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Efficacy of Virtual Reality Incorporation in Post-Stroke Rehabilitation

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Abstract

Introduction: Stroke is one of the leading causes of death and morbidity in the United States, with one of the largest concerns being persistent neurological deficits. Traditionally, conventional rehabilitation has been initiated as soon as possible in post-stroke patients in attempt to improve function and neuroplasticity either back to patient baseline levels or to a new maintained baseline. Recently, virtual reality (VR) supported rehabilitation has been studied in comparison to traditional therapy to determine if there is potential for its utilization in patient care.

Methods: A PubMed database search was used and narrowed down to 6 articles to be interpreted in this analysis. This selection consists of 3 systemic review articles, 2 randomized control trials (RCTs), and 1 meta-analysis article that met inclusion criteria regarding utilization of virtual reality in post-stoke rehabilitation.

Results: Throughout the 6 studies, VR therapy had an association with significant improvement of upper extremity motor function, range of motion, upper extremity muscle strength, balance, gait performance of the lower extremities, executive function, memory, visuospatial ability, dizziness, trunk control, and reduction of motor deficit. There was no statistically significant improvement in either grip strength or spasticity.

Discussion: Majority of the studies found data supporting utilization of VR-supported rehabilitation, either independently or in conjuncture with conventional therapy in post-stroke patients. Combination therapy seemed to be the preferred route based on currently available data, especially to cover deficits in VR-supported rehabilitation. Further studies are recommended.

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INTRODUCTION

According to the Centers for Disease Control and Prevention (CDC), every 40 seconds someone in the United States has a stroke.[1] Stroke is the leading cause of serious long-term disability, and stroke-related expenses within the United States equated to 56.5 billion dollars in 2018-2019.[1]

A cerebral vascular accident (CVA), or stroke, is the interruption of blood flow to brain tissue. This occurs either from occlusion or rupture of vasculature. The main classifications of stroke are thus ischemic and hemorrhagic; ischemic by far being the more common of the two.[1] Causes of ischemia include thrombosis, embolus, and hypoperfusion. The effects of ischemia include development of parenchymal edema and petechial hemorrhages—which leads to hypoxemia, glucose starvation, and neuronal cell and cerebral parenchymal death. Hemorrhagic variations consist of intracerebral, or parenchymal, hemorrhage and subarachnoid hemorrhage.[2,3] This results in direct damage to the brain tissue in the form of compression or mass effect.[2,4] However, there are also neurotoxic effects from contact with blood and brain tissue resulting in directly mediated neuronal cell death via tissue damage and apoptosis, vasospasm, and/or contribution to inflammation.[4] This results particularly from thrombin, fibrinogen, free iron, complement, hemoglobin, leukocytes, and platelets.[4]

One of the largest concerns regarding CVA is persistent neurological deficits. These include cognitive, physical, emotional, and behavioral alterations. Memory impairment, disorders in speech, vision loss, weakness, paresis, dysphagia, depression and mood disorders are only a few of the potential long-term implications of stroke. To combat this and potentially improve the outcomes in post-stroke patients, rehabilitation is started as soon as possible. Traditional post-stroke rehabilitation includes exercises for range-of-motion, strength, coordination, flexibility, balance, weightbearing, gross motor, fine motor, forced-use, sensory re-education, swallowing, eye, speech, language, cognition, and mirror therapy.[5]

Recently, there has been an increased demand for telemedicine. Increase in the usage and research in this aspect of medicine has been influenced by its convenience for patients who live in rural or secluded areas with limited or zero access to transportation, its cost-effectiveness, its limitation of pathogenic exposure, and its overall efficacy of care .[6] In post-stroke patients, there is now a new niche for rehabilitation delivery. The concept of virtual reality (VR), which is defined as being an artificial environment and stimuli that can be interacted with through use of electronic equipment, is becoming a focus of study. Incorporation of VR into post-stroke therapy is thought to have potential for additional benefit and perhaps equivalent benefit to traditional rehabilitation services.[7] Theories of enhanced neuroplasticity and increased patient enthusiasm, with the goal of improved patient compliance, are currently being researched.[7]

The main categories of VR are non-immersive, semi-immersive, and fully-immersive. Non-immersive is classically 2-dimensional and is delivered through a computer or gaming console system. A person would utilize a tool, such as a mouse, joystick, or sensors, to interact with their environment.[7] Semi-immersive systems are 3-dimensional and incorporate stereoscopic projections.[7] Participants utilizing semi-immersive systems tend to feel a deeper connectivity and interaction than non-immersive systems.[7] Fully-immersive systems often utilize head-mounted displays to collect head and body movements so that real-time interaction can occur between visualized images and interactions of the real world.[7]

The purpose of this paper is to explore the possible benefits and efficacy of utilizing VR as a delivery mechanism for post-stroke rehabilitation in comparison or addition to traditional rehabilitation methods.

METHODS

A search using PubMed database for "stroke" AND "virtual" while selecting the parameters of free full-text, articles published within 3 years, randomized control trials (RCT), meta-analysis, systemic review, and those published in the English language resulted in 126 articles. Since this is a limited systemic review, only 6 articles were selected out of the 126. This selection consists of 3 systemic review articles, 2 RTCs, and 1 meta-analysis article that met inclusion criteria regarding utilization of virtual reality in post-stoke rehabilitation. These peer-reviewed articles will be assessed to determine if there is a supported future for VR providing adequate recovery in post-stroke patients. Whether or not this is synergistic, superior, or inadequate to traditional therapy will be further discussed.

RESULTS

Chen et al[8] conducted a systemic review of 42 publications, consisting of 43 trials, with a calculated aggregated sample size of 1,893.[8] Control groups were either those utilizing conventional or no therapy in contrast with those incorporating VR-supported exercise therapy for upper extremity motor function in post-stroke patients. Their study followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines along with independently assessed risk of bias for each included trial.[8] When comparing to the control groups, those incorporating VR therapy had an association with upper extremity motor function improvement; standard mean differences (SMD) 0.45, 95% CI 0.21-0.68; $P<0.001$, or SMD 0.35, 95% CI 0.19-0.50; $P<0.001$ post-outlier removal.[8] There was also significant improvement in range of motion in VR-inclusive groups compared to the controls, with SMD 1.01, 95% CI 0.50-1.52; $P<0.001$, along with improvement in upper extremity muscle strength (SMD 0.79, 95% CI 0.28-1.30; $P=0.002$).[8] Overall, the use of VR therapy was associated with significant improvements in independence in daily activities (SMD 0.23, 95% CI 0.06-0.40; $P=0.01$, with modified Rankin Scale scores; SMD 0.57, 95% CI 0.01-1.12; $P=0.046$).[8] There was no statistically significant improvement in either grip strength or spasticity (i.e. "involuntary muscle contraction, stiffening, and tightening upon the movements of body parts").[8] The statistics of age-based groups and chronicity of post-stroke patients was also discussed. The type of VR program used was assessed and showed that specialized programs specific for rehabilitation resulted in an improvement in quality of life more so than those utilizing commercial games (SMD 0.49, 95% CI −0.11 to 1.10; *P*=0.11 vs SMD −0.20, 95% CI −0.46 to 0.06; *P*=0.13); the difference between the groups was significant (*P*=0.04).[8] Combination therapy of both conventional and VR-supported resulted in overall greater improvement in hand dexterity and quality of life in comparison to utilizing VR therapy on its own (per hand dexterity, SMD 0.52, 95% CI −0.01 to 1.05; *P*=0.052 vs SMD −0.08, 95% CI −0.34 to 0.18 with difference between combined vs stand-alone VR of *P*=0.046; per quality of life, *P*=0.56; SMD 0.49, 95% CI −0.11 to 1.10; *P*=.11 vs SMD −0.20, 95% CI −0.46 to 0.06; *P*=0.13, difference between the groups *P*=0.04).[8] Duration of therapy and trial length was also discussed. Final results suggest, with limitations due to smaller sample size and detected publication biases, that VR-supported rehabilitation therapy could be effective at improving upper extremity gross motor function and independent daily living in post-stroke patients when compared to conventional therapy or no therapy at all. There was no correlation with improvement of fine motor function when compared to the controls. Further studies were recommended.[8]

Demeco et al[7] also conducted a systemic review that included 12 RCTs out of 4,623, "involving post-acute and chronic stroke survivors, with a total of 350 patients (234 men and 115 women; mean age 58.36 years").[7] There were 4,369 articles excluded due to not being written in English, being duplicate articles, not being RTC studies, or no full-text availability. The remaining 19 articles were further narrowed down per the Physiotherapy Evidence Database Scale (PEDro) score checklist.[7] This review was guided by PRISMA and 2 reviewers independently screened articles by title and abstract or full text for study selection. Risk of bias was determined by stratification per the Oxford Center for Evidence-Based Medicine (OCEBM) along with 2 authors' independent assessments.[7] The studies either consisted of patients at the hospital, medical center, or rehabilitation clinic. Ten trials involved chronic stroke patients, 1 post-acute stroke, and 1 trial between 2 weeks to 6 months post-stroke. One study focused on ischemic stroke only, 8 focused on both ischemic and hemorrhagic, and 3 did not clarify. Seven studies were on upper limb, and 5 studies on lower limb. The trials used different association devices for their VR therapies. There was also variation between using a 2-step rehabilitation protocol, interactive labs, game usage, occupational training, and so forth.[7] There was noted improvement in the VR mirror therapy group of 1 study regarding total score and hand component Fugl-Meyer Upper Extremity Scale (FM-UE) ($p = 0.033$ and $p = 0.008$, respectively) compared to mirror therapy group.[7] Another of the 12 studies showed a difference between virtual reality therapy and conventional therapy ($p = 0.014$ vs. $p = 0.021$).[7] Another included study showed improvement in both upper limb measures that was higher in the virtual reality group compared with the control group ($p < 0.001$).[7] A fourth article included in this review, analyzed kinematic data from arm and trunk movements. They found that the virtual reality group had better results than the control group in terms of motor functioning ($p < 0.05$) and smoothness of movements ($p < 0.001$).[7] This same study found correlation with “minor cognitive deficits in memory, attention, visual perception capacity and problem solving.[7]” The last included study regarding upper extremities found no clinical differences in the groups for both the measures ($p = 0.485$ and $p = 0.139$) for upper extremity motricity.[7] A study assessing lower extremity balance and gait performance with use of treadmill VR-supported therapy saw a statistical difference in participation ($p < 0.001$) and dynamic balance (Mini-Balance Evaluation Systems Test (Mini-BESTest) $p < 0.001$) at T1, but no statistical difference between group participation ($p = 0.221$).[7] A second lower extremity study found statistical improvement in the timed up and go test (TUG), Activities-Specific Balance Confidence (ABC) and 6 minute walking test (6-MWT), both in the virtual reality group and the community ambulation group (VR: TUG $p = 0.001$, ABC $p = 0.018$, 6-MWT $p = 0.007$; CA: TUG $p = 0.000$, ABC $p = 0.000$, 6-

MWT $p = 0.004$), with no significant difference found in the control group.[7] Temporal and spatial gait data between groups saw a statistical difference on TUG ($p = 0.048$) and ABC ($p = 0.043$) between the virtual reality and control groups.[7] A third lower extremity study saw that, when studying spatio-temporal gait values, that using virtual reality had “positive influence on locomotor function under single task situation with an improvement in gait speed” ($p = 0.000$), cadence ($p = 0.000$), step length ($p = 0.000$) and stride length ($p = 0.000$).[7] The end results of this review suggested that VR integration in post-stroke rehabilitation could offer additional benefits to conventional therapy; especially due to the majority of stroke survivors dealing with limb dysfunction. They found that VR-supported therapies benefited balance and gait performance of the lower extremities, with limited adverse effects. They also found that VR-supported therapies increased results on upper extremities when compared to occupational therapy on its own. Lastly, they found increase in patient motivation with the goal of increasing neuroplasticity.[7]

Zhang et al’s[9] systemic review consists of 23 RCTs, a total of 894 patients, for meta-analysis. Of those selected, 23 trials were in Korea, 3 in Portugal, 2 in Spain, 2 in China, 2 in Australia, 1 in Lithuania, 1 in Brazil, and 1 in Turkey. Sample sizes ranged from 18-145 per trail. VR therapies ranged from 3-10 weeks—majority being 4 weeks. Frequency of intervention ranged from 2-5 times per week. Most of the studies consisted of VR-supported therapy with occupational therapy, with 2 studies combining VR-supported therapy with computer-assisted cognitive rehabilitation.[9] The review was conducted according to PRISMA guidelines. Participants included those 18 years or older without restriction to other stroke populations. The VR “had to consist of a screen or a head-mounted device, including games with immersive, semi-immersive, and non-immersive systems, simulating virtual environments using computers, video consoles, mobile apps, and VR. The intervention setting, duration, and frequency were not restricted. Participants in the control group could undergo usual care or non-VR interventions.[9]” Two reviewers independently assessed articles for inclusion criteria, and all 23 articles “showed an acceptable risk of bias” with the Egger test of global cognitive function being insignificant (*P*=0.29).[9] They found that when compared to the control, there was no evidence that VR-supported therapies could significantly improve global cognitive function in post-stroke patients (SMD=0.32, 95% CI=–0.43-1.06, *P*=0.41).[9] They were able to use 5 of the trials to find that VR-supported therapies significantly improved executive function when compared to the control (SMD=0.88, 95% CI=0.06-1.70, *P*=0.03).[9] Regarding memory, they found that VR-supported therapies had a positive effect on memory in post-stroke patients (SMD=1.44, 95% CI=0.21-2.68, *P*=0.02).[9] Two of the trials, 64 patients, resulted in no statistical significance on verbal fluency (SMD=0.11, 95% CI=–0.38-0.61, *P*=0.65).[9] Two trials, 56 patients, found that VR-supported therapies had a significant effect on visuospatial ability when compared with the control (SMD=0.78, 95% CI=0.23-1.33, *P*=0.006).[9] Six trials assessed attention in post-stroke patients, with a sample of 166 total patients, concluding that there was no significant effect on attention between groups (SMD=–0.09, 95% CI=–0.39-0.22, *P*=0.58).[9] Depression symptoms were evaluated with 5 of the trails, 255 participants, finding no statistical significance between the VR and control groups (SMD=0.20, 95% CI=–0.25-0.64, *P*=0.39).[9] Quality of life was assessed through 7 trials, 272 participants, with no significant beneficial effect with VR-supported therapies (SMD=0.07, 95% CI=–0.17-0.31, *P*=0.55).[9] The conclusion was that VR therapy was effective in improving executive function, memory, and visuospatial ability in patients with stroke. They did not produce enough evidence supporting VR-based therapies improving global cognitive function, attention, verbal fluency, depression, or quality of life.[9]

Sana et al[10] conducted an RCT single-blinded study that included 34 subacute stroke patients aged 40-70 years that were randomly assigned to 2 groups; 1 receiving vestibular rehabilitation therapy (VRT), which focused on improving balance, gait, and gaze stability, and the other partaking in VR rehabilitation. The Time Up and Go test, Dynamic Gait index, and the Dizziness Handicap Inventory were used for group assessments.[10] Each group received 24 sessions for 3 days a week for 8 weeks total. They found that balance ($P-0.01$) and gait ($P-0.01$) were significantly improved within the VR group, while dizziness was significantly improved in the VRT group with $P < 0.001$.[10] Both groups had improvement in balance, gait, and dizziness with $P < 0.001$.[10] They concluded that both groups, and thus both rehabilitation methods, were effective and had evident patient benefit. However, they stated that VR-supported rehabilitation had a greater impact on improving balance and gait in subacute stroke patients, and that VRT therapy had greater effect on dizziness reduction.[10]

Peláez-Vélez et al[11] conducted an RCT with 24 participants randomly assigned to either a control group or an experimental group. Thirteen of the patients had a right-sided “condition” and 11 patients had a left-sided “condition” post-stroke—all occurring within 6 months.[11] All 24 participants received therapy at home or in outpatient setting. Both groups received a 1-h neurological physiotherapy session 5 times per week, and the experimental group received an additional VR-supported therapy session 3 times per week. The study lasted a total of 6 weeks.[11] The neurological physiotherapy consisted of various upper and lower extremity exercises assessing strength, resistance, kinesiology, gait, fine motor, balance, and postural stability.[11] The exercises were performed in various positions depending on the condition of each patient.[11] The VR-supported therapy consisted of immersive VR with glasses, computer, camera sensor, and router with a supervising physiotherapist.[11] The video games utilized were selected based on patient’s laterality; options included chopping motion, rowing movement, or climbing motions. Measurements of muscle strength, spasticity, functionality, trunk control, balance, and gait were priority.[11] They found that there was no significant difference between groups in muscle strength improvement with the muscle groups assessed (p-values ranging from 0.154 for wrist-extensors to 0.897 for elbow-flexors).[11] Spasticity also had no statistically significant difference in improvement between groups, with p-value range from 0.227 (hip-flexors) to 0.882 (knee-flexors).[11] Functionality, determined via Motricity Index, showed significant difference in improvement of trunk control with the experimental VR-supported group in comparison to the control (trunk control *p*-value 0.008 in experimental; *p*-value 0.083 in the control).[11] Balance between groups showed a *p*-value of 0.251 (Tinetti) and 0.111 (Berg) in the control, and *p*-value of 0.004 (Tinetti) and 0.007 (Berg) in the VR group, per test performed.[11] Gait comparison between the groups saw *p*-value of 0.105 in the control and *p*-value of 0.006 in the VR group; gait functionality resulted in a *p*-value of 0.280 in the control and *p*-value of 0.038 in the experimental.[11] Their conclusion was that the addition of VR-supported therapy to existing neurological physiotherapy was more effective than neurological physiotherapy on its own. They acknowledge that their focus of study may be difficult to compare with others due to variations test choices for balance, gait, and VR approach. They state that their experimental group improved efficacy and efficiency of balance, gait, trunk control, and motor deficit.[11] They found no significant difference regarding strength or spasticity between the control and VR-supported groups.[11] They also state that with further development and research, that VR-supported therapies will become an affordable option for at-home rehabilitation.[11]

Soleimani et al[12]performed meta-analysis screening 11,834 studies, and ultimately selecting 55 that met their criteria (consisting of 2,142 participants total).[12] All participants were 18 years or older and had to have inclusion of upper limb impairment.[12] The analysis met PRISMA guidelines and 2 authors independently screened articles per their inclusion criteria. They also employed EndNote and Rayyan software for detection of duplicate entries and assist in determination of eligibility.[12] Eligible RCTs included a control group of conventional therapy or other control condition, and VR groups were included of varying intensity. Non-immersive, semi-immersive, and fully-immersive VR therapies were included.[12] Primary outcomes assessed were upper extremity motor function (assessed by Fugl-Meyer assessment scale (FMA), Action Research Arm Test (ARAT), Wolf Motor Function Test (WMFT), Jebsen Taylor hand function test (JTHFT), grip strength, Manual Muscle Testing (MMT), and Passive Range of Motion (ROM)), functional independence (measured by Barthel Index (BI), Functional Independence Measure (FIM), or similar tools), quality of life (assessed by SIS), spasticity (rated by Modified Ashworth Scale (MAS)), and functional use and dexterity (assessed by the Motor Activity Log (MAL), Box and Block Test (BBT), or similar).[12] The authors utilized a formula to estimate missing standard deviations from certain included studies. Two authors also independently assessed risk of bias with the Cochrane Risk of Bias 2 tool with varying range of low-high bias (a majority listed as having 69.6%), and heterogeneity and reporting bias was inspected.[12] Subgroup and sensitivity analysis was performed. Blinding was identified as an issue in nearly half of the studies (48.2%).[12] FMA results for neuromuscular function (SMD 0.63, 95% CI 0.33–0.92); full-immersive VR resulted in a mean FMA improvement of 5.4 points (95% CI 5.02–5.77) over conventional therapy.[12] ARAT (for motor function, dexterity, and grip force) had significant data for VR intervention over conventional therapy (SMD 1.56, 95% CI 0.72–2.4).[12] Full-immersive VR therapy yielded the greatest improvement with a mean ARAT of 7.08 points (95% CI 6.67–7.49) over conventional therapy. [12] Semi-immersive VR therapy had a mean ARAT increase of 4.83 points (95% CI 4.53 to 5.13) compared to full-immersion, and non-immersive VR's impact on ARAT scores was a 2.52-point mean advantage (95% CI 1.83 to 2.66).[12] WMFT (for manipulation, dexterity, and fine motor) showed a pooled effect size significant for VR intervention (SMD 0.93, 95% CI: 0.08–1.78).[12] Grip strength had significant increase in VR groups (SMD 0.32, 95% CI 0.11–0.53); fully-immersive (95% CI 5.76–10.43) more than conventional.[12] JTHFT for dexterity found significant improvement in VR groups (SMD 0.71, 95% CI 0.21–1.22).[12] FIAs assessing instrumental daily livings found (SMD 0.41, 95% CI: -0.06-0.88) when assessing with BI. Semi-immersive VR therapy correlated with an average of a 4.6-point higher BI score compared to conventional therapy (95% CI: 4.09–5.09 points higher).[12] FIM (motor and cognitive) found increase in VR (SMD 0.49, 95% CI: -0.10-1.08); fully-immersive (95% CI: 3.54–4.59 points higher).[12] Postural assessment scale for stroke (version of FMA) found VR groups had 0.36 points higher than the conventional therapy group (95% CI 0.3 to 0.39 points higher).[12] SIS scores (assessing memory, cognition, manual dexterity, depressive symptoms, fatigue, and perceived severity of residual stroke-related deficits) found slight increase in VR groups (SMD 0.14, 95% CI: -0.79-1.08).[12] MAS with (95% CI: -0.03-0.54) for VR group.[12] MAL-AOU (self-reported utilization of the paretic limb) found increase in VR groups (0.70, 95% CI: 0.15–1.24).[12] BBT with increase in VR compared to control (pooled SMD 0.48, 95% CI: -0.05-1.2).[12] UEFI had only 1 study with 20 participants could be assessed with VR (95% CI: 2 lower to 8.7 higher) over conventional therapy.[12] Summaries of the data suggested a significant advantage of VR interventions over conventional therapy (SMD of 0.63, assessed by FMA), where fully immersive therapies resulted in significance improvement with FMA (SMD of 1.76), and semi-immersive groups exhibited greater enhancements in fine dexterity assessed by ARAT (SMD of 3.53).[12] They found significant improvements within VR-supported groups regarding functional independence (SMD of 0.41), improvements in quality of life (SMD = 0.14), and a reduction in spasticity (SMD = 0.25).[12] Significant enhancements in dexterity (SMD = 0.70) within VR groups were found to be consistent with findings reported 2 outside studies (SMD = 0.38 and SMD = 0.09), supporting VR-supported therapies improved fine motor skills and dexterity post-stroke.[12] They also found that higher levels of immersion were associated with greater functional improvements (SMD = 0.62 and SMD = 0.58).[12] Their conclusion being that utilization of fully immersive VR modalities could optimize recovery of gross motor skills in post-stroke patients, and that less immersive VR-therapies could benefit fine motor dexterity deficits. VR-based interventions improved neuroplasticity within the first 6 months post-CVA, and continued therapy over 6 weeks was thought to be essential for eliciting maximal therapeutic gains.[12]

DISCUSSION

Overall, most studies suggest that VR-supported rehabilitation provides benefit to post-stroke patient recovery. Though some studies showed evidence that VR therapy on its own showed improvement in function, majority provided evidence that the combination of VR-supported therapy with conventional therapy showed marked improvement and benefit. The main discrepancy would be the variance in which function is being studied in post-stroke patients, as there are many different aspects to compare in these studies: e.g. gait, balance, strength, memory, and so forth. Combination therapy may be more useful in aspects such as improvement of strength or grip strength – two categories that seemed to vary in improvement with VR-therapy alone per study.

Some of the articles, Soleimani et al[12], had such vast inclusion of different aspects of post-stroke rehabilitation being assessed that the display of this data appeared to cater to summarization and not raw data from the studies included. Though meta-analysis and systematic reviews are helpful, some seemed far reaching with inclusion of incomparable variables.

In the future, larger sample sizes should be utilized to improve the quality of these studies. With time, it is expected to see more studies including the various mediums of VR therapy and appearance of more congruity with results. The issue appears to be that there are a multitude of therapy options available, even within the VR category, that can make comparison of data difficult. The other difficulty being that when assessing post-stroke patients for improvement of function, there are variances in the “function” category. This form of rehabilitation has so far provided promising data and is expected to continue to demonstrate promise in post-stroke care.

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