersive and again bring along less constraints for the user.

Another category of question was the content mode of the interventions. In all three settings, especially games were included. As indicated by Schröder et al. (2018) and Llorens et al. (2016), exercising in game-like virtual environments might contribute to the enjoyment factor and increase the motivation in cognitive rehabilitation. As a consequence, the user might engage in longer and more frequent sessions. Those findings might be transferable to cognitive rehabilitation and mental health improvement utilizing VR and therefore, might provide a rationale for the choice of game-based training found in this review.

With regards to the interventions primary goal, the majority of treatments targeted upper extremity/ motor function or cognitive rehabilitation. This deviation holds true for all three settings. When it comes to mental well-being, this aspect could only be found as a secondary outcome, if at all. In the home setting, the inpatient setting as well as the mixed setting mental well-being was merely taken into consideration. If it was included, a focus lay on reducing factors such as depression or anxiety, that one might develop or already have.

We could find only one intervention via VR that emphasized mental well-being in their primary outcomes, whereas the rest focused on the treatment of extremity/ motor function or cognitive rehabilitation as aforementioned. Studies conducted among other comparable target groups such as Multiple Sclerosis patients suggested that VR can contribute to a patients psychological well-being (Calabro et al. 2017). Enhancing a patient's mental well-being might be beneficial in other domains as well. Previous studies in the field of positive psychology indicated for example that “positive emotions, positive social connections, and physical health influence one another in a self-sustaining upward spiral dynamic” (Kok et al., 2013). As stroke survivors suffered from a life-changing event, which possibly restricts them from living their former life, VR might give them a slight sense to be back, present in their previous daily life.

Next to the positive mental well-being, only a few studies measured mental health as a secondary outcome. No reviews regarding VR, neither in the home nor in the inpatient setting could be found, that concerned mental health. Aspects such as fatigue were not addressed at all. As indicated by Kirkevold et al. (2018) experiencing mental issues such as depression or anxiety might affect a stroke survivors long-term functioning, impede the rehabilitation process, and could impair one's quality of life. Especially, when taking a look at numbers indicating that about one-third of stroke patients experiences depressive symptoms after a while, partly leading to a full depression, one should put greater emphasis on stroke survivor's mental health. As depression remains undiagnosed and untreated most of the time, it might come handy that a VR assessment tool for measuring depressive systems was invented (Dodakian et al., 2017), which is applicable for home use. By the means of such a screening tool, depressive symptoms might be detected early and hence be counteracted in time.

In terms of the effectiveness of VR for the treatment of cognitive impairments and mental health, the following results could be drawns from the systematic review. As indicated by the outcomes of two randomized controlled trials, VR-interventions might be beneficial in cognitive rehabilitation in the inpatient setting (Kannan et al., 2019; Oh et al., 2019). The author Wiley et al. (2019) reported, that VR would not be more effective than conventional therapies for cognitive functioning. Different technologies such as tablets and computers were used. However, none of the technologies were fully immersive possibly due to the disadvantages such as nausea or dizziness.

Since about 50% of stroke survivors still experience cognitive restrains 6 months after the onset or even two years later (Nijsse et al., 2017; Kapoor, 2017), one should think of a way to treat those impairments after discharge. Therefore, when transferring those findings to the home setting, VR-therapy might still benefit to the process of cognitive rehabilitation, as it is still as efficient as conventional therapy. It may benefit to our health care system since the advantage of VR in the home setting might lie in independence and cost-efficiency variables. Despite, the special needs of stroke survivors have to be taken into account. Some might not be able to conduct VR therapy on their own due to physical restrains, making them dependent on e.g. caregivers. Additionally, prolonged use might lead to unfavorable side effects such as eye strains (Wiley et al. 2019). For that reason, it has to be taken care of a suitable intervention in terms of technology, user-friendliness, and proper use.

Surprisingly, it came up during the research process that no sharp line should be drawn between the inpatient and at-home settings as rehabilitation is an ongoing process, that is not necessarily finished overnight. For both aspects, cognitive impairments, and mental health, researchers of the studies revealed that a combination of conventional therapy and VR might be appreciated in the clinical field for therapists as well as patients. This way, therapists can still work with their patients, especially at the inpatient setting, and simultaneously prepare them for discharge by including VR in the early rehabilitation phase so that a patient can get familiar and comfortable with the technology and become able to implement it on his own when returning home.

Based on the findings of this systematic review, the following suggestions are made for possible improvements in interventions for cognitive impairments and mental health among stroke survivors. Non-immersive VR should be used for the treatment of stroke patients. The findings within different settings have shown a preference towards computer-based workstations or tablets. Therefore, we advise to keep those hardware devices, as they better fulfill a patients needs than e.g. fully immersive VR-glasses. Additionally, the integration of different assessment tools in the VR-Application is advisable. By means of such assessment tools, mental issues such as depression can be identified early and counteracted. Further, if e.g. the current affective state of the patient is assessed, tasks and exercise levels could be adjusted appropriately. With regards to the content mode, at least a game-based intervention is advised, preferably supplemented by educational and telerehabilitation modules. It is to mention, that the technology should not serve as a sole treatment component but be preferably accompanied by conventional therapy. However, one might consider minimizing the patient and therapist contact as time passes by and a preferable progress could be identified. One way to implement this might be by starting VR-treatment initially after the onset of stroke during the in-patient setting and to keep it running after discharge.

Strengths and limitations of this study

Implementing this systematic review with a single researcher might be seen as a limitation towards the quality of this paper, as several biases might have occurred such as outcome reporting biases. However, due to the supervision and careful treatment of the data, it was attempted to maximize objectivity to the greatest extent.

Another aspect that could be seen as a limitation as well, is the big scope of the review. Including several topics, might have hampered the ability to compare different factors on a more detailed level. Due to time and resources restraints, this was not possible. Further, the variety of study designs and the limited number of statistically quantifiable outcomes caused by the novelty of the topic might have confined the comparison between the different modalities. Still, since this is a state-of-the-art-review, an overview of what is already present and what is still missing in nowadays research, could be created. Additionally, keeping the review to such a wide scope might have been beneficial as well since this allowed to reflect on different angles of the topic and show where possible future research might be directed to.

For that reason, one indication for future research would be to further explore the possibility of VR in the field of mental health among stroke survivors at home as well as in the inpatient or mixed setting as a primary intervention outcome to check for possible correlations. Further, one might consider to not only focus on mental health in the form of the absence of symptoms but to elicit positive psychological well-being. Another field to look into in future research could be the integration of inpatient and at home, VR-therapy to create a smooth transition from the one into the other setting, and simultaneously allow for a continuation of rehabilitation as cognitive deficits and poor mental health can continue far longer.

In conclusion, this review offers an overview of the current state of scientific knowledge with regards to Virtual Reality interventions for cognitive impairments and mental health among stroke survivors, which was necessary due to the rapid pace at which technology advances. Even though this review does not provide sufficient quantitative support to already allow an introduction of VR in the applied field, it sets directional guidance for future research. Due to the lack of well-established guidelines for the treatment of cognitive impairments and mental health among stroke survivors, this work might serve as a basis by contributing not only to our healthcare system but mainly to the recovery of the many stroke survivors who are affected annually by its consequences.

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Appendices

Appendix A

Search strategy: *Scopus, PubMed, Web of Science*:

#1(“stroke” OR “poststroke” OR “CVA” OR “brain attack” OR “cerebrovascular accident*” OR “cerebrovascular apoplexy” OR “ brain injur*”)

#2 (“virtual Reality” OR “VR” OR “gaming exercise*” OR “game*”)

#3 (cognition OR cognitive OR percept* OR visuo-spatial OR visuo-perceptual OR attention)

#4 (“mental health” OR “mental well-being” OR “psychological health” OR “psychological well-being” OR “psychological” OR “mental disorder” OR “Depressi*” OR “Fatigue” OR “Anxiety”)

#5 #3 OR #4

#6 #1 AND #2 AND #5

Appendix B

PART I. MMAT criteria & one-page template (to be included in appraisal forms)

Types of mixed methods study components or primary studies	Methodological quality criteria (see tutorial for definitions and examples)	Responses			
		Yes	No	Can't tell	Comments
Screening questions (for all types)	• Are there clear qualitative and quantitative research questions (or objectives*), or a clear mixed methods question (or objective*)?				
	• Do the collected data allow address the research question (objective)? E.g., consider whether the follow-up period is long enough for the outcome to occur (for longitudinal studies or study components).				
	Further appraisal may be not feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.				
1. Qualitative	1.1. Are the sources of qualitative data (archives, documents, informants, observations) relevant to address the research question (objective)?				
	1.2. Is the process for analyzing qualitative data relevant to address the research question (objective)?				
	1.3. Is appropriate consideration given to how findings relate to the context, e.g., the setting, in which the data were collected?				
	1.4. Is appropriate consideration given to how findings relate to researchers' influence, e.g., through their interactions with participants?				
2. Quantitative randomized controlled (trials)	2.1. Is there a clear description of the randomization (or an appropriate sequence generation)?				
	2.2. Is there a clear description of the allocation concealment (or blinding when applicable)?				
	2.3. Are there complete outcome data (80% or above)?				
	2.4. Is there low withdrawal/drop-out (below 20%)?				
3. Quantitative non-randomized	3.1. Are participants (organizations) recruited in a way that minimizes selection bias?				
	3.2. Are measurements appropriate (clear origin, or validity known, or standard instrument; and absence of contamination between groups when appropriate) regarding the exposure/intervention and outcomes?				
	3.3. In the groups being compared (exposed vs. non-exposed; with intervention vs. without; cases vs. controls), are the participants comparable, or do researchers take into account (control for) the difference between these groups?				
	3.4. Are there complete outcome data (80% or above), and, when applicable, an acceptable response rate (60% or above), or an acceptable follow-up rate for cohort studies (depending on the duration of follow-up)?				
4. Quantitative descriptive	4.1. Is the sampling strategy relevant to address the quantitative research question (quantitative aspect of the mixed methods question)?				
	4.2. Is the sample representative of the population understudy?				
	4.3. Are measurements appropriate (clear origin, or validity known, or standard instrument)?				
	4.4. Is there an acceptable response rate (60% or above)?				
5. Mixed methods	5.1. Is the mixed methods research design relevant to address the qualitative and quantitative research questions (or objectives), or the qualitative and quantitative aspects of the mixed methods question (or objective)?				
	5.2. Is the integration of qualitative and quantitative data (or results*) relevant to address the research question (objective)?				
	5.3. Is appropriate consideration given to the limitations associated with this integration, e.g., the divergence of qualitative and quantitative data (or results*) in a triangulation design?				
	Criteria for the qualitative component (1.1 to 1.4), and appropriate criteria for the quantitative component (2.1 to 2.4, or 3.1 to 3.4, or 4.1 to 4.4), must be also applied.				

*These two items are not considered as double-barreled items since in mixed methods research, (1) there may be research questions (quantitative research) or research objectives (qualitative research), and (2) data may be integrated, and/or qualitative findings and quantitative results can be integrated.

Appendix C

SIGN	Methodology Checklist 1: Systematic Reviews and Meta-analyses SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C,. et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007,* ***7****:10 doi:10.1186/1471-2288-7-10. Available from* http://www.biomedcentral.com/1471-2288/7/10 *[cited 10 Sep 2012]*

Study identification (*Include author, title, year of publication, journal title, pages*)	
Guideline topic:	Key Question No:
Before completing this checklist, consider: Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.	
Checklist completed by:	

Section 1: Internal validity		
In a well conducted systematic review:		*Does this study do it?*
1.1	The research question is clearly defined and the inclusion/ exclusion criteria must be listed in the paper.	Yes ☐ No ☐ **If no reject**
1.2	A comprehensive literature search is carried out.	Yes ☐ No ☐ Not applicable ☐ **If no reject**
1.3	At least two people should have selected studies.	Yes ☐ No ☐ Can't say ☐
1.4	At least two people should have extracted data.	Yes ☐ No ☐ Can't say ☐
1.5	The status of publication was not used as an inclusion criterion.	Yes ☐ No ☐
1.6	The excluded studies are listed.	Yes ☐ No ☐

1.7	The relevant characteristics of the included studies are provided.	Yes ☐ No ☐
1.8	The scientific quality of the included studies was assessed and reported.	Yes ☐ No ☐
1.9	Was the scientific quality of the included studies used appropriately?	Yes ☐ No ☐
1.10	Appropriate methods are used to combine the individual study findings.	Yes ☐ No ☐ Can't say ☐ Not applicable ☐
1.11	The likelihood of publication bias was assessed appropriately.	Yes ☐ No ☐ Not applicable ☐
1.12	Conflicts of interest are declared.	Yes ☐ No ☐
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review?	High quality (++) ☐ Acceptable (+) ☐ Low quality (-)☐ Unacceptable – reject 0 ☐
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes ☐ No ☐
2.3	**Notes:**	

Appendix D

Table 9- hardware and software

Author.	Hardware	**Software**
Burdea et al., 2019	VIVE (3Darm tracking, finger flexion), BBG controller, screen	BrightBrainer System;
Calabro et al., 2018	PC-Based workstation, Virtual Reality Rehabilitation System (VRRS)	advanced videoconferencing system
Cano-Manas et al., 2020	Xbox 360° video games console and the Kinect® (Microsoft Corporation, Redmond, WA, USA)	Commercial video games
Chen et al., 2020	Folding chair. Computer with monitor, microphone, and speakers, Verizon wireless modem, Myo Band, Wiimote in a pistol-shaped holder, PowerMate, PlayStation 3 Eye Move Controller, Joystick, Logitech Trackpad, Standard rehabilitation therapy devices for the upper extremity	-
Dodakian et al. 2017	24″ × 48″ table, bridge chair, Dell Latitude E5420 laptop (with 14″ display, internal webcam, and added fisheye lens), Verizon wireless USB modem, USB-based wrist blood pressure cuff, and custom-made USB-based mat	Polycom Converged Management Application client software;
Fu et al., 2019	2400 touchscreen Windows 8 (Microsoft Corp., Redmond, WA) PC (Figure 1, Dell Inspiron 2330, Dell Corp., Round Rock, TX); Game input from the paretic hand was sensed by a bend sensor (Images SI, Inc., Staten Island, NY) that was attached to a fingerless mitten (Handana Corp., Austin, TX)	-games were programmed using Unity 3D (Unity Technologies, San Francisco, CA)
Kannan et al., 2019	Wii Fit (Nintendo Co, Ltd. Kyoto, Japan)	Wii-fit games (Bubble Balance, Table Tilt, Tight-Rope Walking, Soccer Head)
Kilbride et al., 2018	Portable Non-immersive device for gamification, Hand controller, Neuroball, armbands, Neurobands	Neurofenix platform
Lee et al., 2020	RAPAEL smart rehabilitation 179 solution (consisting of a smart glove as a wireless and 180 real-time biofeedback device), a non-immersive VR training tool	-
Lin et al., 2020	wireless VR device, Kinect sensor (Microsoft Corporation, Redmond, WA, USA)	-
Maggio et al., 2019		-
Maier et al., 2020	RGS set-up, a VR-base rehabilitation tool desktop computer, a Microsoft Kinect and two wristbands with reflective markers	-

Table 9 continued		
Author.	Hardware	**Software**
Maresca et al., 2019	Touchscreen tablet with VR system	-
McKay et al., 2019	Touchscreen tablet	-
Mohd et al., 2019	HTC Vive virtual reality headset	-
Oh et al., 2019	Monitor, conventional computer, various real instruments	Joystim, a 3D manipulator
Paulino et al., 2019	-PC Screen; 2D Natural UI (2D NUI) (joystick); AnTS, a camera-based tracking software	-Reh@City software¸ tracking software
Pugliese et al., 2019	RecoverNow tablet	RecoverNow
Rai et al., 2017	Any PC or mobile-devices web-browser	HTML5, CSS3, JavaScript, PHP and MySQL frameworks
Rivas et al., 2019	Computer, webcam, gripper	tracking system, a simulated environment system with serious games, trunk compensation detector system, Adaption system
Torrisi et al., 2019	VRRS- system including a tablet at a workstation at home	
Wall et al., 2018	Android Samsung Galaxy NotePro (12.2 inch) tablet	Unity game engine (version 4.6) software development
Wiley et al., 2019	IREX motion detection system and Head Mounted Display system combined with computerized cognitive training/cognitive rehabilitation	, Reh@Task, Elements, or BTs-Nirvana combined with conventional therapy, Serious games, Reh@City, Joystim

Table 10- Characteristics of Intervention

Author.	Intervention	Duration	Assistance/additional intervention
Burdea et al., 2019	VR game-based (e.g. car race, tower of Hanoi, card paring games)telerehabilitation system to enhance bimanual upper extremity motor function, cognition, and wellbeing	○ 20-40 minutes ○ 5 days per week ○ 4 weeks ○ 20 sessions in total	○ Initial introduction ○ Access to online tutorials ○ Caregivers assisted, if necessary
Calabro et al., 2018	Telerehabilitation for motor and cognitive function	○ 60 minutes ○ 5 days per week ○ 12 weeks	○ Videoconference with therapist to monitor process ○ Therapist can monitor patients work and adjust exercises on their platform
Cano-Manas et al., 2020	conventional rehabilitation + video-game based therapy on balance, postural control, functionality, quality of life, and level of motivation	○ 20 minutes ○ 3 days per week ○ 8 weeks	-
Chen et al., 2020	telerehabilitation system is comprised of four main components: games, exercises, education, and telecommunication	○ 70 min ○ 6 days per week ○ 6-8 weeks	○ Research team delivered and set up equipment at home ○ Initial introduction
Dodakian et al. 2017	Games focused on arm motor therapy. Stroke education, videoconferences	○ 60 minutes ○ 7 days per week ○ 4 weeks	○ physical or occupational therapist assesses clients progress online and adjusts daily program
Fu et al., 2019	Treatment for upper extremity hemiplegia that integrates contralaterally controlled functional electrical stimulation with hand therapy video games	○ 45 min ○ 10 per week at home ○ 4 timer per week in lab ○ 12 weeks	○ in lab, therapist guided
Kannan et al., 2019	Cognitive-motor exergame training (CMT) games	○ 60 min ○ 3,5 sessions per week ○ 6 weeks	
Kilbride et al., 2018	Rehabilitation via HOMe Based gaming exercise for the Upper-limb	○ 45 min ○ 5 days per week ○ 6 weeks	○ initial introduction, if requested with caregiver
Lee et al., 2020	virtual training program with smart glove on the upper extremity function and quality of life; game-like exercises	○ 30 min ○ 3 days per week ○ 8 weeks	-

Table 10 continued

Author.	Intervention	Duration	Assistance/additional intervention
Lin et al., 2020	Muscle Strength, Mood State, and Functional Status: conventional therapy comprised of standardized stroke care +VR training; exercises	○ 15 min ○ 2x per day ○ 5 days	○ fully supervised by stroke care experienced registered nurses
Maggio et al., 2019		-	○
Maier et al., 2020	Adaptive conjunctive cognitive training (ACCT) in VR for chronic stroke Patients; games	○ 30 min ○ 7 times per weeks ○ 6 weeks	○ Initial introduction
Maresca et al., 2019	linguistic treatment performed using the VRRS-Tablet; exercises	○ 50 minutes ○ 5 days per weeks ○ 12 weeks in hospital ○ 12 weeks at home	○ Initial introduction for patient and caregiver ○ After discharge Videoconference with neuropsychologist 2x a week for monitoring
McKay et al., 2019	adaptive game-based attention training program	○ 20 min ○ 5 days per week ○ 5 weeks	-
Mohd et al., 2019	Dual cognitive task VR game -strategy game storytelling mode	-	○ - minimal assistance from therapist needed
Oh et al., 2019	real instrument training in VR environment for improving upper-extremity and cognitive function	○ 30 mins ○ 3 days per week ○ 6 weeks	○ -supervision of occupational therapist
Paulino et al., 2019	VR cognitive training VR simulation of a city where patients can train a variety of cognitive skills while performing simulated activities of daily living	-	○ Minimal assistance form therapist needed
Pugliese et al., 2019	preselected, modality-specific therapeutic apps for stroke-induced deficits related to communication, cognition, and fine-motor ability	○ 60 min ○ 7 days per week ○ 12 weeks	○ Initial training session for usage of platform ○ Web-based administration portal for therapists available to monitor and adjust therapy
Rai et al., 2017	Cognitive retraining via min 17 different engagement games such as rotating symbol matching, map search, sequence organization, etc.	-	○ Online platform to monitor and adjust progress
Rivas et al., 2019	multimodal affective states recognition system; games	○ 1 rehabilitation session ○ ○	-

Table 10 continued

Author.	Intervention	Duration	Assistance/additional intervention
Torrisi et al., 2019	VR rehabilitation system in improving cognitive function, 2D and 3D exercises	○ 50 minutes ○ 5 days per week ○ 12 weeks in the rehabilitation center ○ 12 weeks at home	○ VRRS training in center ○ After discharge Videoconference with psychologist 2x a week for monitoring
Wall et al., 2018	Non-immersive VR Cognitive assessment of attention, visual memory, executive functioning, and visuoperceptual skills	○ 20 minutes ○ 1 session	-
Wiley et al., 2019	combination of VR therapy and conventional therapy, combination of VR therapy and computer-based cognitive training, VR therapy alone fully immersive, non-immersive, semi-immersive environments	○ 20-180 minutes ○ 2-7 days per week ○ 4-8 weeks	-

Table 11 - Study outcomes

Author.	Outcome measures of interest	Results	Conclusion
Burdea et al., 2019	Emotive and cognitive instruments ○ Primary outcome: NAB ○ Secondary outcome: (BDI-II, BNT, BVMT-R, HVLT, NAB TMT-A, TMT-B, VFT)	○ executive function improvement of 3.3 points (p = .03) ○ average depression severity dropped a statistically significant 3.4 points (p = .03)	Significant gains in executive function and depression reduction for people with chronic stroke
Calabro et al., 2018	Cognitive assessment: ○ (MoCA), Frontal Assessment Battery Mental wellbeing: ○ Beck Depression Inventory (BDI) ○ Coping orientation to problem experienced Psychological General Well-being Index Short-Form-36 health outcome	-	-
Cano-Manas et al., 2020	EuroQoL (for anxiety/depression), Scale of Satisfaction	○ Intragroup: Significant improvement for controlgroup for anxiety/depression dimension (*p* � 0.03) ○ Intergroup: significant difference for anxiety/depression dimension (*p* < 0.01)	Concerning the quality of life, our results indicate that the combination of conventional treatment with a semi-immersive video-game approach produced positive effects on the perception of pain/discomfort, sensation of anxiety/ depression, and an increased subjective perception of patients regarding their health status
Chen et al., 2020	Qualitative semi-structured interviews with open coding scheme	○ Patients experienced enhanced cognitive Skills, memory through playing games ○ Participants felt more socially connected after using the system. ○ participants reported barriers in their technical skills, limited living space to place the devices	-
Dodakian et al. 2017	Depression measured by GDS and patient health questionnaire (PHQ)-9 and PHQ-2 scales	GDS scores obtained in person at visit 1 correlated significantly with these telerehabilitation-derived PHQ-2 scores (ρ = 0.88, *P* = .0001, Spearman’s rank correlation Coefficient)	study validated a home-based telerehabilitation system for measuring depressive symptoms

Table 11 continued

Author.	Outcome measures of interest	Results	Conclusion
Fu et al., 2019	Cognition: -reading subtest from the Wide Range Achievement Test – Fourth Ed. - Digit Span subtest from the Wechsler Adult Intelligence Scale – Third Ed. Symbol Digit Modalities Test (processing speed),32 Judgment of Line Orientation (visuospatial perception),33 the Hopkins Verbal Learning Test (episodic memory),34 and the Tower Test subtest from the Delis–Kaplan Executive Functioning Systems (executive function).35	○ Towers Test of executive function was only significant outcome measure of cognition	Indication that treatment influences cognitive and motor processes independently.
Kannan et al., 2019	Primary outcomes: -cognition (Direct RT Empirisoft software) assessing working memory, attention, information processing speed Dual-task condition(Slip perturbation test, Limits of Stability Test, Letter-Number Sequencing) Secondary outcomes: -cognitive-motor exergaming scores	○ no significant main effect of either time [(f (1, 18) = 2.674; $p > 0.05$)] or group [(f (1, 18) = 3.849; $p > 0.05$)], but there was a significant time x group interaction [(f (1, 18) = 5.809; $p < 0.05$)] for cognitive accuracy on the letter number sequencing (LNS) task ○ LNS cognitive task during the SPT, significant main effects of time [f (1,14) = 3.420; $p < 0.05$] and group [Group effect: f (1,14) = 3.697; $p < 0.05$] were observed, with theCMTgroup showing a significant increase in accuracy from pre- to post-training ($p < 0.05$) but with no change observed for the CT group ($p > 0.05$). This resulted in significantly greater post-training accuracy for theCMTgroup than for the CT group ($p < 0.05$)	efficacious method for improving balance and cognition, and ultimately reducing cognitive-motor interference (CMI).
Kilbride et al., 2018	-fatigue (FSS-7) -quality of life (EuroQoL 5, including Anxiety/depression)	-	-

Table 11 continued

Author.	Outcome measures of interest	Results	Conclusion
Lee et al., 2020	visual attention and task switching (TMT)	-	The VR-training in the intervention group did not differ from recreational activities of control group, cognitive function in chronic phase would require more continuous training
Lin et al., 2020	-Mood state: (Hospital Anxiety and Depression Scale (HADS)) -Functional status (PASS, Barthel Scale)	○ At discharge, there were significant differences in depression (*p* < .001) and anxiety (*p* = .003) between the groups after controlling for baseline levels ○ Participants in the EG reported decreased depression (s = −2.82, *p* < .001) and anxiety (s = −1.74, *p* < .001) after the intervention ○ The significant group–time interaction for depression and anxiety revealed that the EG had a greater decrease in both the depression and anxiety at discharge than the CG (s = −2.31, *p* = .011; s = −1.63, *p* = .047)	addition of VR training during early rehabilitation results in improvements in mood state including depression and anxiety
Maggio et al., 2019	-	-	Effects of conventional cognitive rehabilitation may be enhanced by VR "Vstimulating cognitive abilities (amnesic-attentive functions and visuospatial cognition), executive processes, and behavioral abilities in patients with neurological disorders"
Maier et al., 2020	Primary outcomes: attention, memory, executive function, spatial awareness (Neuropsychological test battery) Secondary outcome: MoCA, BI, FM-UE, Hamilton Depression Rating Scale, MMSE	○ Experimental group showed improvements in attention (χ2 F (2) = 9.57, p < .01), spatial awareness (χ2 F (2) = 11.23, p < .01) and generalized cognitive functioning (χ2 F (2) = 15.5, p < .001). ○ No significant change was seen in the executive function and memory domain. ○ For the control group, no significant change over time was found. They worsened in their depression level after treatment (T = 45, r = .72, p < .01) but returned to baseline at follow-up. ○ The experimental group displayed a lower level of depression than the control group after treatment (Ws = 81.5, z = − 2.76, r = − .60, p < .01) and (Ws = 92, z = − 2.03, r = − .44, p < .05) – EGD group continues to	ACCT positively influences attention and spatial awareness, as well as depressive mood in chronic stroke Patients -trend for EG to reduce their depression level

		express lower depression levels at T2 (mean of 4.40) than the CGD (mean 6.30).	
Maresca et al., 2019	Depression- (ADRS) -health related quality of live (Euro-Qol-5D -functional independence and psychological well-being (PIADS)	○ at the end of the studythere was a significant difference in all test scores. Indeed, the EG scores improved during the whole study, differently from those of the CG which significantly improved only from T0 to T1 (i.e., TT and ADRS) or from T1 to T2 (i.e., EQ-5D). ○ type of the rehabilitative treatment affected comprehension (X2(3) = 18.14; P< .001; R2 = .92), repetition (X2(3) = 16.77; P< .001; R2 = .94), reading (X2(3) = 28.23; P< .001; R2 = .91), naming (X2(3) = 15.22; P< .01; R2 = .98), and calculation (X2(3) = 37.77; P< .001; R2 = .98) domains	home training influenced positively the recovery of the linguistic functions, mood, and perception of one's state of health -could be used to reduce depression and promote psychological well-being
McKay et al., 2019	Primary outcomes: Assessment of selective, sustained and executive attention, Secondary outcomes: behavioral attention, working memory, social skills	-	-
Mohd et al., 2019	Attentional skills test	-	-
Oh et al., 2019	Korean Mini-Mental State Examination, and Korean-Montreal Cognitive Assessment	○ In both groups K-MoCA scores were significantly improved at the posttraining and followup evaluations KMoCA (P<.001 for both)	Combination of VR and real instruments Effective in promoting cognitive function
Paulino et al., 2019			
Pugliese et al., 2019	Primary outcome: Feasibility		Acute stroke patients are interested in attempting tablet-based stroke rehabilitation and are easily recruited early post-stroke. However, tablet-based therapy may be challenging due to patient, device and system-related barriers
Rivas et al., 2019		○ proposed multimodal computational model FSNB got results over 93 % with a standard deviation of around 0.06	

Table 11 contniued

Author.	Outcome measures of interest	Results	Conclusion
Torrisi et al., 2019	Cognition (MOCA) Executive Functions (FAB, Weigl Test), attentive processes (AM, TMT A, B and B-A), Autidory verbal Learning test (RAVLT), Digit span to verify memory abilities, phonemic and semantic verbal fluency, Anxiety (HRS-D), Depression (HRS-D)	○ MOCA ($\chi2(3) = 21.93$; $P < 0.001$), AM ($\chi2(3) = 19.01$; $P <0.001$), ○ TMT.B ($\chi2(3) = 12.80$; $P < 0.01$), TMT.B-A ($\chi2(3)= 17.80$; $P < 0.01$), ○ Phonemic Fluency ($\chi2(3) = 17.92$; $P <0.001$), Semantic Fluency ($\chi2(3) = 27.69$; $P < 0.001$), ○ RAVL.I ($\chi2(3) = 15.05$; $P < 0.01$), ○ HRS-A ($\chi2(3) = 15.68$; $P < 0.01$) and HRS-D ($\chi2(3) = 37.17$; $P < 0.001$) Scores affected by treatment option	-Demonstreated effectiveness of VRRS treatment of cognitive disorders -at the end of the study, we found a more significant improvement in the global cognitive level, as well as in the attentive, memory and linguistic skills
Wall et al., 2018	-	-	Preliminary support for the Cognitive Assessment App to be a feasible cognitive assessment for stroke survivors with and without aphasia
Wiley et al., 2019	Global cognition, Attention, Memory, Executive function, Visuospatial abilities, Language	○ VR therapy was not more effective than control for improving global cognition (n¼5, SMD ¼ 0.24, 95%CI:_0.30,0.78, p¼.38), memory (n¼2 studies, SMD¼ 0.00, 95%CI: _0.58, 0.59, p¼.99), attention (n¼2 studies, MD ¼ 8.90, 95%CI: _27.89, 45.70, p¼.64) or language (n¼2 studies, SMD ¼ 0.56, 95%CI: _0.08,1.21, p¼.09).	