### USING VIRTUAL REALITY TO MANAGE STRESS IN CHILDREN AND YOUNG ADULTS

#### Ph.D. thesis

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#### 1. Introduction

The rising prevalence of psychological stress highlights the urgent need for innovative and effective interventions. This dissertation investigates the potential of virtual reality (VR) technology as a tool for managing stress, particularly in children and young adults. The introduction chapter explores the theoretical background of stress, its physiological and psychological mechanisms, current assessment and treatment methods, and the potential of VR in medical settings with special emphasis on acute stress and mindfulness-based interventions.

Physiologically, stress affects multiple organ systems. Acute stress activates the SAM and HPA axes, leading to increased heart rate, blood pressure, and cortisol release. Chronic stress causes persistent neuroendocrine dysregulation, which in turn promotes inflammation, cardiovascular disease, gastrointestinal issues, immunosuppression, and musculoskeletal problems. Neurologically, prolonged stress impairs brain areas such as the hippocampus and prefrontal cortex, affecting memory, executive functioning, and emotional regulation. Stress is closely linked with the pathogenesis of depression and anxiety, with shared neurobiological and cognitive mechanisms.

Virtual reality offers a novel approach to psychological treatment. VR systems generate immersive, interactive 3d environments that create a strong sense of presence—the feeling of "being there". This experience enhances emotional engagement, attention, and learning. VR enables safe, repeatable simulations and can be personalised to individual needs. Despite potential side effects such as cybersickness, visual strain, and rare contraindications (e.g. photosensitive epilepsy or psychosis), VR is generally safe, and its long-term cost-effectiveness may surpass traditional therapeutic methods.

In healthcare, VR is used in diverse contexts including medical training, emergency response simulations, pain

management, rehabilitation, and mental health treatment. In exposure therapy, VR has proven effective for phobias and post-traumatic stress disorder. In child psychiatry, VR is increasingly being used for diagnostic and therapeutic purposes. Studies show promising results in reducing symptoms of generalised anxiety disorder and social anxiety disorder using VR relaxation or exposure.

The application of VR in managing stress in medical settings is of growing interest. A particularly innovative area is the integration of VR with mindfulness-based interventions. Traditional mindfulness practices such as meditation and breathing exercises have been adapted to virtual environments, offering immersive experiences that minimise external distractions and facilitate focus. Several pilot studies have demonstrated that VR-based mindfulness can reduce anxiety, elevate mood, and improve emotional regulation, often outperforming video or desktop-based interventions. These findings are especially relevant for populations who may find traditional mindfulness techniques inaccessible or challenging to engage with.

Medical procedures such as chemotherapy and diagnostic imaging often provoke significant stress responses in both children and adults. These stress reactions may adversely impact treatment adherence, increase the need for sedation or analgesia, and compromise the quality of care. VR has been shown to mitigate these effects by providing calming, immersive environments that distract patients from anxiety-inducing stimuli. For example, several randomised controlled trials have shown that VR use during chemotherapy can reduce anxiety, pain, fatigue, and even alter time perception, making the procedure more tolerable. Some studies have reported positive physiological changes, such as reductions in blood pressure and heart rate, associated with VR use. In the context of MRI procedures, stress is particularly problematic in paediatric

populations. Claustrophobia and discomfort can lead to scan failure or the need for general anaesthesia (GA), which carries additional risks and costs. Research indicates that adequate preparation, including VR simulations of MRI environments, can reduce anxiety and improve compliance. Preliminary studies suggest that VR may lower the incidence of GA during MRI, although larger-scale trials are required to confirm these findings.

Early evidence suggests that VR is a promising tool for mitigating stress in clinical settings. Its ability to create engaging, controlled environments has the potential to revolutionise stress management in both paediatric and young adult populations. This dissertation aims to systematically explore these possibilities and to establish the scientific basis for integrating VR into standard care practices. This dissertation focuses on three original research projects evaluating VR's impact on stress reduction:

Project I. compares VR-based mindfulness interventions to tablet-based meditation among young adults. Project II. examines the effect of VR on children undergoing chemotherapy, assessing both psychological and physiological markers. Project III. investigates whether VR preparation can reduce pre-MRI anxiety and the need for general anaesthesia in children. A randomised controlled trial explores both children's and parents' stress responses, aiming to improve procedural compliance and comfort.

### 2. Objectives

Our research focuses on the stress-reducing effects of VR technology among children and young adults. We conducted three studies examining the relationship between VR and stress. First, we studied the effects of mindfulness-based virtual experiences among young adults (Project I.), and then we conducted a study among children with cancer undergoing chemotherapy (Project II.). Finally, our research centred on reducing the stress associated with MRI examinations in children (Project III.).

## Project I. – Effects of a VR-based mindfulness exercise on young people

While the number of studies investigating VR-based mindfulness interventions is growing, very few have directly compared VR with other digital modalities, such as tablet or desktop devices. Most notably, prior comparative studies used between-subject designs with limited outcome scopes. In contrast, our study used a within-subject design to compare VR and tablet-based mindfulness, reducing interindividual variability. It uniquely combined psychological, physiological, and time perception measures to assess immersion, flow state and emotional impact, offering a more comprehensive view of the user experience than prior studies.

The first study evaluated and compared the effectiveness of mindfulness exercises delivered via a VR headset and a tablet. We hypothesised that the VR condition contributed to a significant reduction in anxiety compared to the tablet condition. Additionally, we investigated whether VR would promote greater parasympathetic dominance reflected in lower HR, stabilised body temperature, and reduced EDA both during and after the intervention. Finally, we expected that participants immersed in the VR experience would perceive the duration of the exercise as shorter than its actual length.

# Project II. – The impact of VR on children undergoing chemotherapy

To date, very few studies have explored the application of VR for stress reduction during paediatric chemotherapy. Among those, none to our knowledge has used a within-subject design, which significantly reduces noise from between-subject variability arising from different diagnoses and temperament. Another novel aspect is the inclusion of physiological data, such as EDA and peripheral temperature, which offer objective insights into stress response. The VR content was also custom-developed, which may maximise the stress reduction effect of VR in phase II.

Our second study investigated the impact of VR in chemotherapy-treated children. It had two phases; the first phase examined the effects of an interactive VR experience and a mobile phone condition through a crossover design on multiple psychological and physiological variables during chemotherapy, assessing its potential to enhance patient well-being within a clinical context. We hypothesised that VR sessions would reduce anxiety, nausea, and fatigue while also improving mood during chemotherapy. Additionally, we anticipate that VR would attenuate sympathetic nervous system activity, as evidenced by reductions in HR, SBP, and EDA.

A crossover design was again utilised in the second phase of the investigation. We developed a custom-made VR experience and compared it to the VR experience used in Phase I. We hypothesised that the specifically developed VR experience would reduce anxiety, HR, EDA, and peripheral temperature more effectively than a freely available VR game.

## Project III. – Efficacy of a VR-based simulation in preparing children for MRI examinations

Most existing studies on MRI preparation in children have been limited by small sample sizes, lack of randomised controlled designs, and implementation in experimental settings. Furthermore, while passive interventions such as videos, role play, or mock scanners are commonly used, immersive virtual reality tools remain underexplored.

In contrast, a randomised controlled trial was designed to evaluate the efficacy of a VR-based preparatory approach in children before MRI examinations. We hypothesised that a smaller proportion of children in the VR group would require anaesthesia for MRI compared to those in the booklet and control groups. Furthermore, we expected that children in the VR group would show more significant improvements in fear, mood, and distress and a higher level of familiarity with the MRI procedure. We also anticipated a stronger preference for the VR intervention among children compared to the booklet and control groups and an increased willingness among VR group participants to undergo future MRI scans. Additionally, we hypothesised that the VR intervention has the potential to reduce the required dose of anaesthesia in comparison to the control groups.

#### Methods

### Project I. – Effects of VR-based mindfulness on young adults

Project I evaluated the effects of a VR-delivered mindfulness session versus a tablet-based equivalent on physiological and psychological outcomes in young adults (N=50, aged 18–30). A randomised crossover design ensured each participant received both interventions in a counterbalanced sequence. Sessions consisted of a 20-minute guided meditation using the Guided Meditation VR application or an identical audio-visual experience delivered via tablet.

Participants wore the Empatica E4 wristband throughout each session, allowing continuous measurement of HR, EDA, and skin temperature. State anxiety was assessed pre- and post-session using the STAI-Y, and participants' perception of time duration was recorded post-intervention. Data processing and analysis were conducted using repeated-measures ANOVA, paired t-tests.

# Project II. – The impact of VR on children undergoing chemotherapy

Project II. investigated whether immersive VR experiences can mitigate stress-related responses in children receiving chemotherapy. Participants were hospitalised patients aged 8–18 years at the Semmelweis University Paediatric Centre oncology units. Across two phases (N=35 in Phase I., N=30 in Phase II.), a crossover design was implemented, with each child participating in both experimental and control conditions. In Phase I., the experimental intervention featured A Night Sky, a commercially available VR game, and the control condition was a mobile game. In Phase II., we compared a custom-designed VR game tailored for hospitalised children (OncoVR game) and the experience which was used in Phase I.

Sessions were delivered using Samsung Gear VR and Oculus Go devices. In both phases, physiological parameters

(heart rate [HR], electrodermal activity [EDA], blood pressure [BP], and peripheral temperature) were recorded pre- and post-intervention. Phase I. employed manual BP monitors and Obimon EDA sensors, while Phase II. used the Empatica E4 wristband for continuous physiological monitoring. Psychological data were collected using an 11-point Likert scale in Phase I. and the State-Trait Anxiety Inventory (STAI-Y) in Phase II. Data analysis included repeated-measures ANOVAs and ordinal logistic regression, accounting for crossover design and individual variability.

## **Project III.** – Efficacy of a VR-Based simulation for preparing children for MRI examinations

Project III. employed a three-arm randomised controlled trial to evaluate the effectiveness of a custom-built VR experience in reducing anxiety and the need for anaesthesia use among children undergoing MRI scans. Participants (ages 4–18 years) were recruited from Semmelweis University's Paediatric Centre and randomly assigned to one of three groups: VR intervention, active control (educational booklet), or passive control (standard verbal preparation).

The VR experience was designed to simulate an MRI environment while incorporating acceptance-based coping techniques. The session duration varied (16–25 minutes), depending on individual needs. Data were collected at three time points using visual analogue scales (VAS) assessing nervousness, fear, mood, and familiarity. Parental responses and their evaluations of their child's emotional state were also recorded. Anaesthesia usage and medication dosages were obtained from hospital records.

Logistic regression was used to compare anaesthesia needs across groups. ANCOVA models and post-hoc tests assessed the effects of the intervention. This is an ongoing study; we added an interim analysis that included data collected between November 2023 and November 2024.

#### Results

### Project I. - Mindfulness-Based VR in Young Adults

Fifty participants (mean age = 23.02 years, SD = 1.92) completed both VR and tablet-based mindfulness sessions. A significant main effect of time was found on STAI-Y anxiety scores (F(1,48) = 164.47, P < .001,  $\eta^2$  = 0.23), indicating reduced anxiety in both conditions. However, no significant effect of condition (F(1,48) = 0.76, P = .39) or interaction (F(1,48) = 0.06, P = .81) was found.

A sign test showed that participants underestimated session time significantly more often in the VR condition (P = .006), indicating stronger immersion, whereas no significant difference was observed in the tablet condition (P = .39).

Repeated measures ANOVA indicated no significant condition or interaction effects for HR (F(1,45) = 1.31, P = .26), EDA (F(1,46) = 0.007, P = .93), or body temperature (F(1,46) = 3.33, P = .07). However, session effects were significant for HR (F(2,90) = 10.58, P < .001,  $\eta^2$  = .03) and body temperature (F(1.09,50.36) = 60.93, P < .001,  $\eta^2$  = 0.09). Post-hoc tests confirmed reduced HR during the session (P < .001) and increased body temperature pre-to-post session (P < .001).

## Project II. – The impact of VR on children undergoing chemotherapy

Phase I.

Data from 29 children (mean age = 15.28 years, SD = 2.44) were analysed. A significant time-by-condition interaction was observed for happiness (F(1,28) = 10.56, P = .003,  $\eta^2$  = 0.031) and joy (F(1,28) = 6.68, P = .015,  $\eta^2$  = 0.01). Post-hoc tests confirmed significant improvements in happiness (P < .001, MD = 22.21, 95% CI = [11.39, 33.03]) and joy (P = .003, MD = 16.59, 95% CI = [6.09, 27.08]) in the VR condition.

Fear showed a significant main effect of condition  $(F(1,28) = 4.78, P = .037, \eta^2 = 0.029)$ , with higher fear levels before the VR intervention (P = .005), but no significant difference post-intervention (P = .276).

Anxiety and patience exhibited main effects of time only (anxiety: F(1,28) = 11.43, P = .002,  $\eta^2 = 0.03$ ; patience: F(1,28) = 6.66, P = .015,  $\eta^2 = 0.019$ ), with significant within-condition improvements. No significant effects were found for nervousness or alertness.

For physiological outcomes, EDA showed a significant main effect of time (F(1,28) = 7.16, P = .012,  $\eta^2$  = 0.008) and a time-by-condition interaction (F(1,28) = 4.97, P = .034,  $\eta^2$  = 0.008). Post-hoc tests showed a significant reduction in EDA in the control condition (P = .005, MD = -10.2, 95% CI = [-17.03, -3.32]), but not in the VR condition (P = .993). No significant changes were detected in heart rate (F(1,28) = 0.71, P = .407) or systolic blood pressure (F(1,28) = 1.51, P = .230).

Ordinal regression models revealed no significant effects of condition on changes in pain ( $\beta$  = 0.31, P = .698, OR = 1.37, 95% CI = [0.28, 7.53]) or nausea ( $\beta$  = -0.14, P = .810, OR = 0.87, 95% CI = [0.26, 2.81]).

#### Phase II.

Data from 19 children (mean age = 14.5 years, SD = 2.1) were analysed. A significant main effect of time was found for STAI-Y anxiety scores (F(1,18) = 25.06, P < .001,  $\eta^2$  = 0.097), with no significant effect of condition (F(1,18) = 0.226, P = .640) or time-by-condition interaction (F(1,18) = 1.437, P = .246). Post-hoc tests revealed anxiety levels decreased significantly in both groups (custom-developed VR: P = .001; control VR: P < .001).

A two-way ANOVA showed no significant effect of repeated exposure to VR on anxiety reduction (condition: F(1,34) = 0.754, P = .391; occasion: F(1,34) = 0.089, P = .767; interaction: F(1,34) = 0.789, P = .381).

Peripheral temperature showed a significant main effect of time (F(2,36) = 12.24, P < .001,  $\eta^2$  = 0.037), with a post-hoc increase observed in the control VR condition (P = .016), but not in the custom VR group (P = .213). No significant effects were observed for EDA (F(1,18) = 1.963, P = .146) or HR (F(1,18) = 0.478, P = .621).

## **Project III.** – Efficacy of a VR-Based simulation for preparing children for MRI examinations

A total of 740 children were pre-screened until December 2024, out of which 581 were excluded due to not meeting the inclusion criteria. The most common reasons for exclusion included being outside the age range (n=415), intellectual disability (n=74), and hearing or visual impairments (n=65). Additional exclusion criteria included epilepsy (n=13), craniofacial abnormalities (n=10), other unspecified reasons (n=3), and insufficient fluency in Hungarian (n=1). This resulted in 159 eligible patients, of whom 38 were further excluded due to declined participation (n=21) or insufficient data collection (n=17). 120 participants were enrolled and randomised into three study groups: VR group (n=36), booklet group (n=40), and control group (n=45).

Interim data from 120 children (mean age = 6.0 years, SD = 2.06) were analysed. Multivariate logistic regression revealed that participants in the booklet condition had significantly higher odds of requiring anaesthesia compared to the control group (OR = 3.84, 95% CI = 1.24, 13.17, P = .024). No significant difference was found for the VR group (OR = 2.05, 95% CI = 0.67, 6.67, P = .218).

Linear regression found no significant effects of condition on willingness to undergo future MRI (booklet:  $\beta = 1.737$ , P = .867; VR:  $\beta = -2.389$ , P = .817). Repeated measures ANOVA showed a significant main effect of time on children's anxiety (F(2,166) = 3.43, P = .034,  $\eta^2 = 0.039$ ), with post-hoc comparisons indicating a decrease from T0 to T1 (P = .039).

Parental anxiety also decreased significantly over time (F(2,196) = 6.37, P = .002,  $\eta^2 = 0.06$ ), particularly from T0 to T2 (P = .024).

Familiarity with MRI improved significantly over time  $(F(2,160)=7.03, P=.001, \eta^2=0.07)$ , with a significant time-by-condition interaction  $(F(4,160)=3.73, P=.006, \eta^2=0.07)$ . At T1, familiarity was significantly higher in the VR group than in the control (P=.02), and at T2, the booklet group also showed significantly greater familiarity compared to the control (P=.003). No significant main or interaction effects were found for mood or fear.

#### Conclusion

Stress is a complex process with significant physiological and psychological impacts. The findings of this thesis highlight the pressing need for innovative interventions to mitigate stress. VR emerges as a promising, state-of-the-art tool for stress management in clinical settings, offering immersive and engaging experiences that extend beyond traditional psychological and pharmacological methods.

Project I. explored the application of VR in mindfulnessbased interventions for young adults. The results showed that VR significantly enhanced time perception, creating a sense of accelerated time passage during meditation sessions. This effect has implications for improving long-term adherence to mindfulness practices. Physiological measurements, including reduced heart rate and increased peripheral temperature, confirmed the calming effects of VR-mediated mindfulness, indicating parasympathetic nervous system dominance. although the reduction was similar to that of the control group. No side effects were reported by participants. These findings demonstrate the potential of VR to enrich meditation experiences safely, reduce stress, and promote mental wellbeing in young adults.

In Project II., which investigated the impact of VR on children undergoing chemotherapy, VR interventions demonstrated notable benefits for emotional states. Children reported increased happiness and joy following VR experiences, while anxiety reduction was comparable between VR and mobile-based interventions. Fearfulness decreased, and patience improved after interventions, potentially influenced by the games and experimenter interactions. VR did not cause significant cybersickness, although one child withdrew due to this issue, and no changes were observed in pain, tiredness, or nausea. In Phase II., the custom-developed VR experience produced an anxiety reduction effect similar to the control group

(standard VR game). Physiological findings showed a decrease in peripheral temperature, indicating reduced stress, while other measures, such as HR and EDA, remained unaffected. Importantly, VR was well-received, easily integrated into clinical routines, and supported by children, parents, and staff. These findings suggest that VR is a feasible tool for mood enhancement and stress management in paediatric oncology.

Project III. evaluated the efficacy of a VR-based preparatory method for children undergoing MRI scans. Since this is only an interim analysis, no definitive conclusions can be drawn. However, the preliminary findings suggest that the implementation of VR preparation is feasible in real-world clinical settings. Furthermore, VR may positively influence children's anxiety levels and familiarity. These findings may validate the psychological benefits of VR-based preparation in a real-world medical diagnostic context, demonstrating its potential to enhance the MRI experience for children and their parents.

Across all projects, VR was shown to be a practical and well-tolerated tool, with mild and transient side effects reported in a minority of participants. The findings highlight the of integrating VR feasibility into clinical settings. complementing traditional stress management methods and enhancing patient experiences. Several significant findings have been achieved regarding the role of VR in stress management in adults. Our current study contributes to the growing body of research on paediatric populations, providing positive outcomes on its practical applications. Future research should prioritise large-scale, multi-centre, randomised controlled trials focusing on specific clinical populations (e.g., paediatric oncology patients or children before a medical procedure) to validate the efficacy of VR interventions in reducing psychological and physiological variables. Longitudinal studies are also needed to assess the sustained impact of VR on stress reduction, providing

insights into long-term benefits and the necessity of repeated sessions. Developing personalised VR content tailored to age, cultural background, and specific needs could enhance engagement and outcomes.

### Bibliography of the candidate's publications

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