RESEARCH PAPER

SYNAPSE VR for Post-Stroke Recovery: DEVELOPMENT AND CLINICAL FEASIBILITY OF A NOVEL VIRTUAL REALITY INTERVENTION "SYNAPSE VR" IN HAND MOTOR REHABILITATION AMONG HEMIPARETICS: A RANDOMIZED CONTROLLED PILOT STUDY

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ABSTRACT

Background: Virtual reality (VR) accelerates post-stroke recovery by engaging patients in interactive environments. SYNAPSE VR is an innovative virtual reality application containing a head-mounted display and 12 game activities designed to improve upper limb motor function and neuroplasticity in hemiparetic stroke patients.

Methods: A randomized, parallel group, active-controlled trial was conducted on 10 acute to sub-acute hemiparetic stroke patients (aged 45-60 years). Participants were randomly assigned to a group: Group A (experimental), Group B (Control), 5 in each group. Group A and B were provided immersive VR gaming intervention and conventional hand functional activities respectively along with their regular upper limb physiotherapy. Both groups received 4 therapy sessions per week for 6 weeks. Fugl-Meyer assessment for Upper Extremity (FMA-UE) and Box and Block test (BBT) were evaluated at baseline, post-test (7th week) and at 12-weeks follow up.

Results: The VR intervention was feasible, with 100% adherence and no adverse events. Both groups showed significant improvement within the group in FMA-UE (p=0.018) and BBT (p=0.007) scores over 12 weeks. Although the difference between groups lacked statistical significance, there was an absolute mean improvement of 22.00 blocks on the BBT (versus 11.20 in controls) in Group A, exceeding the Minimal Clinically Important Difference (MCID) of 6 blocks, indicating high clinical motor gains.

Conclusion: SYNAPSE VR provides immersive and engaging motor training environment by simulating real-life tasks with the advantage of customizability and interactive scenarios. This mode of treatment is expected to maximize motor function recovery in hemiparetic stroke patients.

Keywords: Virtual Reality, Stroke Rehabilitation, Upper Extremity, Recovery of Function.

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Introduction

Stroke is a leading cause of long-term physical disability globally which often results in upper limb hemiparesis. Upper limb hemiparesis can drastically limit patient's ability to perform activities of daily living, adversely affecting their coordination and independence reducing their overall quality of life.[1] Conventional rehabilitation includes high intensity, repetitive and task specific exercises to improve motor function and enhance neuroplasticity.[2] However, these traditional approaches can lead to reduced patient compliance and motivation over time. Additionally, the conventional therapy imposes a heavy burden on resources and healthcare facilities.[1,3]

The use of virtual reality (VR) in motor rehabilitation of the upper limb is an emerging approach to enhance recovery outcomes.[4]By immersing patients in interactive, gamified environments, VR based interventions increase the patient's interest, reduces psychological stress and enhances engagement and motivation.[5]Immersive VR enable adaptive task difficulty and provide real-time audio-visual feedback. These features are critical for facilitating motor learning, promoting cortical reorganization and preventing learned non-use of the paretic upper limb.[1,6]

Despite the advantages of VR in upper limb rehabilitation, there exists a significant research gap regarding VR interventions, specifically tailored for motor recovery. Many existing VR systems and applications are not designed to specifically address the needs of stroke survivors with severe distal impairments. An innovative virtual reality software framework called SYNAPSE VR, was conceptualized and developed to overcome the clinical challenges faced in conventional rehabilitation exercises and to address the need for immersive and adaptable interventions for upper limb motor rehabilitation in stroke patients[1,7]. Furthermore, custom rehabilitation platforms are expensive, require complex haptic exoskeletons making them difficult for the hemiparetic patients to wear or largely rely on flat screen monitors lacking fully immersive 3D depth perception necessary for fine motor execution.[7,8]

To address these challenges, an innovative VR framework, SYNAPSE VR was conceptualized and developed. The novelty of this newly developed software lies in its integration of well-structured task specific, game-based activities each tailored to target diverse hand functions. [8]

The aim of this study was to evaluate the clinical feasibility and preliminary efficacy of the novel SYNAPSE VR platform for upper limb motor rehabilitation.

Materials and methods

Study design: A pilot randomized, parallel group, active-controlled trial was conducted to assess the feasibility and efficacy of the VR platform. The study protocol was prospectively registered with Clinical Trials Registry-India (CTRI/2024/12/077668). Ethical approval was obtained from the institutional ethical committee of VELS Institute of Science, Technology & Advanced Studies **(**Approval No. ECR/288/Indt/TN/2018/RR-21/073**)**. As a pilot study, a sample size of 10 participants was selected to evaluate the feasibility and obtain preliminary data for future large scale clinical trials.

Participants: The study included acute to sub-acute stroke patients. Inclusion criteria required 1-6 months post-onset patients aged 45 to 60 years with hemiparesis resulting from either ischemic or haemorrhagic stroke. Participants with a basic educational qualification, a Mini-Mental State Examination (MMSE) score between 24 and 30 and a minimum Brunnstrom voluntary control grade of 2-3 for hand motor function were included. Patients with motion sickness susceptibility, multiple infarcts, severe visual impairment, cognitive impairment, vertigo and other neurological conditions were excluded from the study.

Randomization and Blinding: Informed consent was acquired from the participants after which they were allocated randomly into two group in a 1:1 allocation ration (n=5 per group). A computer-generated sequence was used as the method of randomization. The outcome assessors were blinded to minimize the detection bias during clinical evaluations.

Software description: The SYNAPSE VR software [Figure 1] is a fully immersive 3D virtual environment deployed through a head-mounted display. Navigated through a home-page interface[Figure 2], the application provides continuous audio-visual feedback to guide the patient interactions which is an approach that has proven as an effective training signal for motor skill development and cognitive-motor coupling.[4] The software comprises of 12 functional games activities specifically designed to improve diverse components of hand motor functions such as mass grasp (spherical, cylindrical and hook) and precision grips (finger to tip and finger to pad)[Figure 3]. These are the 12 activities: Pick up and drop the coins [Figure 3 A]: Designed to improve hand-eye coordination. It requires the patient to pick up and sort visual objects, Pour water in the glasses [Figure 3B]: Designed to challenge the patient's wrist tilt control and flow precision, Water the plants [Figure 3C]:Designed to promote environmental awareness and precise spatial manipulation, Sketch a circle [Figure 3D]:Designed to validate geometric accuracy and shape precision, Blast the balloons [Figure 3E]: Focuses on reflex training, decision-making and reaction time, Play the drums

[Figure 3F]: Trains the muscles through rhythmic synchronization through motor coordination, Bowling ball [Figure 3G]:Simulates arm motion and appropriate force application, Cut the fruits [Figure 3H]:Utilizes gesture-based swipes to improve rapid decision-making, Play the keyboard [Figure 3I]:Multi-finger interaction and auditory-motor coupling, Pegboard [Figure 3J]:Models special cognition and fine motor coordination through object placement, Hand gesture [Figure 3K]:detects predefined hand poses like open palm or fist to encourage specific finger extensions, Building blocks [Figure 3L]: Develops special reasoning and stability through structural alignment.

Figure 1: The official logo of the SYNAPSE VR application

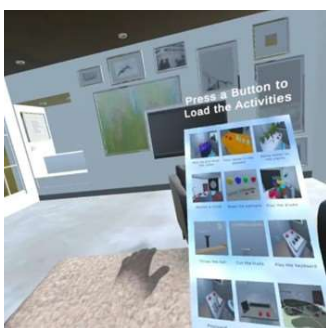

Figure 2: Graphical user interface of the SYNAPSE VR home page

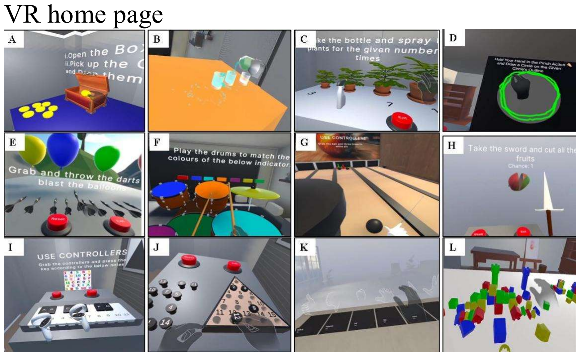

Figure 3: Visual representations of the 12 gamified functional activities (A–L) integrated within the SYNAPSE VR application.

Intervention protocol: Group A (Experimental): All participants in the experimental group received a virtual reality gaming intervention along with their regular upper limb physiotherapy sessions. Patients were seated comfortably and performed the 12 game-based activities on the SYNAPSE VR software (Copyright Registration No. 41506/2024-CO/L; Patent Application No. 202541023070). Group B (control) Participants of this group received conventional hand rehabilitation such as active assisted movements, pegboard exercises and table paper-pencil activities along with the regular upper limb physiotherapy sessions.

Both groups underwent their interventions for 30 minutes per day, 4 sessions per week for a total of 6 weeks. Task completion rates and session attendance were taken to record the participants' adherence. Participants were constantly monitored throughout the sessions for adverse events such as dizziness, fatigue or cybersickness.

Outcome Measures: Clinical evaluations to track upper limb motor recovery were conducted at different phases of the study: Baseline test (pre-test), immediately post-intervention (7^{th} week) and a follow-up assessment (12^{th} week).

Primary outcome: The Fugl-Meyer Assessment for Upper Extremity (FMA-UE) hand component was used to measure isolated motor function recovery.

Secondary outcome: The Box and Block test was used to measure the gross dexterity and functional skill transfer, a largely accepted test for the upper limb in physical as well as virtual rehabilitation environments.[4,8]

Statistical analysis: Statistical analysis was done using SPSS version 22.2 (IBM Corp.). Descriptive statistics were used to summarize the demographic and clinical data. Mean and standard deviation of the continuous variables such as FMA-UE and BBT were calculated. Baseline compatibility was tested using the chi-square test. The differences between the groups were analysed at baseline, 7^{th} week and 12^{th} week. The changes within the group across the 3 phases was assessed using repeated measures ANOVA followed by post hoc pairwise comparison. Statistical significance was set at $p<0.05$.

Results

Baseline Characteristics and Demographics: All 10 acute-to-sub-acute stroke patients who participated in the pilot study completed the 6-week intervention and the 12-week follow-up. There were 6 male (60%) and 4 female (40%) patients with a mean age of 55±5.87 years. 5 patients were ischemic, whereas 5 patients were haemorrhagic. The baseline characteristics of both Group A (Experimental) and Group B (Control) were comparable, and there were no statistically significant differences between the gender (p=1.000), stroke type (p=0.236) and affected side (p=0.527). There was no significant difference in the presence of comorbidities between the two groups, hypertension (p = 0.197) and diabetes (p = 0.114). The baseline FMA-UE scores (p = 1.000) and BBT scores (p = 0.446) were also comparable with no statistically significant difference **[Table 1]**.

Software Performance, Safety and Adherence: Across all 12 game modules of the software, a stable frame rate of 60 frames per second was maintained without performance lag. The system functioned reliably throughout the intervention, with no technical interruptions during the therapy sessions. The intervention was well-tolerated by the patients, with 100% adherence in the experimental group. There were no observed or reported adverse effects such as cybersickness, dizziness, nausea, or fatigue during or after the session.

Primary outcome: FMA-UE Hand Component: FMA-UE scores improved in both the experimental and control groups at the 7th and 12th week compared to baseline **[Table 2]**.

In Group A, the mean scores increased from 8.00 ± 1.58 at baseline to 8.80 ± 1.10 at 7 weeks, and to 9.40 ± 1.52 at 12 weeks (p = 0.018), and the post hoc analysis showed a significant improvement across the three time points. (p ≤ 0.022). In Group B, the mean scores increased from 8.00 ± 2.00 at baseline to 9.20 ± 1.92 at 7 weeks, and to 10.00 ± 2.00 at 12 weeks (p = 0.018), with significant pairwise differences (p ≤ 0.022). There was no statistically significant difference between the two groups observed at either 7 weeks (p = 0.697) or 12 weeks (p = 0.608).

Secondary outcome: Box and Block test (BBT): The Box and Block test (BBT) shows improvement in both experimental and control groups at the 7th and 12th week compared to baseline **[Table 2].** In Group A, the mean scores increased from 29.00 ± 6.52 blocks at baseline to 43.20 ± 4.21 at 7 weeks, and to 51.00 ± 5.57 at 12 weeks (p = 0.007), with significant pairwise differences (p < 0.001).In Group B, the mean scores increased from 33.20 ± 9.73 blocks at baseline to 39.00 ± 11.81 at 7 weeks, and to 44.40 ± 11.10 at 12 weeks (p = 0.007), with significant pairwise differences (p < 0.001). There was a higher overall mean improvement observed in Group A (22.00 blocks) compared to Group B (11.20 blocks). However, there was no statistically significant difference at 7 weeks (p = 0.475) or 12 weeks (p = 0.269) **[Table 2]**.

Table 1: Baseline Demographics and Clinical Characteristics

Characteristics	**Group A (SYNAPSE VR) (n=5)**	**Group B (Control) (n=5)**	**p-value**
Age (years), Mean ± SD	55.00 ± 5.92	55.00 ± 6.52	1.000
Gender, n (%)			1.000
Male	3 (60%)	3 (60%)	
Female	2 (40%)	2 (40%)	
Stroke Type, n (%)			0.333
Ischemic	2 (40%)	3 (60%)	
Hemorrhagic	3 (60%)	2 (40%)	
Affected Side, n (%)			0.527
Right	2 (40%)	3 (60%)	
Left	3 (60%)	2 (40%)	
Comorbidities, n (%)			
Hypertension (Yes)	4 (80%)	2 (40%)	0.197
Diabetes (Yes)	3 (60%)	5 (100%)	0.114
Baseline Clinical Scores			
FMA-UE	8.00 ± 1.58	8.00 ± 2.00	1.000
Box and Block Test (BBT)	29.00 ± 6.52	33.20 ± 9.73	0.446

Data is expressed as Mean ± Standard Deviation or frequency (percentage). Baseline comparability was assessed using the Chi-square test for categorical variables and independent comparisons for continuous variables.

Table 2: Between-Group and Within-Group Comparisons of Clinical Outcomes

Outcome Measure	**Timepoint**	**Group A (SYNAPSE VR) (Mean ± SD)**	**Group B (Control) (Mean ± SD)**	**Between-Group p-value**
FMA-UE	Baseline	8.00 ± 1.58	8.00 ± 2.00	1.000
	7th Week	8.80 ± 1.10	9.20 ± 1.92	0.697
	12th Week	9.40 ± 1.52	10.00 ± 2.00	0.608
	Within-Group p-value (Time)	p = 0.018	p = 0.018	
Box and Block	Baseline	29.00 ± 6.52	33.20 ± 9.73	0.446

Test (BBT)				
	7th Week	43.20 ± 4.21	39.00 ± 11.81	0.475
	12th Week	51.00 ± 5.57	44.40 ± 11.10	0.269
	Within-Group p-value (Time)	p = 0.007	p = 0.007	

FMA-UE = Fugl-Meyer Assessment for Upper Extremity. Between-group differences were evaluated at each time point. Within-group changes over time were evaluated using Repeated Measures ANOVA. Statistical significance was set at $p < 0.05$.

Discussion

The results of the current pilot study demonstrated that the SYNAPSE VR software for upper limb rehabilitation in acute and sub-acute stroke patients was highly feasible, well tolerated by the patients and had a 100% adherence. Although both the experimental and control groups exhibited a significant improvement in isolated motor function (FMA-UE) and gross manual dexterity (BBT) over the 12-week study period, there was no statistically significant difference between the groups. In contrast to the present study, the research conducted by Amin et al combined immersive VRF gaming with real-time electromyography (EMG) to evaluate neuromuscular consistency and observed a statistically significant difference between the two groups in both the FMA-UE and BBT tests.[9] The absence of a significant difference in the present pilot study can be attributed to the small sample size, which limits its statistical power.

A study by Mekbib et al highlights the importance of strictly dose-matching the VR intervention against conventional therapy to ensure that the motor gains are intrinsic to the VR environment and not due to the increased session time.[10] In the present study, there was a notably greater mean improvement in blocks in Group A compared to Group B on the BBT. Considering that both the VR intervention and conventional therapy sessions were dose-matched and both groups received 30-minute sessions, the higher mean difference validates the effectiveness of the VR intervention.

Studies conducted by Amin et al and Meyer et al establish the Minimal Clinically Important Difference (MCID) for BBT in stroke patients to be 6 blocks.[9,11] In the present study Group A exceeds this threshold, demonstrating positive motor gains. The accelerated functional improvements recorded at the 7th week in the current study is comparable to the results obtained in the research conducted by da Silva Cameirão et al., which proves that integration of an action observation paradigm in VR therapy can accelerate the recovery in acute and sub-acute phases of stroke.[12]

A study by Herrera et al. noted that the requirement for patients to grasp physical controllers is a potential barrier for individuals with motor impairments, such as in the case of acute and subacute stroke patients[5]. The SYNAPSE VR software targets diverse hand functions (mass grasps and precision grips) using a controller-free approach, accommodating patients with limited grip strength, allowing for a more comfortable training environment.

Table 3: Comparison of SYNAPSE VR with Previous Virtual Reality Rehabilitation Systems

System / Study	Features & Interaction	Advantages	Disadvantages
SYNAPSE VR Current Study	Immersive head-mounted display; controller-free hand tracking; 12 task-specific gamified activities.	No controllers required; feasible for motor impairment and spasticity; audio-visual feedback.	Small cohort pilot study lacks integrated physical haptic feedback.
Rehab-Immersive Herrera et al.[5]	Immersive VR; controller-free tracking; virtual BBT.	Eliminates the need for physical controllers; customizable patient parameters.	Lacks tactile feedback; primarily tested in spinal cord injury
VR Rehab Games Amin et al[9]	Immersive VR: visual feedback with EMG tracking.	Integrates objective neurophysiological assessment (EMG).	Limited number of exercises; Complex clinical setup
Elements VR Rogers et al.[4]	Semi-immersive 42-inch tabletop surface display; tangible physical interfaces.	Natural interaction via tangible objects; improves both motor and cognitive deficits.	Non-immersive display limits 3D depth perception

Rehabilitation Gaming System (RGS) da Silva Cameirão et al[12]	Vision-based tracking; action observation; game-based grasping and placing.	Accelerates functional recovery; automatically adjusts task difficulty.	Requires physical interaction with objects Lacks haptic feedback on the effectiveness of movement.

Technical Feasibility and Study Limitations

During the software development, technical glitches such as synchronizing movement sensors, capturing precise hand functions and isolating specific motor controls were resolved successfully.

Operational challenges including patient positioning, device charging, and real-time performance monitoring using secondary screens where effectively managed. Initial patient reluctance, eye strain, postural discomfort and stress were addressed using demonstration videos, preliminary trial sessions and adequate rest intervals. All the technical and functional challenges were manageable, supporting SYNAPSE VR'S feasibility.

The present study has a few methodological limitations. The small sample size limits generalizability and statistical power required to detect significant differences between the two groups. The short 6-week intervention and the 12-week follow up restrict the long-term motor retention assessment. In spite of these limitations, the findings of the pilot study strongly support SYNAPSE VR as an accessible and efficient adjunctive therapy for post-stroke motor recovery.

Conclusion

The present pilot study demonstrates that the novel SYNAPSE VR software is a highly feasible, well-tolerated therapy for upper limb motor rehabilitation in acute and sub-acute stroke patients. Although the small sample size limited the statistical power to identify statistical significance between the VR and conventional therapy groups, there was substantial within-group improvement in the group that received the VR intervention that exceeded the MCID threshold. By providing a customizable, engaging and task-specific training environment, SYNAPSE VR overcomes the limitations of conventional therapy. Future large-scale randomized controlled trials with long term interventions and follow-up periods, are necessary to validate the long-term clinical benefits of SYNAPSE VR.

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