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# An attempt to identify factors influencing the effectiveness of physical exercise in virtual reality conditions in the treatment of anxiety and depressive disorders – study design

Próba identyfikacji czynników wpływających na skuteczność wysiłku fizycznego w warunkach wirtualnej rzeczywistości w leczeniu zaburzeń lękowych i depresyjnych - projekt badania

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**Abstract**

**Introduction:** Virtual reality (VR) has been shown to have beneficial effects in the treatment of depressive disorders, anxiety disorders, eating disorders, and addictions. This method is relatively safe and noninvasive, but its effectiveness is variable, and predictors of effectiveness have been investigated in a limited manner. We hypothesized that personality traits could impact VR effectiveness, and that cognitive impairments might relate to its therapeutic success.

**Material and methods:** The study involves a randomized sample of 40 patients diagnosed with anxiety and mood disorders (ICD-10 F3x and F4x) from a psychiatric rehabilitation daily unit. Over 12 weeks, they will participate in a therapeutic program that includes exercise sessions enhanced with virtual reality (VR) interventions lasting 10 to 12 minutes each. A control group of 40 patients will follow a standard therapeutic program without VR. During the screening phase, we will assess anxiety and depression severity using the HADS and STAI. We will also evaluate patients' physical fitness by using the 6MWT, personality traits by using the HEXACO-60 Personality Inventory, and cognitive functioning by the ACE III, MoCA, FAB and RAVL tests.

**Results:** The procedure's effectiveness will be measured using HADS and STAI assessments for anxiety and depression at weeks 6, 12, and 4 weeks after the program.

**Conclusions:** Defining the subpopulation of patients sensitive to the proposed therapeutic interventions and analyzing the factors influencing their treatment will allow offering therapy in virtual reality to those who will benefit the most from it.

*Keywords*: virtual reality, physical exercise, depression, anxiety disorder, HADS

**Streszczenie**

**Wstęp:** Wykorzystanie wirtualnej rzeczywistości (VR) ma korzystny wpływ na leczenie zaburzeń depresyjnych, lękowych, zaburzeń odżywiania i uzależnień. Metoda ta jest stosunkowo bezpieczna i nieinwazyjna, ale jej skuteczność jest zmienna, a predyktory skuteczności nie zostały dostatecznie zbadane. Na potrzeby tego badania postawiliśmy hipotezę, że pewne cechy osobowości, w szczególności wysoki poziom neurotyzmu, mogą wpływać na skuteczność VR. Ponadto zakładamy, że obecność zaburzeń poznawczych koreluje z ogólną skutecznością terapeutyczną VR.

**Materiał i metody:** Badanie obejmuje randomizowaną próbę 40 pacjentów z dziennego oddziału rehabilitacji psychiatrycznej, u których zdiagnozowano zaburzenia lękowe i zaburzenia nastroju (grupy ICD-10 F3x i F4x). W ciągu 12 tygodni pacjenci będą uczestniczyć w programie terapeutycznym z uwzględnieniem sesji ćwiczeń fizycznych wzbogaconych o interwencje VR (10-12 minut podczas każdej sesji). Grupa kontrolna składa się z kolejnych 40 pacjentów z tego samego dziennego oddziału rehabilitacji psychiatrycznej. Osoby te będą również uczestniczyć w standardowym programie terapeutycznym, jednak bez interwencji VR. Podczas fazy przesiewowej ocenimy nasilenie lęku i depresji u pacjentów za pomocą skal HADS i STAI. Dodatkowo, sprawność

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fizyczna pacjentów zostanie oceniona za pomocą 6MWT, cechy osobowości zmierzone za pomocą Inwentarza Osobowości HEXACO-60, a funkcjonowanie poznawcze przetestowane za pomocą testów ACE III, MoCA, FAB i RAVL.

**Wyniki:** Skuteczność procedury zostanie oceniona poprzez pomiar poziomu lęku i depresji za pomocą HADS i STAI w 6. i 12. tygodniu programu oraz w 4. tygodniu po zakończeniu programu.

**Wnioski:** Określenie wrażliwej na proponowane interwencje terapeutyczne subpopulacji pacjentów oraz analiza czynników wpływających na ich leczenie umożliwi zaoferowanie terapii w wirtualnej rzeczywistości tym, którzy odniosą z tego największe korzyści.

*Słowa kluczowe*: wirtualna rzeczywistość, wysiłek fizyczny, depresja, zaburzenia lękowe, HADS

## 1. Background

Virtual Reality (VR), a digital representation of a 3D environment, offers a wide range of tools available for adaptation in healthcare services through the possibilities of users' interaction with virtual settings and characters. [1] A rapidly developing field of VR use is education and clinical training. The research so far emphasizes that with adequate implementation of VR technology, interactive classes and simulations can be created to imitate actual treatment and diagnostic scenarios, providing added value without unnecessary risk to patients. It is essential to ensure that both lecturers and students are competent in technology use. Additionally, involving end-users in the technology development process is crucial for joint participation. [2] It is also important to note the regional limitations of the analyzed data, which stem from the unequal distribution of digital medical education resources around the world. This disparity not only hampers medical education in less developed areas but also exacerbates inequality instead of alleviating it through improved access to technology. [3] VR simulators have demonstrated their effectiveness in acquiring surgical skills and providing a realistic environment for spatial training. [4] At the same time, there have been reports comparing the impact of virtual medical education with the traditional method. While VR can effectively improve knowledge, it is not more effective. [5]

Another widely developing field of VR use is the therapeutic aspect. Tailored VR experiences can assist in physical therapy, mental health interventions, pain management and rehabilitation exercises. VR's interactive and engaging nature can motivate patients to adhere to their treatment plans, improving outcomes. [6] The use of virtual reality (VR) gives beneficial effects in the treatment of depressive disorders, anxiety disorders, eating disorders and addictions, often combined with counseling and cognitive behavioral therapy. [7] VR has also been used in cognitive rehabilitation. When evaluating the impact of VR interventions focused on cognition, the authors highlight the limited number of studies, small sample sizes, heterogeneity of outcomes, and potential questions around quality and inconsistent methodology as the primary challenges in drawing general conclusions. At the same time, overall results might suggest that VR-based cognitive training could be at least as practical as conventional cognitive training sessions for patients with mild cognitive impairment (MCI), being a good alternative and possibly a solution to tailor personalized rehabilitation for individual patients. Because of age and perhaps lack of experience with technology, the efficacy of VR interventions for people with MCI may vary. Many factors, such as the type of technology, previous experience, and living situation, should be considered. [8] A meta-analysis study on VR rehabilitation training's effects on cognitive function and daily living activities in post-stroke patients suggests it may serve as an excellent complement to traditional cognitive interventions. [9] Four independent meta-analyses support the notion that VR-based interventions, by providing exposure therapy, psychoeducation, and relaxation therapy, significantly alleviate symptoms associated with anxiety and depression. [10] Immersive VR therapy that addresses both functional activities and depressive symptoms, when combined with neurological rehabilitation, has shown a positive impact on improving mood and reducing symptoms in post-stroke patients. This is particularly significant because depression can diminish quality of life, reduce physical activity, impair social functioning, and strain interpersonal relationships, ultimately leading to poorer overall therapy outcomes for these patients. [11] Systematic review from 2023 on the treatment efficacy of immersive VR or AR technologies on different symptom domains of schizophrenia spectrum disorders indicates how different symptom domains can be targeted through VR interventions. [12] The method is relatively safe and noninvasive, but its effectiveness varies and the predictors of effectiveness have been investigated in a limited manner. It is also worth noting that at the moment not much is known about the side effects of VR therapy. A systematic review from 2023 indicates cybersickness (when exposure to a virtual environment causes symptoms similar to those of motion sickness),

worsening of symptoms (posttraumatic stress disorder, anxiety, and cravings), tiredness, dizziness, back pain, and carelessness. Available evidence indicates that adverse effects associated with VR are likely to be common, but the identified lack of robust data makes it difficult to estimate their prevalence with confidence. [13]

Among the most frequently mentioned barriers related to the introduction of therapeutic programs based on VR technology, there were resourcing and financial constraints, lack of knowledge and trust on the part of medical staff, limited strength of scientific evidence, lack of specific clinical guidelines, treatment protocols and training program leading to safety and ethical concerns. One of the main factors influencing the final effect is an adequate qualification of patients for the programs and functional individualization of the proposed solutions. [14,15] A 2023 study emphasized the importance of behavior change among all stakeholders involved, including healthcare providers, patients, support staff, and managers, through a participatory development process. The study also noted that there is often insufficient focus on creating a systematic implementation plan with specific objectives. This oversight results in a gap in research between identifying factors that influence implementation and connecting them to practical strategies and outcomes, thereby hindering the formation of a coherent implementation intervention. [16]

The exact mechanism of how exercises have a protective effect on mental state is not clearly explained and is still a subject to intensive scientific analyzes both in general population (prevention) and those who suffer from mental disorders (treatment). Most theories focus on modulation of neurotransmitters and growth factors, neurogenesis and neuroplasticity, reduction of inflammatory reaction or strengthening the immune system. [17] Structural and functional changes in the central nervous system under the influence of exercise benefit both from a biological as well as a psychological and social perspective. The studies published so far confirm that physical exercise, understood as planned, ordered and repetitive activity, reduces the severity of depression (including symptoms such as depressed mood, disturbances in circadian rhythms, and appetite disorders). Full remission and reduction of the risk of relapse are also documented. The results of the meta-analyzes also show that physical exercise can improve clinical symptoms in terms of the severity of symptoms, general functioning, and quality of life in patients with schizophrenia, depression, anxiety, PTSD or addictions. [18,19] The available evidence suggests that aerobic exercise, regardless of the type of subject and the duration of the intervention, is beneficial for improving the mental health of adults aged 60 years and older. Importantly, low-frequency, long-term, regular aerobic exercise has been shown to be particularly effective for older adults, providing a reassuring path to improved mental health. [20]

Physical exercise in virtual reality has recently gained significant attention. This approach enhances the benefits of movement as a therapeutic method. VR provides precise presentation and control of stimuli within a dynamic environment, allowing for multimodal changes while creating safe and motivating conditions for exercise. This helps prevent injuries and reduces the risk of burnout. Experiences using immersive virtual reality (IVR) to encourage physical activity have been shown to stimulate heart rates at various intensity levels significantly. This suggests that IVR for moderate and vigorous-intensity activities could be a promising tool to help individuals meet the WHO's recommended physical activity volume and intensity, fostering a sense of optimism about its potential. [21]

There is ongoing debate regarding the influence of personality disorders on treatment outcomes across various medical fields. The relationships between personality traits, psychopathology, and treatment outcomes are complex. However, research primarily focuses on one psychopathological condition: depression. [22] Research suggests that high scores on neuroticism or related measures, such as harm avoidance, are linked to worse treatment outcomes for depression (both for pharmacotherapy and psychotherapy). [23] A 2013 study found that individuals with both a personality disorder and depression had more than double the likelihood of experiencing poor outcomes compared to those without a personality disorder. [24] Recent reports highlight the importance of considering personality disorders when evaluating their impact on treatment outcomes for eating disorders and chronic pain. For instance, patients with more pronounced borderline personality traits tend to benefit more from treatment for eating disorders, while those diagnosed with histrionic personality features show a significantly better response to pain treatment. [25,26] There are no studies on relationship between personality disorders/ personality traits and effectiveness of VR therapy.

The method in question is time-consuming and costly compared to traditional non-pharmacological treatments, highlighting the need to identify groups of patients who may benefit from this technique. Key factors that are likely to influence the effectiveness of the treatment include specific personality traits and existing comorbidities. By identifying a subpopulation of patients who are potentially receptive to virtual reality treatment, we can better target our efforts toward those who are most likely to benefit from it.

The aim of the study is to verify two hypotheses: 1. there are personality traits (especially high levels of neuroticism) that influence the effectiveness of VR; 2. the preexistence of cognitive impairment correlates with the overall therapeutic effectiveness of VR.

## 2. Material and methods

*2.1 Study and control group*

The study involves a randomized sample of 40 patients from the daily psychiatric rehabilitation unit, all diagnosed with anxiety disorders and mood disorders (ICD-10 groups F3x and F4x). These patients will receive standard treatment and additional group exercise sessions incorporating virtual reality (VR) for up to one-third of a planned 30-40 minute session. The control group consists of another 40 patients from the same daily psychiatric rehabilitation unit with identical diagnoses. These individuals will also undergo pharmacological therapy and participate in a standard therapeutic program without VR interventions.

Inclusion criteria for the study group are as follows: age 18 -75 years, diagnosis from the F3x-F4x group according to ICD-10, full legal capacity, informed consent to participate in the study, regular participation in the extended therapeutic program. Inclusion criteria for the control group are as follows: age 18 -75 years, diagnosis from the F3x-F4x group according to ICD-10, full legal capacity, informed consent to participate in the study, regular participation in the standard therapeutic program.

Exclusion criteria for the study group are as follows: mental condition that impairs the ability to give informed consent, health condition that prevents active participation in the kinesitherapy program with VR interventions (including strong symptoms of motion sickness in the past, including severe dizziness and fainting, as well as a diagnosis of epilepsy or epileptic seizures in the past), diagnosis of dementia, diagnosis from group F1x (related to psychoactive substances) except for disorders related to the use of sedatives and hypnotics according to ICD-10, diagnosis of disorders from group F2x according to ICD-10 (schizophrenia and schizophrenia-type disorders), visual or hearing impairment that prevents the use of diagnostic tools, other mental or somatic disorders that prevent understanding the instructions or implementing the program.

*2.2 Psychometric tools and physical fitness test planned*

***Hospital Anxiety and Depression Scale (HADS)***

The HADS is a user-friendly scale, making it suitable for the initial diagnosis of depressive and anxiety disorders and for assessing the severity or resolution of their symptoms. It consists of 14 questions, with 7 addressing anxiety (HADS-A subscale) and 7 focusing on depression (HADS-D subscale). Each question is rated on a scale of 0 to 3 points, making it straightforward for both the examiner and the patient. The scoring range is the same for both independent subscales. A higher point value corresponds to a greater severity of symptoms.

***State-Trait Anxiety Inventory (STAI)***

The STAI is a comprehensive tool for examining anxiety, offering insights into different aspects of anxiety, such as worry, fear, discomfort, nervousness, and stress. It consists of two separate sections of twenty questions each on state anxiety and trait anxiety, providing a thorough assessment of the individual's anxiety levels.

***Addenbrooke's Cognitive Examination-III (ACE-III)***

The ACE-III is a screening tool used to assess cognitive functions. It helps in the early detection of cognitive disorders, initial differential diagnosis of dementia syndromes, and monitoring the disease's progression. The ACE-III assesses attention and orientation, memory, verbal fluency, language, and visuospatial functions.

***Montreal Cognitive Assessment Scale (MoCA)***

The MoCA is an efficient tool for detecting mild cognitive disorders, as the entire research procedure takes approximately 10 minutes. It assesses abstraction, short-term memory, visuospatial and executive functions, language, verbal fluency, allopsychic orientation, and attention, providing a comprehensive evaluation in a short amount of time.

***Frontal Assessment Battery (FAB)***

The FAB is a tool for assessing frontal lobe functions, including conceptualization, mental flexibility, motor planning, susceptibility to interference, inhibitory control, and environmental independence.

***Rey Auditory Verbal Learning Test (RAVLT)***

The RAVL test enables the assessment of verbal memory, auditory declarative memory skills, both immediate and delayed, and verbal learning skills. It involves remembering a list of 15 words after being presented five times (list A), which the examinee recreates immediately after being read by the examiner. Then, the examiner presents a new list of words (list B), played back after hearing it once. Then, the subject is asked to reproduce the remembered words from the previously presented list, and after 20 minutes, the words from list A are repeated.

***HEXACO–60 Personality Inventory (HEXACO-60)***

The HEXACO–60 Personality Inventory is designed to

evaluate various personality traits. Six personality factors are widely recognized in psychological studies across different languages and are included in the six-factor model: Honesty-Humility, Emotionality, Extraversion, Agreeableness, Conscientiousness, and Openness to Experience. Each item is scored on a scale of 1 to 5, and the overall score for the inventory is calculated by summing specific items.

***Physical performance assessment tool***

A 6-Minute Walk Test (6MWT) is an exercise test used to determine the longest possible distance that can be covered by a patient moving on a flat, hard surface in a specific time; it can be performed both outdoors and indoors. The test allows us to determine the submaximal level of exercise capacity and tolerance in patients with respiratory and circulatory system diseases, as well as the integrated reactions of neuromuscular units, muscle metabolism, and the level of motor control.

*2.3 Description of the experiment*

The screening phase, conducted from 14 to 1 day before the start of the study, is divided into two assessment days. This phase includes several key components:

1. Review of inclusion and exclusion criteria.
2. Provision of information about the study to the participants.
3. Acquisition of informed consent from the participants.
4. Conducting psychiatric and somatic examinations.
5. Assessing anxiety and depression using the Hospital Anxiety and Depression Scale (HADS) and the State-Trait Anxiety Inventory (STAI).
6. Evaluating personality traits with the HEXACO-60 Personality Inventory.
7. Assessing physical capacity using a designated assessment tool (6MWT).
8. Evaluating cognitive functioning through the ACE III, MoCA, FAB, and RAVL test.

This structured approach ensures a thorough evaluation of participants before the study begins.

Over a period of 12 weeks, patients in the study group will participate in physical exercise sessions that incorporate VR components for 10-12 minutes during each session. They will attend three sessions per week, with each session lasting 30-40 minutes. The sessions will include group fitness exercises, as well as relaxation and breathing techniques. The training program will follow a consistent schedule, with adjustments in intensity tailored to meet each patient's individual capabilities and needs. In contrast, the control group will engage in the same exercise approach but no VR interventions will be included.

Patients from the study group and the control group receive antidepressant or antianxiety pharmacotherapy as usual, excluding tricyclic antidepressants and antipsychotics. Treatment of concomitant somatic diseases will be carried out as before.

The procedure's effectiveness will be evaluated by measuring anxiety and depression levels using HADS and STAI during the 6th and 12th weeks of the program and in the 4th week after the program concludes. The 6MWT test will be administered in the 12th week.

The main objective of the study is to compare the reduction in depressive and anxiety symptoms between the study group and the control group. Additional objectives include examining the differences in the persistence of improvement and the time taken to achieve improvement between the two groups.

## 3. Discussion

Reviews published to date have concluded that physical activity can help prevent future episodes of depression in the general population. Proposed explanations include neuroendocrine and inflammatory responses to exercise and long-term brain adaptations like changes in the neural architecture. Researchers have also suggested that psychosocial and behavioral factors may play an essential role in the healing process, including positive self-perception changes, understanding of the physiological body reactions and improved body image, expanded social interactions, and developing personal coping strategies. [27] Metanalysis from 2022 indicates substantial mental health benefits can be already achieved when keeping physical activity levels below the WHO recommendations, with some additional benefits for meeting the minimum target. [28] Combining medication with exercise has been shown to have significant effects on depressive symptoms. In particular, adding exercise to antidepressant treatment mainly impacts the core symptoms of depression. In some groups of patients, exercise-based treatment programs can be as effective as those achieved with pharmacotherapy. [29] According to NICE guidelines, patients experiencing less severe depression have several first-line treatment options available, including exercise among cognitive behavioral therapy (CBT), counseling, and psychotherapy. [30] Unfortunately, these interventions are often underutilized in clinical practice, primarily due to a lack of knowledge among clinicians about how to prescribe exercise and the environmental constraints they face, such as insufficient dedicated spaces in healthcare facilities and a lack of equipment. [31] Most evidence indicates that primarily aerobic training—though research on resistance training is limited—can improve anxiety-related outcomes and

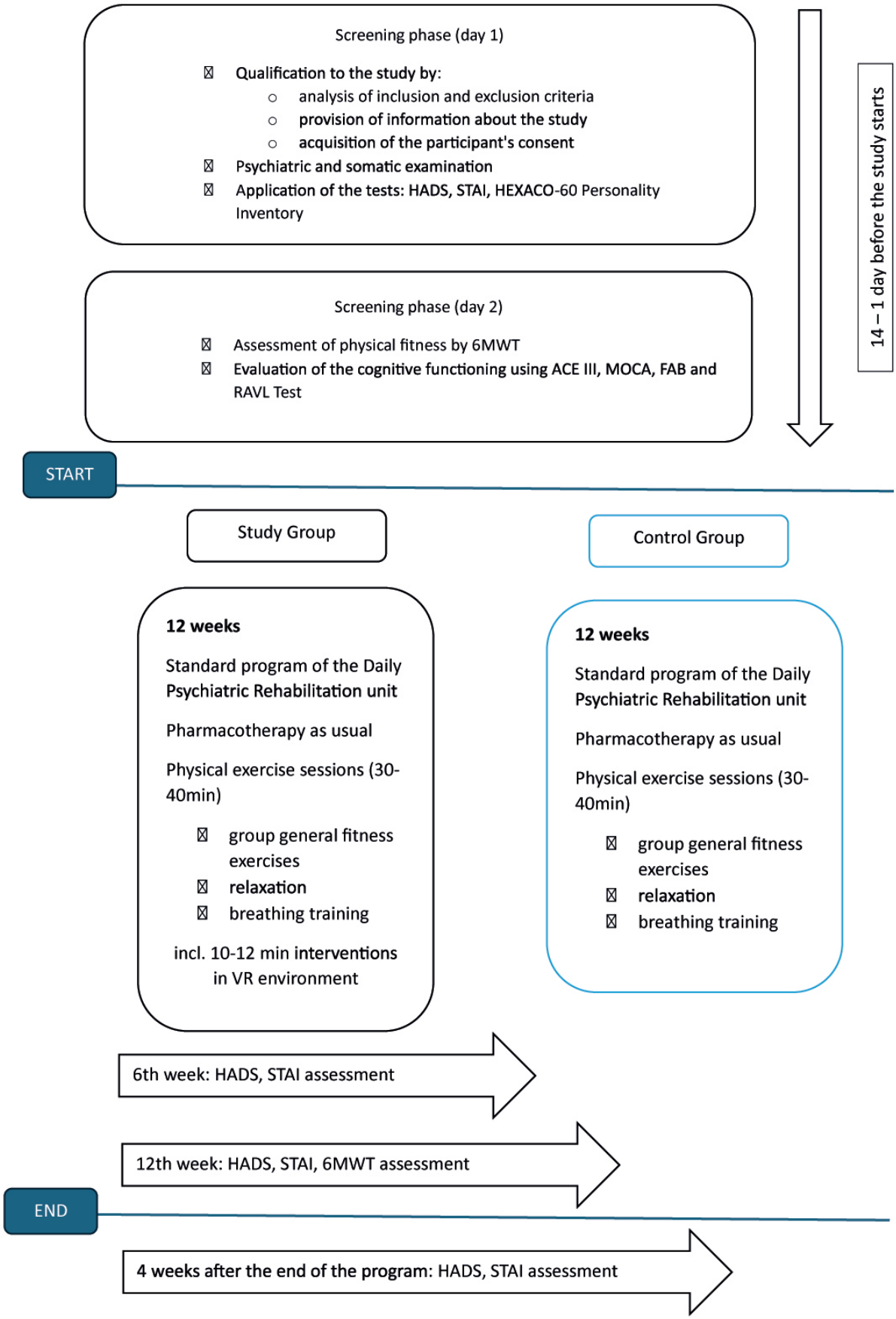


*Fig.1 Subsequent stages of the experiment*

decrease anxiety sensitivity. However, some studies suggest that these benefits are maintained only in individuals who continue to exercise after discontinuing active treatment. [32]

Exposure to nature, breathing exercises, mental imagery, progressive muscle relaxation, and mindfulness are commonly used interventions to reduce stress in routine mental health care support programs. Several studies have specifically investigated the effects of VR relaxation on stress levels, both in healthy individuals and those with psychiatric conditions, primarily through exposure to VR natural environments. A 2021 study indicated that VR relaxation immediately reduced negative emotional states and improved positive emotional states in patients receiving outpatient psychiatric treatment. [33] While the mechanisms behind these effects are not yet fully understood, it is likely that the VR experience distracts users from negative thoughts and stimuli. VR relaxation has potential as a low-intensity intervention to promote relaxation and alleviate stress in adults with mental health conditions, particularly those dealing with anxiety and stress-related issues. However, it is important to note that existing research primarily includes small clinical samples of working-age adults, predominantly female participants, and individuals with anxiety disorders or stress-related problems. Consequently, the number of studies on other diagnoses is insufficient to draw broad conclusions. [34] Numerous studies support the idea that VR can effectively alleviate negative feelings while enhancing cognitive abilities in older patients. Published research shows improvements in areas such as visual memory, linguistic fluency and expression, and physical engagement, along with positive emotional outcomes like feelings of relief. [35] A meta-analysis conducted in 2021 also suggests that VR exergames can positively impact cognition, memory, and depression among older adults. [36] However, considering that older individuals often experience decreased cognitive ability due to mental deterioration, VR therapy may sometimes lead to further discomfort and challenges. Additionally, a lack of technological understanding and physical limitations can make older individuals apprehensive about using VR, posing barriers to its effective implementation as a therapeutic intervention. [37]

Currently, there is limited research that systematically evaluates the role of personality in VR therapy. A study conducted in 2021 assessed whether personality traits influence VR sickness symptoms. The results confirmed that individuals with higher emotionality scores tend to experience greater sickness, and there was a correlation between the personality trait of neuroticism and motion sickness. [38]

## 4. Conclusions

Targeting a subpopulation of patients who are suffering from depressive and anxiety disorders and analyzing the factors influencing their treatment will enable us to offer virtual reality therapy to those who are most likely to benefit from it.

## Conflict of interest

The authors have declared no conflict of interest.

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