

ADDRESSING THE PARADOX OF REST WITH INNOVATIVE TECHNOLOGIES PREMAGOVANJE PARADOKSA POČITKA Z INOVATIVNIMI TEHNOLOGIJAMI

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ABSTRACT

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The paradox of rest lies in its dual nature: essential for recovery yet potentially harmful when prolonged. Prolonged physical inactivity (PI) significantly contributes to non-communicable diseases (NCDs). Studies show nearly a third of adults worldwide were insufficiently active in 2022, with the economic costs of PI projected to reach INT\$520 billion by 2030.

Bedrest models have illuminated the rapid onset of insulin resistance, general functional decline and muscle atrophy associated with PI, particularly in hospitalised older adults. Innovative technologies, such as extended reality (XR), offer promising solutions for mitigating the effects of PI and can enhance non-physical rehabilitation techniques such as motor imagery and action observation. These technologies provide immersive, personalised therapeutic experiences that engage multiple senses, transforming passive recovery into an active process and addressing both the physical and cognitive consequences of inactivity.

Results of bedrest study showed significant preservation of muscle mass, improved strength and enhanced insulin sensitivity in the intervention group compared to controls. These findings highlight the potential of XR-based strategies in addressing structural and functional declines during inactivity. As part of the Interreg VI-A Italia-Slovenija project X-BRAIN.net, advanced XR-equipped active rooms were developed to aid post-stroke rehabilitation in acute care settings. XR technologies, particularly VR, have shown promise in providing dynamic and adaptable therapeutic environments that facilitate early and targeted interventions. Future advancements focus on integrating XR with brain-computer interfaces (BCIs) and synchronised visual-haptic neurofeedback, enhancing sensorimotor cortical activation and improving rehabilitation outcomes. Comprehensive multimodal approaches, including nutritional, physical and non-physical interventions, are emerging as effective strategies to personalise and optimise patient recovery.

IZVLEČEK

Ključne besede:

gibalna neaktivnost
funkcionalni in kognitivni upad
rehabilitacija
razširjena resničnost
multimodalne intervencije

Paradoks počitka leži v njegovem dvojnem značaju: nujen je za okrevanje, vendar lahko postane škodljiv, če traja predolgo. Dolgotrajna gibalna neaktivnost (GN) pomembno prispeva k nastanku kroničnih nenalezljivih bolezni (KNB). Študije kažejo, da je bilo leta 2022 skoraj tretjina odraslih na svetu premalo telesno aktivnih, ekonomski stroški KNB pa naj bi do leta 2030 dosegli 520 milijard ameriških dolarjev.

Modeli raziskovanja GN z dolgotrajnim ležanjem v postelji so osvetlili hitro pojavljanje inzulinske rezistence, splošnega funkcionalnega upada ter mišične atrofije, povezane s GN, zlasti pri starejših bolnikih v bolnišnicah. Inovativne tehnologije, kot je razširjena resničnost (XR), ponujajo obetavne rešitve za omilitev učinkov GN in lahko izboljšajo ne-fizične rehabilitacijske tehnike, kot sta lastna predstavnost gibanja in opazovanje gibanja. Te tehnologije omogočajo poglobljeno, personalizirano terapevtsko izkušnjo, ki vključuje več čutov, ter spreminjajo pasivno okrevanje v aktiven proces, ki naslovi tako fizične kot kognitivne posledice neaktivnosti.

Rezultati študije dolgotrajnega ležanja v postelji so pokazali znatno ohranitev mišične mase, izboljšanje moči in občutljivosti na inzulin v intervencijski skupini v primerjavi s kontrolno skupino. Ti rezultati poudarjajo potencial strategij, temelječih na XR, za reševanje strukturnih in funkcionalnih upadov med neaktivnostjo. V okviru projekta Interreg VI-A Italia-Slovenija X-BRAIN.net so bile razvite napredne aktivne sobe, opremljene z XR tehnologijami, za pomoč pri rehabilitaciji po možganski kapi v akutni fazi zdravljenja. XR tehnologije, zlasti VR, so obetavne pri zagotavljanju dinamičnih in prilagodljivih terapevtskih okolij, ki omogočajo zgodnje in ciljno usmerjene intervencije. Prihodnji napredek se osredotoča na integracijo XR z možgansko-računalniškimi vmesniki (BCI) in usklajenim vidno-haptičnim nevrofeedbackom, ki izboljšujeta aktivacijo senzor motorične skorje in izboljšujeta rezultate rehabilitacije. Celostni multimodalni pristopi, ki vključujejo prehranske, fizične in ne-fizične intervencije, postajajo učinkovite strategije za personalizacijo in optimizacijo okrevanja pacientov.

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1 INTRODUCTION TO THE PARADOX OF REST

The paradox of rest lies in its dual nature: while rest is essential for recovery and healing, particularly for patients, prolonged physical inactivity (PI) can be detrimental. Extended periods of rest can negatively impact various systems of the body, especially the musculoskeletal system, leading to muscle atrophy, weakened bones and decreased overall function (1-4). In the *Art of Medicine* (5) Galen warns: when, for example, the body is in need of motion, exercise is healthy and rest morbid; when it is in need of a break, rest is healthy and exercise morbid. Balancing rest and activity are crucial to ensure recovery without causing harm.

PI has emerged as a critical global health challenge, significantly contributing to the rise of non-communicable diseases (NCDs) such as cardiovascular disease, stroke, type 2 diabetes, and certain cancers (6). The World Health Organization (WHO) highlights that physical inactivity is a primary, modifiable risk factor for NCDs and mortality. According to the WHO, physical inactivity is responsible for approximately 6% of deaths worldwide, making it one of the top four risk factors for mortality. People who are insufficiently active have a 20% to 30% increased risk of death compared to people who are sufficiently active (7). There is an estimate that nearly a third of adults globally (31.3%; 1.8 billion) were insufficiently physically active in 2022, an increase from 23.4% (900 million) in 2000 (8). A recent analysis (9) estimated that the global economic cost of physical inactivity could amount to approximately INT\$520 billion between 2020 and 2030 if current physical activity levels remain unchanged. The study further identified the European region as bearing the highest economic burden attributable to physical inactivity during this period.

It has long been understood that rest is vital for healing. It facilitates regeneration and affects every system, from cognitive function to immune health. However, research into the effects of physical inactivity on the human body highlights numerous consequences, including the deterioration of various subsystems—ranging from the musculoskeletal and cardiovascular systems to respiratory function, motor control, perception and overall well-being. These processes are especially pronounced in older individuals, where recovery is often slower (1). Such catabolic phases can significantly impact not only the return to normal life but also the recurrence of injuries and illnesses, along with increased mortality rates. These insights underscore our responsibility to thoroughly study the mechanisms behind these changes and, most importantly, to develop effective interventions that can slow down deterioration and promote the maintenance and swift recovery of patients' functional abilities.

The physiological consequences of PI have been extensively studied through controlled models such as bedrest campaigns. Bedrest protocols vary in duration, ranging from short-term campaigns of a few days to long-term studies lasting several weeks or even months. These protocols follow strict guidelines to ensure consistency across studies, such as maintaining a horizontal position with only minimal movements permitted and controlled dietary intake. These conditions help researchers isolate the effects of inactivity from other variables, providing valuable insights into its physiological consequences. Studies have highlighted critical changes in neuromuscular function, including the remodeling of motor units and the underlying mechanisms driving muscle deterioration (10-12). Acute exposure to inactivity has been strongly linked to a rapid onset of insulin resistance in muscle tissue, reduced glucose uptake and utilisation, and accelerated muscle protein degradation, ultimately leading to muscle atrophy (13, 14). These findings underscore the metabolic and structural vulnerability of skeletal muscle to even short-term reductions in PI. This challenge is particularly acute in hospital settings, where prolonged bedrest is often unavoidable. Research indicates that hospitalised older adults may spend as much as 86% of their time inactive (15). Such extended periods of inactivity significantly threaten both physical and mental health, accelerating muscle atrophy, impairing functional independence and substantially increasing the risk of chronic disability (16). Our research team recognises the urgent need to make more meaningful use of the time patients spend confined to their beds. One promising solution lies in leveraging innovative technologies, such as extended reality (XR), to immerse patients in synthetically produced enriched environments that support rehabilitation efforts (17). In short, XR encompasses immersive technologies such as Virtual Reality (VR), Augmented Reality (AR) and Mixed Reality (MR), which blend physical and virtual environments to enhance user experiences (18). These technologies offer an opportunity to enhance non-physical rehabilitation techniques, including motor imagery (MI) and action observation (AO). MI involves the mental rehearsal of movements through kinesthetic experiences or visual representations, while AO involves observing the execution of movements. Both MI and AO have been shown to alleviate the detrimental effects of prolonged immobilisation (19-21). By integrating these approaches, we can transform passive recovery into an active process, addressing both the physical and cognitive consequences of inactivity in hospitalised patients while fostering their active participation in the rehabilitation process.

2 HARNESSING XR FOR ACTIVE REHABILITATION

While MI and AO have proven effective in reducing

physiological decline and promoting motor recovery in bedridden patients, their application is significantly constrained by the patient's ability to generate vivid mental imagery and maintain focused attention in rehabilitation settings that are often sensory-deprived or filled with distractions, such as clinical environments. These traditional settings fail to replicate the dynamic and unpredictable challenges of real-life scenarios, limiting the practical applicability of these approaches beyond the controlled clinical context. In contrast, XR systems provide a unique advantage in rehabilitation by allowing precise control over treatment parameters, including the ability to adjust stimuli and distractors. This flexibility enables highly personalised therapy sessions tailored to individual needs. By immersing patients in a fully synthetic environment, XR systems deliver a multisensory experience that extends beyond visual stimuli, effectively engaging kinesthetic, visual and auditory senses for a more immersive and impactful therapeutic experience (17).

2.1 Innovative technologies in practice

In Šlosar et al. (17), we hypothesised that combining XR interventions with MI and AO could effectively mitigate muscle strength decline. This hypothesis was confirmed by findings from our 2023 bedrest campaign, where older adults engaged in a multimodal intervention approach. This included exercise prehabilitation prior to bedrest, a leucine-rich, high-protein diet and a daily VR-based brain training programme. Compared to the control group, participants demonstrated significant benefits, including the preservation of muscle mass and strength and significant improvements in insulin resistance (22). These findings underscore the promise of XR-based strategies, especially when integrated with complementary practices, in mitigating both structural and functional declines during periods of physical inactivity, as illustrated in Figure 1.

As part of the EU project Interreg VI-A Italia-Slovenija: X-BRAIN.net, our team played a key role in the development of active rooms, state-of-the-art spaces equipped with advanced XR technologies designed to support the rehabilitation of post-stroke patients in the acute stage in the General Hospital of Izola and ASUGI - Azienda sanitaria universitaria Giuliano Isontina, Trieste, Italy (22). Healthcare professionals involved in the project highlighted the potential of XR systems, particularly VR, to facilitate earlier and more targeted interventions. By immersing patients in a controlled yet engaging therapeutic environment, XR technologies align with modern rehabilitation practices, offering a more dynamic and

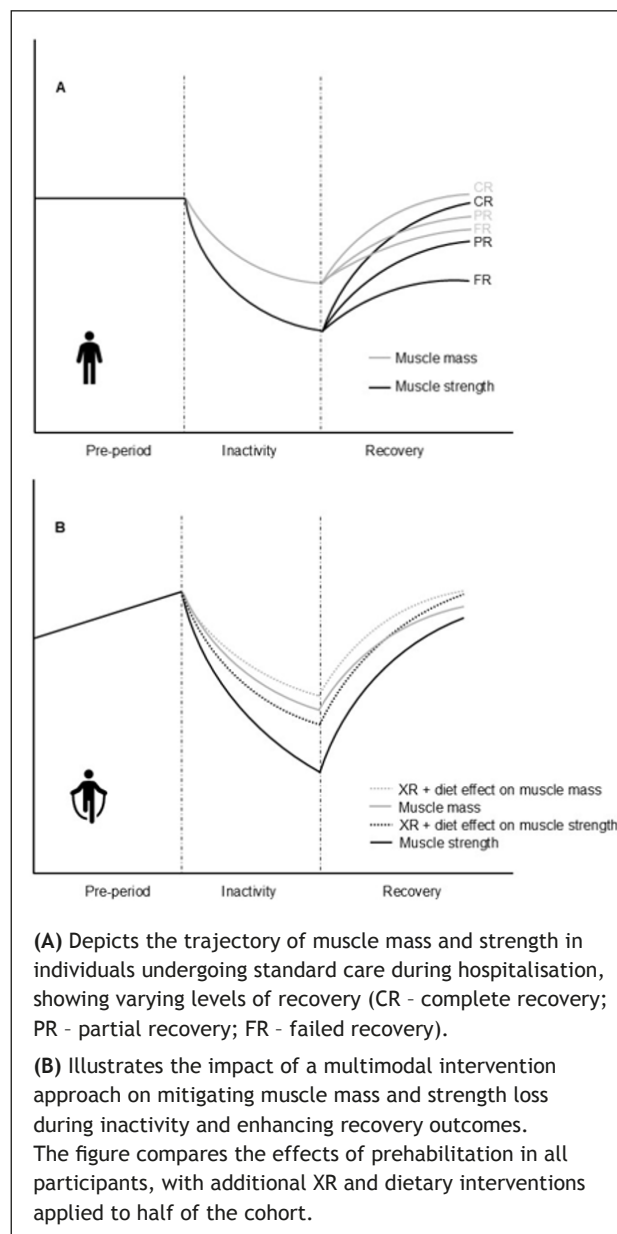


Figure 1. Comparative effects of standard care and multimodal intervention approach on muscle mass and strength during periods of inactivity and recovery. Adapted from Soendenbroe et al. (23).

adaptable approach to recovery. This initiative represents a pioneering step in post-stroke care, integrating advanced technologies to complement traditional rehabilitation techniques while addressing the unique needs of each patient. Such anticipatory approaches have shown promise in promoting neurological function improvement and potentially accelerating recovery timelines, particularly for neurological patients (24).

3 SHAPING THE FUTURE OF REHABILITATION

Future directions in this field emphasise the potential of synchronised visual-haptic neurofeedback during MI, a technique that combines visual and tactile feedback to enhance mental rehearsal of movements. For example, a typical setup might involve a participant wearing a VR headset to visualise a limb movement while receiving corresponding tactile feedback through a haptic glove or device. Studies have demonstrated that this approach can improve outcomes compared to traditional neurofeedback training by providing more immersive and realistic sensory input (25). Additionally, the integration of XR solutions with brain-computer interfaces (BCIs) (26-28), particularly in stimulating sensorimotor cortical activation, represents a significant milestone in refining rehabilitation processes. Multimodal and comprehensive interventions, incorporating both traditional physical treatments and non-physical strategies, are emerging as optimal approaches for rehabilitation in hospital settings. These include non-physical interventions such as multisensory stimulation, nutrition-focused programmes and prehabilitative processes designed to prepare patients for physical recovery. For instance, multisensory stimulation delivered through XR or virtual environments can promote neural plasticity and improve patient engagement. Proper nutritional interventions further support the body's recovery by addressing metabolic needs during inactivity or recovery phases. Prehabilitative exercise programmes, which aim to maintain neuromuscular integrity and prepare patients for post-disuse recovery, complement these innovative approaches (23).

However, while these advancements hold great promise, several limitations must be acknowledged. Challenges such as cybersickness—a form of motion sickness induced by VR—can hinder patient adherence and comfort. Additionally, the high cost of advanced technologies like BCIs and VR systems, as well as the technical expertise required to implement and maintain them, may limit accessibility and scalability in clinical settings. These barriers highlight the need for developing more cost-efficient, user-friendly and widely accessible methods to ensure equitable adoption across healthcare systems.

Despite these challenges, the integration of advanced technologies with traditional rehabilitation methods offers precise control over therapeutic structures and functions, paving the way for more personalised, effective and sustainable interventions. By addressing current limitations and fostering further research in this promising field, the future of rehabilitation can evolve to be both patient-centered and holistically impactful, ensuring that innovative solutions are not only effective but also practical and inclusive.

CONFLICTS OF INTEREST

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