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Virtual Reality-Based Intervention in Neurorehabilitation

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Definition

Virtual Reality is an interactive technology that creates immersive, computer-generated three-dimensional environments for therapeutic and rehabilitative purposes. In neurorehabilitation, it has been increasingly adopted to support motor, cognitive, emotional, and functional recovery via task-oriented, multisensory, and feedback-driven interventions. Originally developed for exposure-based therapies, its applications have expanded to neurological conditions such as stroke, traumatic brain injury, Parkinson's disease, multiple sclerosis, spinal cord injury, and chronic pain. Its therapeutic rationale is thought to rely on mechanisms including neuroplasticity, multisensory integration, motor learning, embodiment, and adaptive feedback. Despite the fact that standardized clinical protocols are still evolving, VR is considered a complement to conventional neurorehabilitation, with advances in artificial intelligence and wearable technologies expected to further enhance its clinical applications.

Keywords: virtual reality; neurological rehabilitation; stroke; Parkinson's disease; traumatic brain injury; chronic pain

1. Introduction

The history of the application of virtual reality (VR) in healthcare reflects the convergence of behavioural psychology, rehabilitation sciences, computer science and immersive simulation. Its conceptual origins can be traced to exposure-based behavioural interventions developed during the mid-twentieth century, particularly by Joseph Wolpe, who introduced systematic desensitization as a therapeutic approach based on the gradual and controlled exposure of individuals to feared stimuli in order to reduce maladaptive emotional and behavioural responses [1]. These principles later provided a theoretical foundation for virtual exposure paradigms, enabling real-world situations to be recreated within controlled, customisable and reproducible digital environments.

Subsequently, significant advances in computer graphics, simulation systems and human–computer interaction throughout the second half of the twentieth century paved the way for the development of immersive virtual environments. Among the earliest technological milestones were Morton Heilig's "Sensorama", stereoscopic visualization systems, and pioneering head-mounted displays (HMDs), particularly Ivan Sutherland's "Sword

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of Damocles", which established the technological foundations for creating computer-generated environments of interactive and multisensory experiences [2,3].

During the 1980s, the conceptual maturation of VR—widely associated with the pioneering work of Jaron Lanier—together with the growing interest in the concepts of immersion, presence, and user interaction, further broadened the potential applications of virtual technologies across a wide range of fields, particularly within healthcare [4]. Building upon these technological advances, the first clinical applications of VR emerged during the 1990s, primarily within psychiatry and clinical psychology.

In particular, studies by researchers such as Barbara Rothbaum and Larry Hodges showed the feasibility of using immersive environments to deliver exposure-based interventions for anxiety-related disorders and specific phobias in safe and reproducible settings [5]. These pioneering investigations ultimately led to the development of Virtual Reality Exposure Therapy (VRET), which remains one of the earliest and most extensively studied therapeutic applications of VR.

As VR technologies continued to evolve, substantial advances in motion tracking, stereoscopic rendering, haptic interfaces, wearable devices, and interactive gaming systems facilitated their progressive incorporation into neurological rehabilitation. As a result, VR increasingly emerged as a complementary therapeutic approach to support motor, cognitive, and psychological rehabilitation through repetitive, task-oriented, multisensory, and feedback-driven interventions. Since then, VR-based interventions have been evaluated across a wide spectrum of neurological conditions, including traumatic brain injury (TBI), stroke, Parkinson's disease (PD), Multiple Sclerosis (MS), spinal cord injury (SCI), and pain-related disorders [6,7].

Despite sharing common technological foundations, it is important to distinguish between VRET and VR-based neurorehabilitation. Although VRET is grounded in exposure-based mechanisms—including habituation, inhibitory learning, extinction processes, emotional processing and the reduction in fear-avoidance behaviours—VR encompasses a broader range of interventions designed to enhance motor acquisition, functional and cognitive recovery and sustained patient participation through interactive and task-oriented activities [8–10].

Although both approaches rely on similar technological platforms, they differ fundamentally in their theoretical foundations, therapeutic aims, mechanisms of action, and expected clinical outcomes. To contextualize these developments historically and illustrate the progressive evolution of VR applications in healthcare, the main milestones in the development of VR in neurorehabilitation—from its conceptual origins to its current clinical implementation—are summarized in Table 1.

Table 1. Historical milestones in the development of VR. Abbreviations: AI, artificial intelligence; CAVE, cave automatic virtual environment; HMD, head-mounted display; PTSD, post-traumatic stress disorder; TBI, traumatic brain injury; VR, virtual reality; VRET, virtual reality-based exposure therapy; XR, extended reality.

Period	Milestone	Principal Contributors	Main Contributions
1950s–1970s	• Development of systematic desensitization and behavioural exposure therapies	• Joseph Wolpe	• Gradual exposure to feared stimuli • Behavioural conditioning principles • Controlled reduction in maladaptive responses
1960s	• Development of the "Sensorama"	• Morton Heilig	• Multisensory immersive simulation • Integration of visual, auditory, vibratory, and olfactory stimuli • Early environmental realism

Table 1. *Cont.*

Period	Milestone	Principal Contributors	Main Contributions
1968	• Creation of the first HMD, the "Sword of Damocles"	• Ivan Sutherland	• First stereoscopic HMD • Head-tracked visualization • Spatial interaction with virtual objects
1980s	• Popularization of the term "Virtual Reality"	• Jaron Lanier	• Immersive digital environments • Human–computer interaction • Interactive simulation systems
1980s–1990s	• Development of presence and immersion theories	• Mel Slater • Paul Milgram	• Theory of presence ("being there") • Reality–Virtuality continuum • Embodiment and immersion frameworks
1990s	• First clinical implementation of VR exposure therapy for phobias	• Barbara Rothbaum; Larry Hodges	• Controlled virtual exposure • Reproducible therapeutic scenarios • Safe simulation of feared environments
Late 1990s–2000s	• Expansion toward PTSD, anxiety, and emotional disorders	• Albert Rizzo	• Military simulations • Trauma-related virtual scenarios • Emotionally adaptive environments
2006–2012	• Introduction of commercial gaming systems	• Nintendo (Nintendo Co., Ltd., Japan) • Microsoft (Microsoft Corporation, United States)	• Motion-based interaction • Affordable rehabilitation interfaces • Home-based therapeutic engagement
2010s	• Emergence of immersive HMD systems	• Meta (Meta Platforms, Inc., United States) • HTC Vive (HTC Corporation, Taiwan; Valve Corporation, United States)	• High-fidelity immersion • Motion tracking • Stereoscopic visualization • Enhanced presence and embodiment
2020s–Present	• Integration of AI, wearable sensors, and adaptive systems	• Interdisciplinary neuroscience and engineering groups	• Artificial intelligence • Wearable sensors • Adaptive feedback systems • Telerehabilitation • Digital biomarkers

2. Definition of Virtual Reality

VR refers to computer-generated environments that enable users to interact with simulated objects and activities through visual, auditory, and, in some systems, haptic feedback [11–13]. Within this context, three characteristics are particularly relevant: immersion, or the degree to which the system limits awareness of the physical scenarios; interaction, or the capacity to respond to virtual stimuli in real time; and presence, or the subjective experience of being located within the virtual environment [14,15].

In neurological settings, VR enables repetitive, task-oriented, and progressively adapted practice in controlled environments. These characteristics may facilitate motor learning, cognitive training, multisensory integration, and patient engagement while allowing clinicians to adjust task demands according to the patient's functional capacity and therapeutic goals [16].

3. Main Components of Virtual Reality

VR systems combine immersive displays, motion-tracking sensors, and interactive interfaces to recreate a responsive environment [11,17,18]. HMDs are most common, although projection-based systems and Cave Automatic Virtual Environments (CAVE) installations may be used depending on infrastructure and therapeutic goals [19,20]. Likewise, motion sensors track head, limb, and trunk movements, enabling real-time interaction and performance assessment while controllers, wearables, gloves, and force-sensitive platforms support task-specific interaction [21–25]. In neurological rehabilitation, haptic and force

feedback provide tactile and proprioceptive input that may enhance integration, motor relearning, and patient engagement [26,27].

Beyond the main hardware components, software generates and updates virtual environments in real time, synchronizing movements with therapeutic tasks while maintaining responsiveness and immersion [28,29]. In addition, AI algorithms can adapt task difficulty, exercise parameters, and feedback according to individual performance, thereby supporting personalized rehabilitation as patients' abilities evolve over time [30–32]. Figure 1 summarizes the main hardware and software components of clinical VR systems.

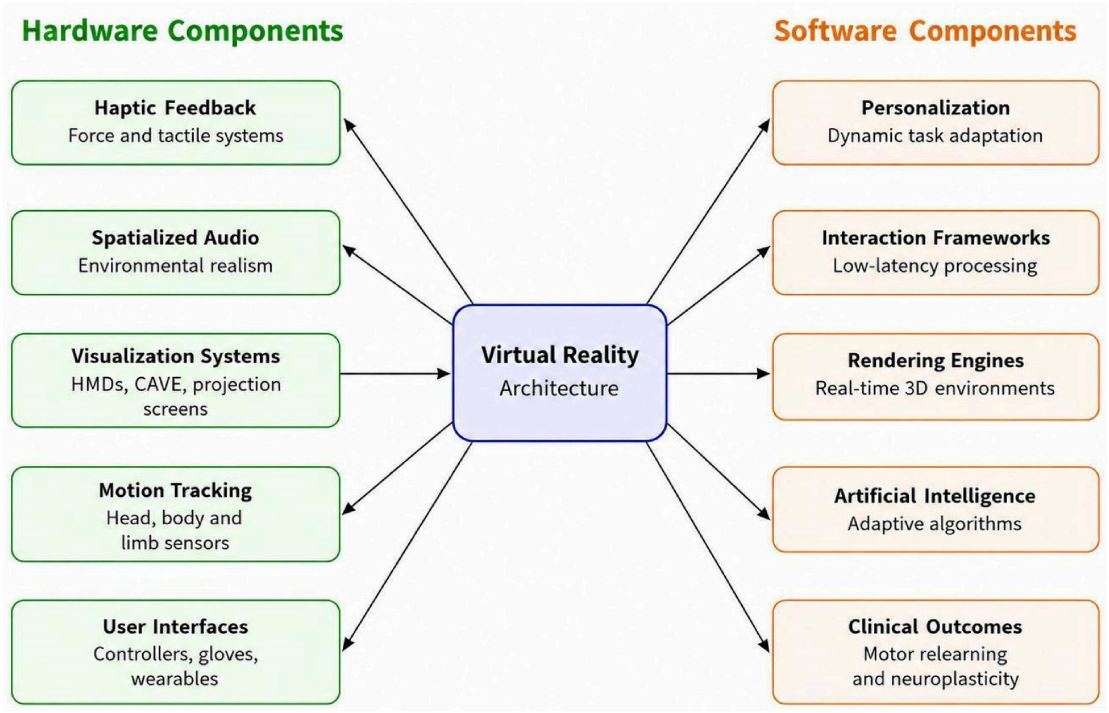


Figure 1. Main components of Virtual Reality systems. Overview of the hardware (green) and software (orange) architecture underlying VR systems, illustrating the synergistic integration of sensory displays, motion tracking, real-time computational processing, and adaptive AI-based mechanisms to deliver meaningful experiences. Source: Own work.

4. Classification of Virtual Reality

4.1. According to Extended Reality Continuum

Extended reality (XR) is an umbrella term that comprises VR, augmented reality (AR), and mixed reality (MR). Within Milgram's Reality–Virtuality Continuum [33], these technologies are distinguished by the degree to which real-world and digitally generated content coexist and interact [34–37]. Within this Continuum, VR usually provides the highest level of immersion by replacing most or all sensory stimuli from the physical environment with computer-generated stimuli, typically delivered through an HMD [38,39].

By contrast, MR combines virtual and real objects that interact in real time, whereas AR overlays digital information onto the physical environment while preserving direct interaction with the real world [40–43]. In neurorehabilitation, these XR modalities offer different levels of immersion, ecological validity, interaction, and experimental control. Consequently, their suitability depends on the patient's characteristics, goals, and clinical setting. The Reality–Virtuality Continuum and the relationship among these modalities are illustrated in Figure 2.

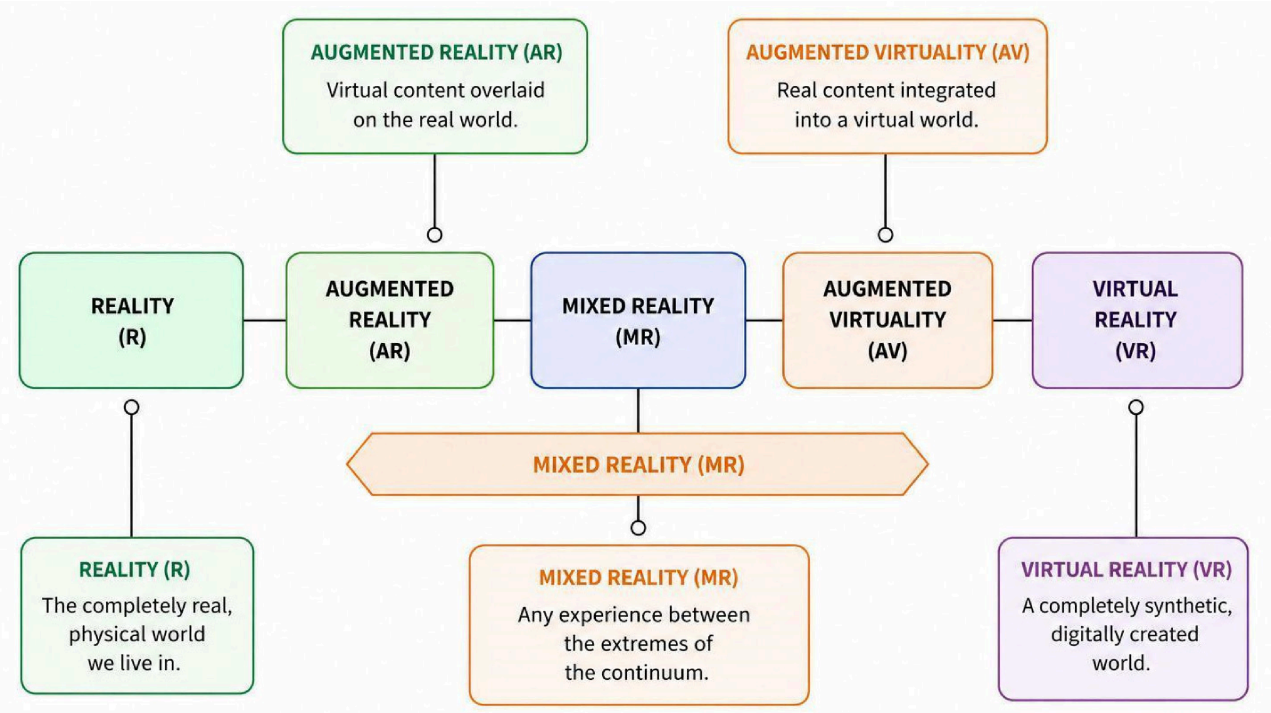


Figure 2. Reality–virtuality Continuum. Conceptual spectrum ranging from the real environment to fully immersive virtual reality, encompassing intermediate technologies such as augmented reality, mixed reality, and augmented virtuality, according to the degree of integration between physical and computer-generated elements. Source: Own work.

4.2. According to Level of Immersion

VR systems used in neurorehabilitation are commonly classified according to their level of immersion. Non-immersive systems deliver virtual environments through monitors, tablets, or commercial gaming devices, allowing patients to remain aware of their physical surroundings [44–48]. Their accessibility, low cost, and reduced risk of cybersickness make them appropriate for home-based treatment and patients with limited tolerance to immersion [49–53].

Semi-immersive systems use large screens or projection-based environments to provide an intermediate sense of presence while preserving therapist supervision and partial awareness of the physical environment. Accordingly, they may be suitable for gait, balance, postural-control, and cognitive training, particularly in those with balance impairments, vestibular dysfunction, or limited tolerance to fully immersive systems [54–56].

Fully immersion integrates HMDs and motion-tracking systems, thereby enhancing the sense of presence and allowing greater control over the therapeutic environment. These systems enable realistic, task-oriented interventions targeting motor and cognitive functions. Nevertheless, their use requires careful patient selection and close clinical supervision because of the potential for cybersickness, sensory overload, disorientation, and postural instability [57–63].

Therefore, the level of immersion should be selected according to the therapeutic aim, clinical setting, cognitive capacity, balance, visual and vestibular function, fatigue, and individual safety profile, as summarized in Figure 3.

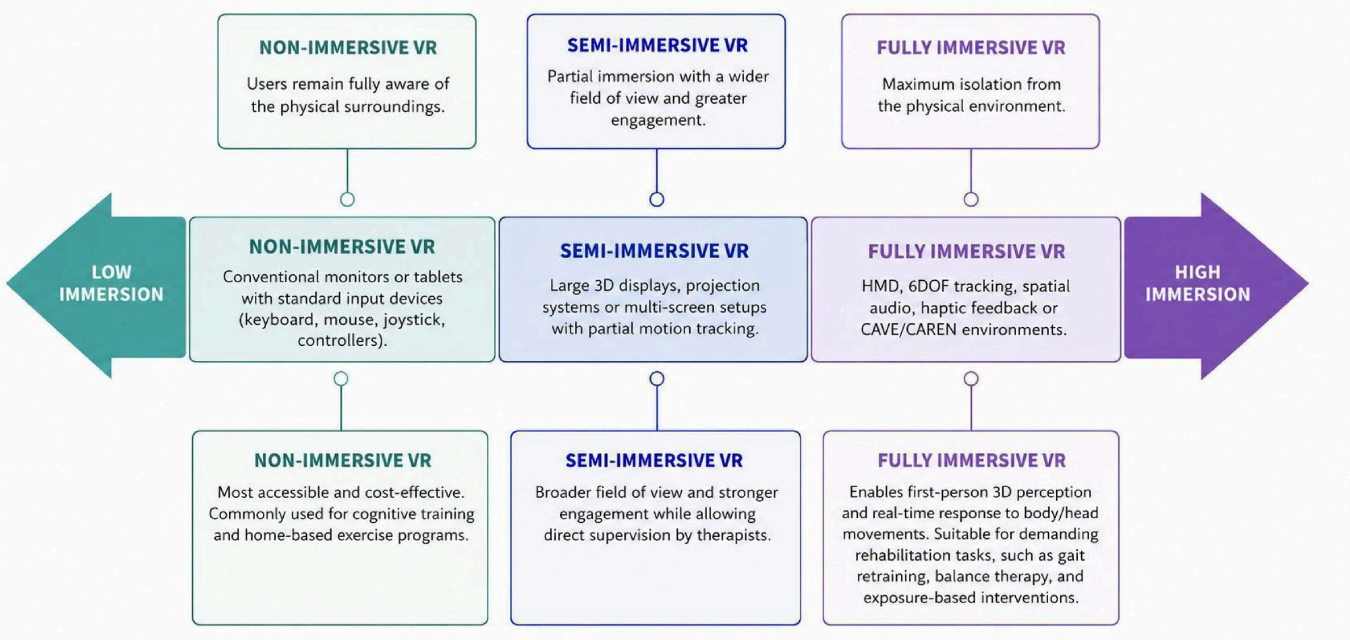


Figure 3. Classification of virtual reality systems according to the level of immersion. The spectrum ranges from non-immersive VR (lowest immersion), through semi-immersive VR, to fully immersive VR (highest immersion), reflecting the degree to which users are isolated from the environment and engaged in computer-generated virtual experiences. Source: Own work.

5. Clinical Applications of Virtual Reality

5.1. Mechanism of Therapeutic Actions

The therapeutic value of VR in neurorehabilitation stems from the interaction of immersion, motor-learning principles, and neurophysiological mechanisms that support recovery across neurological conditions [64,65]. By providing enriched, task-oriented, and multisensory environments, VR enhances patient engagement and facilitates both motor and cognitive training. It can also recreate meaningful real-life situations that stimulate movement, perception, cognition, motivation, and emotional regulation, thereby promoting the transfer of acquired skills to activities of daily living (ADLs) [66].

Neuroplasticity constitutes one of the principal theoretical frameworks supporting the use of VR in neurorehabilitation [67]. Rather than representing a single mechanism, neuroplasticity encompasses a range of adaptive processes through which the nervous system modifies its structural and functional organization in response to experience or injury [68]. Neurophysiological evidence suggests that VR-based interventions may be linked to changes in corticospinal excitability, cortical reorganization, sensorimotor integration, and functional connectivity across distributed neural networks involved in motor control, sensory processing, cognition, and behaviour. These adaptations may contribute to motor relearning and functional recovery [69–71].

Repetitive and task-specific practice may promote experience-dependent neural reorganization through synaptic plasticity, long-term potentiation, cortical remapping, dendritic remodelling, and reinforcement of sensorimotor pathways [72,73]. These adaptive processes are consistent with the principles of Hebbian learning, according to which the repeated and synchronized activation of neuronal populations strengthens synaptic efficacy and functional network connectivity. In the context of neurological injury, these changes may support the acquisition, refinement, and retention of motor skills [74–76].

Neuroimaging and neurophysiological studies show that VR-based interventions engage cortical and subcortical regions involved in motor control, sensory processing, attention, and cognition, including the primary motor cortex (M1), premotor cortex (PMC),

supplementary motor area (SMA), cerebellum, basal ganglia, posterior parietal cortex (PPC), and frontoparietal networks [77–80]. Transcranial magnetic stimulation (TMS), electroencephalography (EEG), functional magnetic resonance imaging (fMRI), functional near-infrared spectroscopy (fNIRS), and diffusion tensor imaging (DTI) [81–86] further help characterize VR-induced neural responses and clarify mechanisms of neuroplasticity, motor recovery, and functional restoration.

Multisensory integration represents another key central mechanism underlying VR-based neurorehabilitation. In this sense, virtual environments can synchronously combine visual, auditory, sensitive, proprioceptive, and haptic information, potentially strengthening sensorimotor coupling and optimizing the processing of afferent inputs involved in movement control, stability, balance, spatial orientation, and environmental interaction [11,87]. Repeated exposure to coherent multisensory feedback may also enhance body awareness, movement precision [88], anticipatory postural adjustments [89], and spatial cognition [90]. These effects may support the transfer of acquired motor skills from virtual environments to real-world functional activities.

Closely related to multisensory integration is the concept of embodiment [91], defined as the subjective experience of perceiving a virtual body, avatar, or virtual limb as part of one's own body representation [92,93]. Through visuomotor congruence, synchronized multisensory feedback, and the sense of agency over virtual movements, embodiment has been proposed to promote sensorimotor recalibration, reinforce body ownership, reduce distorted body representations and facilitate functional recovery [94]. Particularly, these mechanisms may be relevant in neurological conditions characterized by hemispatial neglect, chronic pain, phantom limb pain, stroke, traumatic brain injury and other neurological disorders associated with sensorimotor impairment.

Attentional modulation may further contribute to the therapeutic effects of VR, particularly in pain conditions accompanied by emotional distress [76,95]. Immersive environments can redirect mental resources away from nociceptive signals, fear-related stimuli, maladaptive thoughts, and negative emotional states. This competition for attention may reduce perceived pain and psychological distress while promoting active participation [96]. From a neurocognitive perspective, these effects may reflect the allocation of limited attentional resources and the engagement of top-down executive mechanisms that influence perception, emotional salience, and cognitive appraisal [97,98].

In parallel, the sense of presence, agency, immersion, and environmental control may be associated with the promotion of emotional engagement, self-efficacy, and anxiety reduction during rehabilitation [99]. Interactive virtual experiences may also engage motivational and reward-related neural circuits, including dopaminergic pathways [100]. Consequently, VR may enhance enjoyment, perceived competence, treatment adherence, and sustained participation in rehabilitation programmes [101].

Finally, real-time feedback and adaptive task progression are relevant determinants of its effectiveness. Continuous monitoring of patient performance enables the dynamic adjustment of complexity, motor demands, sensory stimulation, cognitive load, and difficulty according to the patient's progress and goals [102]. This progression may help maintain an appropriate level of challenge, optimize motor behaviour, and support motivation and autonomy while reducing frustration, disengagement, fatigue, and excessive cognitive burden [103]. The main therapeutic mechanisms and their potential clinical implications are summarized in Table 2.

Table 2. Proposed therapeutic mechanisms of VR, their primary functions, and clinical outcomes reported in the literature. The outcomes summarized represent associations observed across the included studies and should not be interpreted as evidence of direct causal relationships between specific VR mechanisms and potential outcomes. Note: ↑ indicates an increase, enhancement, or improvement in the corresponding variable or clinical outcome; ↓ indicates a decrease, reduction, or attenuation.

Condition	Main Function	Potentially Associated Outcomes
Neuroplasticity stimulation	• Repetitive, task-oriented practice	• ↑ Motor relearning • ↑ Functional recovery
Multisensory integration	• Visual, auditory, and haptic stimulation	• ↑ Improved balance • ↑ Coordination and cognitive performance
Task-specific training	• Goal-directed functional activities	• ↑ Transfer to daily-life skills
Attentional redirection	• Focus shifted away from pain or stress	• ↓ Pain reduction • ↑ Improved treatment engagement
Emotional engagement and presence	• Perceived control, immersion, and interaction	• ↓ Anxiety • ↑ Emotional regulation
Real-time feedback	• Immediate performance information and correction	• ↑ Enhanced sensorimotor learning • ↑ Motivation and participation
Adaptive therapeutic challenge	• Personalized adjustment of task difficulty	• ↑ Adherence • ↑ Self-efficacy • ↓ Frustration

5.2. Clinical Effects

The clinical effectiveness of VR-based neurorehabilitation depends not only on the quality of the virtual environment but also on the appropriate prescription of the intervention. Although considerable heterogeneity remains across protocols, several common principles have emerged regarding treatment dose, intensity, progression, and recovery periods.

5.2.1. Treatment Prescription and Intervention Characteristics

- Treatment Dose and Frequency

VR interventions typically last between 4 and 12 weeks, with 2 to 5 sessions per week and individual sessions lasting approximately 20–60 min [104,105]. However, the optimal treatment dose has not yet been established and may vary according to the neurological condition, disease stage, rehabilitation objective, and patient tolerance.

In most clinical settings, VR is used as an adjunct to conventional rehabilitation rather than as a standalone treatment [106,107]. This combined approach may increase the number of task-specific repetitions while supporting motivation, engagement, and treatment adherence. Nevertheless, clinicians should consider the total rehabilitation workload to avoid excessive physical or cognitive demands when VR is added to an existing treatment programme.

- Training Intensity and Task Progression

Training intensity should be individualized according to the patient's motor, cognitive, sensory, and cardiorespiratory capacities. Unlike conventional aerobic or resistance exercise,

the intensity of many VR-based interventions is primarily regulated through task demands and performance rather than predefined physiological thresholds [64,108]. Accordingly, progression should be guided by improvements in movement quality, accuracy, range of motion, balance, gait, reaction time, task completion, or cognitive performance [27,109].

Task difficulty can be progressively increased by modifying movement speed, range of motion, environmental complexity, cognitive load, dual-task requirements, external assistance, and the type or frequency of sensory feedback [110]. These adjustments allow the intervention to remain aligned with the patient's evolving functional abilities while maintaining an appropriate level of challenge. Performance-based progression may therefore facilitate motor learning and neuroplasticity without exposing the patient to excessive physical or cognitive demands.

- Rest Periods, Fatigue, and Clinical Monitoring

Treatment progression should remain flexible and responsive to the patient's clinical status. Session duration, task complexity, and rest periods should be adjusted according to severity, perceived exertion, fatigue, pain, cognitive load, cybersickness symptoms, and clinical judgement.

Because rest intervals are rarely standardized, work-to-rest ratios vary considerably across protocols. Consequently, rest periods should be prescribed individually and modified throughout the session when signs of physical fatigue, cognitive overload, postural instability, visual discomfort, or reduced performance are observed. The prescribed treatment dose should therefore be regarded as an individualized and dynamic component of VR-based rehabilitation rather than a fixed parameter.

5.2.2. Condition-Specific Clinical Evidence

- Traumatic Brain Injury (TBI)

TBI may cause motor, cognitive, visuospatial, and behavioural impairments that restrict daily functioning and community participation. Consequently, VR has been incorporated into multidisciplinary rehabilitation programmes targeting gait, balance, upper-limb function, cognition, dual-task performance, and ADLs [111,112]. Current evidence is derived mainly from small randomized controlled trials, pilot studies, and cohort studies involving patients in the subacute and chronic phases. Most interventions combine immersive or semi-immersive VR with conventional rehabilitation [113].

Reported benefits include improvements in balance, mobility, executive function, and dual-task performance, although findings regarding attention and working memory remain inconclusive [114]. VR supports cognitive–motor training through structured tasks involving planning, attentional control, cognitive flexibility, and simultaneous cognitive and physical activity. Adverse events are uncommon and usually consist of transient cybersickness, visual discomfort, or fatigue [115,116].

- Stroke

Stroke has the largest body of evidence supporting the clinical use of VR among neurological conditions. Studies have primarily examined individuals in the subacute and chronic phases, using immersive, semi-immersive, or non-immersive systems alongside conventional rehabilitation [106,108,117,118]. The strongest findings relate to upper-limb recovery, with RCTs and systematic reviews showing benefits in arm function, dexterity, balance, mobility, and quality of life [119,120].

Findings for gait recovery are less consistent and appear to vary according to stroke severity, treatment intensity, and patient selection. Potential benefits have also been observed in visuospatial and executive functioning, motivation, and visual disorders such as homonymous hemianopia [121,122]. Home-based programmes have also shown good

feasibility and adherence. By facilitating intensive, repetitive, and task-specific practice, VR may promote motor relearning.

- Parkinson's Disease (PD)

PD is a progressive neurodegenerative disorder characterized by a broad spectrum of motor and non-motor impairments that can significantly affect gait, postural stability, cognition, mobility, and overall functional independence, ultimately reducing patients' quality of life. Evidence from RCTs and systematic reviews involves individuals with mild-to-moderate severity, with VR complementing rehabilitation programmes to target balance, gait, mobility, and quality of life [123–128].

Reported benefits include improvements in gait performance, dynamic balance, mobility, and freezing of gait. Positive effects on executive function, global cognition, and motivation have also been observed, particularly in patients with mild cognitive impairment (PD-MCI) [123–126]. Outcomes are commonly assessed using the Timed Up and Go test, Berg Balance Scale, 10-Metre Walk Test, Unified Parkinson's Disease Rating Scale, and cognitive screening instruments [123,124].

The therapeutic rationale for VR in PD centres on external visual and auditory cues that may compensate for impaired movement initiation and sequencing caused by basal ganglia dysfunction. Such cues may facilitate gait initiation and automaticity, reduce freezing episodes, and enhance performance during complex motor tasks [124,127].

- Multiple Sclerosis (MS)

MS is a chronic immune-mediated neurological disease characterized by motor, sensory, visual, cognitive, and autonomic impairments that may progressively limit mobility, functional independence, and overall quality of life. In this sense, current evidence comes from RCTs involving individuals with mild-to-moderate disability, in which VR complements conventional rehabilitation to target balance, postural control, upper-limb coordination, and dual-tasking [64,129–132].

Reported benefits include improvements in balance, walking ability, functional mobility, and independence. Positive effects on executive function, cognitive processing, dual-task performance, and perceived fatigue have also been observed [129–132]. Common assessment instruments include the Berg Balance Scale, Timed Up and Go test, Six-Minute Walk Test, 12-Item Multiple Sclerosis Walking Scale, and fatigue-specific questionnaires [129,130]. A notable advantage of VR in MS rehabilitation is its capacity to adjust task demands and training intensity according to fatigue and fluctuations in neurological function, thereby accommodating changes in patients' functional capacity [131,132].

- Spinal Cord Injury (SCI)

SCI can cause motor paralysis, sensory impairment, autonomic dysfunction, and chronic pain, substantially limiting mobility and functional independence [133]. Current evidence comes primarily from pilot studies and RCTs involving individuals with complete or incomplete injuries. In these studies, VR is integrated into multidisciplinary rehabilitation to target upper-limb function, wheelchair skills, standing balance, gait, and functional task performance [134–136].

Reported benefits include improvements in upper-limb function, wheelchair mobility, balance, quality of life, and gait among individuals with incomplete SCI [135–137]. Outcomes are commonly evaluated using the Walking Index for Spinal Cord Injury, Spinal Cord Independence Measure, 10-Metre Walk Test (10MWT), and balance assessments [135–137]. Consequently, VR-based rehabilitation may facilitate intensive training of residual motor pathways while promoting compensatory strategies for functions affected by persistent deficits [136,137].

- Pain

Pain comprises a heterogeneous group of conditions arising from interactions among peripheral, spinal, and supraspinal mechanisms [138]. Thus, the application of VR may differ across nociceptive, neuropathic, and nociplastic pain phenotypes [139–141]. Evidence for nociceptive pain comes from musculoskeletal and postoperative rehabilitation, where VR is combined with exercise to facilitate graded movement and functionality. Reported benefits include reductions in pain intensity and improvements in range of motion, physical performance, and confidence in movement, commonly assessed through pain scales, disability questionnaires, and functional tests [139–142].

In neuropathic conditions—including phantom limb pain, complex regional pain syndrome [143,144], and pain following peripheral nerve injury [145]—VR has shown potential to target pain, motor performance, body perception, and body representation [140,146–149]. However, the supporting studies generally have small samples.

In nociplastic pain, immersive interventions integrating movement, relaxation, and cognitive activities have also been linked to improvements in pain, functionality, fatigue, kinesiophobia, catastrophizing, anxiety and quality of life. Assessment commonly combines disease-specific instruments, such as the Fibromyalgia Impact Questionnaire, with pain, fatigue, and quality-of-life scales [146,150].

Proposed mechanisms include attentional distraction, graded exposure to feared movements, embodiment-related modulation of body perception, and sensorimotor recalibration. The characteristics, principal findings, and limitations of representative studies assessing VR-based interventions across several pain conditions are summarized in Table S1.

5.2.3. Comparison of Clinical Evidence Across Neurological Conditions

Evidence supporting VR-based rehabilitation differs across neurological conditions. Stroke has the largest and most developed evidence base, particularly for upper-limb motor rehabilitation, whereas findings for gait, cognition, and long-term functional independence remain more heterogeneous. In PD, the most consistent benefits concern gait, balance, mobility, and freezing of gait, especially when VR provides external visual or auditory cues. In MS, VR has shown benefits for balance and mobility; however, fatigue, severity, and symptom fluctuations may influence tolerance and response.

Evidence for traumatic brain injury and SCI remains less conclusive because it is predominantly derived from small trials, pilot studies, and clinically heterogeneous samples. In TBI, improvements have also been reported in balance, mobility, executive function, and dual-task performance, but findings for attention and working memory remain inconsistent. Particularly, in SCI, improvements depend strongly on injury level and completeness, residual motor function, and whether the VR intervention targets restorative or compensatory strategies. Pain studies report reductions in pain intensity and fear of movement, but the magnitude and durability of these effects vary according to pain phenotype, intervention content, and the degree to which VR is combined with active exercise or graded exposure.

Discrepancies across studies may reflect differences in sample size, disease stage and severity, degree of immersion, duration of the exposure and intensity, comparator treatments, and outcome measures. In addition, commercial exergaming systems, customized platforms, and fully immersive environments should not be regarded as equivalent interventions. Statistically significant changes in impairment-based measures may not translate into clinically meaningful gains in adherence, participation or quality of life. Overall, evidence supports VR as a complement to, rather than a replacement for, conventional rehabilitation. Therefore, protocols should be chosen according to the condition, goals, safety considerations, cognitive capacity, and tolerance of immersive environments. Table 3

summarizes the mechanisms of VR together with the principal clinical outcomes reported across different neurological conditions.

Table 3. Proposed mechanisms of VR and outcomes reported in the literature across different clinical populations. Outcomes represent findings described in the included studies and should be interpreted as reported associations rather than established causal effects. ↑ indicates outcomes that were reported as improved or enhanced in some studies; ↓ indicates outcomes reported as reduced. Abbreviations: AEs, adverse events; QoL, quality of life; PD, Parkinson's disease; TBI, traumatic brain injury; VR, virtual reality.

Condition	Predominant Mechanism	Potential Outcomes
TBI	• Experience-dependent neuroplasticity • Cortical reorganization • Multisensory integration • Attentional modulation	• ↑ Executive function • ↑ Balance/mobility • ↑ Motivation • ↓ Pain/emotional distress
Stroke	• Cortical reorganization • Corticospinal network recruitment • Sensorimotor integration • Motor relearning	• ↑ Upper-limb function • ↑ QoL/motivation • ↑ Visual recovery • = Mixed gait findings
Parkinson's Disease	• External sensory cueing • Cortico-basal ganglia circuit compensation • Multisensory integration • Sensorimotor learning	• ↑ Gait/balance/mobility • ↑ Cognition • AEs: mild dizziness/cybersickness
Multiple Sclerosis	• Adaptive neuroplasticity • Multisensory integration • Task-specific motor learning • Sensorimotor integration • Dual-task cognitive–motor training	• ↑ Dynamic balance/postural control • ↑ Walking performance/mobility • ↑ ADLs participation • ↑ Executive function/dual-task performance • ↓ Fatigue
Spinal Cord Injury	• Activity-dependent neuroplasticity • Residual corticospinal pathway recruitment • Multisensory integration • Task-specific motor learning • Compensatory motor strategies	• ↑ Upper-limb function • ↑ Balance/wheelchair mobility • ↑ Gait • ↑ ADLs participation • ↑ Motivation/treatment adherence
Pain	• Descending pain modulation • Attentional modulation • Sensorimotor recalibration cortical plasticity • Graded exposure	• ↓ Pain/fear of movement • ↑ Function/QoL

5.3. Safety, Adverse Events, and Tolerability of VR

VR is commonly considered a safe, well-tolerated, and effective intervention across neurological rehabilitation settings, with most studies reporting a low incidence of adverse events when intervention is appropriately supervised and individualized. Nevertheless, immersive systems require careful safety assessment, particularly in patients with impairments affecting balance, vision, cognition, vestibular function, or autonomic regulation. The occurrence and severity of adverse events depend on the interaction between patient- and technology-related factors.

Cybersickness is the most generally reported adverse effect and may involve dizziness, nausea, headache, eyestrain, blurred vision, sweating, fatigue, and postural instability [151,152]. Sensory Conflict theory attributes these symptoms to mismatches among visual, vestibular, and proprioceptive inputs that disrupt sensory integration and elicit autonomic responses [153,154]. Other models, including Postural Instability Theory [155]

and Eye Movement Theory [156], suggest that impaired postural adaptation and abnormal oculomotor responses may also contribute.

Patient-related risk factors include older age, vestibular dysfunction, impaired balance, susceptibility to motion sickness, acute migraine, visual impairment, anxiety, fatigue, cognitive deficits, autonomic dysfunction, and neurological disorders affecting sensory integration [157,158]. Technology-related factors include high visual immersion, prolonged exposure, low refresh rates, system latency, mismatches between virtual and physical movement, rapid optic flow, and poorly calibrated HMDs [152,159]. Although cybersickness is usually mild and self-limiting, it can reduce patient comfort, treatment adherence, and the overall effectiveness of VR-based rehabilitation.

Comprehensive screening before initiating VR-based rehabilitation is essential for a safe implementation. Clinicians should assess the patient's medical history, neurological status, balance, visual and vestibular function, cognitive capacity, seizure history, cardiovascular stability, and ability to interact safely with the virtual environment [160]. Particular caution is warranted in patients with uncontrolled epilepsy, severe vestibular dysfunction, acute migraine, significant visual impairment, marked susceptibility to motion sickness, poorly controlled psychiatric disorders, or any condition that may compromise safe participation [161].

Several practical measures can significantly reduce adverse events and improve treatment tolerability. These include gradual familiarization with the VR environment, short initial sessions, progressive increases in exposure duration and task complexity, scheduled rest periods, appropriate HMD fitting and display calibration, adequate environmental lighting, and supervision by well-trained healthcare professionals [162]. Continuous monitoring of patient-reported symptoms also allows discomfort to be identified early and enables timely modification or discontinuation when necessary [163]. Standardized instruments, such as the Simulator Sickness Questionnaire (SSQ), may facilitate the systematic assessment of cybersickness in both clinical practice and research.

To sum up, serious adverse events appear to be uncommon, and most reported symptoms resolve rapidly after VR exposure is discontinued without requiring medical intervention. However, appropriate patient selection, gradual exposure, and continuous clinical monitoring remain essential. The principal adverse events associated with VR and the recommended strategies for their prevention and management are summarized in Table 4.

5.4. Clinical Decision-Making for VR

The clinical implementation of VR should follow a graded decision-making process based on treatment goals, patient characteristics, safety considerations, and individual tolerance. First, clinicians should define whether the main objective is improving motor, balance, gait, cognitive, functional, or pain-related management. Second, patients should be screened for cognitive ability to understand and follow instructions, visual and vestibular function, balance and fall risk, fatigue, cardiovascular stability, seizure history, and susceptibility to suffer from motion sickness. Patients with epilepsy, acute vestibular symptoms, severe visual impairment, unstable cardiovascular disease, severe behavioural dysregulation, or inability to communicate discomfort should not begin immersive VR until these risks have been appropriately assessed or controlled.

Table 4. Most common adverse effects associated with VR and strategies to improve safety and tolerability. The proposed mechanisms and management strategies summarize current evidence from the included studies and should be interpreted as practical clinical recommendations to optimize patient safety during VR-based rehabilitation. Abbreviations: SSQ, simulator sickness questionnaire; VR, virtual reality.

Adverse Effect	Symptoms	Mechanism	Strategies to Improve
Cybersickness	• Dizziness • Nausea • Headache • Eye strain • Blurred vision • Fatigue • Postural instability	• Visual–vestibular conflict • Postural instability • Abnormal eye movements	• Gradual familiarization • Short initial sessions • Progressive exposure • Rest breaks • Optimize headset calibration • Reduce latency and visual motion • Continuous clinical supervision • Monitor symptoms (SSQ)
Visual discomfort	• Eye fatigue • Blurred vision • Dry eyes	• Prolonged visual accommodation • Display characteristics	• Regular breaks • Proper headset fitting • Correct interpupillary distance (IPD) • Adequate room lighting
Postural instability	• Unsteadiness • Loss of balance	• Altered sensory integration	• Seated exercises (high-risk patients) • Safe environment • Therapist supervision • Use safety harness/support if needed
Fatigue	• Physical or cognitive exhaustion	• High cognitive load • Prolonged sessions	• Individualize session duration • Progressive task difficulty • Adequate recovery periods

The initial level of immersion should be selected according to clinical risk and rehabilitation objectives. Non-immersive VR is recommended as the initial option for patients with limited tolerance to sensory stimulation, marked fatigue, substantial fall risk, or home-based rehabilitation needs. Semi-immersive VR may be considered for patients who require greater environmental engagement while maintaining therapist supervision and awareness of their physical surroundings. Fully immersive VR should be reserved for those with adequate cognitive, visual, vestibular, and postural tolerance when a high degree of presence or controlled environmental simulation is clinically relevant.

Pathology-specific selection should also be considered. In stroke, VR may be prioritized for repetitive practice, visuospatial training, balance, and task-specific gait rehabilitation. In PD, systems delivering external visual or auditory cues may be used to facilitate gait initiation, reduce freezing episodes, and support balance and dual-task training. In MS, treatment intensity and session duration should be adjusted according to fatigue, heat sensitivity, and daily symptom fluctuations.

In TBI, cognitive load and environmental complexity should be introduced gradually, particularly in those patients with moderate to severe attention, executive, behavioural, or sensory-processing deficits. In SCI, the intervention should be selected according to injury level and completeness, residual motor function, autonomic stability, and the need for restorative or compensatory training. In patients with pain, VR may be particularly useful for those with deficits in attentional modulation, graded exposure, motor confidence, or sensorimotor recalibration, provided that symptom exacerbation and excessive fear-related exposure are avoided.

A short familiarization session of approximately 5–10 min should precede the full intervention. If no relevant adverse events occur, session duration and task complexity may be progressively increased. Treatment should be modified or even discontinued if the patient develops nausea, dizziness, headache, visual discomfort, disorientation, postural instability, autonomic symptoms, substantial pain exacerbation, or a clinically meaningful decline in performance. VR should normally be integrated as an adjunct to multidisciplinary rehabilitation, and continuation should depend on objective functional progress, patient-reported benefit, treatment adherence, and tolerability. Table 5 links clinical profiles to VR modality, progression, and monitoring.

Table 5. Clinical framework for selecting the initial VR modality, guiding treatment progression, and monitoring safety and tolerance according to the patient's clinical profile.

Clinical Profile	Initial Modality	Progression	Monitoring
High fall risk, vestibular symptoms, substantial fatigue, or low tolerance	• Non-immersive; seated tasks	• Progress only after showing stable tolerance	• Balance • Fatigue • Nausea • Dizziness
Moderate impairment requiring supervision	• Semi-immersive	• Increase sensory and task complexity gradually	• Postural control • Cognitive load • Symptoms
Clinically stable with adequate cognitive and sensory tolerance	• Fully immersive	• Increase duration, movement demands, and dual-task complexity	• Cybersickness • Performance • Adherence
Home-based rehabilitation	• Non-immersive or carefully supervised standalone system	• Remote monitoring and periodic reassessment	• Safety • Adherence • Caregiver support

6. Conclusions and Prospects

VR-based interventions have become an adjunctive therapy for neurorehabilitation, providing immersive, interactive, and task-oriented environments that may support motor, emotional, and functional recovery. Across a wide range of neurological conditions, its reported benefits appear to be mediated by complementary mechanisms, such as experience-dependent neuroplasticity, multisensory integration, motor learning, attentional modulation, adaptive feedback and enhanced patient participation.

Despite these promising findings, the available evidence remains heterogeneous with respect to patient populations, intervention protocols, VR technologies, outcome measures and methodological quality. Accordingly, VR should not be regarded as a replacement for conventional rehabilitation but rather as an adjunctive intervention that increases intensity, promotes repetitive task-oriented practice, enhances motivation and facilitates personalized rehabilitation pathways. Furthermore, careful patient selection, consideration of functional status and cognitive capacity, and appropriate monitoring of AEs, especially cybersickness, remain essential for the safe and effective implementation of VR in clinical practice.

Looking ahead, several technological advances are expected to reshape the role of VR in neurorehabilitation. The integration of AI and machine learning (ML) is expected to enable increasingly adaptive rehabilitation systems capable of automatically adjusting task difficulty according to real-time patient performance. Likewise, wearable sensors and digital biomarkers may facilitate continuous monitoring of movement quality, physiological responses, treatment adherence, and recovery trajectories, thus supporting data-driven clinical decision-making. The convergence of VR with telerehabilitation platforms and

XR technologies may expand access to intensive neurorehabilitation beyond specialized centres while improving long-term follow-up and continuity of care.

Lastly, VR is likely to continue evolving towards the precision neurorehabilitation paradigm, in which immersive interventions are dynamically personalized according to each patient's neurological profile, functional abilities, rehabilitation goals and longitudinal clinical data. Future high-quality multicentre clinical trials, incorporating standardized treatment protocols, longer follow-up periods, cost-effectiveness analyses, and validated digital outcome measures, will be essential to determine the optimal indications, implementation strategies, and long-term clinical value of VR.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/encyclopedia6080164/s1, Table S1: Summary of Studies on Virtual Reality-Based Interventions in Neurological Conditions.

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Abbreviations

The following abbreviations are used in this manuscript:

6DOF	Six Degrees of Freedom
ADL	Activities of Daily Living
AE	Adverse Event
DTI	Diffusion Tensor Imaging
EEG	Electroencephalography
FIQ	Fibromyalgia Impact Questionnaire
fMRI	Functional Magnetic Resonance Imaging
fNIRS	Functional Near-Infrared Spectroscopy
IPD	Interpupillary Distance
M1	Primary Motor Cortex
ML	Machine Learning
MS	Multiple Sclerosis
PMC	Premotor Cortex
PPC	Posterior Parietal Cortex
PTSD	Post-Traumatic Stress Disorder

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