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Integrating Neurofeedback and Virtual Reality to Enhance Exposure Therapy for Anxiety and Food Aversion

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ABSTRACT

In recent years, integrating virtual reality (VR) with neurofeedback (NF) and biofeedback methods, such as electroencephalography (EEG) and electrocardiography (ECG), has shown promise in enhancing therapeutic interventions. This research explores the potential of a combined EEG-ECG-VR system designed to support neurofeedback-based therapies aimed at managing anxiety, stress, and food aversion. Leveraging the immersion and adaptability of VR environments, the system seeks to offer a controlled setting that engages patients in exposure tasks while allowing real-time monitoring of brain and heart activity.

The proposed system was developed around a VR-based serious game, Pikita VR Quest, initially intended for children with food aversion and verified with adult participants to refine the system's framework. The primary goals were to assess the efficacy of NF in modulating brain activity in VR environments and to determine the feasibility of concurrent EEG and ECG monitoring within these immersive settings.

To evaluate the system, participants were exposed to VR sessions while undergoing EEG and ECG monitoring. Data were collected on critical biomarkers, the N200 and P300 components, to assess cognitive responses related to attention, relaxation, and stress. The collected EEG and ECG data provided insights into the effects of VR immersion on neural activity and physiological responses. Additionally, pre- and post-session comfort surveys helped gauge participant acceptance of the technology.

Preliminary results demonstrated that the VR-based neurofeedback system facilitated meaningful engagement and contributed to adaptive responses, particularly in stress-related scenarios. Analysis of EEG and ECG data further validated the potential of VR to support dynamic, real-time adjustments in therapeutic tasks, suggesting a promising avenue for clinical applications. Future work will focus on validation and refining the system for pediatric use, optimizing the interface, and evaluating long-term therapeutic effects in populations with specific therapeutic needs.

Keywords: Neurofeedback, Biofeedback, Virtual Reality, Serious Games, Electroencephalography

RESUMO

Nos últimos anos, a integração da realidade virtual (VR) com métodos de neurofeedback (NF) e biofeedback, como a eletroencefalografia (EEG) e a eletrocardiografia (ECG), tem demonstrado potencial em melhorar intervenções terapêuticas. Esta investigação explora o potencial de um sistema combinado EEG-ECG-VR, desenvolvido para apoiar terapias baseadas em neurofeedback, visando a gestão de ansiedade, stress e aversão alimentar. Tirando partido da imersão e adaptabilidade dos ambientes de VR, o sistema procura oferecer um cenário controlado que envolve os pacientes em tarefas de exposição, permitindo ao mesmo tempo o monitoramento em tempo real da atividade cerebral e cardíaca.

O sistema proposto foi desenvolvido em torno de um jogo sério baseado em VR, o Pikita VR Quest, inicialmente destinado a crianças com aversão alimentar, mas verificado com participantes adultos para refinar o enquadramento do sistema. Os objetivos principais foram avaliar a eficácia do NF na modulação da atividade cerebral em ambientes de VR e determinar a viabilidade do monitoramento simultâneo de EEG e ECG nesses cenários imersivos.

Para avaliar o sistema, os participantes foram expostos a sessões de VR enquanto realizavam monitorização de EEG e ECG. Foram recolhidos dados sobre biomarcadores críticos, incluindo os componentes N200 e P300, para avaliar respostas cognitivas relacionadas com atenção, relaxamento e stress. Os dados de EEG e ECG recolhidos forneceram insights sobre os efeitos da imersão em VR na atividade neural e nas respostas fisiológicas. Adicionalmente, questionários de conforto pré e pós-sessão ajudaram a avaliar a aceitação dos participantes relativamente à tecnologia.

Os resultados preliminares demonstraram que o sistema de neurofeedback baseado em VR facilitou um envolvimento significativo e contribuiu para respostas adaptativas, especialmente em cenários relacionados com o stress. A análise dos dados de EEG e ECG validou ainda mais o potencial da VR para suportar ajustes dinâmicos e em tempo real em tarefas terapêuticas, sugerindo uma via promissora para aplicações clínicas. Trabalhos futuros centrar-se-ão em validar e aperfeiçoar o sistema para uso pediátrico, otimizar a interface e avaliar os efeitos terapêuticos a longo prazo em populações com necessidades terapêuticas específicas.

Palavras-chave: Neurofeedback, Biofeedback, Realidade Virtual, Jogos Sérios, Eletroencefalografia

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ACRONYMS

3D	Three-dimensional
6DoF	Six Degrees of Freedom
ABM	Attentional Bias Modification
ADD	Attention Deficit Disorder
ADHD	Attention Deficit Hyperactivity Disorder
AI	Artificial Intelligence
ANS	Autonomic nervous system
AR	Augmented Reality
ARFID	Avoidant/Restrictive Food Intake Disorder
ASD	Autism Spectrum Disorder
AV	Augmented Virtuality
BCI	Brain-computer interfaces
BF	Biofeedback
BRV	Breathing Rate Variability
CBT	Cognitive Behaviour Therapy
ECG	Electrocardiogram
EDA	Electrodermal Activity
EEG	Electroencephalogram
ERPs	Event-related Potentials
FCUL	Faculty of Sciences of the University of Lisbon
fMRI	Functional Magnetic Resonance Imaging
GABA	Gamma-Aminobutyric Acid
HMD	Head Mounted Display
HPA	Hypothalamic-pituitary-adrenal
HRV	Heart Rate Variability
IBEB	Institute of Biophysics and Biomedical Engineering

ICA	Independent Component Analysis
ICF	International Classification of Functioning
MEG	Electromyography
ML	Machine Learning
MR	Mixed Reality
NFB	Neurofeedback
PFC	Prefrontal Cortex
PNS	Parasympathetic Nervous System
PTSD	Post-traumatic Stress Disorder
qEEG	Quantitative Electroencephalogram
SCP	Slow Cortical Potentials
SMR	Sensorimotor Rhythm
SNS	Sympathetic Nervous System
TMS	Transcranial Magnetic Stimulation
VR	Virtual Reality
VRET	VR-based Exposure Therapy
WCF	Warp Correlation Filter
XR	Extended Reality

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INTRODUCTION

Health and medical therapies are undergoing a transformative shift, fueled by rapid technological advancements that are redefining traditional care models. Emerging tools such as Virtual Reality (VR), artificial intelligence (AI), and machine learning (ML) are paving the way for more personalized and effective treatment strategies across a wide range of clinical conditions. These technologies not only enhance the precision of diagnoses and the efficiency of interventions, but also introduce innovative methods for patient engagement and monitoring. In particular, VR has revolutionized healthcare by providing immersive and interactive environments that enable clinicians to simulate scenarios and tailor treatments to individual patient needs. This integration of cutting-edge digital solutions represents a pivotal moment in healthcare innovation, offering both opportunities to elevate patient care and challenges in balancing technological reliance with ethical and privacy concerns.

These technological advancements have brought about significant improvements in healthcare, including enhanced diagnostics, more efficient therapies, and a reduction in medical errors. However, they also raise important ethical concerns, including issues related to the privacy and security of patient data, as well as the potential over-reliance on technology in clinical decision-making. These challenges must be carefully considered to ensure that the integration of new technologies enhances, rather than compromises, patient care.

Among these emerging technologies, VR-based applications have shown remarkable potential in treating neurological and psychological conditions, such as anxiety and food aversion. These conditions, when left untreated, significantly hinder patients' quality of life and recovery. The ability to create safe, immersive, and controlled environments for therapeutic exposure through VR addresses a critical gap in traditional approaches. Furthermore, the integration of physiological monitoring tools, such as Electroencephalography (EEG) and Electrocardiography (ECG), enables real-time insights into neural and cardiac activity, providing clinicians with valuable data to tailor interventions. This research is motivated by the need to explore and develop a system that combines these technologies to optimize therapeutic outcomes, particularly for stress-induced and food-related disorders. Thus, understanding the interplay between these innovative tools and their impact on patient care is vital.

1.1 Motivation

The motivation for this research lies in enhancing healthcare quality through innovative tools for patient data analysis and ethical therapeutic approaches. It addresses the growing need for personalized strategies in treating neurological and psychological conditions, such as anxiety and food aversion, which often require adaptable solutions beyond traditional exposure therapy.

Integrating neurofeedback with VR-based gamified applications offers novel ways to improve patient engagement and therapeutic outcomes. EEG and ECG provide real-time insights into brain and heart activity, enabling a controlled and tailored approach to therapy. Serious games further enhance engagement by creating safe, interactive spaces that reduce psychological barriers, particularly in pediatric populations.

This research leverages existing platforms to generate data that informs treatment strategies and supports personalized clinical decisions. By focusing on the integration of EEG, ECG, and VR systems, it aims to bridge technological innovation with therapeutic practice, enhancing the precision and accessibility of exposure therapy for anxiety and food aversion.

1.2 Context, Objectives and Research Questions

As previously highlighted, integrating digital technologies into therapeutic contexts needs the collection of diverse data types to create models that accurately reflect patient responses. This includes not only biological data, such as brain activity (EEG) and heart activity (ECG), but also behavioral and performance metrics gathered from the VR-based gamified applications. Additionally, subjective information provided through structured forms and surveys complements the objective data, capturing patient-reported outcomes, preferences, and comfort levels. Together, these data sources enable a comprehensive understanding of individual patients, incorporating factors beyond their conscious control and aligning therapeutic interventions with both their physiological and psychological profiles.

Furthermore, the integration of technologies such as AI and ML can play a pivotal role in advancing personalized healthcare. By using these technologies to generate digital twins, healthcare professionals could simulate different treatment scenarios and predict the outcomes for individual patients. These digital models could provide deeper insights into the patient's physiological responses, offering a more precise understanding of how they may respond to various treatments. Data generated from digital therapeutic tools, such as serious game-based virtual reality applications, would enable a more accurate simulation, as these platforms naturally collect data on patient performance, movement patterns, and other relevant factors.

Building on previous work by the team, a framework and web-based platform, PLAY, were conceptualized and developed [11]. PLAY is a multiuser platform designed to support patients, therapists, and clinics by providing tools for creating and managing serious games, as well as backend services for data handling and communication. The platform employs an HTTP REST API and WebSockets (WS) for real-time, bidirectional communication with external devices and applications, enabling seamless integration with Internet of Things (IoT) devices, external serious games, and other applications.

The PLAY platform also serves as a foundational component for a proposed Digital Twin framework—a virtual replica of the physical patient. This digital twin aims to enable comprehensive status assessments, scenario applications, simulations, and predictions, paving the way for personalized therapy [13]. By leveraging the capabilities of the PLAY platform, the team has worked toward a model that integrates serious game-based therapy with the unique physiological and behavioral data of individual patients, enhancing the personalization and effectiveness of therapeutic interventions.

Moreover, this research uses the Pikita VR Quest, which is a gamified VR-based application to tackle anxiety and food aversion in children, focusing on speech and occupational therapy [101].

The structure of Pikita is set up in PLAY using the Serious Games design tools. When a patient starts the application, the configuration for the game session is requested from PLAY. Each patient may have a distinct combination of game parameters and these can also change in different sessions to reflect the current patient needs. The game parameters are configured in the therapist interface and sent to Pikita.

Therefore, this research aims to explore the integration of biological data, specifically electroencephalogram (EEG) and electrocardiogram (ECG), to enhance the development of PLAY's digital twin framework. By leveraging these methods, the study seeks to capture data that are critical for evaluating and improving therapeutic performance, such as neurophysiological and physiological markers. The objective is to determine the most effective approach—whether using EEG, ECG, or a combination of both—for providing actionable insights that can refine and personalize the therapeutic process. The Pikita VR Quest application serves as the testbed for this investigation, offering a gamified VR-based application to apply and validate the use of EEG and ECG in real-time therapeutic scenarios.

In order to proceed with the objectives of this research, the following main research questions arose:

1. **RQ1.** How feasible is the application of neurofeedback using real-time EEG data to enhance patient outcomes, such as brain activity modulation, performance, and engagement, in therapeutic contexts involving VR-based gamified applications?

   The goal is to investigate whether neurofeedback using real-time EEG data can assist in modulating brain activity during therapy that employs VR-based gamified applications. This research seeks to determine how effectively neurofeedback can enhance patient performance and engagement in tasks designed to reduce anxiety or address food aversion within immersive, gamified virtual environments.

2. **RQ2.** How feasible and effective is the simultaneous integration of multiple technological devices (e.g., EEG and ECG) in therapeutic settings, considering potential impacts on patient comfort, data quality, and therapeutic outcomes?

   This research aims to evaluate the feasibility and effectiveness of integrating multiple technological devices, such as EEG and ECG, in therapeutic settings that involve VR-based gamified applications. It explores the impact of device integration on patient comfort, usability, and data quality. Specifically, the study examines whether the simultaneous use of multiple devices within confined therapy spaces introduces stress or discomfort, potentially hindering therapeutic outcomes, and whether such configurations are viable for reliable, real-time data acquisition.

3. **RQ3.** Under what circumstances is it necessary or beneficial to employ the integrated EEG-ECG-VR tool in therapy sessions, considering aspects such as patient stress, setup time, and session objectives?

   Given the complexity and potential time constraints associated with setting up multiple integrated devices, this research investigates the contexts in which the proposed EEG-ECG-VR tool is most beneficial. It seeks to identify scenarios where its use is critical for achieving therapeutic objectives, such as managing severe anxiety or food aversion, while considering the possibility of alternative or simplified setups for less intensive sessions. The study aims to establish guidelines for optimal tool usage, balancing therapeutic effectiveness with practical considerations like patient stress and session efficiency.

1.3 Contributions

This dissertation offers the following key contributions:

- Biological Data Acquisition System: A system was developed to collect essential biological data, enabling the monitoring of performance and progress in VR-based therapy through EEG, enhancing assessment of cognitive and emotional states.
- Technological Enhancement Framework: A framework was proposed to guide future improvements to the system, ensuring scalability and adaptability to clinical needs.
- Human-Factors Study: A two-phase usability study was conducted to validate the system, addressing challenges from the initial phase and refining the design for improved user experience and effectiveness.

  These contributions support the integration of neurofeedback and EEG into therapeutic practices, advancing patient treatment and engagement.

Furthermore, this research was submitted to the **32nd IEEE Conference on Virtual Reality and 3D User Interfaces (IEEE VR 2025)**, the premier international event for presenting research in virtual, augmented, and mixed reality. The poster paper "Integrating Real-Time ECG and EEG to Improve VR-Based Interventions in Exposure Therapy" is under review.

1.4 Structure

This dissertation is organized into five main chapters with corresponding sub-chapters, a references section, and 10 appendices. A brief overview of each chapter is presented below:

- Chapter 2: Reviews essential concepts relevant to the research, including stress and anxiety disorders, pediatric eating disorders, autism spectrum disorder (ASD), various therapeutic approaches (like exposure therapy), the role of physical activity in mental health, virtual reality (VR), neurofeedback (NFB), and serious games.
- Chapter 3: Describes the materials, devices, and approaches used in the research, including the PLAY platform and Pikita VR Quest, biological analysis tools, and EEG and ECG monitoring setups. It also details the experimental setup and procedures for validating the approach.
- Chapter 4: Presents and analyzes the outcomes from the initial and validation tests, focusing on EEG and ECG data, comfort assessments, and overall system effectiveness. It includes insights on how these measurements support or refine the proposed therapeutic framework.
- Chapter 5: Suggests a practical framework for implementing the findings in therapeutic contexts, including neurofeedback integration, use of stress and anxiety tools, and specific recommendations for utilizing EEG, ECG, and VR in clinical settings.
- Chapter 6: Summarizes the findings, contributions, and limitations of the research, along with potential future directions to further integrate digital and biological data in therapeutic applications.

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BACKGROUND

In the context of this research, understanding the importance of interdisciplinarity is crucial. This project is inherently multidisciplinary, requiring exploration across diverse areas to enhance both the understanding and treatment of eating disorders and mental health. Interdisciplinarity not only deepens the study but also expands the scope for intervention, allowing for more comprehensive and effective approaches to emerging challenges.

A key focus of this study is the exploration of food aversion, stress, and anxiety, which are often interrelated and significantly affect an individual's health and quality of life. In severe cases, such as food phobia and malnutrition, identifying appropriate therapeutic approaches is essential for successful outcomes. A deep understanding of these disorders and their connections is vital for effective intervention.

Additionally, technologies such as virtual reality, serious games, and other innovations present unique opportunities for advancing research and intervention in mental health and eating disorders. Understanding their capabilities is key to developing accessible and effective treatments.

Finally, neurofeedback (NF), with its complexity and distinction from biofeedback, emerges as a promising tool in this research. Assessing its potential in treating eating disorders and mental health is a critical step in identifying innovative and effective therapeutic methods.

2.1 Stress and Anxiety Disorders

Stress and anxiety are often used interchangeably, though they are distinct yet interrelated. Stress is a natural physiological response to perceived threats or changes, triggering a state of alert in the body, which leads to the release of hormones like epinephrine and norepinephrine for quick responses. Prolonged exposure to stress can result in excessive cortisol production, leading to chronic stress, which is detrimental to health [31, 45, 65]. Stress can be caused by both real and perceived threats, and its symptoms include muscle pain, fatigue, headaches, irritability, and sleep disturbances [65]. The frontal lobe plays a key role in stress detection, with altered brain activity such as alpha asymmetry and high beta or theta activity indicating stress and anxiety states [65].

Anxiety, in contrast, is typically a psychological response to perceived threats with a low likelihood of occurring [31, 45]. It is categorized into state anxiety (a transient response to specific stressors) and trait anxiety (a predisposition to anxiety in various situations) [31, 45, 91, 132]. Anxiety is more common in women and individuals aged 18-29 [16, 52, 37, 60]. While both stress and anxiety can be protective in the short term, chronic or frequent activation of these responses can lead to significant mental health issues, including alterations in brain function.

2.1.1 Stress and anxiety in children

Childhood and adolescence are critical periods for physical and mental development, where stress and anxiety are common due to changing circumstances and perceptions. Factors such as environment, genetics, and personality traits contribute to the development of anxiety in children [14, 145, 78]. Anxiety disorders are the most common mental health issues in children, affecting up to 18% of youth, with subclinical anxiety affecting 40% [135]. Anxiety is more prevalent among children with special needs, such as those with autism spectrum disorder (ASD) or attention-deficit hyperactivity disorder (ADHD), and can impact their social interactions and therapy outcomes [39, 42, 82, 106].

The development of the prefrontal cortex (PFC) in children occurs more slowly than other regions involved in emotion and behavior, which may heighten the risk of anxiety if stress is not well-managed [147]. Early intervention, including cognitive-behavioral therapy (CBT), has been shown to reduce the long-term impact of anxiety disorders, particularly in children with chronic conditions like ADHD or ASD [66, 78, 100, 147, 72, 33, 83, 122]. Additionally, integrating caregiver support into treatment can enhance the effectiveness of interventions for younger children [114].

A comprehensive, multidimensional approach is essential for addressing anxiety in children and adolescents, incorporating environmental, biological, and social factors, and employing targeted therapeutic strategies to minimize the long-term effects of these disorders.

2.1.2 Biological Mechanisms in Anxiety Development

The brain remains a largely uncharted area, though certain regions are linked to anxiety when dysregulated, notably the hippocampus, hypothalamus, amygdala, and prefrontal cortex (PFC), which are central to emotional regulation and stress response [19, 104, 130].

Hormonal imbalances in well-being and stress hormones also contribute to anxiety. Key well-being hormones include serotonin, oxytocin, and dopamine, while cortisol, epinephrine, and norepinephrine regulate stress responses [48]. Gamma-aminobutyric acid (GABA) and glutamate further modulate these hormones; GABA inhibits neuronal activity, while glutamate excites it, maintaining essential neural balance for emotional regulation [77, 119]. Understanding these complex interactions informs effective interventions for anxiety disorders.

2.1.2.1 Hippocampus

The hippocampus, crucial for memory and spatial navigation, is highly sensitive to stress, with chronic stress impairing cellular regeneration and increasing glutamate, which can negatively affect learning and memory [56, 71, 104, 119]. Linked closely to the limbic system (including the thalamus, basal ganglia, hypothalamus, and amygdala), the hippocampus influences the hypothalamus in cortisol production, playing a central role in stress regulation [56]. The hypothalamic-pituitary-adrenal (HPA) axis, involving the hypothalamus, pituitary, and adrenal glands, mediates physiological stress responses. Dysregulation of the HPA axis elevates cortisol, potentially causing harm [117, 137].

2.1.2.2 Autonomic Nervous System

The autonomic nervous system (ANS) regulates involuntary stress responses and comprises the sympathetic nervous system (SNS), parasympathetic (PNS), and enteric systems [43, 153]. The SNS activates "fight-or-flight" responses, while the PNS facilitates recovery. The enteric system regulates reflexes and communicates with both SNS and PNS [153]. The ANS also assesses fear responses, such as heart rate and pupil dilation, by balancing SNS and PNS activity [19].

2.1.2.3 Amygdala

The amygdala, part of the limbic system, is crucial for fear perception and response, integrating inputs from the hippocampus and PFC for appropriate emotional reactions [64, 71, 94]. Dysfunction in the amygdala can impede learning from fearful experiences, increasing anxiety vulnerability [4]. During stress, high cortisol may impair hippocampus-amygdala communication, weakening emotional response and memory formation, while increased oxytocin in the amygdala can moderate fear [48, 104].

2.1.2.4 Prefrontal cortex

The prefrontal cortex (PFC) is considered the centre of personality and is essential for processing, comparing and reacting to external stimuli [69]. The development of an individual's personality characteristics is closely linked to the functions of the PFC, as it is responsible for decision-making, impulse control and social behaviour [69]. When there is damage to the PFC, significant impairments can occur, such as memory problems, difficulties in carrying out tasks and emotional disturbances.

In stressful situations, there is an increase in the levels of neurotransmitters such as dopamine, serotonin and norepinephrine in the PFC [111]. During stress, both the PFC and the amygdala release neurotransmitters that interact with each other, emphasising the functional connection between these two structures. Changes in the amygdala can affect the release of dopamine by the PFC, highlighting the complexity of emotional regulation and the stress response. Similar to the amygdala's response to chronic stress, the PFC also experiences a reduction in glutamate levels, which can contribute to difficulties in attention and concentration [119].

The role of oxytocin in controlling anxiety may be related to its action in the PFC, which may explain the differences in stress response observed between genders [104]. In the PFC, an increase in neuronal activity is also recorded during the execution of working memory tasks, which helps to maintain the temporary memory required to complete these tasks [110]. This activity, characterised by increased levels of 'spiking' (firing of neurons), is crucial for short-term retention of information and effective performance in complex cognitive tasks [110].

In addition, the PFC is fundamental for regulating emotions, controlling impulsive behaviour and planning future actions, allowing individuals to evaluate the consequences of two actions and make choices that are appropriate and beneficial [69]. Thus, the functional integrity of the PFC is essential for emotional well-being and adaptation to different life situations.

2.2 Paediatric Eating Disorders and Food Aversions

Paediatric eating disorders (PED) are characterized by inappropriate oral intake for the child's developmental stage, leading to medical, nutritional, psychosocial, and feeding difficulties [59].

The ideal progression of oral intake involves a gradual shift from breastfeeding or formula feeding to self-feeding with a variety of foods [59]. In children with developmental delays, feeding skills may be age-appropriate but not developmentally aligned, potentially resulting in a diagnosis of autism spectrum disorder (ASD) [59]. Distinguishing ASD from other eating disorders, like anorexia nervosa, involves the absence of body image disturbances in ASD diagnosis [59].

The International Classification of Functioning (ICF) model posits that disability arises when health issues interact with personal and environmental factors, causing activity limitations or participation restrictions [59]. PED can contribute to disability, especially when mealtime difficulties restrict participation in social settings such as day-care or schools [59]. However, culturally specific eating behaviors are not classified as PED unless dysfunction is present [59].

PED is influenced by four interrelated domains: medical, nutritional, feeding ability, and psychosocial. Issues in one domain often exacerbate others, leading to dysfunction [59]. These domains are outlined below.

Medical, nutritional, and psychosocial factors significantly impact feeding in children. Gastrointestinal issues, respiratory problems, cardiac conditions, and neurological deficits, including cerebral palsy and ASD, can all disrupt feeding [59]. Children with ASD often have restricted diets, leading to potential malnutrition or deficiencies, even with adequate macronutrient intake [59]. Feeding ability may be impaired by illness, injury, or developmental delays, especially with changes in food textures and utensils, and can result from sensorimotor issues, sensory hypersensitivity, or pharyngeal motor problems [59].

Psychosocial factors, such as developmental delays, mental health issues, and cultural expectations, can further disrupt feeding [59]. Disruptions may also arise from mealtime dynamics, including mismatched caregiver expectations, stress, and environmental distractions like television [59]. Psychosocial dysfunctions, such as learned food aversions, mealtime stress, and disruptive behaviors, are common in feeding disorders and can hinder progress to an age-appropriate diet [59]. Additionally, inadequate caregiver strategies, like force-feeding or limiting food variety, can worsen feeding difficulties [59].

Food aversion, distinct from selective eating, is marked by an intense reluctance to try new foods, often due to fear or past negative experiences [58, 96]. This avoidance can be classified as Avoidant/Restrictive Food Intake Disorder (ARFID) and is part of a broader spectrum of sensory aversions [96]. This behavior is often characterized by emotional reactions to unfamiliar foods, supporting the view of food aversion as a type of phobia [96].

Selective eating, on the other hand, refers to the persistent refusal to eat known foods, limiting both food variety and nutrient intake [96]. It is more common in young children and is often considered a developmental phase [58, 96].

The mechanisms behind food aversions involve a complex interplay of biological, psychological, and environmental factors [25, 58, 96]. Negative experiences during mealtimes can reinforce food aversions, shaping a child's perceptions of what foods are safe or acceptable [96]. Visual, olfactory, and tactile stimuli play a significant role in these perceptions, influencing the acceptance of food based on color, texture, and smell [140]. Food color, for example, can significantly affect taste perception, with certain colors linked to specific taste expectations (e.g., red for sweetness, green for sourness) [51, 88, 96].

Research also shows that food color intensity influences the perception of flavor and quality, with brighter, more saturated colors often associated with higher quality and tastier foods [88, 51]. This highlights the importance of visual factors in both food acceptance and therapeutic interventions for feeding disorders.

2.2.1 Underlying Factors of Food Aversion

Children's food preferences are shaped by genetic and environmental factors, including genetic predispositions, prenatal and early postnatal experiences, caregiver practices, and family dynamics [58, 96, 133].

Genetic Factors: Genetics influence food neophobia, with a hereditary component, particularly from mothers [96]. Food neophobia peaks between ages 2 and 6 and may resurface later in life. Traits like low openness and high anxiety are linked to higher neophobia [58, 96]. Genetic variations, such as in the TAS2R38 gene (related to bitter taste sensitivity), also affect preferences, with more sensitive individuals tending to prefer sweeter foods [25, 58]. Both genetics and home environment contribute to selective eating [25, 58].

Prenatal Influences: Maternal diet impacts later food preferences. Flavor exposure through amniotic fluid and breast milk increases acceptance of familiar tastes, while formula-fed infants may show reduced flavor acceptance [58, 25, 41].

Early Postnatal Experiences: Repeated exposure to diverse foods, especially fruits and vegetables, during early post-weaning stages promotes acceptance [58, 96]. Infants under 12 months are more open to new flavors, but this decreases with age, requiring multiple exposures for increased acceptance [58, 96].

Caregiver Feeding Practices: Caregiver behavior, such as positive modeling and involvement in meal preparation, influences children's food preferences, while pressure to eat can increase rejection and food anxiety [58, 96].

Environment: A diverse food environment at home encourages broader food acceptance, while limited exposure reinforces selective eating [25].

Food aversion, including picky eating and neophobia, can lead to nutritional deficiencies, with children avoiding nutrient-dense foods like vegetables and meats, potentially affecting growth and health [58, 96]. Neophobic tendencies may also lead to a preference for calorie-dense, low-nutrient foods, increasing the risk of chronic diseases [58].

For children with health conditions requiring specific diets, like food allergies or diabetes, neophobia complicates adherence [96]. While food neophobia's link to lower body weight is unclear, its impact on nutritional balance remains concerning [58, 96].

Children with autism spectrum disorder (ASD) are more likely to experience anxiety disorders, which affect their outcomes [82]. Kerns et al. (2021) found that anxiety was more common in children with ASD, often with unique fears not captured by traditional assessments [82]. Cognitive behavioral therapy (CBT) is a promising approach for managing anxiety in children with ASD [82, 83].

2.3 Current therapeutic approaches

The treatment of ARFID typically requires a multidisciplinary approach, involving a specialized team that may include pediatricians, child psychiatrists, therapists, nurses, nutritionists, and occupational therapists [30]. The complexity and multifaceted nature of ARFID necessitate collaboration among various healthcare professionals to provide comprehensive and effective intervention. Each team member plays a unique and complementary role in the treatment process, contributing their specific skills and expertise to address the individual needs of each patient.

2.3.1 Exposure Therapy

Eating disorders (EDs) are linked to significant medical, psychosocial complications, and an increased risk of mortality. They often co-occur with anxiety and mood disorders, complicating treatment [54, 53]. Prompt intervention, often requiring hospitalization for nutritional stabilization, is necessary, though cognitive-behavioral aspects are less addressed in hospital care [54].

Cognitive-behavioral therapy (CBT) is the most effective treatment for EDs, with strong evidence supporting its use [27, 54, 53, 135]. CBT for EDs (CBT-ED) targets eating-related anxiety and behaviors [53] and is also the primary treatment for mood and anxiety disorders in children, focusing on thoughts, emotions, and behaviors through psychoeducation, cognitive restructuring, and exposure techniques [83].

In CBT-ED, exposure therapy targets anxiety-inducing situations, such as specific foods, and reduces safety behaviors like compulsive exercise [32, 54, 53, 135, 83]. The therapy emphasizes inhibitory learning, helping individuals realize feared stimuli are not harmful [32], and addresses anxiety from internal bodily sensations, encouraging confrontation without avoidance [27, 123].

Exposure therapy has been shown to reduce ED symptoms, with increased exposure yielding better outcomes [53]. Hospital-based interventions focusing on food-related fears also reduce avoidance behaviors [54]. An acceptance-based interoceptive exposure approach, combining mindfulness and counter-conditioning, has improved food tolerance and body mass [123]. Interoceptive exposure, when combined with CBT, reduces anxiety sensitivity and ED symptoms [27].

Gradual exposure to foods effectively increases children's acceptance of previously rejected foods, especially when combined with incentives [58]. A multidisciplinary approach, including sensory integration therapy, improves sensory processing and eating behaviors in children with selective eating [20].

Given the high comorbidity between EDs and anxiety disorders, transdiagnostic approaches effective for anxiety may benefit ED treatment [27]. Research shows that interoceptive sensitivity, where heightened sensitivity to internal sensations related to eating is linked to ED risk, is addressed by CBT through exposure techniques and reappraisal skills [135].

2.3.2 Physical Activity

Scientific evidence supports the anxiolytic effects of regular physical activity, which can reduce anxiety and increase neurotransmitters like glutamate and GABA, which have complementary roles in the brain [16, 136, 119]. Research indicates that physical activities such as stretching and resistance training are particularly effective in alleviating anxiety, especially among university students [156]. These activities offer immediate relief from anxiety symptoms and enhance overall mental health.

Studies also show that women are more prone to anxiety than men, suggesting that the impact of physical activity on anxiety may differ by gender, possibly due to variations in the type or intensity of exercise [15, 156]. Svensson et al. (2021) found that physical activity reduced anxiety risk in both men and women, regardless of activity type [142].

These findings highlight the importance of maintaining a regular physical activity routine to improve mental health, reduce anxiety, and promote overall well-being, making physical activity a crucial component of a healthy lifestyle.

2.4 Virtual Reality

Virtual Reality (VR) is a rapidly evolving technology with diverse applications in entertainment, education, medicine, and industry, offering immersive and interactive experiences that bridge the physical and digital worlds [2]. VR involves a 3D computer-generated environment that simulates real-world situations through devices like head-mounted displays (HMD), providing visual, auditory, and sometimes haptic stimuli [50, 76, 151]. More advanced systems include accessories like haptic gloves and multidimensional treadmills to enhance immersion [155].

The effectiveness of VR lies in its ability to immerse users so convincingly that experiences within virtual environments can translate to real-world situations [68]. This sense of presence, where individuals respond to virtual stimuli as if real, is crucial, and physiological markers such as heart rate and skin conductance help measure it [68, 2]. The key distinction in information processing between real scenarios and VR environments lies in how stimuli are presented to the individual, as illustrated in Appendix K. Although virtual environments can be very realistic, they may also cause mental and physical fatigue, or even malaise. Depending on the system's complexity and quality, movements within VR environments can result in motion sickness or discomfort.

VR is commonly used in therapeutic settings, such as exposure therapy for anxiety disorders, psychosis, and eating disorders, with significant evidence supporting its clinical effectiveness [29, 50]. Augmented Reality (AR) overlays virtual elements onto the real world, allowing users to interact with both simultaneously [1, 151]. Augmented Virtuality (AV) involves adding virtual elements to virtual environments, blending real and virtual elements into Mixed Reality (MR) and Extended Reality (XR) [155, 34].

For immersive experiences, VR systems must respond accurately to user actions, such as head movements and interaction with virtual objects [112]. While VR environments can be highly realistic, they may also cause fatigue, motion sickness, or discomfort. Some systems, like the Meta Quest 2, address these issues with adjustable lenses, 6DoF sensors, and 3D positional audio to enhance immersion and comfort [113, 128].

2.4.1 Virtual Reality Based Therapeutic Treatment

In recent years, there has been a significant increase in interest and the use of innovative technologies for delivering health and wellness programs and interventions [151]. Technological advancements over the past decade have made high-quality VR experiences accessible to the general population, thereby expanding the reach and impact of these systems. Some clinical applications demonstrate the unique benefits of these technologies, such as VR-based exposure therapy for treating phobias and post-traumatic stress disorder (PTSD) [151].

In a therapeutic context, VR emerges as an innovative and effective tool in the treatment of eating disorders, offering patients immersive experiences designed to improve their behavior and address specific challenges [50, 151]. One of the most promising therapeutic approaches is VR-based exposure therapy (VRET), in which patients are repeatedly and controlledly exposed to food-related situations, allowing them to practice and familiarize themselves with these situations before confronting them in real life [50].

VRET offers several advantages over traditional exposure therapy methods, including greater patient receptivity and the ability to gradually adjust virtual environments according to individual discomfort levels [50]. This means that therapists can customize exposure therapy sessions to meet the specific needs of each patient, providing a highly controlled and adaptable treatment environment.

Moreover, VR also plays a crucial role in food training, aiming to reduce aversion and anxiety related to food, which are key factors in maintaining a state of nutritional deprivation [89, 61, 126]. Through carefully developed virtual environments, patients can gradually and safely practice exposure to food stimuli under the guidance of specialized health professionals [89, 126]. This approach allows patients to develop a healthier and more balanced relationship with food while learning to confront and overcome their fears and concerns associated with eating [89, 61]. Studies have demonstrated that food stimuli in VR can be just as effective as real food, and in some instances, even more stronger. Moreover, VR-based stimuli have proven to be more effective than static images in eliciting emotional responses [61, 126].

The benefits of VR in the therapeutic context extend beyond mere controlled exposure to food stimuli. It offers the possibility of repeated exposures, which is essential for consolidating behavioral knowledge and progressively reducing patient anxiety [89]. Additionally, VR is a highly generalizable technology, meaning that the skills and strategies learned during therapy sessions can be easily transferred to real-world situations, increasing the long-term effectiveness of the treatment.

Ammann et al. (2020) emphasize the key role of visual perception in food selection, often influencing decisions more than taste or aroma [6]. Their research demonstrates how food color impacts flavor identification, with VR offering a tool to manipulate visual appearance without altering food composition [6]. By testing an orange-flavored drink altered to green and a cake sample in VR, they found consistent results with real-life studies, showing that visual cues influence flavor perception and can aid in promoting healthier food choices [6].

2.5 Neurofeedback

Known as a brain training technique, NF is a kind of biofeedback that has garnered increasing interest in recent decades due to its potential in treating a variety of neurological and psychiatric conditions [18, 23, 26, 36, 103]. This technique has therapeutic and restorative effects on neuropsychological and neurophysiological issues, such as attention deficit disorder (ADD), ADHD, and cognitive disorders related to addictions [75, 26, 57, 65, 23, 74]. NF is also used in reducing anxiety, depression, and stress [65, 10, 103].

NF represents a neurocognitive therapy technique based on human-computer interaction, allowing the brain to adjust its synapses to a more appropriate or regular state, whether that involves increased responsiveness, decision-making, relaxation, or memory performance [18, 36, 65, 74]. NF training sessions aim to enhance self-regulation on two levels: neurophysiological and cognitive-behavioral [26]. Additionally, NF is used in the treatment of stress and anxiety, enabling the brain to control synapses, form new connections, and strengthen brain waves during times of stress and anxiety [65]. Learning control over specific neural pathways has been demonstrated to alter particular behaviors [138].

The primary objective of NF is to enable individuals to learn to voluntarily regulate their brain activity through real-time feedback provided by their own brain waves, obtained via EEG [18, 21, 23, 36, 65, 74].

The NF process involves capturing EEG signals through non-invasive electrodes (placed on the scalp or other areas of the head, such as the earlobes, mastoids, chin, or the tip of the nose), amplifying and processing them, performing quantitative EEG (qEEG) analysis using various filters and classifiers, and presenting the results to the brain in the form of a reward (such as scores in games, auditory stimuli, color changes, or bar graphs) [18, 21, 65, 108]. Thus, NF uses the presentation of visual and/or auditory stimuli that directly represent real-time brain activity to facilitate self-regulation of the putative neural substrates that underlie a specific behaviour or pathology, allowing the individual to explore the impact of their own mental activity on this representation [18, 21, 65, 108, 103, 138]. The processed data are used to control the stimulus in NF, regulating the real-time reward system that provides feedback to the brain, as illustrated in Figure 2.1 [18, 21, 65, 108]. For instance, users may observe a bar graph that rises or falls depending on whether their brainwave patterns are above or below a specific threshold. The goal of the training is for users to learn to maintain the bars within this threshold by controlling and regulating their brain activity [18, 21, 65, 108].

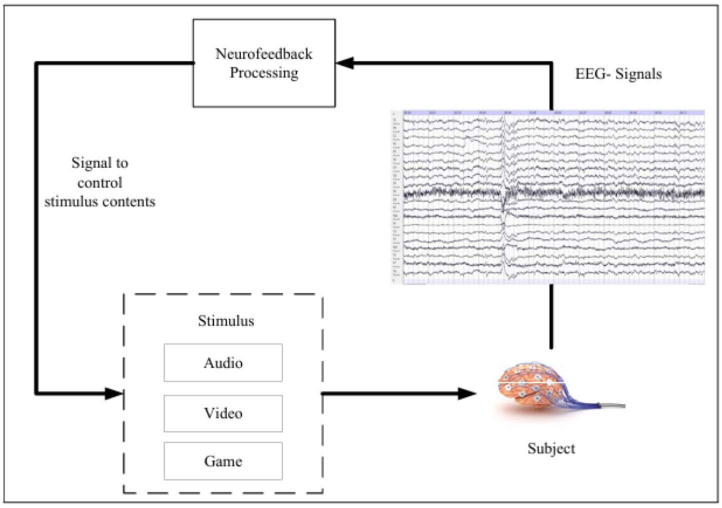


Figure 2.1: Neurofeedback process [65].

Through the use of this technique and via a process of learning and training, individuals will develop the ability to modulate their brain activity more effectively, which may result in improvements in clinical symptoms and cognitive performance [18, 21, 36, 65].

In this way, the approach aims to empower individuals to train and voluntarily modify specific functional biomarkers (psychophysiological variables objectively measured and assessed as indicators of pathological processes or therapeutic responses) related to mental disorders, with the goal of improving associated symptoms or cognitive processes [18, 21, 36, 65]. However, most EEG-based neurofeedback protocols focus on modulating certain spontaneous brain oscillations, specifically defined by the frequency of their oscillation [18].

Each neurofeedback training session typically lasts between 20 and 30 minutes after the electrodes have been placed. If the session exceeds 30 minutes, users may experience fatigue or headaches [108]. To prevent these symptoms, especially in new users, it is advisable to divide the session into activity blocks of 3 to 10 minutes each, with short breaks of 1 to 3 minutes between blocks [108]. Research indicates that within the first five to ten neurofeedback training sessions, and depending on the severity of the issue, users begin to notice initial improvements, particularly in cognitive flexibility and control [108]. These cognitive improvements tend to persist in the long term, even after the training is discontinued, in contrast to pharmacological treatments, where symptoms may reappear after discontinuation [108]. NF is also effective in a shorter time frame compared to other behavioral interventions and has fewer side effects than pharmacological treatments [44].

2.5.1 Neurophysiological Foundations of Neurofeedback

2.5.1.1 EEG and neurofeedback

Electroencephalography (EEG) is a technique that allows for the recording of brain electrical activity through non-invasive electrodes placed on the scalp of an individual [8, 18, 65, 80, 38]. Brain activity is generated by ionic exchanges across cell membranes and synapses during neuronal activity. When neuronal activity in a specific region occurs synchronously over time, EEG measures the summed electric potentials, resulting in fluctuations in the signal [18]. Changes in the amplitude of these fluctuations reflect the degree of synchronization of neuronal populations within the cerebral cortex, influenced by both the intrinsic excitability of neuronal populations and synaptic input from other brain regions [18]. This dynamic brain activity can be categorized into different frequency bands, including infralow (<1 Hz), delta (1-4 Hz) – produced during deep sleep, theta (4-8 Hz) – associated with sleep, learning, memory, and attention, alpha (8-12 Hz) – linked to a relaxed state of mind, sigma (12-15 Hz), beta (15-30 Hz) – related to emotional arousal and cognitive performance, and gamma (>30 Hz) – used as biomarkers for diagnosing brain pathologies, reflecting different neuronal processes [18, 127]. Further details can be found in Appendix L.

These brainwave bands are measured in hertz, or cycles per second. The synchronized neural activity within different bands can be linked to various cognitive and emotional states, depending on the electrode placement. For instance, EEG sensors placed on the prefrontal cortex can help monitor states such as relaxation, anxiety, and attention [9].

NF games are becoming increasingly popular for inducing states of meditation and relaxation by detecting oscillatory neurophysiological rhythms, specifically theta and beta, recorded in the frontal lobe [75]. The most common NF training methods for anxiety self-regulation focus on increasing activity in the alpha band, enhancing the alpha/theta (A/T) ratio, or reducing high beta band activity [9]. For attention and hyperactivity self-regulation, typical approaches include reducing the theta/beta (T/B) ratio, boosting amplitude in the lower beta range (known as sensory motor rhythm or SMR), or decreasing the negativity of slow cortical potentials (SCP) [9]. In other words, for the treatment of ADHD and ADD, games are used as stimuli in NF to reduce theta activity and increase beta activity in young individuals [65, 9]. Elevated theta activity is associated with lower alertness, while suppressed beta activity is linked to decreased attention [65, 38]. NF is also employed to enhance the SMR (12-15 Hz) in the Cz region, as behavioral inhibition is related to the sensorimotor rhythm [65]. Cz, located at the scalp's top center, corresponds to the sensorimotor cortex and is targeted in neurofeedback to enhance SMR for motor control and attention regulation.

Regarding stress reduction, NF has also been successfully used [10]. By using audio content as stimuli, alpha power in the right prefrontal lobe was increased, leading to a reduction in stress levels [65].

Studies conducted on neurotypical populations present varied results when analyzing the effects of NF [21]. Although some findings are occasionally conflicting, there is extensive research in this field within cognitive science, revealing both functional and structural changes resulting from NF [21]. Thus, two competing theories about alpha oscillations exist: one suggests that large alpha oscillations in a cortical region indicate inactivity of the underlying neuronal substrate (the cortical idling hypothesis), while the other proposes that increased alpha oscillations reflect more efficient cognitive processing (the neuronal efficiency hypothesis) [21]. NF research tests these hypotheses by investigating how training to increase or decrease alpha oscillations can impact cognitive performance and attention control.

The therapeutic efficacy of NF is based on the patient's ability to significantly self-regulate the parameters trained during feedback, followed by long-term changes in brain activity induced by neuroplasticity mechanisms [18, 65]. This neuroplasticity can manifest during training sessions (online—changes in the trained signal relative to the resting baseline) or outside of them (offline—absolute change in resting baseline between sessions, possibly related to skill acquisition), resulting in functional changes that can be either Hebbian or homeostatic [18].

Hebbian plasticity induced by NF produces functional changes in the same direction as the NF training (e.g., long-term increases in alpha frequency following up-regulation alpha training). In this process, during more intense oscillations, synchronized neuronal populations involved in the oscillatory pattern strengthen their connections over time, further facilitating the occurrence of these oscillations in the future. Conversely, maintaining a cortical region at low amplitude reduces synaptic correlations and weakens the connections that support synchronization [18].

Homeostatic plasticity produces changes in the opposite direction, actively counterbalancing Hebbian-type plasticity to prevent extreme expressions (e.g., long-term increases in alpha frequency following down-regulation alpha training). These changes are influenced by synaptic potentiation and neuronal synchronization, demonstrating the close relationship between brain oscillations and brain plasticity. Therefore, from an NF perspective, it would be expected that homeostatic forms of plasticity would produce changes opposite to those induced by training [18].

2.5.1.2 Neurophysiological Measures of Neurofeedback

In addition to EEG-based measures, the neuroplastic effects of NF are increasingly being researched using various techniques, such as transcranial magnetic stimulation (TMS) and functional magnetic resonance imaging (fMRI) [17, 57, 138].

It is crucial to note that while the quality of EEG recordings and the design parameters of NF protocols, such as the frequency and number of sessions, are fundamental factors that need improvement to enhance the training process, this optimization will never fully compensate for the potential negative effects of a lack of precise understanding of the brain/mental processes underlying any psychological or cognitive condition [18]. Recognizing this limitation (common to any functional method used for recording brain activity) is a valuable starting point for guiding research and the development of NF-based therapeutic approaches [18]. As an initial step in addressing this challenge, it is crucial to inventory the current list of EEG biomarkers and their associations with cognitive functions [18].

Research using temporally precise event-related potentials (ERPs) derived from electroencephalography (EEG) has identified two key components of inhibition: N200 and P300, as presented in Figure 2.2.

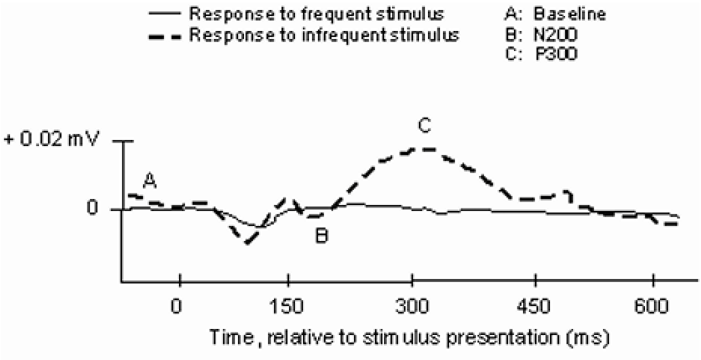


Figure 2.2: EEG signal showing the N200 and P300 components [120].

The N200, a fronto-central negativity that occurs approximately at 200 ms after the stimulus but can vary from 150-350 ms after an inhibitory cue, is linked to conflict monitoring, visual encoding, and response inhibition, as well as attentional engagement [115, 118]. However, the latency of the N200 can vary depending on the age of participants, highlighting age-related changes in processing speed and inhibitory control [84]. This component's characteristics are influenced by task demands and specific stimulus features, which modulate attentional allocation.

The amplitude of the N200 component typically ranges between -1 and -5 µV, although it may vary depending on various factors. In general, the N200 exhibits a negative deflection in the EEG signal and is most commonly observed in tasks requiring attention [120, 84]. The amplitude can be influenced by individual differences, including age, neurological condition, and cognitive performance. Additionally, factors such as electrode placement and the experimental design can contribute to variability in the N200 amplitude. In certain conditions, such as increased cognitive load or greater task difficulty, the N200 amplitude may be enhanced, reflecting heightened attentional or processing demands.

The P300, a positive-going wave that appears approximately at 300 ms but can range from 300-500 ms post-inhibitory stimulus, is another crucial component associated with inhibitory control. In most tasks, the P300 reaches its peak amplitude over parietal electrodes, though in inhibition-specific tasks, it is often larger over fronto-central sites. This component is linked with response inhibition, performance monitoring, error correction, and working memory updating. The inhibitory P300 is further associated with increased delta power, which reflects heightened motivated attention and performance evaluation, supporting its role in self-monitoring and regulatory processes [118]. In healthy young adults, the mean P300 latency and amplitude were found to be 281.38 ± 33.39 ms and 4.53 ± 1.67 µV, respectively [139]. There are also studies indicating that the classical P300 deflection typically appears between 300 and 400 ms following stimulus presentation. However, the timing of the P300 can vary widely, ranging from 250 ms to 900 ms, with amplitudes generally between 5 µV and 20 µV in response to auditory and visual stimuli, though values up to 40 µV have also been documented [120]. However, these values can vary depending on factors such as age and cognitive tasks.

Together, the N200 and P300 components offer valuable insights into cognitive processes involved in inhibition, attentional control, and performance evaluation. They hold potential as biomarkers for distinguishing cognitive patterns across developmental stages and for assessing cognitive function in clinical populations.

2.5.2 Biofeedback (electrocardiogram and electrodermal activity)

Biofeedback (BF) is a method aimed at teaching individuals to control their physiological processes by exposing them to real-time information about specific bodily activities [21, 26]. Once acquired, this skill should ideally remain effective beyond the training context, providing individuals with a way to improve their health and performance without the need for external interventions [21].

Emotional regulation is crucial to the human experience, enabling adaptation to various daily challenges and needs [93]. Several methodologies exist for identifying emotions and cognitive states, using both non-physiological signals, such as speech, facial expressions, and body movements, and physiological signals, such as electromyography (MEG), electrocardiography (ECG), electrodermal activity (EDA) and electroencephalography (EEG) [21, 26, 80, 93, 2]. EEG, in particular, stands out for its ability to measure cortical electrical activity with millisecond precision, making it an effective and accessible tool for investigating the neural mechanisms of emotions [80, 93].

Heart rate variability (HRV) and breathing rate variability (BRV) have been identified as significant biomarkers for anxiety detection, with parameters such as mean heart rate, standard deviation of heart rate, and SDNN showing significant changes between non-anxiety and anxiety-induced states [129].

2.5.3 Brain-Computer Interfaces Using NF

The ability of brain-computer interfaces (BCI) to seamlessly control video games highlights their potential to make neurofeedback training more accessible and increasingly popular [107]. BCI enable direct communication between individuals and computers through electrical impulses generated by neurons in the brain, which serve as inputs for computer programs [8, 23, 57, 65, 152, 157, 108, 9]. One form of BCI uses an EEG headset to measure the amplitude and frequency of specific brainwaves, which are associated with different cognitive and emotional states depending on the placement of the electrodes on the user [8, 57]. These measurements can reveal the user's brain states, such as whether they are calm, anxious, attentive, or distracted [8]. By transferring these pre-processed data to a computer, it is possible to transform them, displaying information about current brain states and real-time brain processes [8].

When examining how users are trained in NF using a BCI, it is crucial to consider how the learning processes of both the user and the machine can mutually influence each other. In the context of EEG-based NF/BCI, machine learning typically aims to identify specific EEG patterns in the user that correspond to the target of self-regulation. For example, machine learning techniques can be used to detect patterns in EEG signals that vary with different levels of attention or relaxation [8, 18, 36].

Conversely, user learning is essential in both NF and BCI, particularly in their ability to learn how to self-regulate the target neurophysiological pattern based on the feedback received during NF/BCI training [18, 152]. This interaction between the machine and the user represents a form of co-adaptation and co-learning. Therefore, it is necessary to consider the cognitive, motivational, and technological acceptance factors of patients when designing protocols tailored to each individual's profile, which may involve adapting both tasks and feedback to optimize long-term learning [18].

The task's complexity can be determined by the amount of mental effort the patient needs to apply to successfully complete it, which is directly related to their ability to control their

own brain activity. It is important that the task difficulty aligns with the user's skills to avoid it being too easy, which could lead to boredom, or too difficult, which could cause frustration. This difficulty can be adaptively adjusted, increasing or decreasing based on the user's progress and individual abilities. Typically, adaptive difficulty is initially determined based on the user's physiology and is regularly updated throughout the training sessions [18].
Feedback is provided to users to help them learn how to modulate their brain activity. Many studies have focused on the types, content, and social aspects of feedback. Regarding the types of feedback, the effects of visual, auditory, tactile, and even multi-sensory feedback have been studied. These types of feedback can enhance how users exert control, influencing their level of technological acceptance. Additionally, adapting the types of feedback allows for consideration of general cognitive principles, such as presenting information in multiple modalities for a quicker response and adapting to the users' sensory impairments [18]. Regarding the content of the feedback, specific task elements have been studied. For example, to effectively control a BCI, users need to understand the impact of their brain activity on task performance. These mechanisms show the user an engaging representation of their own brain activity in real-time to help them understand which EEG patterns should be generated [18]. In terms of social aspects, some studies offer emotional support and social presence to compensate for the lack of interaction during NF/BCI sessions, using a virtual assistant. Each intervention by the assistant consists of facial animation and/or speech, taking into account the user's performance and progress to positively reinforce good practices [3, 18, 26].

Currently, the task and feedback are adapted before and during training. A crucial aspect is determining an appropriate threshold and feedback type for each situation. Traditionally, the threshold can be set either automatically or manually [18]. In the automatic method, the threshold is continuously updated to provide patients with positive reinforcement when they spend a certain percentage of time above or below the designated threshold, which is continuously estimated based on the EEG signal recorded just before. A limitation of this scenario is that patients are only rewarded for changing their brain signal relative to the previous average period, which greatly reduces the opportunity for learning across sessions. When the threshold is set manually by the professional, it is based on a baseline recorded before the session, where the patient is rewarded if their signal is above or below (depending on the protocol) the previously designated threshold [18].

2.5.4 Virtual Reality Based Neurofeedback Training

NF is heavily influenced by psychological factors such as motivation, subjective sense of presence, and the feeling of control. Therefore, it is crucial to investigate elements that could enhance these subjective states, making the training more engaging and less fatiguing [23].

VR-based NF training represents an innovative and promising approach in the fields of neuroscience and cognitive rehabilitation. By combining NF principles with the immersion and interactivity provided by VR, this training modality offers a range of potential advantages in terms of user engagement, training efficacy, and skill transfer to real-world situations [3, 26, 65, 80, 86, 87, 85, 36, 74].

VR-based NF training scenarios can positively impact both performance and training outcomes for several reasons [8, 85]. Initially, an immersive and engaging VR feedback design can enhance user motivation, interest, and adherence to the training process. Studies have shown that VR-based NF training results in increased motivation and interest among neurological patients compared to traditional 2D feedback [22, 26, 65, 80]. Additionally, the use of advanced technology such as VR can provide users with more realistic, engaging, and explanatory feedback about their brain activity during training, potentially enriching their understanding of the process [3, 26, 65, 80, 86, 87, 85].

Evidence suggests that VR systems are more effective than traditional 2D representations in capturing participants' attention [23, 36]. Previous studies have explored the use of 3D brain models to provide explanatory feedback on brain activity during NF training. There is evidence that using 3D virtual bodies as feedback scenarios can create a sense of control and ownership over the virtual body, enhancing user performance [36, 86, 87, 85].

Li et al. (2024) [93] developed an EEG-based BCI system for emotional regulation, integrating (NF) within a VR environment. Eighteen participants were exposed to music clips evoking positive, neutral, or negative emotions and used NF to regulate their emotional states. The VR interface featured a virtual pop star whose facial expressions provided real-time feedback on participants' emotional status, enhancing intuitive engagement compared to traditional numerical feedback [93]. The study demonstrated that NF in VR significantly improved participants' accuracy in emotional regulation over time, underscoring the effectiveness of this approach [93].

Despite the benefits of VR for NF training, challenges remain, including potential cognitive overload, technical requirements, and physical discomfort, such as interference with EEG signals and cyber sickness, affecting 25% to 80% of VR users [23, 85]. Symptoms like dizziness often diminish within 2 to 6 minutes, though they can reduce the sense of presence, which may impact NF training outcomes [23].

In VR-EEG setups, VR headsets are worn over EEG electrodes; while discomfort like pressure or headaches is not typically reported, further studies are needed to verify comfort across configurations [23]. Physiological measures such as EEG, eye tracking, and EDA offer insights into users' emotional responses in VR, where a heightened sense of presence can elicit strong emotions [2]. Integrating these sensors in VR gaming shows promise for enhancing user experience: a neurofeedback loop can adapt game parameters to optimize players' affective states, improving overall engagement [2]. Measuring these responses and adapting VR environments accordingly is essential for a more user-centered experience [2].

AmbuRun, a VR game developed by Hamdi Ben et al. (2018), was designed to test a NF system where players control an ambulance, navigating it to the hospital while avoiding traffic. The game dynamically adjusts elements like traffic density and ambulance speed based on players' real-time emotional states, leveraging 3D assets in Unity3D and optimized for the FOVE headset with integrated eye tracking and accelerometer [2].

The NF system comprises three core components: the VR environment (AmbuRun), a measuring module, and a neural agent. The VR environment adapts dynamically to the user's physiological data, creating an immersive NF loop. The measuring module collects EEG, eye tracking, and EDA data to assess emotional states, with data stored for further analysis. The neural agent processes these data to adjust the VR environment, enhancing the user experience by modulating game elements in response to the player's emotions [2].

In the study, 20 participants played AmbuRun while the NF system adapted game difficulty and speed based on frustration and excitement levels. Participants wore an Emotiv EPOC headset and the FOVE VR headset, and real-time adjustments were made according to detected emotions. Post-session feedback indicated improved gaming experiences, and analysis confirmed that frustration and excitement levels adjusted as anticipated with system interventions [2].

In conclusion, the AmbuRun NF system effectively modulated game difficulty and speed in response to emotional states, enhancing gameplay and highlighting potential applications in fields like education and healthcare. Future research could further refine this system by incorporating additional rules and emotional responses [2].

2.6 Serious games

Serious games offer an innovative approach in education and healthcare, using game mechanics to achieve educational, therapeutic, and training goals beyond entertainment. They serve purposes like skill development, behavior modification, and cognitive enhancement. In healthcare, serious games are increasingly used to support mental well-being for both children and adults, addressing conditions like depression, PTSD, ASD, and ADHD, while promoting cognitive health [75, 33, 40, 57, 98, 79].

These games are especially valuable in mental health and rehabilitation, showing potential in treating depression, anxiety, and neurobehavioral challenges associated with neurodevelopmental disorders [102, 149]. Studies suggest their efficacy in various therapeutic applications, including prevention, detection, and intervention [102]. In psychological therapy, serious games and video games offer preliminary support for clinical mental health treatment, while VR-based games enhance motor rehabilitation by increasing patient engagement and motivation for physical therapy [99, 55].

For children with ASD, who often face challenges with social interaction and communication, traditional therapies may heighten anxiety due to complex sensory stimuli and direct verbal interaction. Serious games in virtual environments provide a safe space for practicing skills, reducing stress and fostering social learning [33, 40, 98, 46]. Many children with ASD also show a preference for technology-based interactions, which serious games leverage to create immersive, beneficial experiences that support learning, cognitive development, and emotional health [33, 40, 57]. Play-based serious games further aid in developing motor, communication, social, and problem-solving skills, making them an ideal tool for long-term NF training where sustained engagement is key [57, 98].

Specifically, video games can create more efficient learning environments compared to traditional classroom programs for several reasons [135]:

a) Motivation – Children participating in prevention or treatment programs within classroom settings are rarely motivated to change their behavioral and emotional patterns. In contrast, games are inherently motivating, providing a strong sense of control and enjoyment, and rewarding children for achieving goals and improvements [135];

b) Practice – Most prevention programs are predominantly psychoeducational, offering substantial information but few opportunities for practical application. CBT attempts to bridge this gap through simulations and homework, but these exercises can be limited, awkward, unrealistic, and tedious. Video games, on the other hand, engage participants in genuine emotional experiences and provide the opportunity to practice new regulation skills until they become automatic and can be applied outside the game context [135];

c) Personalization – Conventional prevention approaches often fail to tailor interventions to the diverse needs and learning paces of at-risk children. Video games, however, are designed as adaptable systems that dynamically adjust to user needs. The game's progress determines the level of difficulty and reinforcements, maintaining an optimal balance for each case [135];

d) Access and Cost – Approximately 80% of young individuals requiring mental health care do not receive any services. Those needing clinical support often face barriers to accessing programs due to sociodemographic factors. Cost is also a significant barrier for many in need of assistance. Games offer a relatively affordable solution and provide easy access from home to a large number of individuals needing support [135].

Schoneveld et al. (2016) [135] developed MindLight, a game designed through interdisciplinary collaboration to help children manage anxiety. By integrating evidence-based techniques like NF and CBT, the game teaches emotional regulation in a playful context. Players control an avatar's "mindlight" using an EEG headset, learning to calm down and reduce anxiety when the light dims. The game also incorporates exposure training and attentional bias modification (ABM) to address fear and encourage focus on positive stimuli.

A study comparing MindLight to a control game, Max, showed both significantly reduced anxiety after three months, with no major differences between the groups. MindLight was rated more anxiety-inducing, aiding emotional regulation, while Max was more engaging. Future versions of MindLight could improve by enhancing fun elements. Overall, while promising, the effectiveness of MindLight depends on factors like player motivation, warranting further research to optimize its impact [135].

2.6.1 Virtual reality based serious games integrating neurofeedback/brain computer interfaces as a therapeutic approach for children

When combined with VR technology, serious games take on an even greater dimension, providing an immersive experience that allows users to become fully immersed in three-dimensional virtual environments [40]. This deep immersion can be particularly effective in a therapeutic context for children, creating a safe and controlled environment in which they can explore, learn and develop [40]. For children with emotional, behavioural or learning challenges, serious games that incorporate NF can be a powerful therapeutic tool [40, 157]. They provide a fun and motivating approach to learning self-regulation strategies and promote the development of essential socio-emotional skills.

In the study by Coenen et al. (2020) [40], an NF game was developed which claimed that in the relaxation condition it would increase the activity of alpha waves in the brain, resulting in a high alpha/beta ratio, and that in the concentration condition it would increase the activity of beta waves, resulting in a low alpha/beta ratio. In other words, the NF game 'Daydream' was designed to train different types of brainwaves based on two specific conditions. In the relaxation condition, players were encouraged to relax in order to increase the activity of alpha waves, which have a frequency of 8 to 12 Hz and are associated with states of relaxation and calm [40]. The aim was for players to increase the alpha/beta ratio, which indicates a more relaxed state. In the concentration condition, players were asked to concentrate, which should increase the activity of beta waves, which have a frequency of 13-20 Hz and are associated with states of alertness, concentration and focus [40]. The aim in this case was for the players to reduce the alpha/beta ratio, indicating a more concentrated state [40].

Based on these objectives, this research also aims to explore the effectiveness of serious games as therapeutic tools, specifically whether games using neurofeedback can be designed to train different mental states and whether this can be validated with objective measures of brain activity.

2.6.2 Design of Serious Games Based on Virtual Reality and Neurofeedback/Brain Computer Interfaces

In most NF models, visual feedback is commonly used, typically displayed as bars that rise and fall according to brain activity [22, 85]. However, overly simple and unengaging designs tend to make training sessions demotivating and tedious [22]. Therefore, it is important to seek more engaging feedback designs, with VR emerging as a solution to this issue [22]. Studies indicate that patients who received 3D feedback reported high levels of satisfaction and attention, demonstrating a desire to continue training [23, 86, 85, 92]. This underscores the significance of the type of feedback in motivating training, which is positively related to participant performance.

Highly immersive 3D virtual environments have already been used in therapeutic sessions to mitigate phobic manifestations, aiding in neurorehabilitation [22]. With the use of low-cost consumer headsets and custom software, it is possible to develop NF/BCI games that allow children to learn and practice self-regulation of different brain states [8]. This could benefit millions of children worldwide, particularly those facing mental and emotional health issues such as anxiety disorders, which can negatively impact their education, health, and overall well-being [3, 8].

Several considerations must be addressed in the development of an NF/BCI system to ensure the tool is effective and user-friendly, including [8]:

a) Interaction Model – It is crucial that children understand how to interact with the system, specifically how to alter their brain state to use the BCI effectively;

b) Feedback – Children should receive clear feedback about their brain state, indicating whether they are performing correctly or need corrective guidance;

c) Input – Children should be able to complete NF training tasks and use other BCI functions even if they deviate significantly from the desired brain state;

d) Calibration – The system should not require lengthy calibration or training procedures, particularly for children who struggle to maintain a specific brain state for extended periods;

e) Sensing – The system must operate reliably, even when the data collected by the headsets are noisy or of low quality [8].

These considerations help define the design requirements when developing a game intended for use by children [8]. Serious games represent a new domain that supports the treatment of clinical symptoms and the enhancement of adaptive functioning across various patient groups [148].

2.7 Performance Evaluation of Electroencephalogram, Electrocardiogram, and Virtual Reality System for Neurofeedback Therapy

Recent studies have explored the integration of EEG and VR for applications in neurofeedback, adaptive learning, and architectural design, highlighting both challenges and opportunities. Neurofeedback training in VR environments has shown significant improvements in alpha band power and cognitive test scores, with virtual environments showing more pronounced effects compared to real-world settings [67]. EEG and VR-based adaptive training systems have been developed to adjust task difficulty in real-time based on alpha activity measurements, revealing the brain's ability to compensate for increased workload without impairing visuomotor performance [47]. These adaptive learning systems show great potential, though challenges remain in artifact removal and the identification of relevant features [73].

In the field of design, EEG and VR combinations have been used to investigate the impact of designed environments on specific brain regions, with implications for supporting physiological, psychological, and cognitive functions [143]. These studies suggest that environmental design can directly influence areas of the brain, although further research is needed to fully understand the effects of specific environmental features.

Additionally, the feasibility of using EEG in VR systems is supported by studies showing that EEG signal quality remains largely unaffected by HMDs for frequencies below 50 Hz, consolidating EEG as an effective biometric tool in virtual environments [70]. Therefore, the combination of EEG and VR offers significant opportunities for improving therapeutic techniques, such as neurofeedback, as well as for the development of adaptive learning systems and the creation of environments with measurable neurological impact. EEG is a non-invasive tool with high temporal resolution, and its combination with VR can provide valuable insights, though signal quality must be validated against potential interferences.

Hertweck et al. (2019) investigated the quality of EEG signals in combination with two commercial HMD systems: Oculus Rift and HTC Vive Pro [70]. Using a 2x2 experimental protocol, they compared spectral power measurements under conditions with and without HMD during both eyes-open and eyes-closed tasks. The measurements were conducted using a high-resolution EEG system, and the data were analyzed in MATLAB, focusing on frequencies ranging from 1 Hz to 2.5 kHz [70]. The results showed that EEG signal quality below 50 Hz remained unaffected with both HMDs, which is crucial for most contemporary EEG studies. However, significant artifacts were observed at the 50 Hz frequency and its harmonics, as well as sharp peaks at frequencies above 100 Hz with the Oculus Rift, but not with the HTC Vive Pro [70]. Spectral analysis also revealed that the Berger effect (cortical neural activity modulation) was consistent in both VR and non-VR conditions, validating the effectiveness of EEG for meaningful brain mapping while using an HMD [70]. However, it is essential to consider and compensate for artifacts at higher frequencies. Techniques like independent component analysis (ICA) could improve the accuracy of measurements [70].

EEG artifacts, particularly those caused by movement, can significantly impact signal quality and classification accuracy in VR-based neurorehabilitation paradigms [105]. Artifacts originating from movements, such as muscle activity, eye movements, and head or limb displacements, frequently confuse the measurement of brain signals and may overlap with signals of interest, making it difficult to correctly interpret brain functions [105, 146]. Although these artifacts are generally considered problematic, there are situations where they can be advantageous, such as in brain-computer interface (BCI) communication that uses artificial signals (e.g., eye blinks for letter selection) [105]. Studies like McDermott et al. (2021) emphasize the need for robust approaches to artifact removal in BCI, especially in therapies based on brain states. Machine learning methods should be used to ensure that the signals reflect real brain states, not artifacts [105].

Despite the challenges posed by these artifacts for estimating physiological brain states, researchers have explored methods for their suppression in interactive VR environments [146]. Tremmel et al. (2019) investigated how movement artifacts in EEG could be suppressed during an interactive VR task [146]. In this study, 15 healthy participants aged 18 to 35 (mean age 24.73, 4 females) were recruited. The HTC VIVE system was used, which includes a VR headset

with motion tracking, two handheld controllers, and two base stations that enable 6 degrees of freedom (6 DoF) for movement tracking [146]. EEG was recorded using the g.LADYBIRD electrode cap (Guger Technologies), with 8 electrodes positioned according to the international 10-20 system (F3, F4, C3, C4, P3, Pz, P4). The EEG was amplified by a wireless g.MOBIlab device, with a sampling rate of 256 Hz.
Participants performed a cognitive task known as the n-back, which requires short-term memory and focus. In this task, participants viewed colored balls on a virtual platform and had to move them to containers on the left or right, depending on the color of the ball and whether it matched previously shown balls [146].

To suppress movement artifacts in the EEG data, a method called Warp Correlation Filter (WCF) was applied, which uses the participant's movement trajectory to align and correct the EEG signals [146]. The motion data from the handheld controllers showed that although each participant had a unique movement trajectory, the left and right-reaching movements were highly consistent for each individual [146].

The WCF was applied to the EEG data, and the results showed a significant reduction in movement artifacts. The correlation between the participants' movements and the EEG signals was significantly lower after applying the WCF, especially in the frontal channels, indicating that the WCF was effective in suppressing movement artifacts [146]. It is important to ensure that artifact suppression does not affect the desired EEG signal features. The study demonstrated that movement artifact suppression using the WCF is highly effective, particularly in interactive VR environments where repetitive movements are common [146]. This method can be useful for ensuring the viability of EEG in VR studies, allowing better analysis of cognitive states without interference from movement artifacts. However, this methodology requires motion tracking methods, such as accelerometers or gyroscopes, and thus is not directly applicable to the present investigation, as neither was used.

Electromagnetic noise from HMDs can introduce artifacts in EEG recordings, especially at higher frequencies, although the lower frequency range (<50 Hz) remains largely unaffected [154].

Assessing the quality of ECG signals is crucial for improving diagnostic accuracy in unsupervised ECG analysis systems [131]. Artefacts in ECG signals can be caused by various factors, including patient motion, electrode issues (such as electrode-skin impedance perturbations due to inadequate electrode adhesion and conductance), and environmental disturbances [81, 95]. These artefacts can distort ECG components and potentially lead to incorrect diagnosis and interpretation [121]. The most common types of artefacts include motion artefacts due to shaking or shivering, baseline drift, network interference, muscle tremor and cable movement [81, 121, 144]. Proper design of electrodes and ECG circuits can minimise some artefacts, but motion-related artefacts are still difficult to identify and eliminate [81]. An example of the effect of motion artefacts on the ECG signal is shown in Figure 2.3.

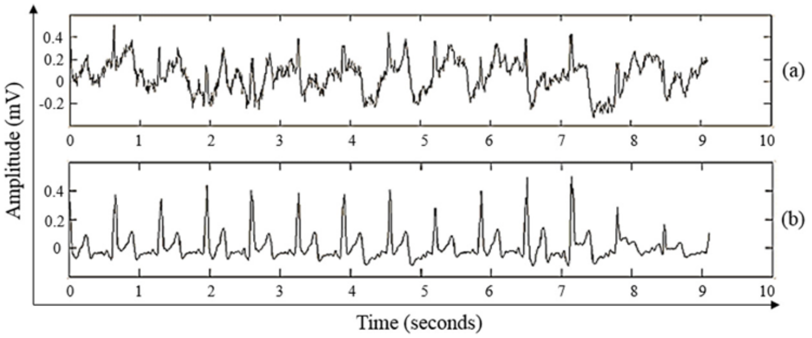


Figure 2.3: (a) Motion artifacts in ECG signal; (b) ECG signal at rest [81].

Strategies to mitigate motion artefacts include both modifying the materials at the electrode-skin interface and developing models and algorithms to minimise their contribution [81]. Although several studies have focused on the removal of stable noise over time, the removal of motion artefacts remains a challenge without a complete solution [81].

Recent research has focused on developing methods to detect and mitigate artefacts in real-time during ECG acquisition [95]. Various techniques have been developed to analyse ECG signals, focusing on the detection of parameters such as P, Q, R, S, T waveforms and intervals [7]. Noise removal is a critical pre-processing step, with methods such as Wavelet-VBE, EMD-MAF and GAN2 showing effectiveness for different types of noise [35, 144]. These methods aim to improve the reliability of ECG analysis, particularly in the context of wearable devices and telemedicine applications [7, 131].

3

METHODS AND MATERIALS

To implement this dissertation practically, it was necessary to define and organize specific methodologies, as well as to select the appropriate materials. This third chapter outlines the methodologies used and also examines the approaches that did not yield the desired outcomes. A detailed explanation is provided for each unsuccessful attempt, along with potential directions for future investigations.

In line with the research objectives, several experimental approaches were selected to enable effective evaluation. Collecting diverse data is essential to determine the most advantageous approach, allowing for comparison of results across different users and tracking each individual's progress. This process is crucial for refining the tools and enhancing their application to the target population. Therefore, data collection should be carried out using both technological devices and questionnaires completed by the participants.

3.1 Materials

In this research, data will be collected, allowing for a detailed analysis of users' responses within a therapeutic context. The main project has resulted in the creation of a web application and serious games, particularly highlighting the PLAY platform, which stores and presents data on users' performance throughout the sessions [12].

Pikita VR Quest, the primary serious game in this study, is continuously developed for the treatment of food aversions, enabling the observation and assessment of patients' movements and overall performance during sessions.

To complement this analysis, eletrophysiological tests such EEG and ECG are utilized to enhance the quality of the data. EEG provides direct visualization of brain activity and facilitates the integration of NF within the game, while ECG offers direct insights to the electric activity of the heart and indirect insight into stress levels which are key indicators of anxiety.

Thus, the combination of this technological method provides a more comprehensive and detailed understanding of patient performance, enabling more precise adaptation of therapeutic interventions.

3.1.1 PLAY

The significant increase in the use of serious games and advanced technologies such as VR in therapeutic contexts has driven the need to develop platforms that not only offer games but also provide detailed statistics and data on patient performance.

The PLAY platform, which supports multiple users, was developed for use in both clinical and home settings, functioning autonomously or under supervision. PLAY offers three distinct profile types: therapist, patient, and clinic. While patients can play games and access their statistics, therapists have tools to manage game settings on a personalized basis for each patient and to schedule their training sessions [12].

The creation of dashboards that track patient progress over time, as illustrated in Appendix M, is crucial for therapeutic monitoring. These dashboards enable therapists to continuously monitor patient progress, identifying patterns of improvement or areas requiring further attention. Additionally, visualizing the data collected during games provides an objective basis for adjusting interventions and personalizing treatment according to the patient's individual responses, which contributes to a more effective and targeted approach.

Based on the data collected during game sessions, the platform facilitates the creation of a digital twin for each patient. This feature allows therapists to evaluate the impact and feedback of a specific game and its associated settings before applying them to the actual patient, thereby minimizing the risk of stress related to exposure to inappropriate games. This is a crucial functionality for personalizing and optimizing therapies, enabling therapists to safely simulate and assess the impact of different games and settings. This results in a more precise and tailored therapeutic approach, ensuring more effective and secure treatment.

In addition to data obtained from motion sensors, NF and biofeedback (ECG) can be integrated as valuable components in building the digital twin. These tools, by analyzing the patient's involuntary responses during activities, provide valuable insights for predicting reactions to new environments and stimuli, thus enhancing the accuracy and effectiveness of therapeutic interventions.

3.1.2 Serious Game Pikita VR Quest

Serious games are designed to address and treat specific health conditions and cognitive skills by combining entertainment elements with therapeutic interventions to promote rehabilitation and learning in an engaging and effective manner. Given the target audience of these interventions, it is crucial that the developed tool provides a safe environment while simultaneously keeping the user motivated.

In the context of this research, the Pikita VR Quest has been developed as a specialized therapeutic tool for food aversion therapy. This intervention is typically implemented through a process of gradual exposure to the stress-inducing element in question. The Pikita VR Quest adopts an approach that creates a playful and less intimidating virtual environment, facilitating a therapeutic experience that helps the patient adapt to the fear factor and reduces their sense of threat.

In the later stages of the game, Pikita VR Quest enables the introduction of real objects into the patient's therapeutic session while they remain immersed in the virtual environment. This strategy aims to minimize fear and anxiety, as the real object is not directly visible but rather integrated into the virtual scenario. The incorporation of real objects within the virtual context acts as a bridge between reality and virtual simulation, providing a smooth and controlled transition in exposure to the feared factor. This approach facilitates a gradual adaptation to the feared object, helping to reduce the patient's aversion response and promoting a more effective therapeutic experience.

Considering the diversity in food aversions among different individuals, the game must offer an extensive variety of virtual foods, allowing the therapist to select the most appropriate feared object for each session, thereby enabling precise personalization of therapy based on each patient's individual needs. As an exposure therapy tool, Pikita VR Quest should promote a controlled induction of stress, ensuring a safe environment where the patient can distance themselves from the fear factor when necessary. The therapist's ability to monitor the patient's progress in real-time and make adjustments to the intervention is crucial due to the adaptive and variable nature of the patient's condition. Detailed data collection on the patient's performance during activities is essential, as it allows for comprehensive and careful analysis after sessions, facilitating continuous adaptation and improvement of the therapy sessions to meet the patient's needs.

During the development of Pikita VR Quest, all relevant considerations were carefully implemented. Data obtained during therapeutic game sessions are transferred to the PLAY system, where they are integrated into each patient's profile for subsequent analysis of session data along with other clinical information. The system records data such as the time taken by the patient to complete a task, the movements executed, and the direction of their gaze, which allows for thorough analysis of specific events.

As a VR tool, Pikita VR Quest utilizes an HMD (Oculus Meta Quest 2, [109]), which is compatible with both controllers and user hand tracking, thanks to the built-in tracking system. During the activities, the therapist monitors the patient's progress via an external device, viewing the patient's experience in real-time. Figure 3.1 illustrates how the therapist controls and supervises the system and the therapy session.

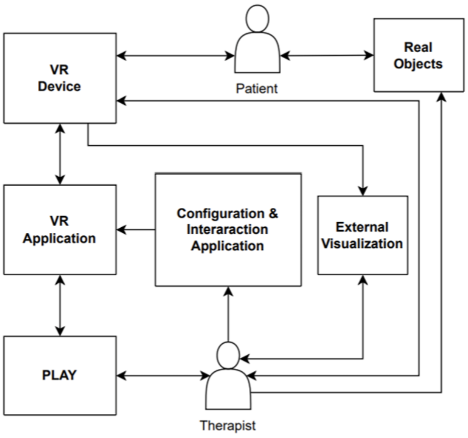


Figure 3.1: Structure of Pikita VR Quest

The Pikita VR Quest is designed to provide gradual exposure to aversive stimuli. Initially, the game introduces an object that may be perceived as similar to the real one, based on characteristics such as color, shape, or even a written word (Figure 3.2A). As the patient progresses, the object becomes progressively more realistic and is presented in various ways, including different tasks or interaction moments—direct contact challenges or reaction challenges, Figure 3.2B. The game also features tasks that require the patient to approach, observe, or grasp the virtual object for specific, pre-designated periods, Figure 3.2C. This progression culminates in physical interaction with the real object while the patient remains immersed in the virtual experience. A primary challenge for treating food aversion involves having the patient grasp the virtual item and bring it close to the mouth to simulate ingestion, Figure 3.2D. To motivate users to complete the tasks, the majority of challenges feature a progress bar displayed above the object, as illustrated in Figure 3.2C and Figure 3.2D.

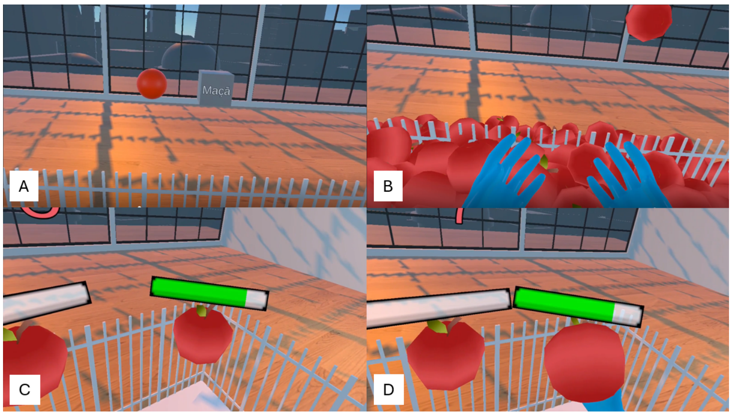


Figure 3.2: Tasks inside the game: A- Object resembling the real stimulus, distinguished by color, shape, or labeling; B- Reaction challenge; C- Tasks involving approaching and observing; D- Task involving holding.

Motivation, comfort, and the patient's sense of security are fundamental elements in the design of Pikita VR Quest. To address these aspects, the game employs a comforting character within the virtual environment to demonstrate tasks and assure the patient that the entire process is safe (Figure 3.3A). Additionally, positive reinforcement within the game, akin to motivational techniques found in entertainment games, is used to encourage the patient and promote improvements in their performance Figure 3.3B. To provide an escape from the stressful environment, a safe zone was established. As shown in Figure 3.3C, the original configuration consisted of a distinct area populated by animals. However, following an evaluation by the therapists, it was suggested that the safe zone should mirror the environment of the activity area, but without the stimuli, to prevent overwhelming the patient.

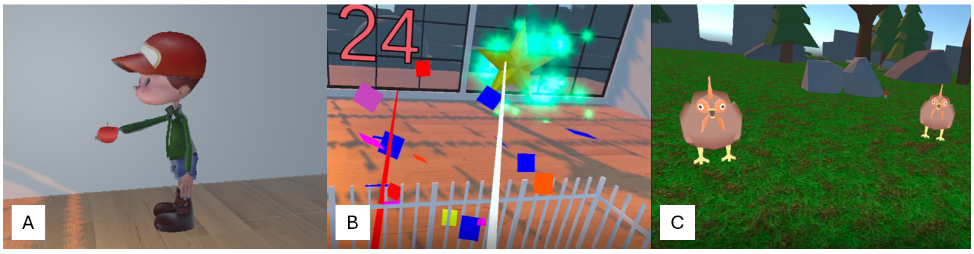


Figure 3.3: A- Comfort character; B- Motivational rewards; C- Safe zone.

These features make Pikita VR Quest an innovative tool for food aversion therapy, integrating VR technology with motivational and safety strategies to optimize treatment and achieve positive outcomes in managing food aversions.

3.1.2.1 Oculus Meta Quest 2

The Oculus Meta Quest 2, released by Meta Platforms, is a standalone VR headset designed to operate independently, meaning it does not require an external PC or console to function (Figure 3.4). This device is designed to be portable and user-friendly, eliminating the need for cables and enabling a more free and immersive VR experience [109].

Figure 3.4: Meta Quest 2 [109].

In terms of performance, the Quest 2 is equipped with the Qualcomm Snapdragon XR2 processor, delivering a smooth and responsive experience. Its LCD screen provides a resolution of 1832x1920 pixels per eye, ensuring sharp and detailed images, which significantly enhances immersion in the virtual environment. The included Touch controllers use infrared tracking, allowing for precise and intuitive interaction with the virtual environment [109]. Additionally, the device employs an Inside-Out tracking system with built-in cameras that monitor user movements without the need for external sensors. Connectivity with PCs is available via Oculus Link or Air Link, expanding the possibilities of use with access to a broader library of games and applications [109].

The device features casting functionality, which enables real-time streaming of what the user is viewing inside the headset to another device, such as a compatible TV, PC, smartphone, or tablet. This feature is particularly useful in contexts where third parties, such as therapists or instructors, need to monitor the user's experience [109].

The Quest 2 is designed to be lightweight and comfortable, with improved padding compared to the previous model, making it suitable for extended sessions of use. This device is widely used for both entertainment and professional applications, such as therapy and rehabilitation, due to its flexibility and ability to deliver highly immersive experiences [109].

3.1.3 Electrophysiological measurement setup

Given the objectives of implementing NF, it is crucial to identify equipments capable of capturing the necessary eletrophysiological signals while ensuring compatibility with the overall system. To address this, a partnership was established with the Institute of Biophysics and Biomedical Engineering (IBEB), a research unit at the Faculty of Sciences of the University of Lisbon (FCUL). This collaboration enabled the use of EEG, ECG, and EDA equipment.

Considering the need to integrate a VR headset into the research and to accommodate children with special needs, it was essential to select an EEG cap that did not require conductive gel for data collection and allowed greater freedom of movement. Accordingly, based on the equipment available at FCUL, the Unicorn Hybrid Black cap was tested [62]. This device supports both gel-based and dry electrode readings. The dry readings are facilitated by the unique design of the electrodes. Although the Unicorn Hybrid Black offers its own software for real-time data visualization (Unicorn Suite [63]), post-processing must be conducted using external software. For this research, EEGLAB was utilized, a free tool developed for Matlab that allows for continuous and event-related processing of biological signals, including EEG [49]. While initially created as a Matlab tool, EEGLAB can also function independently [49].

For data analysis, it is essential to identify task-related events, facilitating the synchronization of all simultaneously acquired data. Typically, this is done using a stopwatch, with relevant data later integrated into the collected signals. However, for this research, a team member developed an application that enabled the marking of three types of events directly within the data ("stimulus" – when the participant receives task instructions, "response start" – when the participant begins task execution, and "response end" – when the participant completes the task), making these markers visible in real-time presentation within Unicorn Suite. This approach allows for the analysis of data during instruction processing and subsequent task execution.

Additionally, it was intended to collect ECG and EDA data during task performance in order to correlate them with EEG data. For this purpose, IBEB provided two BITalino devices: one equipped with ECG sensors and the other with an EDA sensor to be placed on the earlobe [124]. The ECG sensor, which consists of three electrodes, was positioned over the C7 vertebra and the trapezius muscle, as illustrated in Figure 3.5A. The placement of electrodes over the trapezius muscle and the C7 vertebra is justified by evidence suggesting that EMG and ECG measurements from these regions can effectively quantify stress and relate anxiety levels to EEG activity [5]. Initial tests revealed that the EDA sensor placed on the earlobe (Figure 3.5B) was not satisfactory, as the obtained signals were inconclusive and the sensor was uncomfortable.

Thus, an alternative approach was explored. Considering that the EDA sensor manufacturer recommends using the palm of the hand or fingers for electrode placement, attempts were made to attach the EDA electrodes to these areas while simultaneously placing the ECG electrodes (Figure 3.5C). After placing all the electrodes, it became evident that this solution was inadequate because the system requires the user to have controllers in both hands and to move, which was not feasible. As a result, the EDA measurement was temporarily suspended.

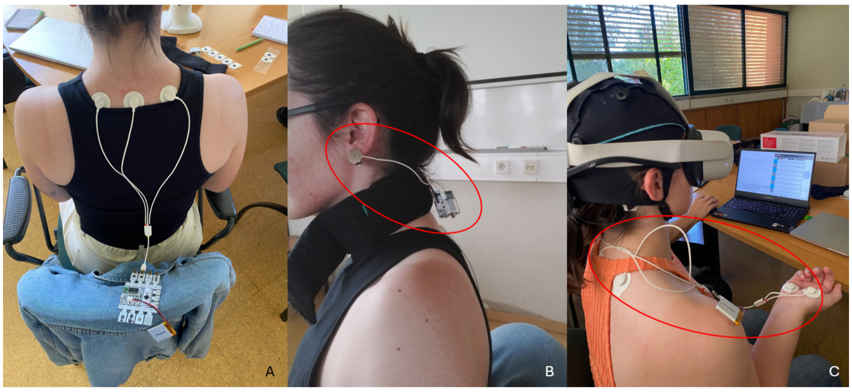


Figure 3.5: (A) ECG sensors placed over the C7 vertebra and the trapezius muscle; (B) EDA sensor on the earlobe; (C) EDA sensor placed on the palm of the hand.

For the acquisition, visualization, and export of ECG data, the manufacturer of BITalino provides free software called OpenSignals, which enables real-time visualization of the collected data [116].

3.1.3.1 Unicorn hybrid black system

The Unicorn Hybrid Black EEG cap (Figure 3.6A) was developed by g.tec neurotechnology, a leading company in BCI solutions and neurotechnology. This company is renowned for creating advanced devices that combine high signal quality with ease of use, catering to a wide range of applications from scientific research to medical rehabilitation. The Unicorn Hybrid Black embodies g.tec's expertise in neurotechnology by offering a product that balances technical precision with practicality. The device was developed with the goal of simplifying the acquisition of brain signals, making it accessible for research laboratories as well as clinical and educational environments. It is particularly notable for its ability to perform both gel-based (wet) and gel-free (dry) readings, making it a practical and adaptable option for various research needs.

The cap is equipped with eight electrodes strategically positioned to capture signals from the major brain regions, including the frontal, central, parietal, and occipital lobes. The design of the electrodes (Figure 3.6B), extending beyond the hairline, facilitates direct contact with the scalp, ensuring high-quality readings without the need for conductive gel.

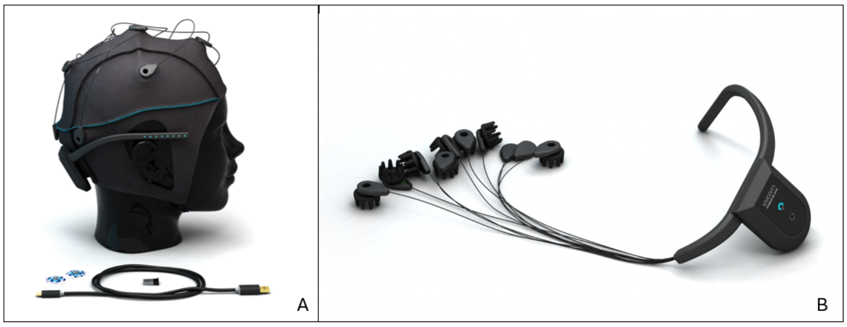


Figure 3.6: A- Unicorn Hybrid Black Bundle; B- Unicorn Hybrid Black electrodes [62].

As illustrated in Figure 3.7, the electrodes are configured to capture the channels Fz, Cz, C3, C4, Pz, PO7, PO8, and Oz. A more detailed analysis of the spatial distribution of the channel locations reveals that Fz corresponds to the frontal lobe, Cz, C3, and C4 to the central lobe, with C3 and C4 located near the temporal lobe. Pz, PO7, and PO8 represent the parietal lobe, while Oz refers to the occipital lobe. These regions are considered suitable for the objectives of this study, as Fz can identify decision-making and attention processes, C3 and C4 can detect auditory and motor events, Oz is primarily responsible for vision, and PO7 and PO8 are associated with memory processing.

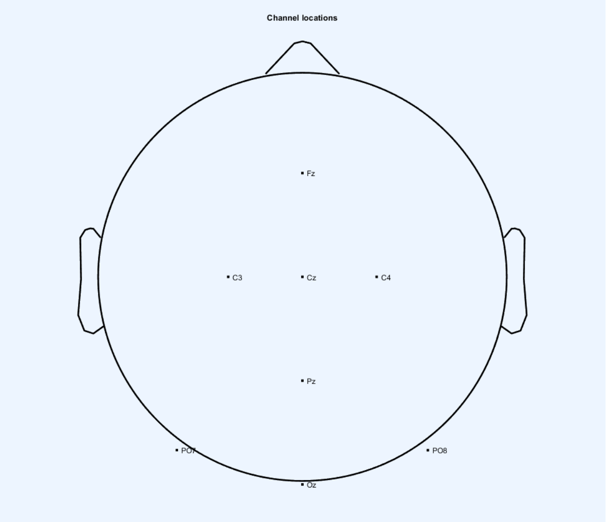


Figure 3.7: Unicorn Hybrid Black channel locations of the 8 electrodes.

This device is also designed to offer good mobility for the user, which is particularly useful in studies involving the simultaneous use of VR headsets or requiring freedom of movement. The EEG cap, Unicorn Hybrid Black, comes with its own software, Unicorn Suite, which enables real-time visualization of brain waves, monitoring of electrode performance, and the quality of collected signals, as well as integration with other applications for more detailed signal analysis, as illustrated in Figure 3.8 [63]. With integrated Bluetooth connectivity, the Unicorn Hybrid

Black facilitates wireless data transmission to a computer, where the information can be recorded and subsequently analyzed.

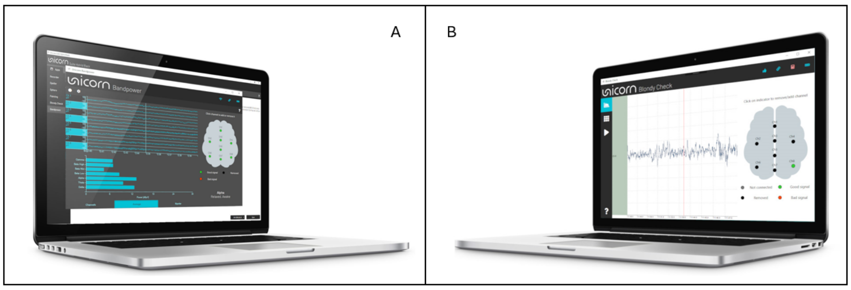


Figure 3.8: Unicorn Suite presenting: A- Signals being shown individually for each electrode and per band; B- Close-up of the captured signal and the performance of each electrode [63].

3.1.3.2 BITalino

The BITalino is a modular and open-source hardware platform developed by the Portuguese company PLUX, which specializes in biomedical technologies and biosensors (Figure 3.9) [124]. This versatile and accessible tool allows for the capture of various physiological signals, including ECG, EMG, EEG, EDA, and others [124].

The main advantage of the BITalino lies in its modularity and ease of use. The device is composed of several modules that can be easily connected to create a customized monitoring system tailored to the specific needs of the user. This flexibility makes it suitable for both beginners looking to explore bioelectronics and for professionals and researchers who require a practical and efficient solution for biomedical data collection [124].

In addition to the hardware, BITalino is compatible with a range of software, including OpenSignals, a platform developed by PLUX for visualizing, analyzing, and exporting acquired data. This integration facilitates real-time analysis of biological signals, allowing users to conduct detailed studies of the monitored subject's physiological activity [124].

The software enables the recording of captured signals, which can be subsequently exported for more detailed analysis. Data can be exported in common formats such as CSV or MATLAB, allowing for utilization across various data analysis and processing platforms [124].

Figure 3.9: BITalino [124].

3.2 Experimental approach

The experimental approach adopted in this research was carefully outlined, considering the specific needs of the target audience and the complexities inherent in developing a system aimed at integrating innovative technologies into a therapeutic context. The selection of materials and methodologies was guided by these considerations, ensuring that each component was not only functional but also suitable for prolonged use by the end-users. Before proceeding with the actual research, it was imperative to assess the comfort and reliability of the system, as these factors are crucial for the successful practical application of the involved technologies. Therefore, the initial tests focused on evaluating the comfort provided by each component and its suitability for the target audience, ensuring that the developed system would be both effective and well-tolerated by the users.

3.2.1 Preliminary analysis approach verification

Before participation in the study, all individuals were thoroughly informed about the nature of the research and the procedures involved. The recruitment process emphasized transparency, ensuring that participants were fully aware of what their involvement would entail.

Each participant was provided with detailed information about the study's objectives, methods, and any potential risks associated with participation. This information was presented both verbally and in written form, allowing participants ample time to review the material and ask any questions they had regarding the study. This ensured they had a clear understanding of the tasks they would be required to complete during the experimental sessions.

In addition, all participants were informed that their participation was entirely voluntary, and they could withdraw from the study at any point without any consequences. To formalize their consent, each participant was asked to complete an informed consent form. This form outlined the study's purpose, the specific procedures involved (including EEG, ECG, and VR tasks), and any potential risks. By signing the consent form, participants confirmed that they understood the information provided, agreed to participate voluntarily, and acknowledged that they could ask questions or seek clarification at any stage of the study.

This process ensured that all participants had the necessary knowledge to make an informed decision about their involvement in the research, upholding ethical standards and respecting their autonomy throughout the study.

With the provision of EEG and ECG devices by FCUL and IBEB, as well as the VR headset, it was essential to test the entire system to validate its comfort, reliability, and safety before introducing it to children, particularly those with special needs. It was also important to assess the effectiveness of the employed methodology and identify areas for improvement. To this end, a series of tasks was developed and tested with a group of adult individuals.

The initial phase of the test involved introducing the EEG and ECG devices to the participants, accompanied by a brief overview of the study and the function of each device. Participants completed a consent form and provided relevant information, such as age, gender, and prior experience with virtual reality.

In the second test, the complete system configuration was utilized. Participants received instructions on the VR headset, which was then placed on them. Guided tasks were conducted in Pikita VR Quest. After the test, each participant was asked to evaluate their level of comfort when using the devices and the overall system.

To obtain accurate biological data, the OpenSignals and Unicorn Suite platforms were used to monitor the collected signals. To enhance data synchronization, it is recommended to connect the BITalino to a different computer than the Unicorn Hybrid Black, facilitating coordination between researchers. The ECG signal was evaluated alongside the EEG to ensure signal clarity and detect noise during simple tasks.

Six tasks were developed in order to measure NF with the EEG, in addition to the initial task designed to establish a baseline, aiming to elicit five specific bands of brain waves: delta, theta, beta, alpha, and gamma (Figure 3.10A and Figure 3.10B). An audio presentation ensured that all participants received the same instructions. The division of tasks for data marking can be found in Appendix C. The team previously followed the tasks to ensure smooth testing, and the testing session allowed for refinement of the approach used.

Figure 3.10: BITalino [124].

To safeguard the integrity of the data against external influences, the study was conducted in a controlled environment where each participant faced a white wall (see Figure 3.11A). In the room, there were four team members present alongside the participant. One member provided instructions and maintained direct contact with the participant during the tasks. This individual was also responsible for fitting the EEG cap and ECG electrodes during the first phase and for placing the VR headset during the second phase.

The remaining three team members had specific roles: one monitored the EEG signal, marked tasks, and triggered the VR activities; another focused on the ECG signal, logged task performance, and timed tasks as needed; the last member managed the VR headset setup, prepared the game, and recorded in-game visuals, Figure 3.11B.

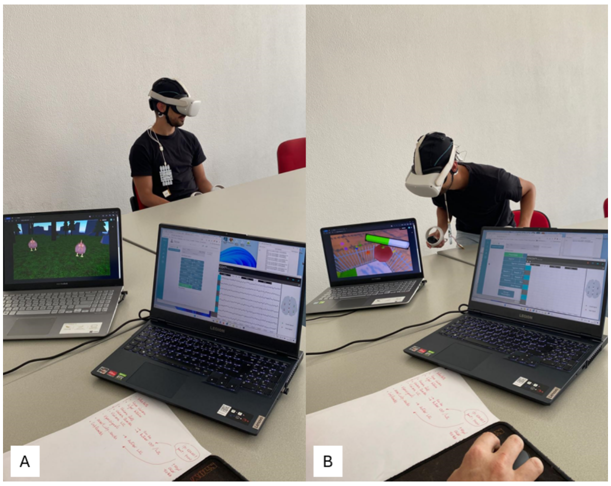


Figure 3.11: A- Room disposition; B- Participant performing a task.

3.2.1.1 Participants

In a preliminary test session six participants were selected for this study using a simple initial criteria: all had to be at least 18 years old and capable to give an informed consent. After this check, participants completed a form to determine if any of the established exclusion criteria applied, the full responses to which are described in Appendix B. Of the six participants, five were male (n=5; 83.33%) and one was female (n=1; 16.67%). Their ages ranged from 22 to 26 years, with an average age of 24.33 years. In terms of manual preference, four participants reported being right-handed (n=4; 66.67%), one was left-handed (n=1; 16.67%) and one was ambidextrous (n=1; 16.67%). This factor is extremely important because brain connectivity patterns varies according to manual dominance.

As the study involved the use of VR, the participants' level of familiarity with the technology was assessed on a scale of 1 to 5, with 5 being the maximum level of familiarity. Only 16.67% of participants (n=1) reported the maximum level of familiarity with the technology (level 5), while 83.33% (n=5) reported an intermediate level (level 3). This information was important for understanding the participants' experience with VR and how this might influence the results.

The exclusion criteria were that participants should not have neurological impairment, severe hearing or vision problems, nor should they suffer from conditions such as epilepsy, cardiovascular disease, addiction or mobility problems. Participants were also excluded if they were taking medication for heart problems or other substances that affect brain activity. To ensure the quality of the data, it was made sure that all participants had slept well and had not taken any substances that affect the nervous system in the 24 hours before the study.

Although severe visual problems were a reason for exclusion, people who wore glasses were allowed to take part because their visual impairment did not affect their performance during the study. Therefore, 50% of the participants (n=3) wore glasses during the study. It should be added that the academic context of the study, coupled with the technical nature of the research, meant that the sample consisted mainly of university students, with a young and predominantly male demographic profile, which may affect the generalisability of the results. Familiarity with the technology, although limited in some cases, was sufficient to ensure that all participants were able to complete the proposed tasks using VR.

3.2.2 Initial assessment strategy validation

During the preliminary tests, key areas for improvement were identified and addressed. A thorough review of all aspects of the study led to several modifications.

To facilitate an accurate assessment of each participant's behavior, all sessions were recorded using a Nikon D5500 mounted on a tripod. This setup is crucial, as the devices employed require minimal movement to avoid contamination of the data by noise. The recorded videos enable the identification of whether any noise in the data is due to participant movement (e.g., leg shaking or arm movement) or other factors. Participant's privacy was maintained by positioning them at an angle that prevented direct filming of their face. The room layout remained consistent with the preliminary assessments, featuring a blank wall devoid of distractions in front of the participant, two computers for data retrieval, and one computer designated for guidance and video playback.

To minimize noise caused by minor movements, the BITalino ECG device was securely attached to the participant's arm rather than being suspended in front of them, as illustrated in Figure 3.12. However, accurately positioning the electrodes proved challenging in several cases; some participants had well-developed back muscles that required alternative configurations, while others had broad shoulders that hindered the BITalino cable's ability to reach the arm and properly secure the electrode. Additionally, the BITalino device's battery level was low by the end of the study, resulting in compromised data quality. Consequently, the data collected from this device is likely inaccurate and was not subjected to comprehensive analysis.

Figure 3.12: A- Initial ECG BITalino disposition; B- Second ECG BITalino disposition.

In light of the tasks conducted by participants using the complete system, and in the absence of the VR headset, certain tasks were deemed unnecessary while others were revised. The analysis utilizing only the EEG and ECG required a reduction in task quantity and a shift in focus regarding the data to be collected. The revised tasks included:

1. Baseline and EEG equipment testing: Participants were instructed to close their eyes for five seconds, open their eyes, blink three times, and repeat this sequence for one minute.

2. Relaxation: Participants engaged in guided relaxation through audio instructions with eyes closed for one minute.

3. Memorization: Participants read a list of ten words for one minute and then repeated the list after a brief pause.

4. Observation and Reaction: Participants viewed an animated video and were instructed to grasp an object upon the appearance of a crocodile.

To enable thorough data analysis, a selection was made based on the brain region of interest, considering the tasks performed in both phases of the study. For the tasks conducted without the VR headset, word memorization was monitored during the reading activity (Figure 3.13B). In relation to the VR tasks, a task involving grasping and bringing the object to the mouth was chosen for analysis (Figure 3.13A). This tasks were chosen with the objective of investigating cognitive processing and auditory response, respectively.

[redacted]

Figure 3.13: A- Grasping and bringing the object to the mouth VR task; B- Word memorization task.

3.2.2.1 Participants

A total of fifteen volunteers were selected for participation in this stage of the study process, adhering to all criteria established in the preliminary tests, which confirmed that all participants were eligible to advance to the testing phase. The study took place in a dedicated room at NOVA FCT.

Among the participants, 40% were female (n=6) and 60% were male (n=9). Their ages ranged from 21 to 62 years, with an average age of 28.07 years. When analyzing the age distribution by gender, females had an average age of 24.17 years, while males averaged 30.67 years. The majority of participants (86.67%, n=13) reported a preference for using their right hand, while 13.33% (n=2) identified as ambidextrous, including two individuals from each gender.

Similar to the preliminary evaluation, some participants exhibited vision impairments; however, these did not pose significant limitations for the tasks involved in the study. Among the fifteen participants, 33.33% (n=5) indicated a need for glasses, all of whom were male. Two female participants initially wore glasses but later determined they were unnecessary and removed them for the activity; these cases were excluded from the percentage calculations.

Regarding prior experience with VR, 40% (n=1) of participants reported no exposure to the technology, 20% (n=2) had encountered the device but had not attempted to use it, 26.67% (n=3) had minimal experience with VR, and 13.33% (n=4) had more extensive experience. Gender-based analysis revealed that a higher proportion of female participants reported greater familiarity with the technology.

4

Results and Discussion

Given the study's complexity, two testing phases were carried out, followed by analysis and discussion of the results. Although both phases utilized similar procedures and a comparable analytical approach, the second phase was informed by findings and insights gathered in the first. Consequently, it was essential to analyze and discuss these phases separately, taking into account both the biological data and the survey responses.

4.1 Preliminary Tests

Two types of tests were conducted: one without the use of VR equipment and one with VR equipment, both conducted simultaneously with EEG and ECG signal monitoring. In the first modality, without VR, participants completed the tasks while only the electrophysiological responses were monitored, allowing data to be collected in a controlled and stable environment. In the second modality, VR equipment was introduced to provide an immersive and more dynamic environment, creating a more complex analysis scenario due to the increase in sensory stimuli and the possibility of greater movement.

This comparative approach is crucial to assess how immersion in VR affects brain and heart activity in real time. The simultaneous use of EEG and ECG in both modalities provides a comprehensive view of physiological responses, allowing analysis of changes in brain connectivity, variations in heart rate and identification of possible artefacts generated by movement in the virtual environment. Comparing data from the two modalities helps to better understand the effects of VR in therapeutic and biofeedback contexts, especially in terms of signal quality and physiological response of participants.

The preliminary tests were conducted primarily to refine the approach, structure, and methodology to be applied. However, the comprehensive data analysis that followed aimed to deepen understanding of device performance and to acquire the software expertise necessary for further progress. Although the sample size was smaller than typically recommended, two participants were excluded from the EEG and ECG analysis due to data retrieval issues. Since these issues did not impact the comfort assessment, their questionnaire responses were included.

4.1.1 Electroencephalogram analysis

In the preliminary tests, EEG results were initially assessed to ensure accurate data capture. For this purpose, a visual and exploratory analysis was conducted using EEGLAB software.

Given that most researchers were unfamiliar with both the software and the data type involved, these results served as an introductory step to establish this methodology. Four data sets were initially analyzed to confirm the presence of identifiable triggers within the signal: the start of task instructions, the beginning of task execution, and the end of task execution. As shown in Appendix N, the signal plot allows for the identification of these three previously specified trigger types.

The data were then filtered according to the specified frequency range, and channel positions were mapped. Since the activities aimed to analyze each brain frequency band, the data were inspected for delta (0.5-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), sigma (12-15 Hz), beta (15-30 Hz), and gamma (30-50 Hz) bands. Any data above 50 Hz were classified as noise, mainly resulting from movement, and excluded from further analysis. Ensuring that the system can detect all relevant bands is essential, as the target audience typically uses lower brain frequencies for the same activities as the study participants. In this study, the beta band is particularly recommended, since it is associated with states of attention, concentration, and cognitive activity, allowing for monitoring of mental engagement, fatigue, and emotional impact during cognitively demanding tasks.

Finally, it was shown that the data could be separated into its individual components, and artifacts could be detected through independent component analysis. As depicted in Figure 4.1, this method yields multiple representations for each component, highlighting the activation across different brain regions. Additionally, this technique allows for the quantification of the percentage of brain activity or artifacts captured by each component.

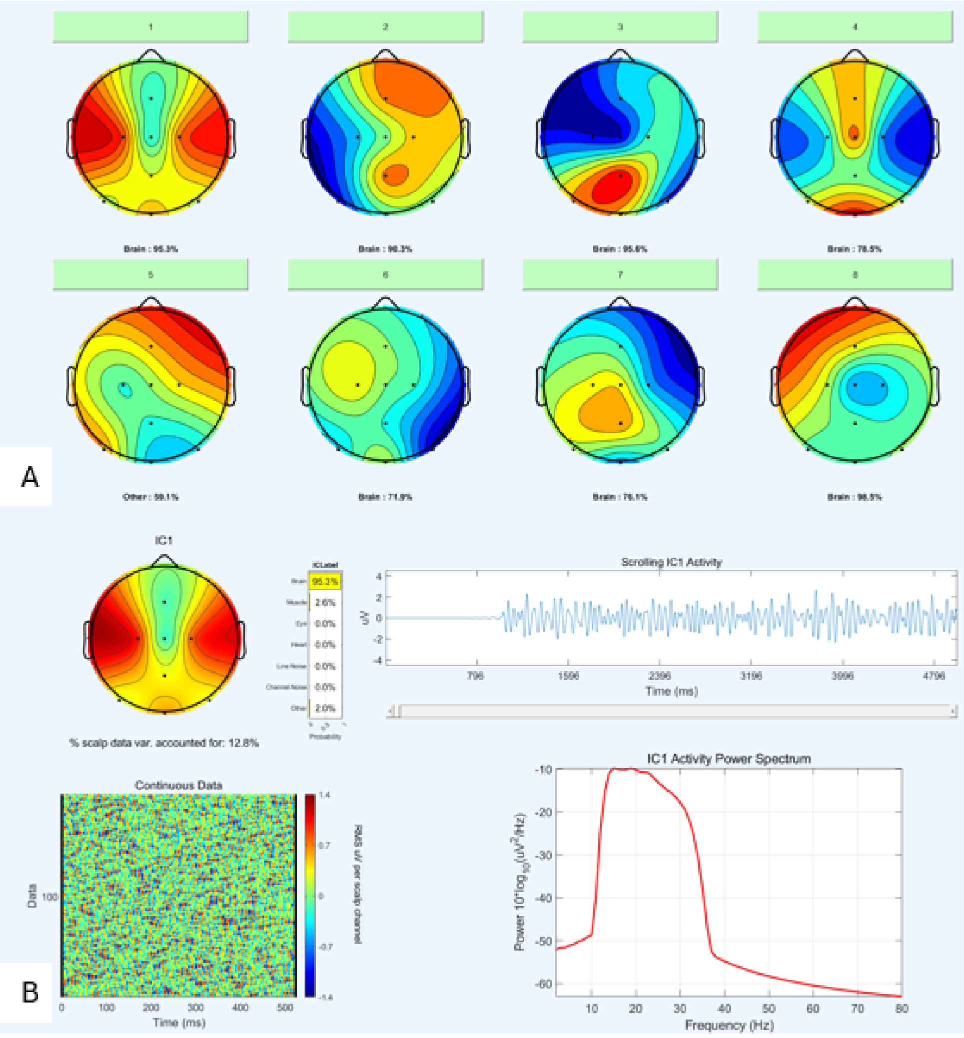


Figure 4.1: ICLabel results: A- 8 components of the signal; B- IC1 analysis.

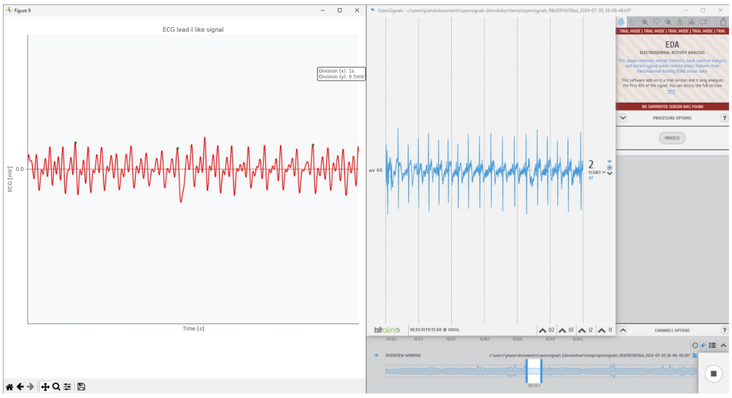
The analysis conducted offered valuable insights into the challenges encountered and provided practical experience with the software. It also played a crucial role in shaping the methodologies and requirements for upcoming testing sessions. Notably, it was observed that participants demonstrated distinct signals and patterns of brain activation across different frequencies while performing identical tasks. This observation emphasizes the necessity of establishing an individual baseline for each participant.

4.1.2 Electrocardiogram analysis

During the tests, the ECG signal was monitored in real time using the OpenSignals software developed by Plux Biosignals. This software provides accurate and immediate visualisation of the signals captured by the sensors, facilitating continuous monitoring during acquisition. However, OpenSignals does not provide data processing tools without a paid add-on, which limits the detailed analysis of the collected data.

To overcome this limitation, we used two Python libraries that can provide the necessary tools to analyse ECG signals free of charge. Based on the work of Pedro Gomes (2022), available in his GitHub repository, the BioSPPy and pyHRV packages were implemented [24, 28, 125]. These libraries offer advanced functionalities for the analysis of biological signals, including peak detection, calculation of heart rate variability (HRV), and processing of signals in different frequency domains. The script (Appendix A) provides various visual analyses of the signal, using the ecg() function from the BioSPPy package as an example. It allows you to see the difference between the data before and after filtering, identify the peaks along the signal, display a clear view of the signal trace, analyse the amplitudes over time and overlay each R-R interval, as shown in Appendix O.

The code used to process the ECG data is described in Appendix A to allow other researchers to replicate the analysis. Comparing the ECG processed by this Python script with that obtained directly from OpenSignals, it is clear that the signal processed by Python is significantly smoother (see Figure 4.2). This smoothing improves the clarity of the data and makes it easier to identify peaks and other features important for clinical and diagnostic analysis.



This plugin computes overall statistics, basic spectral analysis, and extract typical event-related phasic features from Electrodermal Activity (EDA) sensor data.

This software add-on is a trial version and it only analyses the first 60s of the signal. You can access the full version here.

Figure 4.2: Left shows the filtered signal from the Python script; right displays the same signal from OpenSignals.

When comparing the signal obtained with a standard ECG waveform, it can be seen that the signal does not have the same perfection or ideal clarity. However, despite the small imperfections and irregularities, all the characteristic peaks - such as the P waves, QRS complex and T wave - are still visible and identifiable (Figure 4.3). Although the signal is not perfect, it is of sufficient quality to allow functional analysis, especially when additional signal processing or more advanced filtering techniques are used, as was done in this study. This shows that, despite technical or environmental limitations, the system still provides reliable results for practical applications in cardiac monitoring.

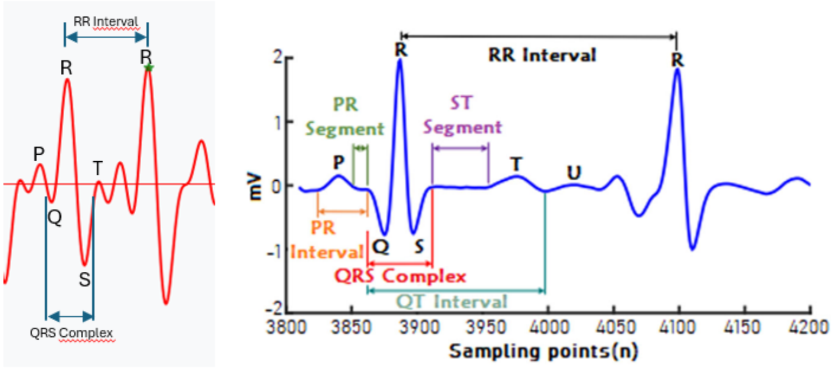


Figure 4.3: Identification of peaks through comparison with the diagram. A: Signal acquired (P1); B: ECG diagram [35].

In the tests carried out both in the condition without the use of VR, simultaneously with the EEG and ECG equipment, and in the condition with the use of VR, the ECG data maintained its quality in terms of waveform and characteristic peaks at times of greater rest. Regardless of the immersive context introduced by virtual reality, the P waves, QRS complex and T wave were consistently identifiable, showing that the inclusion of VR did not significantly interfere with the acquisition of the cardiac signal (Figure 4.4). The signals selected for analysis are detailed in Appendix D and Appendix E, illustrating both test conditions: without VR equipment and with VR equipment, respectively.

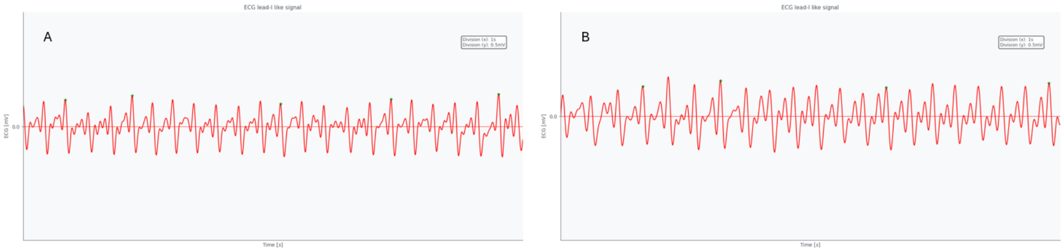


Figure 4.4: Comparison of the signal obtained in P5 in the condition without VR (A) and with VR (B).

This consistency in ECG quality is essential as it allows analyses of HRV and other physiological parameters to be performed with confidence without the need for significant adjustments to the methodology used to interpret the signals. In addition, the consistent quality of the data suggests that the use of VR environments can be explored in future studies without compromising the integrity of ECG measurements, which is particularly relevant for therapeutic and real-time monitoring applications. In the tests conducted, movement artifacts were observed in both conditions - both without the use of VR and with the use of VR simultaneously with the EEG and ECG equipment. However, it was found that the VR condition produced a greater amount of motion artifacts, mainly due to the need for participants to move more when interacting with the virtual reality game (Figure 4.5).

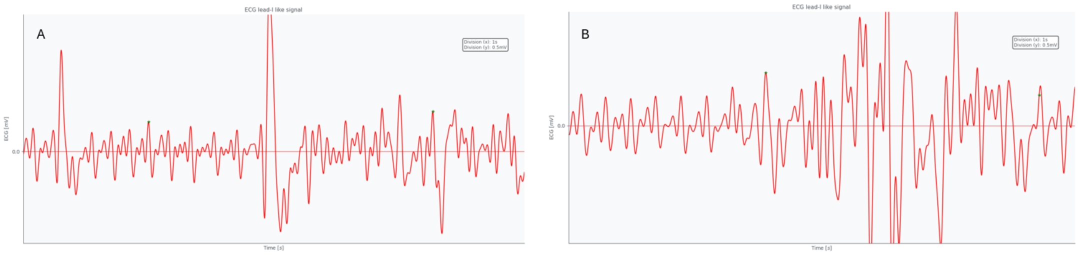


Figure 4.5: Movement artefacts in the P5 ECG signal in the condition without VR (A) and with VR (B).

Although the quality of the ECG signal was maintained during the resting phases, movement artifacts became more pronounced during the moments when the participants moved, causing transient distortions in the signal. These distortions were more frequent in the VR condition, where the immersive environment required more extensive and constant body movements to interact with the game, which amplified the distortions in the signal.

4.1.3 Comfort Questionnaire

At the end of the tests, each participant was asked to complete a questionnaire written in Microsoft Forms. This questionnaire was designed to assess the level of comfort with each component and with the system while performing the tasks. It contained 13 questions with a Likert scale from 1 to 7, where 1 corresponded to ’terrible’ and 7 to ’excellent’. There were also 5 open-ended questions to allow for additional feedback. The full questionnaire responses can be found in Appendix F.

A. Electroencephalogram cap

Regarding the comfort level of the cap, participants were asked how they felt during the cap fitting process and about the comfort of the cap itself. Concerning the setup, 50% (n=3) reported a very good comfort level (level 6), 33.33% (n=2) reported an excellent comfort level (level 7) and 16.7% (n=1) reported a poor comfort level (level 3).

Regarding the comfort of the electrodes (dry electrode structure), 50% (n=3) reported excellent comfort (level 7), 33.33% (n=2) reported poor comfort (level 1) and 16.7% (n=1) reported good comfort (level 5).

Regarding the cap itself, taking into account the fabric and closure mechanism, 50% (n=3) reported excellent comfort (level 7), 16.7% (n=1) very good (level 6), 16.7% (n=1) good (level 5) and 16.7% (n=1) fair (level 4). The participant who rated the cap as level 5 stated that the fastening mechanism was initially too tight, which became uncomfortable as he performed the tasks.

Thus, the cap had an average comfort level of 5.83 during the fitting process; 4.67 in relation to the electrodes and 6 in relation to the device itself.

B. Electrocardiogram electrodes

With regard to the ECG electrodes, three electrodes positioned over the C7 vertebra and the trapezius muscle, participants were asked about their level of comfort during placement, activity and removal.

For the placement of the electrodes, 83.3% (n=5) reported excellent comfort (level 7), while only 16.7% (level 5) reported good comfort (level 5). During activities, there was unanimity in participants’ responses, with 100% (n=6) rating comfort as excellent (level 7). For electrode removal, 66.7% (n=4) reported excellent comfort (level 7), 16.7% (n=4) reported fair comfort (level 4), and 16.7% (n=3) reported poor comfort (level 3).

Thus, the ECG had an average comfort level of 6.67 during the placement of the electrodes, 7 during the performance of the activities, and 5.83 during the process of removing the electrodes.

C. Virtual reality headset

As with the questions about the ECG equipment, participants were asked about the level of comfort when putting the VR equipment on, during the activity and when taking it off. When putting the equipment on, 33.33% (n=2) reported excellent comfort (level 7), 16.7% (n=1) reported very good comfort (level 6), 16.7% reported reasonable comfort (level 4), 16.7% (n=1) reported poor comfort (level 3) and 16.7% (n=1) reported very poor comfort (level 2).

During the activities within the virtual environment, the majority of participants had a more positive experience, with 83.3% (n= 6) reporting an excellent level of comfort (level 7) and only 16.7% (n= 1) reporting a reasonable level of comfort (level 4).

The results were also positive for the process of removing the VR equipment, with 83.3% (n=6) reporting excellent comfort (level 7) and 16.7% (n=1) reporting very good comfort (level 6).

In additional feedback related to the VR equipment, one participant noted that the images within the virtual environment sometimes appeared blurry, which could be attributed to poor headset adjustment. Another participant mentioned the difficulty of adjusting the VR headset while wearing the EEG cap.

These results indicated a final average comfort level of 4.83 for putting on the VR equipment, 6.5 during the activities and 6.83 for the removal.

D. Electroencephalogram-electrocardiogram-virtual reality system

Finally, the overall comfort of the system, the combined weight of all equipment, the level of mobility while wearing the system, and the ease of performing the assigned tasks were evaluated. In general, based on participants' responses, the system showed positive results, with 50% (n=3) indicating an excellent comfort level (level 7), 16.7% (n=1) reporting a very good comfort level (level 6), 16.7% (n=1) indicating a good level of comfort (level 5), and 16.7% (n=1) reporting a poor comfort level (level 3).

Regarding the system's weight, 50% (n=3) of participants rated their comfort as good (level 5), 33.3% (n=2) as excellent (level 7), and 16.7% (n=1) as very poor (level 1).

Although participants were instructed to remain as still as possible during task execution, it is important to assess the degree of mobility allowed by the system. In this regard, 66.7% (n=4) rated their mobility as excellent (level 7), and 33.3% (n=2) as very good (level 6).

With respect to the ease of performing the tasks, 50% (n=3) of participants rated it as excellent (level 7), while the remaining 50% (n=3) rated it as very good (level 6). As a result, the EEG-ECG-VR system presented an average comfort level of 5.63, 5 for the system's weight, 6.67 for mobility while using the system, and 6.5 for the ease of performing the assigned tasks.

4.2 Initial Tests

Based on the results obtained from the initial testing phase, a similar methodology was applied in the following phase, placing greater focus on the analysis of electroencephalography data. The specific marking of triggers and the corresponding tasks proposed to participants are detailed in Appendix J for further reference.

4.2.1 Electroencephalogram Analysis

Given the focus of this dissertation on the implementation of NF in a therapeutic context, the practical application will include an analysis of data derived from memory tasks and activities involving auditory stimuli. In this regard, the electroencephalography data will be examined in relation to the electrodes corresponding to the brain regions associated with the auditory cortex. As for memory, EEG is used as an indirect indicator of brain states involved in memory processes. As illustrated in Figure 4.6, the Fz electrode is associated with cognitive activities related to memory tasks, as it is located near the prefrontal cortex. Conversely, the C3 and C4 electrodes are linked to auditory processing, as they are situated in the temporal regions of the brain.

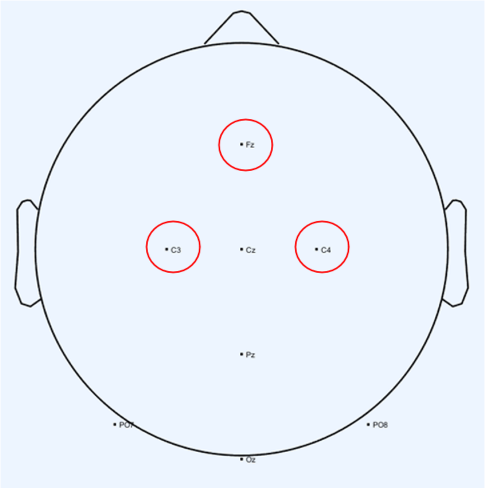


Figure 4.6: Unicorn Black electrodes selected for the targeted brain regions.

This study also aimed to identify the N200 and P300 biomarkers in EEG signals recorded during each VR-based activity. We used the same analysis approach as in previous studies focused on detecting these biomarkers.

Thresholds were set to validate biomarker values: N200 required amplitudes below -1 µV, while P300 required values above 4.5 µV. The results, presented in Appendix G, indicate that the N200 was the most consistently detected biomarker across participants, while P300 only occasionally approached the threshold. The biomarker analyses were conducted within a 20 ms range around the reference point to capture subtle variations in neural response timing. For instance, to analyze the N200 (targeted at 200 ms), assessments were made at 180 ms, 200 ms, and 220 ms. Similarly, for the P300, analyses were performed at 280 ms, 300 ms, and 320 ms. This approach aimed to ensure a precise identification of each biomarker by accounting for individual timing differences in neural processing.

Although exact thresholds weren't always met, waveform analysis around expected biomarker time windows showed irregularities that suggest cognitive responses to stimuli. These disturbances in the waveform indicate possible neural modulation, hinting at cognitive engagement even if the precise biomarker criteria weren't reached.

These findings suggest that N200 is more reliably detected in VR tasks, while P300 may be harder to capture, possibly due to task characteristics or equipment sensitivity. This highlights the potential of EEG biomarkers for assessing cognitive engagement in VR, while also pointing to the need for refined measurement techniques.

4.2.1.1 Memorization task (without virtual reality)

To investigate the activity of brain regions of interest identified by the selected electrodes, the predefined activities (memorization of a list of random words and repeating the words) were analyzed using EEGLAB software. The methodology applied in previous tests was replicated in this analysis, with a specific focus on the beta frequency band. After filtering the data to the specified frequency range and decomposing all components and artifacts, triggers were used to define the epochs for analysis. To obtain results from the first phase of the experiment, conducted without the use of VR, type 2 triggers, which mark the beginning of each task, were selected. These triggers were analyzed within a window from -2 to 2 seconds around each trigger point. From this initial analysis, a power spectrum plot was generated for the electrodes in the baseline condition, including electrode Fz during the reading of the word list.

The primary objective of this study was to assess the occurrence of significant brain activation during cognitively demanding activities, specifically during a word-list memorization task and, subsequently, during the task of recalling the memorized words. These tasks were chosen for their requirement of high levels of concentration and sustained mental processing, which are essential for both memory formation and active information retrieval. The hypothesis was that brain activation would increase relative to the baseline, reflecting the high cognitive demand required by both activities. To evaluate this hypothesis, time-frequency spectra were analyzed under baseline, memorization, and recall conditions. This analysis allows for the identification of variations in brain activity associated with heightened cognitive engagement. The results, presented in the Figure 4.7 below, show a significant increase in brain activation during both tasks compared to baseline. During memorization, a notable increase was observed in the beta frequency band, suggesting an intensified state of attention and mental focus. The recall task, conducted after memorization, also showed increased brain activation, both in the beta band and in slightly higher frequencies. This increase in higher frequencies is associated with processes that require active retrieval and maintenance of information, reflecting the additional cognitive effort involved in recalling the memorized words. Activity in these bands indicates a heightened allocation of neural resources, necessary to access and organize the information stored during the memorization phase.

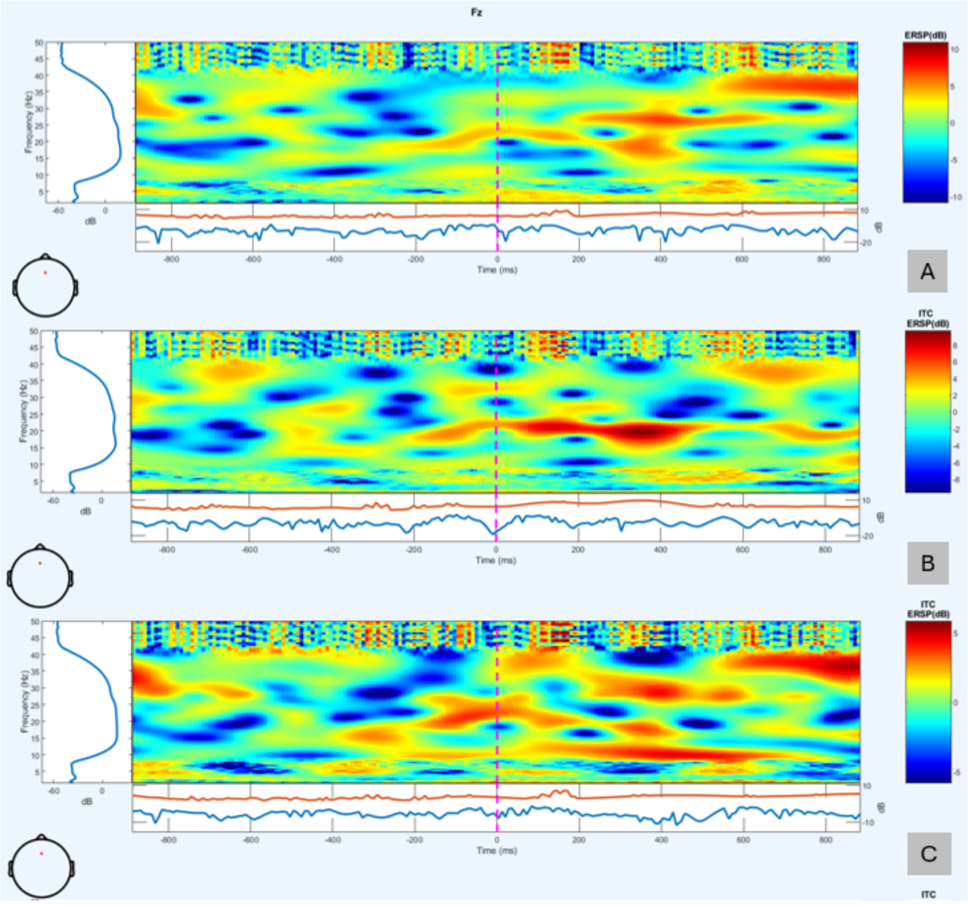


Figure 4.7: Brain activation: A- baseline; B- during word memorization; C- during word recall.

These findings demonstrate not only increased brain activation during both the memorization and recall tasks but also highlight how the brain dynamically adjusts its activity in response to the distinct demands of each task phase.

To assess the quality of the brain signal and ensure that we are capturing relevant information, it is essential to use filtering methods that evaluate the amount of artifacts present in the signal. One commonly used method for this purpose is IClabel, a tool that provides the percentage of the signal derived directly from the brain (referred to as "brain") compared to the percentage of the signal coming from other external sources that are not of interest for this study, such as noise from muscle activity, cardiac activity, eye movements, and others.

In the context of this study, these filtering methods were applied to examine the provenance and overall quality of the obtained signals. The goal was to confirm that the majority of the recorded signal originated from relevant brain activity, particularly in the regions of interest, and that noise from artifacts was minimized.

Examples of the obtained results can be visualized in the Figure 4.8 below, which presents the different components of the signal, as well as the percentages associated with each of these components. The analysis reveals that our main interest is to obtain the highest possible percentage of brain-derived signal, particularly in the prefrontal cortex region, as the task performed by participants involves significant cognitive effort, requiring attention and memory. The prefrontal cortex is widely recognized for its role in executive functions, such as attention control and working memory processing.

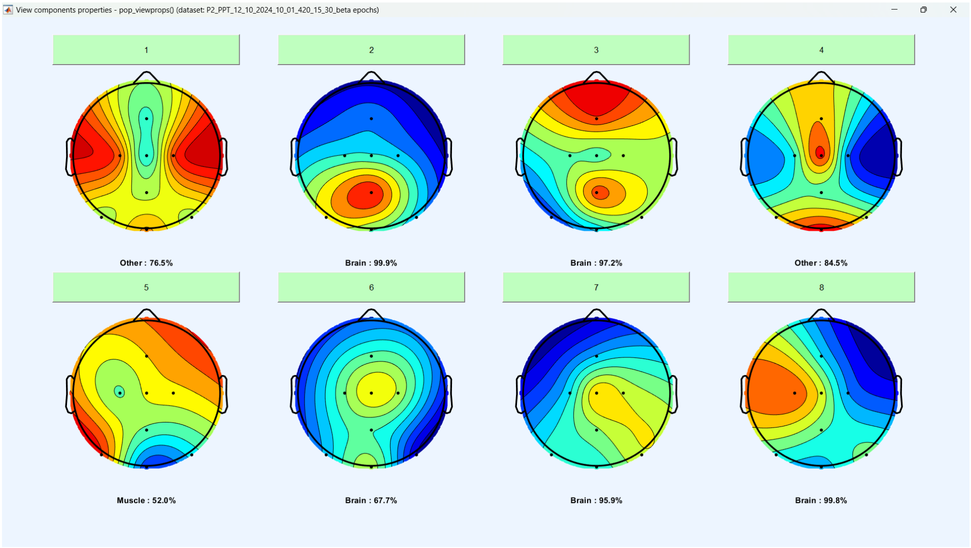


Figure 4.8: IClabel results showing the percentage of brain-derived signal and artifacts in each component.

When performing Independent Component Analysis (ICA) on EEG data recorded with the Unicorn Hybrid Black system, which includes 8 electrodes, the analysis produces exactly 8 Independent Components (ICs). This is because ICA decomposes the recorded signals into a number of components equal to the number of input channels. Each IC represents a statistically independent source contributing to the recorded signals, such as brain activity, muscle artifacts, or eye movements.By separating these components, ICA allows researchers to better identify and isolate the contributions of various signal sources within the EEG data, enhancing the accuracy and interpretability of the analysis. The correspondence between ICA components and the electrodes is as follows: ICA Component 1 corresponds to the signal from Electrode 1 (e.g., Fp1), ICA Component 2 corresponds to Electrode 2 (e.g., Fp2), ICA Component 3 corresponds to Electrode 3 (e.g., C3), ICA Component 4 corresponds to Electrode 4 (e.g., C4), ICA Component 5 corresponds to Electrode 5 (e.g., Pz), ICA Component 6 corresponds to Electrode 6 (e.g., Oz), ICA Component 7 corresponds to Electrode 7 (e.g., Fz), and ICA Component 8 corresponds to Electrode 8 (e.g., Cz).

The Figure 4.9 below clearly illustrates a signal component indicating activation in the correct region of the brain, the prefrontal cortex, with a high percentage of "brain" signal, which is desirable to ensure the captured information is relevant to the research objectives. This high percentage of brain signal, associated with the region of interest, validates the quality of the obtained data, allowing for a more accurate analysis of brain activation related to memory and attention tasks.

Moreover, this result is significant as it confirms the effectiveness of the filtering process, not only in terms of signal cleanliness but also regarding the precise localization of brain activation. The ability to isolate the brain-derived signal and exclude noise from other sources is crucial for the reliable interpretation of data, ensuring the robustness of the results and enabling more consistent conclusions about the relationship between brain activation and performance in the cognitive task at hand.

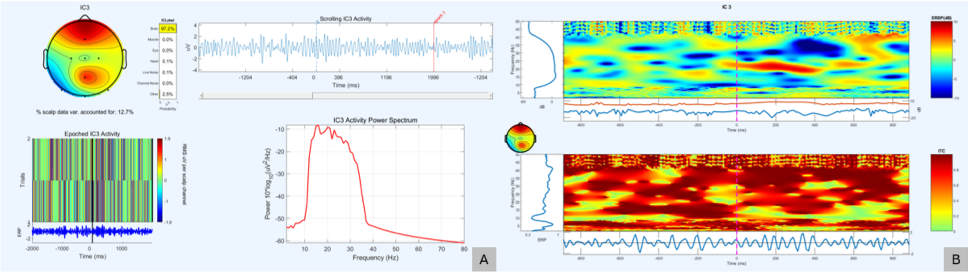


Figure 4.9: Brain activation in the prefrontal cortex identified by IClabel: A- Best component analysis (IC3); B- Time-frequency analysis of IC3.

The time-frequency analysis conducted on component IC3 revealed activity in the beta frequency band, as expected. The presence of beta band activity is particularly relevant, as this range is frequently associated with cognitive processes such as attention, focus, and working memory, making it the target frequency for the task at hand. This result in IC3 confirms that the captured signal reflects the expected brain activity, indicating that neural processing in the beta frequency band is directly involved in task performance and aligns with the study's objectives.

To identify values that could serve as biomarkers in the PLAY platform for NF applications, ERPs were obtained from the Fz channel, located near the prefrontal cortex, a region of interest in this task. The ERP is an electrical response generated by the brain in reaction to specific sensory, motor, or cognitive stimuli, allowing researchers to observe how the central nervous system processes information in real time. This measure is particularly useful in studies on attention and memory as it captures the dynamic changes in neural processing associated with external stimuli.

Among ERP potentials, both negative and positive responses at specific time intervals can be observed, such as the N200 and P300.

For identifying N200 and P300 biomarkers, a rigorous analysis methodology was applied. First, a CSV file containing baseline epoch data was extracted, with a time window of -2 to 2 seconds surrounding the trigger that marks the start of the baseline task. Then, the average signal amplitudes for the Fz channel during this baseline were calculated. Following this, an ERP analysis was conducted for each experimental activity (memorization and word repetition), and the average baseline value was subtracted from the ERP values obtained for each activity. This subtraction isolates the specific amplitude changes related to cognitive activities, providing a more precise measure of the desired biomarkers.

This procedure enables not only the detection of changes in neural response times but also the establishment of consistent parameters for NF use. Since ERPs offer insight into shifts in mental state and attention, obtaining reliable N200 and P300 values from the Fz channel is significant for NF applications. It provides insights into the brain's responsiveness to task stimuli, which can be utilized to enhance interventions aimed at optimizing memory and focus through brain training.

In Appendix P are presented the amplitude values for each participant during baseline and memorization activity conditions. It also includes the results of subtracting the baseline amplitude from the activity amplitude, which provides the true amplitude value for each participant.

In this research, N200 values below -1µV and P300 values above 4.5µV were used as the established thresholds to be considered. Certain results from this study meet these criteria and can be regarded as reliable biomarkers for N200 and P300. Specifically, the N200 values for

Participant 9 and the P300 values for Participant 15 fall within the expected ranges for their respective biomarkers. These findings thus support the validity of these results as biomarkers, in accordance with EEG research standards. However, it is important to note that scientific evidence suggests the range for these biomarkers may be broader than the thresholds used in this study, indicating the possibility that additional values could also fall within the expected range.

In addition, the difference in brain activation during both phases of the study was analyzed: during the baseline phase, where the participant received no stimuli, and during the word memorization task. As shown in Figure 4.10 below, there is a clear distinction in brain activation between these two moments for some participants. In this examples, it is notably that greater activation is observed during the memorization activity compared to the baseline phase, indicating that the task elicited a higher neural response. This increased activation during the cognitive task is consistent with expectations, as memory-related processes typically involve heightened brain activity in areas such as the hippocampus and prefrontal cortex.

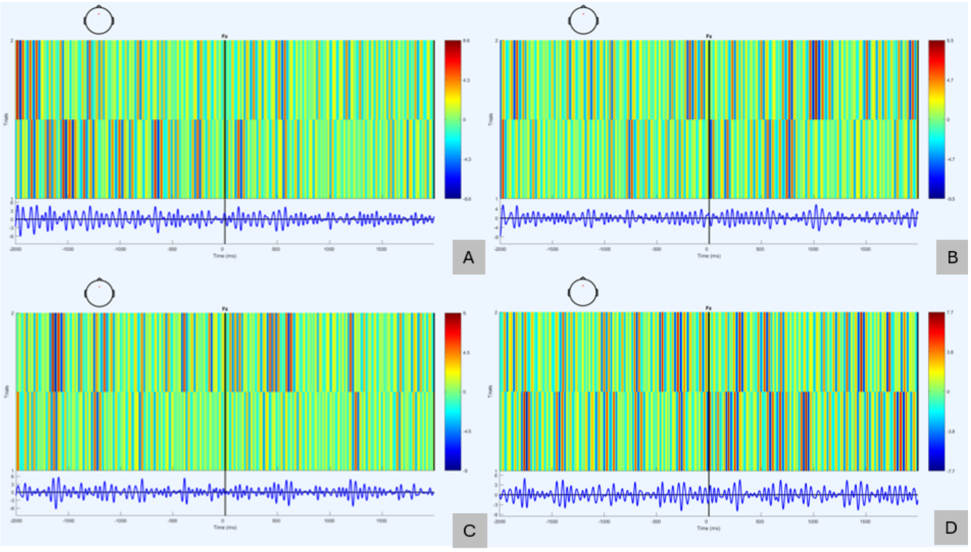


Figure 4.10: Brain activation during the baseline phase (A and C) and the word memorization task (B and D), for participants 9 and 15, respectively.

In Figures 4.10A and 4.10C, the recorded brain activation during the baseline phase is shown. These images reveal relatively low levels of neural activation, consistent with a resting or minimally engaged cognitive state. This observation aligns with the expectation that baseline conditions generally involve reduced cognitive demand, serving as a control phase to assess task-related changes in activation. The activation patterns are localized and less widespread, likely reflecting intrinsic neural activity during resting states or minimal external stimulation.

Conversely, Figures 4.10B and 4.10D depict brain activation during the word memorization task, showing a notable increase in activation levels. This is evidenced by the presence of more extensive and varied colors on the graphs, indicating higher neural engagement. This enhanced activation likely reflects the cognitive processes involved in memory encoding, such as attention allocation, semantic processing, and working memory. Regions associated with these tasks, such as the prefrontal cortex and temporal lobes, may be prominently engaged.

The contrast between the baseline and task phases highlights the task's cognitive demand, emphasizing the sensitivity of the recording methods to capture dynamic changes in brain activity. This comparison underscores the effectiveness of the experimental design in isolating task-specific neural processes. Additionally, participant variability, as seen in differences between participants 9 and 15, could provide valuable insights into individual differences in cognitive strategies, neural efficiency, or task engagement during memory-related activities.

4.2.1.2 Grabbing and eating task (with virtual reality)

A similar procedure of comparing baseline activity to task activity was conducted, this time during the VR-based apple-grasping and eating task. The aim was to verify whether, as hypothesized, there would be greater brain activation during the activity phase. However, the results indicated a less pronounced increase in brain activation during the task than expected, with clear evidence of heightened activation only in one case (Participant 11), as illustrated in Figure 4.11 below. For most participants, brain activation appeared visually similar or even reduced during the VR task compared to the baseline phase.

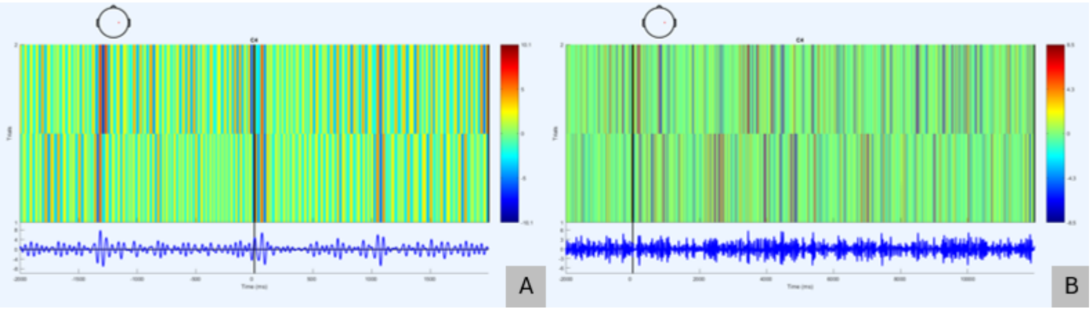


Figure 4.11: Brain activation during the baseline phase (A) and during the apple-grasping and eating task (B).

Several factors may explain this outcome. First, the novelty and immersive nature of VR might have introduced a cognitive overload or sense of disorientation, potentially affecting brain activity patterns. Additionally, the relatively passive and repetitive nature of the apple-grasping task may not have fully engaged the neural networks typically activated in more complex or dynamic tasks. Finally, individual differences in adaptation to VR environments could have influenced the variability in responses, as some participants may have required additional time to acclimate to the VR setup, resulting in varied neural engagement.

The objective was to assess whether cerebral habituation would occur — a neural adaptation characterized by a reduction in brain response to a repetitive activity.

In this study, participants were asked to perform a task of grabbing and eating three apples in sequence, repeating the same action three times. To investigate whether participants exhibited habituation during the task of successively picking up three apples, a detailed analysis of the EEG signal was conducted. The methodology followed these key steps:

1. **Precise Event Marking:** The exact moment when each participant grasped an apple was identified and recorded. This ensured accuracy in pinpointing the key events for analysis.

2. **EEG Signal Segmentation:** For each grasping event, three separate analyses of the EEG signal were performed - A time window of 20 microseconds before and after the central moment (the exact time of the grasp) was analyzed. This approach provided a high-resolution view of neural activity leading up to and immediately following the action. These reference points were then used to map the electroencephalographic (EEG) signal at electrodes C3 and C4, chosen for their optimal placement to capture the motor activity required to grab and bring the apple to the mouth.

This dual-focused temporal window allowed us to capture both action anticipatory neural processes and post-action responses, which are critical for understanding the cognitive and motor dynamics associated with task repetition. By comparing the EEG signals across the three apple-grasping events, patterns of neural activity were examined to identify any reductions in response intensity or changes in activation patterns that might indicate habituation. Such adaptations could reflect neural efficiency improvements or reduced cognitive demand due to task familiarity. This meticulous approach not only ensured the precision of the analysis but also provided a comprehensive understanding of the temporal dynamics of EEG activity during repetitive motor tasks. These findings are crucial for interpreting neural adaptation mechanisms and their implications for task learning and motor control. However, it is important to acknowledge that a degree of uncertainty remains regarding the procedure used to detect the habituation factor, highlighting the need for further validation and refinement in future studies.

The analysis showed that, in twelve cases, there was a progressive decrease in EEG signal amplitude over the three instances of the action, indicating habituation, as seen in Appendix H.

These findings suggest that with repetition, the brain required fewer resources to perform the same motor task, demonstrating neural adaptation, as illustrated in Figure 4.12 below.

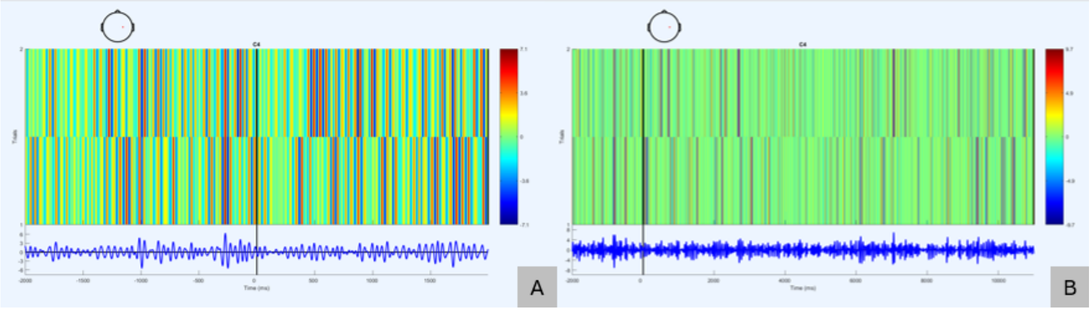


Figure 4.12: Examples of habituation effect in participant 2 (C3 electrode analysis): A - baseline; B - during activity.

The figure compares cerebral activity during baseline (Figure 4.12A) and task execution (Figure 4.12B). The baseline condition shows higher brain activity, while the task execution reveals a noticeable decrease, as indicated by the lighter colors on the graph. This suggests a reduction in neural engagement during the task. A comparison across other participants, showing the habituation factor, can be found in Appendix I.

4.2.2 Electrocardiogram analysis

Although ECG data were collected during the exercises, the analysis of this data was not extensive. This limitation is largely due to the experimental context, where participant movement played a significant role. During the activities, participants performed movements inherent to physical exercise, which naturally generate noise and artifacts in the ECG data. These movements directly impact the quality and accuracy of the recorded signals, introducing variability that makes clear and precise interpretation challenging.

As a result, some noise in the findings is expected, complicating a clean analysis of cardiac signals. This noise can obscure important patterns and reduce the sensitivity needed to detect subtle variations in participants' cardiac activity, particularly in response to specific exercise stimuli. For a more robust and rigorous analysis in the future, it would be advisable to employ more advanced filtering methods or apply motion-correction techniques. These could help minimize the impact of movement-induced noise and improve the accuracy of the ECG data analysis.

4.2.3 Comfort questionnaire

Similar to the initial tests, participants in the validation tests were asked to fill out the same comfort questionnaire concerning the devices utilized during the session.

A. Electroencephalogram cap

Regarding the comfort level of the setup of the cap, 60% (n=9) of the participants reported an excellent comfort level (level 7), 13.3% (n=2) reported a very good comfort level (level 6), 13.3% (n=2) a good comfort level (level 5), 6,7% (n=1) a fair comfort level (level 4), and 6.7% (n=1) reported a poor comfort level (level 3).

Regarding the comfort of the electrodes (dry electrode structure), 53.3% (n=8) reported excellent comfort (level 7), 13.33% (n=2) reported a very good comfort (level 6), 20% (n=3) a good comfort level (level 5) and 13.3% (n=2) reported fair comfort (level 4).

Regarding the cap itself, taking into account the fabric and closure mechanism, 60% (n=9) reported excellent comfort (level 7), 26.7% (n=4) very good (level 6), 6.7% (n=1) good (level 5) and 6.7% (n=1) poor (level 3). As additional feedback, one participant reported experiencing itchiness due to the bottom part of the EEG cap that wrapped around the chin.

Thus, the cap had an average comfort level of 6.13 during the fitting process; 6.06 in relation to the electrodes and 6.33 in relation to the device itself.

B. Electrocardiogram electrodes

With respect to the ECG electrodes, participants were asked to assess their comfort level when the device was applied, while performing tasks, during the removal of the electrodes, and concerning the new strap used to secure the BITalino in place.

For the placement of the electrodes, 86.7% (n=13) reported excellent comfort (level 7), while 13.3% (n=2) reported very good comfort (level 6). During activities, 86.7% (n=13) rated the comfort as excellent (level 7). For electrode removal, 33.3% (n=5) reported excellent comfort (level 7), 26.7% (n=4) reported very good comfort (level 6), 13.3% (n=2) a good comfort level (level 5), 20% (n=3) a fair comfort level (level 4) and 6.7% (n=1) reported a very poor comfort level (level 2).

Furthermore, the fixation device for the BITalino received 80% (n=12) of responses indicating an excellent comfort level (level 7) and 20% (n=3) indicating a very good comfort level (level 6).

Thus, the ECG had an average comfort level of 6.87 during the placement of the electrodes, 6.8 during the performance of the activities, 5.53 during the process of removing the electrodes, and 6.8 regarding the strap holding the BITalino.

C. Virtual reality headset

Participants were asked about the level of comfort when putting the VR equipment on, during the activity and when taking it off. When putting the equipment on, 73.3% (n=11) reported excellent comfort (level 7), and 26.7% (n=4) reported very good comfort (level 6).

During the activities within the virtual environment, 66.7% (n=10) of the participants reported an excellent level of comfort (level 7), 26.7% (n=4) a very good level of comfort (level 6), and only 6.7% (n= 1) reporting a good level of comfort (level 5).

The results were positive for the process of removing the VR equipment, with 86.7% (n=13) reporting excellent comfort (level 7) and 13.3% (n=2) reporting very good comfort (level 6).

In additional feedback regarding the VR equipment, one participant noted that the headset was slightly loose, shifting out of the correct position throughout the experience.

These results indicated a final average comfort level of 6.73 for putting on the VR equipment, 6.6 during the activities and 6.87 for the removal.

D. Electroencephalogram-electrocardiogram-virtual reality system

Finally, the system was assessed based on its overall comfort, weight, mobility, and user-friendliness in completing the tasks. Regarding the level of general comfort, 60% (n=9) indicated an excellent comfort level (level 7), 33.3% (n=5) reported a very good comfort level (level 6), and 6.7% (n=1) reporting a good comfort level (level 5).

Regarding the system's weight, 60% (n=9) of participants rated their comfort as excellent (level 7), 26.7% (n=4) as very good (level 6), 16.7% (n=1) as good (level 5), and 6.7% (n=1) as fair (level 4).

Although participants were instructed once again to remain as still as possible during task execution, it is important to assess the degree of mobility allowed by the system. In this regard, 73.3% (n=11) rated their mobility as excellent (level 7), 20% (n=3) as very good (level 6), and 6.7% (n=1) as fair (level 4).

With respect to the ease of performing the tasks, 86.7% (n=13) of participants rated it as excellent (level 7), while the remaining 13.3% (n=2) rated it as very good (level 6). As a result, the EEG-ECG-VR system presented an average comfort level of 5.53, 6.4 for the system's weight, 6.6 for mobility while using the system, and 6.87 for the ease of performing the assigned tasks.

5

Framework Proposal

This dissertation was initially motivated by the need to explore and propose solutions for integrating NF into an existing system. Although the initial tests did not provide enough data for a full assessment of the research, the subsequent session, along with the analysis and insights gained from this study, contributed to creating a framework that proposes a possible integration of the system into therapeutic sessions.

5.1 Target Population and Key Moments

NF in VR contexts offers promising therapeutic support for children with eating difficulties related to ASD, anxiety disorders, chronic gastrointestinal issues, and ARFID [141, 134, 150]. These conditions often involve sensory hypersensitivities or trauma linked to food, with ASD characterized by selectivity to texture, flavor, or color, and ARFID by severe sensory-based aversions [150].

Effective NF integration relies on selecting appropriate biological metrics, such as EEG or other monitoring methods. Initial EEG data from a VR headset establishes a baseline for comparison. If multiple methods provide similar results, a single, less invasive technique is preferred.

Therapeutic sessions for food aversion should monitor stress and anxiety through cortisol levels or heart rate (ECG). Comparative analysis determines whether both are necessary or if one suffices. While VR supports continuous data collection, focusing on specific tasks, such as the Pikita VR Quest game, improves signal clarity by minimizing movement.

The PLAY platform, integrated with the VR headset, allows therapists to customize interventions, particularly during initial sessions when anxiety is higher. Over time, strategically timed data collection fosters a less invasive and supportive environment, promoting the child's overall development.

5.2 Suggested Approach

Given the need to create a comprehensive tool encompassing various topics, assembling a wide range of resources for the proposed model's development is vital. Based on the tested and available devices, evaluating which components need modification is essential. Alongside the devices and methodologies, establishing the ideal timing for their implementation is crucial.

5.2.1 Neurofeedback

The Unicorn Hybrid Black EEG cap is an innovative solution for NF applications, making it an excellent choice for this research project. Its user-friendly design offers several key advantages that align with our investigation goals.

One notable feature is its ease of use; unlike traditional EEG caps that require conductive gel, this device operates without it, simplifying the setup process. This is particularly beneficial when working with children, as it enhances comfort and minimizes preparation time.

Additionally, the Unicorn Hybrid Black is wireless, allowing for greater freedom of movement during sessions. This mobility is crucial in a VR context, where participants engage in physical activities. The wireless functionality ensures seamless data collection without the constraints of wires, promoting a more immersive experience.

Equipped with advanced EEG technology, the Unicorn Hybrid Black provides accurate brainwave measurements and integrates well with other systems. This facilitates real-time data collection on NF, essential component of our research.

5.2.2 Stress and Anxiety: Tools and Techniques

Since the therapy in this study is based on exposure techniques, participants may experience anxiety, potentially affecting performance and progression. To monitor and manage this, heart rate tracking can be employed to detect abnormal increases during stimulus exposure, as shown effective in previous research.

However, ECG-based heart rate monitoring is prone to motion artifacts, often complicating data quality, especially in active settings like standard Pikita VR Quest sessions, where physical movement is frequent. ECG monitoring is more suitable during assessment periods requiring minimal movement.

Additionally, devices like the PICO 4 Enterprise and Meta Quest Pro, though originally intended for other uses, are valuable for stress and anxiety analysis. Equipped with facial sensors that track and replicate user expressions, these devices offer therapists insights into participants' facial cues, creating a robust dataset for building digital twins within the PLAY platform. Research supports the link between facial expressions and stress levels, and if eye-tracking capabilities are included, these devices could further aid in testing the viability of facial expression monitoring.

5.3 Context of use: therapeutic integration

The treatment of children with food aversion presents unique challenges, particularly regarding their psychological and physiological sensitivities. To address these challenges, a proposed framework emphasizes the gradual integration of advanced technologies, including EEG, ECG, and VR. Although this study did not include EDA measurements due to a lack of equipment, incorporating EDA could offer valuable insights into autonomic nervous system responses, such as stress and emotional arousal, which are highly relevant in therapeutic contexts. This approach could further enhance individualized interventions, as EDA is a well-established tool for monitoring emotional and stress-related changes during therapy. This approach aims to create a supportive environment that fosters trust and comfort, thereby enhancing therapeutic outcomes. By carefully planning the introduction of these devices during critical stages of treatment, clinicians can effectively monitor and manage anxiety, ultimately facilitating a more successful recovery process for young patients.

5.3.1 Integration of Electroencephalogram, Electrocardiogram, and Virtual Reality

The proposed framework emphasizes the gradual integration of devices, particularly during evaluation sessions, to accommodate the sensitivity of the target population, specifically children with food aversion. Since the serious game has not been tested with this demographic, careful introduction to VR headsets and environments is crucial.

The timing of EEG, ECG, and VR implementation should align with each child's therapeutic progression. Gradual exposure to aversive stimuli, while respecting psychological and physiological limits, is essential for reducing anxiety.

Initially, patients should be acclimated to devices incrementally to ensure that any anxiety measured is not system-induced. Therapists should conduct multiple sessions to familiarize patients with the EEG cap, ECG electrodes, and VR headset, ensuring comfort and acceptance of the technology.

The integrated system is particularly effective during the following treatment stages:

a) Initial Assessment - Establish rapport with the child and family, conduct a clinical evaluation, and prepare the child for intervention. Early EEG use can identify brain responses to anxiety or fear.

b) Intermediate VR Intervention - Introduce the EEG-ECG-VR system as part of a gradual exposure program. VR enables controlled engagement with virtual food stimuli, mitigating real ingestion risks.

c) Continuous Monitoring of Emotional and Physiological Responses - EEG and ECG systems track brain activity (e.g., alpha, beta, and theta waves) and heart rate variability during VR exposure, allowing tailored adjustments.

d) Final Transition Phase - Shift from virtual to real-world interactions while maintaining EEG and ECG monitoring to manage stress levels effectively.

5.3.2 Isolated or integrated use of electroencephalography, electrocardiography and virtual reality in a therapeutic context

The choice of EEG, ECG, VR, or their combination depends on session objectives, emotional state, and treatment stage:

a) EEG alone - Suitable for emotional assessment without intense stimuli, such as detecting brainwave patterns linked to anxiety or relaxation.

b) Isolated ECG - Effective for monitoring physiological stress during real-world food introductions, focusing on vital signs without brain activity analysis.

c) Stand-alone VR - Ideal for initial, non-invasive familiarization sessions with virtual food scenarios, promoting gradual engagement.

d) Combined use (EEG-ECG-VR) - Most effective during mid-to-late therapy phases for comprehensive emotional and physiological monitoring while addressing VR challenges.

This structured approach ensures effective, personalized therapy while minimizing stress and fostering gradual progression to real-world exposure.

5.3.3 Running a therapy session with the proposed system

The therapist may use play or distraction techniques (such as soft music or toys) while adjusting the equipment.

Conducting a therapy session with integrated EEG, ECG, and VR requires careful planning to balance effectiveness and the child's comfort. Below are the key steps:

1) Preparation: Introduce the child to the environment gently. Place EEG and ECG sensors playfully, using age-appropriate language to ensure comfort. Use distractions like toys or music if needed.

2) Baseline Phase: Collect EEG and ECG data for 5–10 minutes while the child rests without stimuli. This establishes a relaxation baseline for comparison during exposure.

3) Gradual VR Exposure: Select a VR scenario matching the child's aversion level, progressing from playful to more challenging simulations. EEG tracks stress (beta waves) and relaxation (alpha waves), while ECG monitors heart rate. Adjust exposure intensity based on physiological feedback, using positive reinforcement for encouragement.

4) Feedback and Adjustment: If stress markers rise significantly, pause or reduce stimuli and introduce relaxation techniques like guided breathing. Adjustments are made in real time to ensure safety.

5) Closure: End with decompression activities in a relaxing VR environment, avoiding food exposure. Discuss progress with the child using positive reinforcement. Remove equipment calmly, leaving the child in a relaxed state. Analyze data post-session to guide future treatments.

5.4 Benefits and limitations of the system

The EEG-ECG-VR system offers several benefits and limitations. Among its benefits, the system provides a multi-dimensional approach, addressing emotional, physiological, and behavioral aspects of food aversion. VR allows controlled exposure, while EEG and ECG monitor involuntary stress and anxiety responses, offering objective insights that are particularly useful for children who cannot articulate their discomfort. EEG detects fear-related wave patterns, and ECG tracks heart rate changes, making the system valuable for identifying internal responses. Additionally, the safe simulation environment provided by VR enables children to face sensory challenges without immediate exposure to real food, ensuring a controlled and supportive therapeutic process. The integration of gamification elements, such as visual rewards and playful interactions, enhances engagement and adherence to therapy. Furthermore, the system's ability to leverage real-time physiological data allows for personalized interventions, tailoring therapy to the child's unique needs and progress. This personalization increases treatment efficacy and fosters trust, ultimately supporting long-term success.

However, the system has limitations. Its technical complexity requires a multidisciplinary team to operate and calibrate the EEG, ECG, and VR components, which may not be available in all clinics. Additionally, children with sensory hypersensitivity, such as those with ASD, may find the equipment uncomfortable, necessitating careful adjustments to avoid increasing anxiety. Lastly, the high cost of the required equipment, software, and training can limit the system's accessibility, particularly in resource-constrained settings.

6

Conclusions

This dissertation investigated the integration of advanced technological tools into therapeutic methodologies, addressing the pressing need for innovation in healthcare. The rapid evolution of digital technologies, particularly virtual reality (VR) and gamified strategies, has significantly impacted therapeutic practices. While promising, these approaches require careful evaluation to ensure their efficacy and safety. The intersection of VR, neurofeedback (NF), and biofeedback offers a compelling framework for addressing psychological and behavioral challenges, including anxiety, stress, and food aversion.

The study focused on the development and evaluation of an integrated EEG-ECG-VR system utilizing the serious game Pikita VR Quest, initially designed for children with food aversion. The system aimed to explore the feasibility of monitoring brain and cardiac activity during VR-based therapy, assessing both the impact of immersion and the potential of NF techniques to enhance therapeutic outcomes.

The methodology included the creation of a system combining VR with EEG and ECG sensors, followed by preliminary testing with adults. Participants engaged in controlled exposure tasks while brain activity and cardiac responses were monitored. Results demonstrated the system's ability to facilitate significant engagement and adaptive stress responses, while validating its capacity to provide reliable real-time biometric data. Comfort questionnaires indicated positive acceptance, though challenges related to the simultaneous use of multiple devices were noted.

The research addressed three key questions: the feasibility of using EEG-based NF in therapy, confirmed by the system's success in modulating brain activity; the viability of employing multiple devices, which proved functional but required refinement to improve comfort; and the necessity of applying the system in all sessions, which remains context-dependent.

In conclusion, the integration of EEG, ECG, and VR shows great potential to revolutionize therapeutic interventions, enabling a more personalized and adaptive approach. Despite being tested only with adults, the system provides a robust foundation for future applications in pediatric therapy and other clinical contexts, advancing the use of emerging technologies to enhance treatment efficacy and engagement.

6.1 Limitations

Despite the team's dedicated efforts, not all objectives outlined at the beginning of this dissertation could be fully accomplished. Notably, it was not possible to reach the stage of implementing neurofeedback within the developed system, limiting the evaluation of its potential therapeutic impact. The study also faced some limitations that should be considered when interpreting its findings. First, the population used for testing consisted exclusively of adults, which does not fully reflect the intended application of the system in children, the primary target audience. Second, the simultaneous use of EEG and ECG devices introduced discomfort for some participants, potentially limiting the system's usability in extended or intensive therapeutic sessions. Third, the small sample size of adult participants restricted the ability to draw robust and generalizable conclusions about the system's effectiveness and user acceptance. Finally, the research focused on specific tasks within the Pikita VR Quest game, which may not capture the broader applicability of the system in other therapeutic contexts or conditions. These limitations highlight the need for further studies to validate and refine the system across diverse populations and scenarios.

6.2 Future Work

Future efforts will focus on expanding testing with children, particularly those with food aversions, to validate and refine the system for pediatric needs. Customization will be key to improving user comfort and effectiveness.

The project will also work on optimizing device design to reduce complexity and integrate all components into a single, user-friendly unit.

Additionally, long-term studies will assess the therapeutic effects of the system, evaluating its effectiveness across multiple sessions and stages of therapy to ensure sustained benefits over time in treating food aversion.

By the end of this research, the goal is to establish a robust, user-friendly platform that incorporates neurofeedback, ECG and EEG-based monitoring to provide real-time data to clinicians. This will allow them to track patient performance more accurately, adjust therapies as needed, and potentially improve the overall efficacy of treatments. Ultimately, this system aims to offer a more holistic approach to patient care by combining innovative technology with personalized therapeutic strategies.

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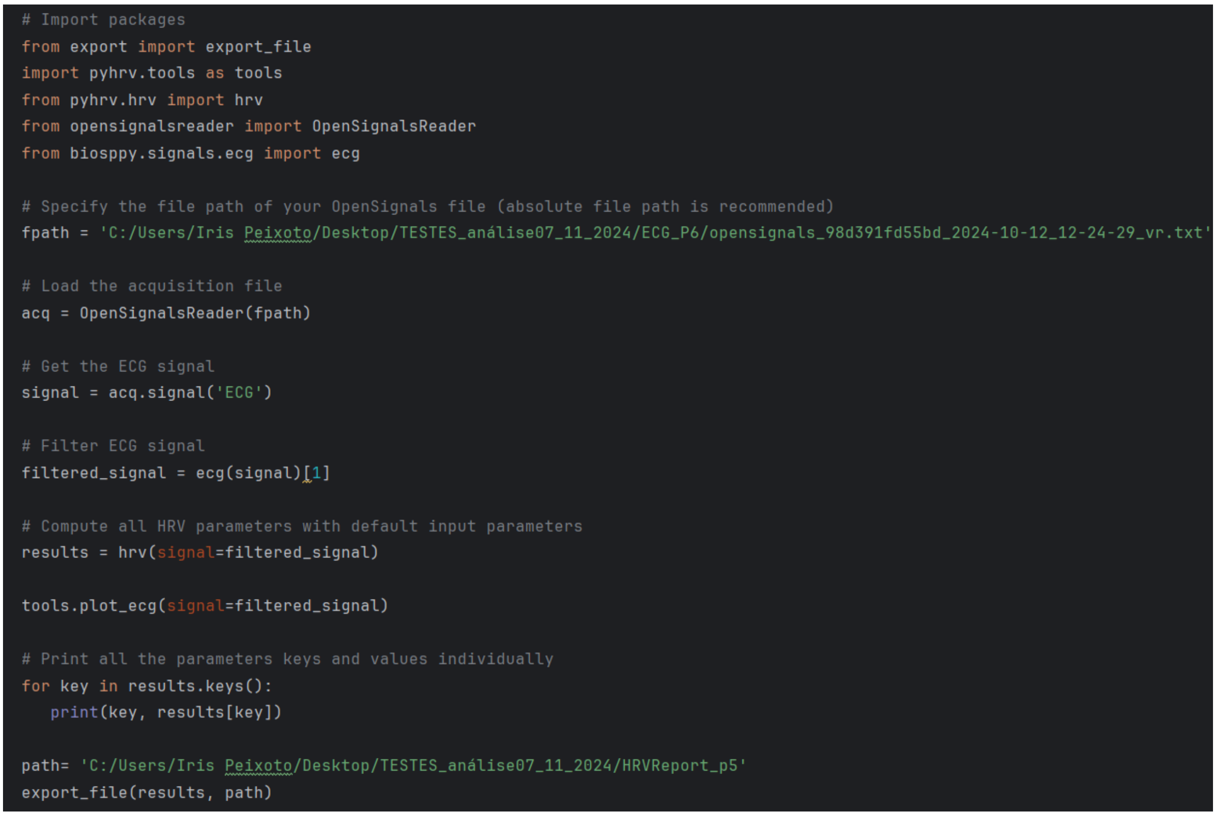
A

PYTHON SCRIPT FOR ECG SIGNAL ANALYSIS AND PROCESSING



```python
# Import packages
from export import export_file
import pyhrv.tools as tools
from pyhrv.hrv import hrv
from opensignalsreader import OpenSignalsReader
from biosppy.signals.ecg import ecg

# Specify the file path of your OpenSignals file (absolute file path is recommended)
fpath = 'C:/Users/Iris Peixoto/Desktop/TESTES_análise07_11_2024/ECG_P6/opensignals_98d391fd55bd_2024-10-12_12-24-29_vr.txt'

# Load the acquisition file
acq = OpenSignalsReader(fpath)

# Get the ECG signal
signal = acq.signal('ECG')

# Filter ECG signal
filtered_signal = ecg(signal)[1]

# Compute all HRV parameters with default input parameters
results = hrv(signal=filtered_signal)

tools.plot_ecg(signal=filtered_signal)

# Print all the parameters keys and values individually
for key in results.keys():
   print(key, results[key])

path= 'C:/Users/Iris Peixoto/Desktop/TESTES_análise07_11_2024/HRVReport_p5'
export_file(results, path)
```

B

PARTICIPANT CHARACTERIZATION QUESTIONNAIRE RESULTS AND EXCLUSION CRITERIA INFORMATION IN THE FIRST TESTING PHASE

Table B.1: Participant responses to the identification and exclusion criteria questionnaire (Part 1)

ID	**Age**	**Sex**	**Dominant hand**	**Level of VR**	**Sleep quality**	**Alcohol consumption**
P1	24	M	Right	5	Yes	No
P2	26	M	Right	3	Yes	No
P3	23	M	Right	3	No	No
P4	26	M	Left	3	Yes	No
P5	25	M	Right	3	Yes	No
P6	22	F	Bidextrous	3	Yes	No

Table B.2: Participant responses to the identification and exclusion criteria questionnaire (Part 2)

ID	**Neuro medication**	**Cardiac medication**	**Neuro disorder**	**Sight disorder**	**Hearing impairment**	**Physical limitations**
P1	No	No	No	No	No	No
P2	No	No	No	Yes	No	No
P3	No	No	No	Yes	No	No
P4	No	No	No	No	No	No
P5	No	No	No	Yes	No	No
P6	No	No	No	No	No	No

C

TASKS AND MARKERS CONDUCTED FOR THE PRELIMINARY TESTING PHASE

Table C.1: Tasks executed by participants, along with their respective objectives and associated marker types.

Task	**Objective**	**Type of Marker**
Task explanation audio	Baseline	Stimulus
Beginning of blinking 3 times, closing the eyes for 5 seconds and repeating the process for 1 minute	Baseline	Response start
Task end	Baseline	Response end
Task explanation audio	Delta frequency	Stimulus
Beginning of guided relaxation audio for 1 minute	Delta frequency	Response start
Task end	Delta frequency	Response end
Task explanation audio	Theta frequency	Stimulus
Beginning of reading and memorizing a list of 10 words for 1 minute	Theta frequency	Response start
Task end	Theta frequency	Response end
Task explanation audio	Theta frequency	Stimulus
Beginning of repeating the list of words	Theta frequency	Response start
Task end	Theta frequency	Response end

Table C.2: Second part of task Overview with Objectives and Marker Types

Task	**Objective**	**Type of Marker**
Task explanation audio	Alpha frequency	Stimulus
Beginning of looking ahead and having relaxing thoughts for 1 minute	Alpha frequency	Response start
Task end	Alpha frequency	Response end
Task explanation audio	Beta frequency	Stimulus
Beginning of sorting 10 cards in ascending order as fast as possible	Beta frequency	Response start
Task end	Beta frequency	Response end
Task explanation audio	Gamma frequency	Stimulus
Beginning of memorizing 10 face-down cards, observing only one card at a time over a duration of 1 minute	Gamma frequency	Response start
Task end	Gamma frequency	Response end
Task explanation audio	Gamma frequency	Stimulus
Beginning of sorting the cards back to the initial positions	Gamma frequency	Response start
Task end	Gamma frequency	Response end

D

ECG data from participants included in the initial testing phase - without VR

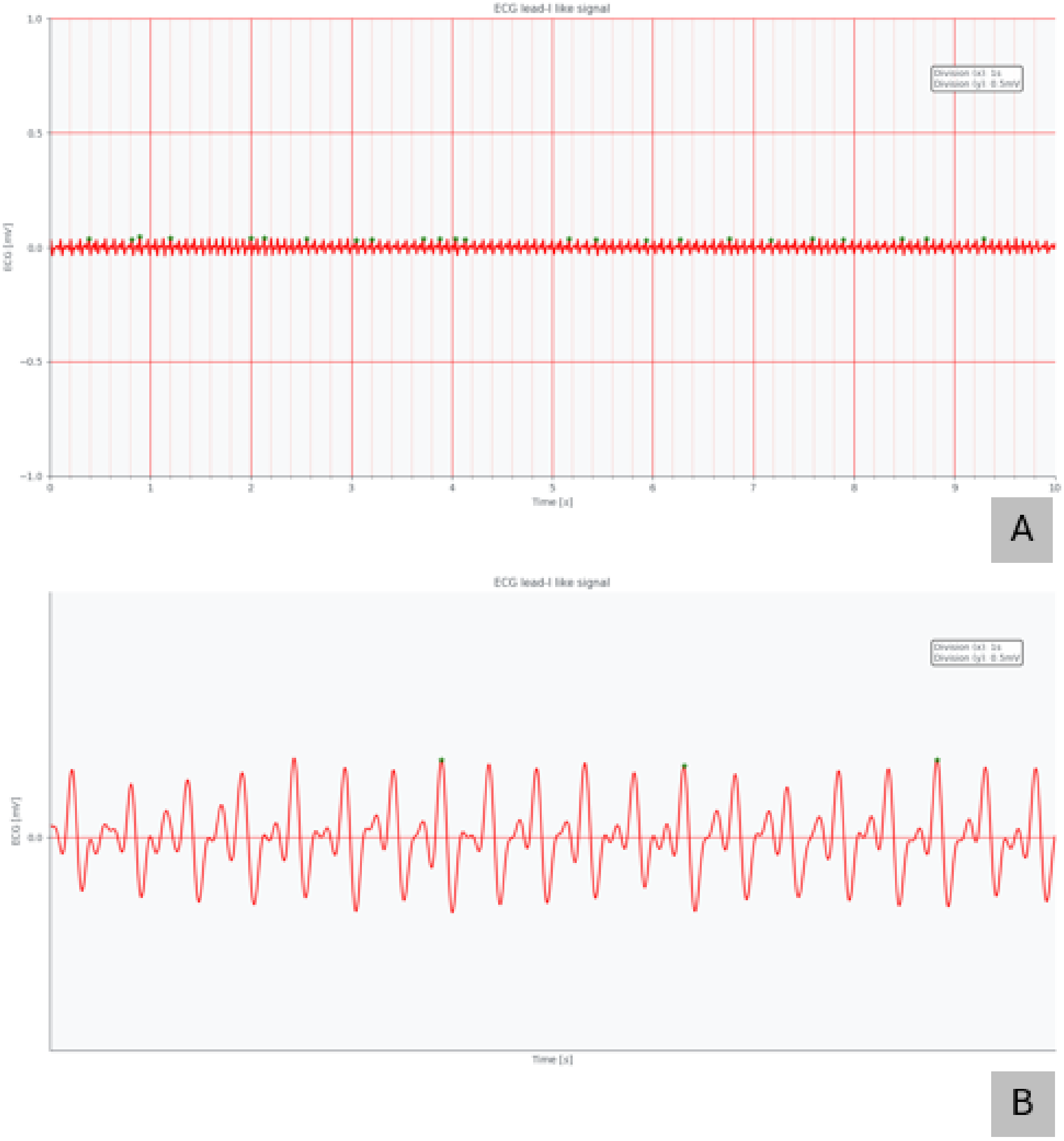


Figure D.1: ECG signal of participant 1.

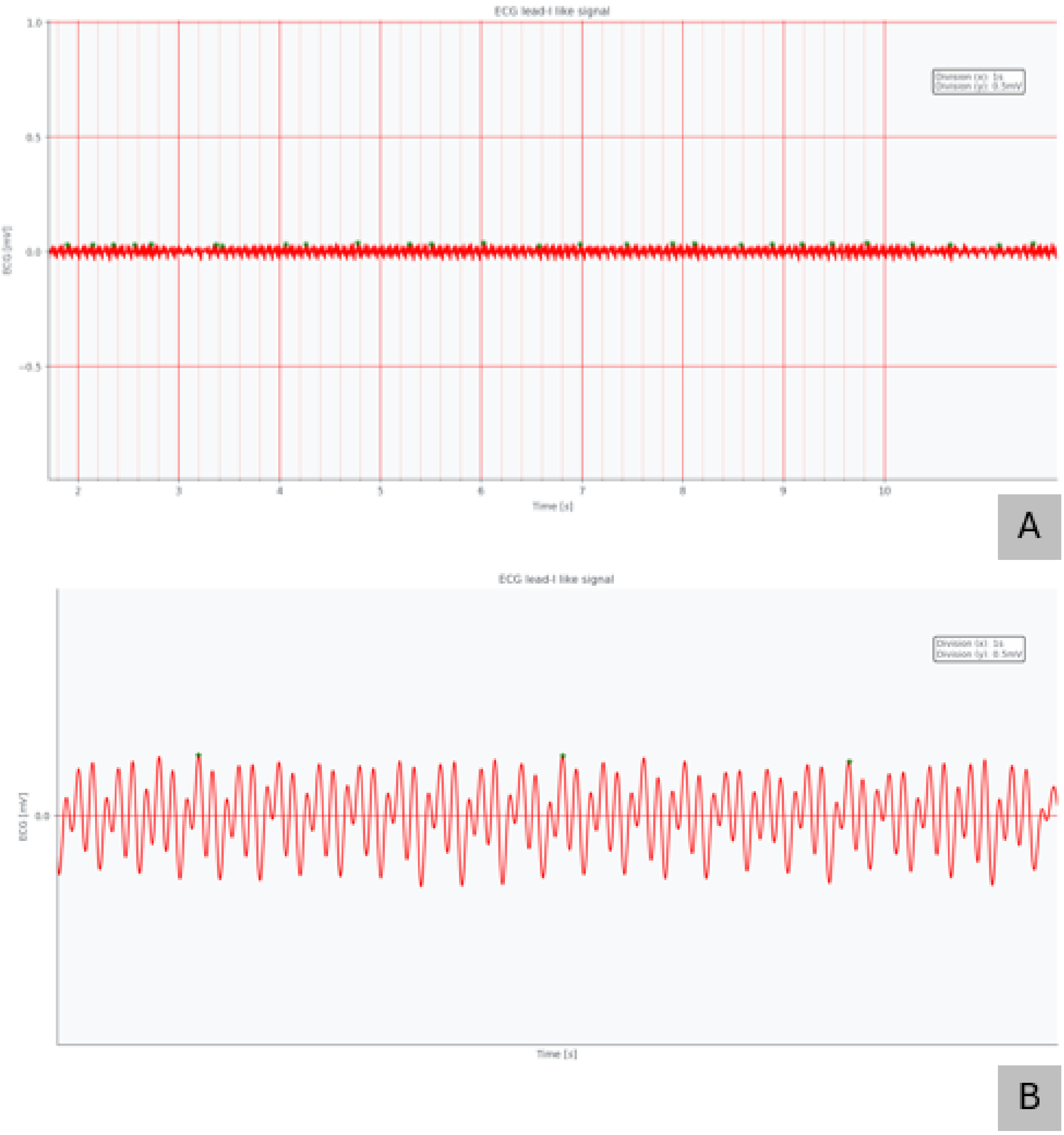


Figure D.2: ECG signal of participant 2.

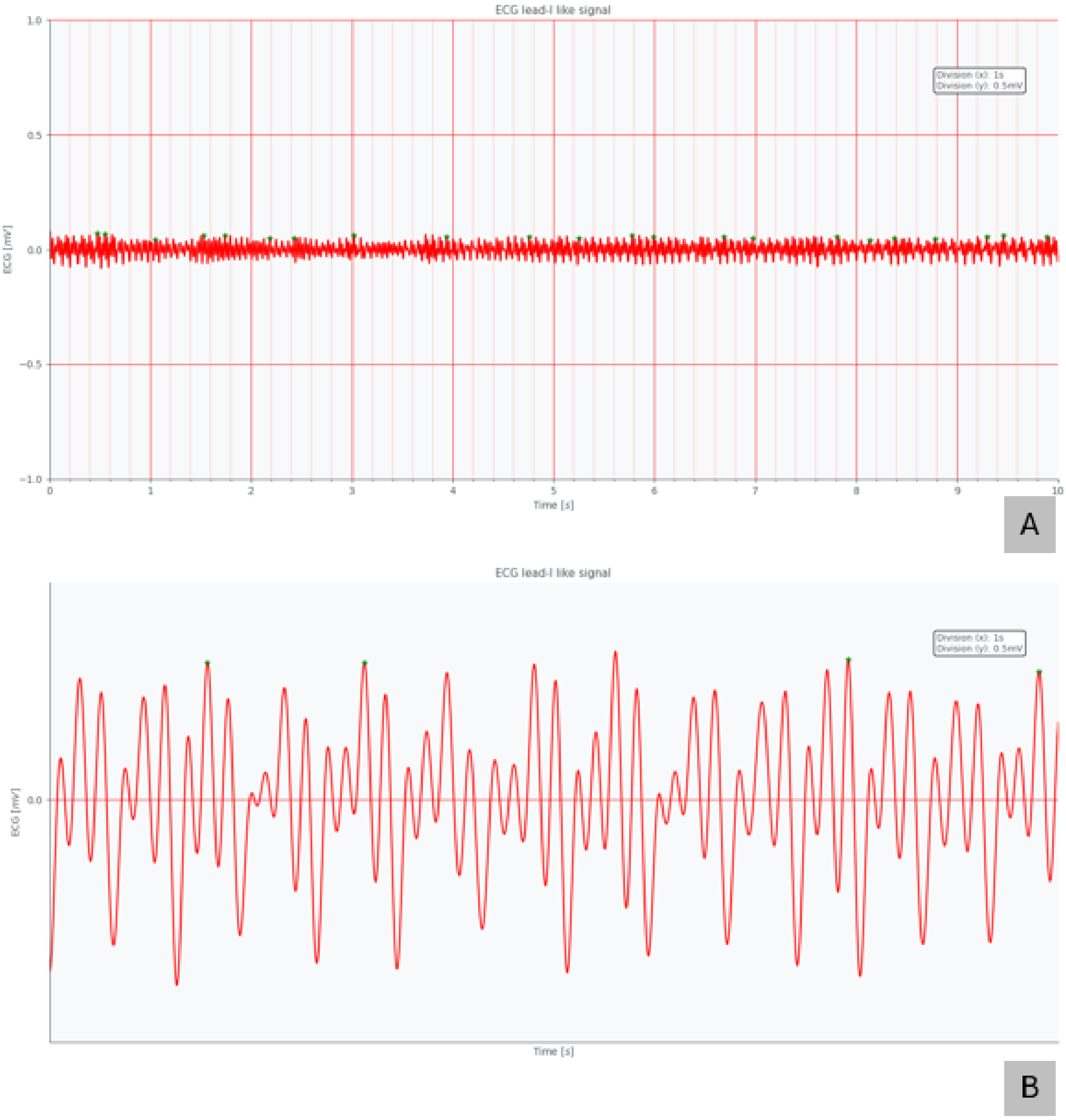


Figure D.3: ECG signal of participant 3.

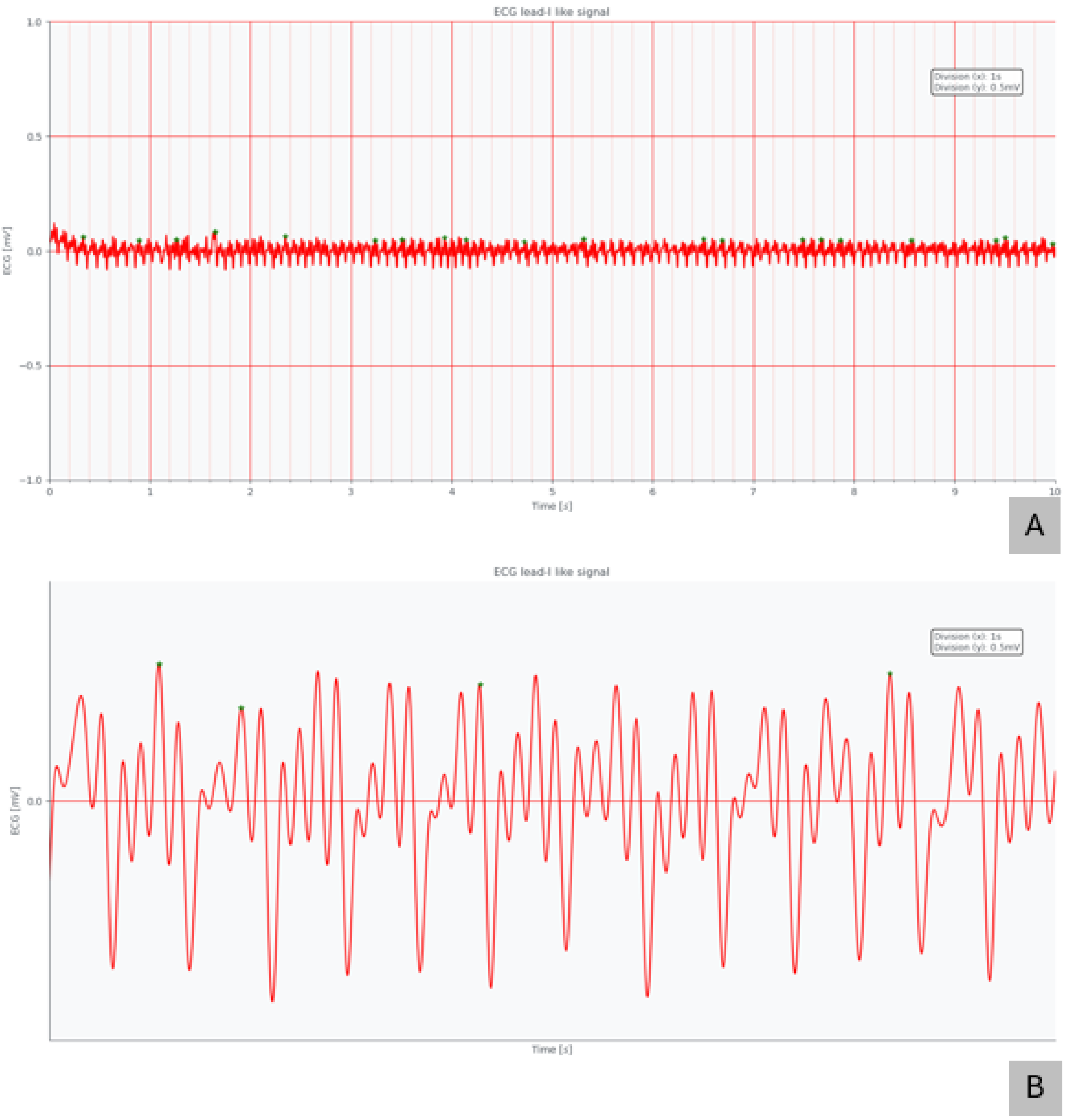


Figure D.4: ECG signal of participant 4.

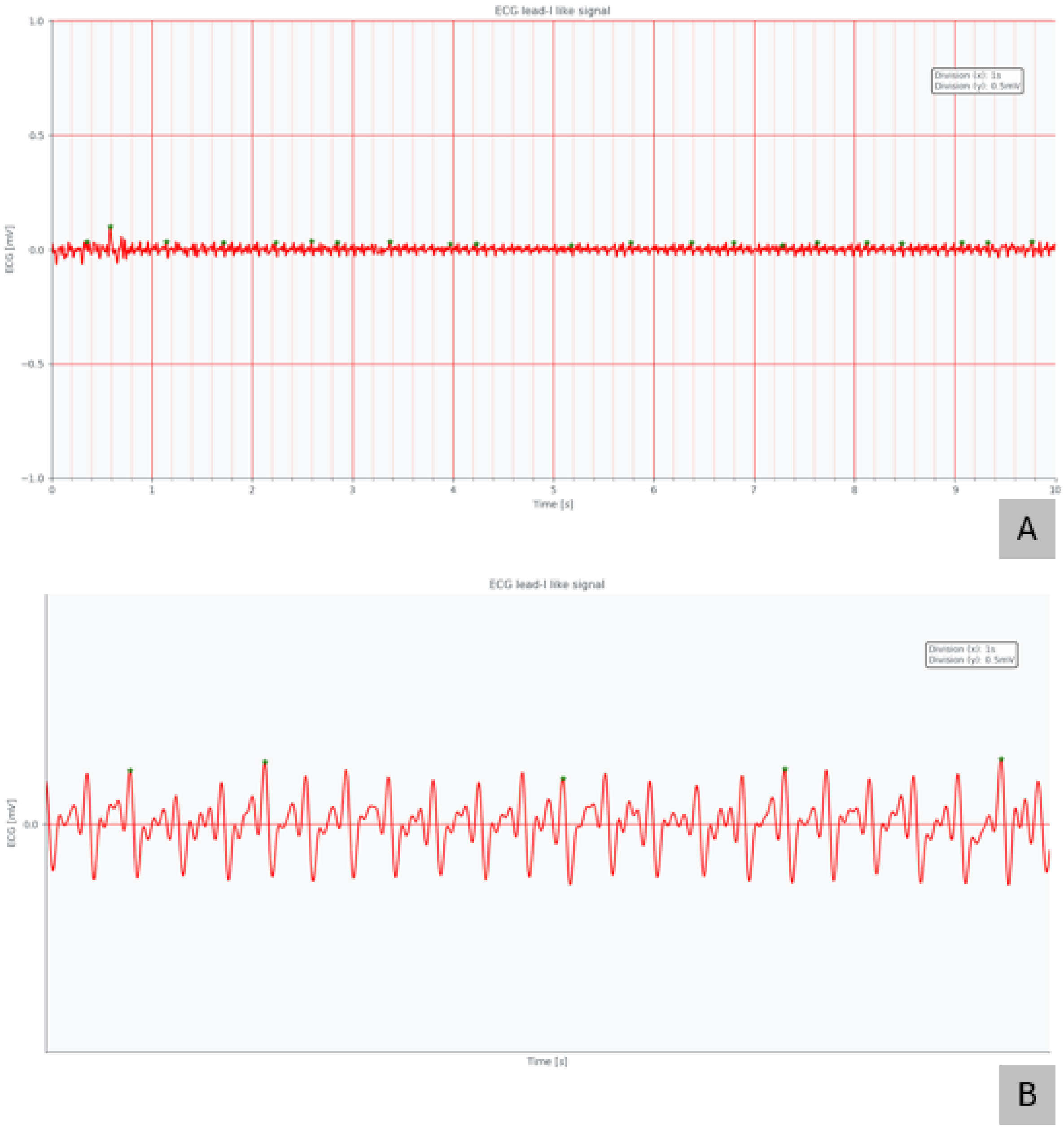


Figure D.5: ECG signal of participant 5.

E

ECG data from participants included in the initial testing phase - with VR

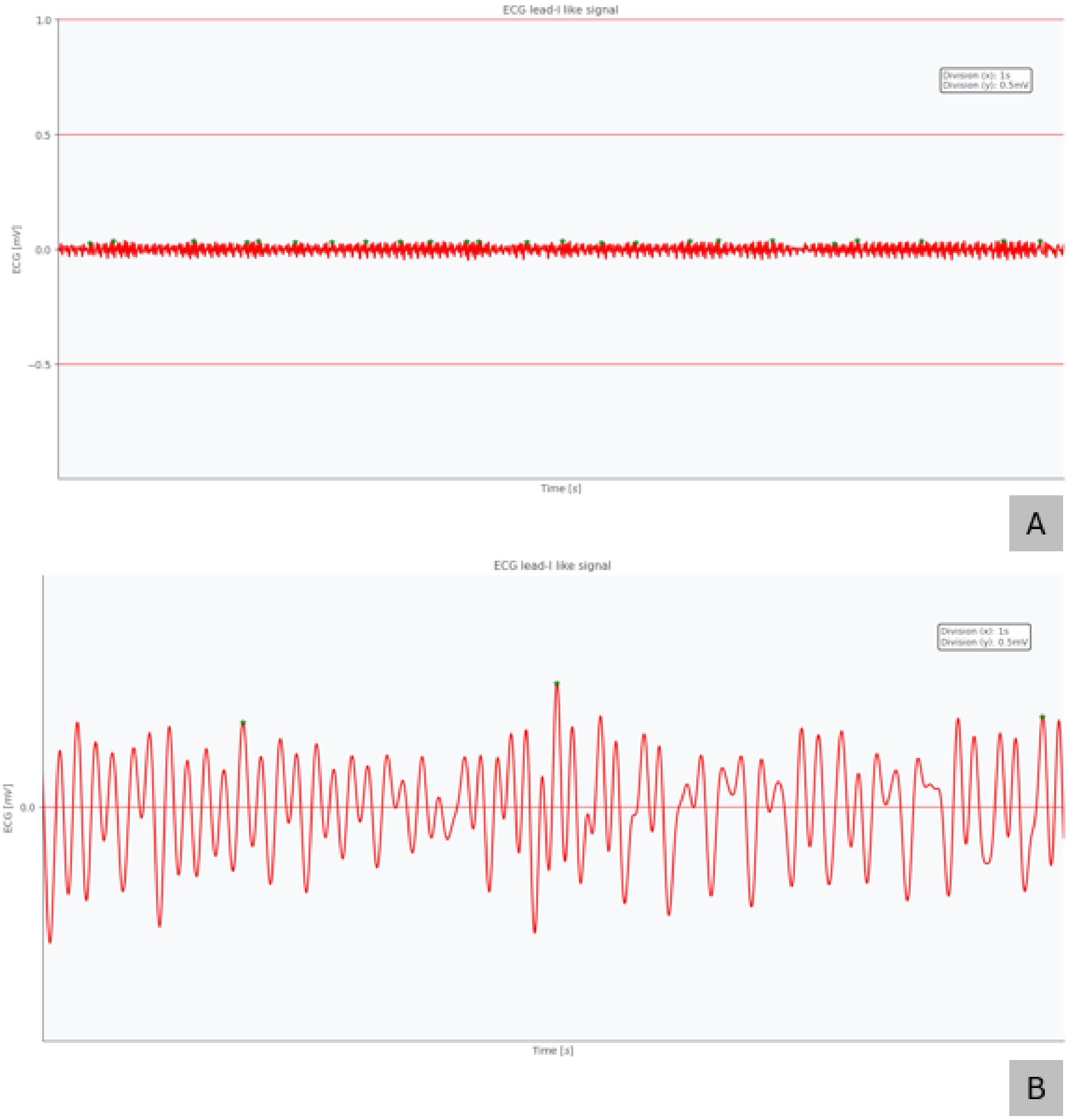


Figure E.1: ECG signal of participant 1.

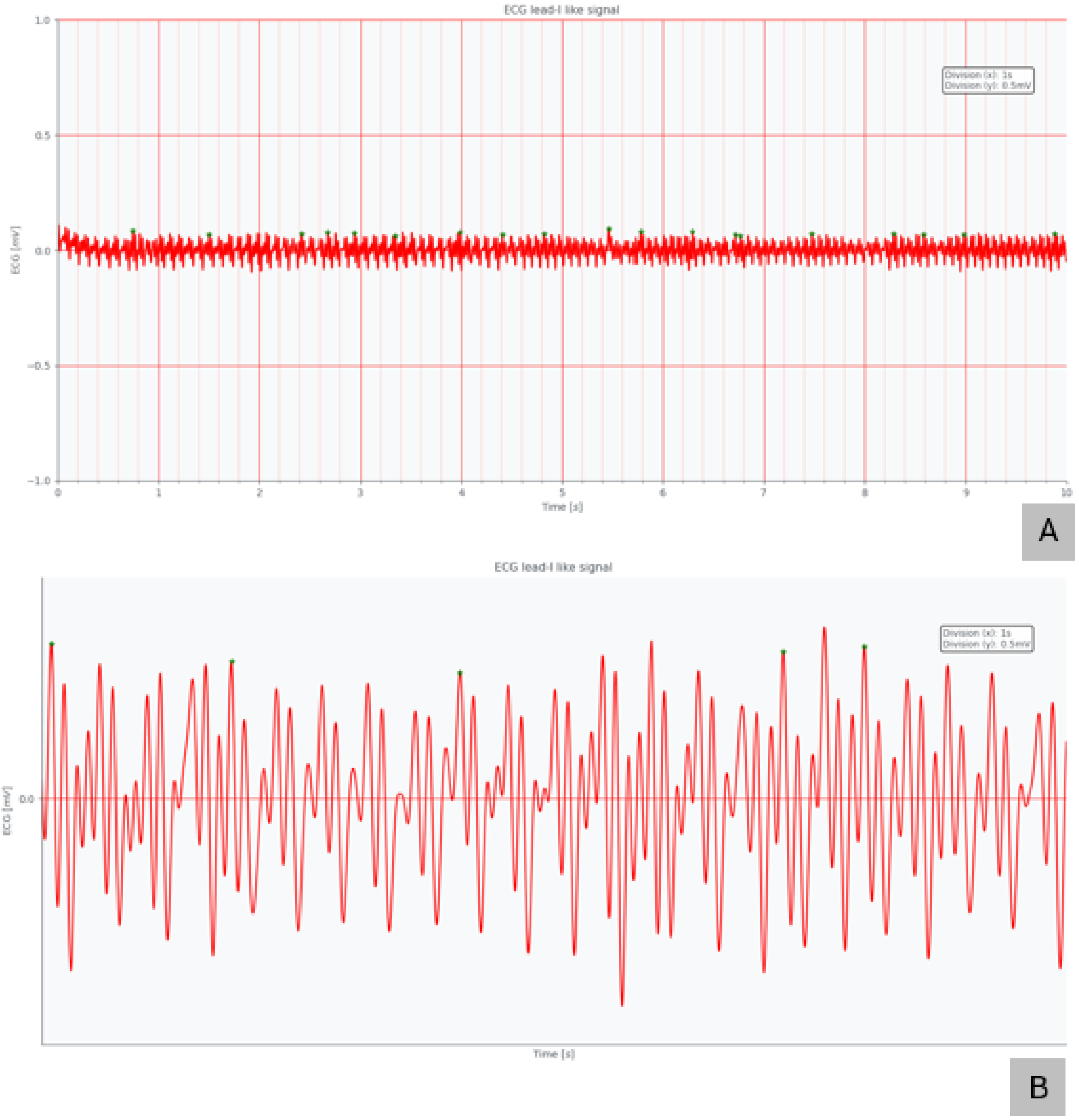


Figure E.2: ECG signal of participant 2.

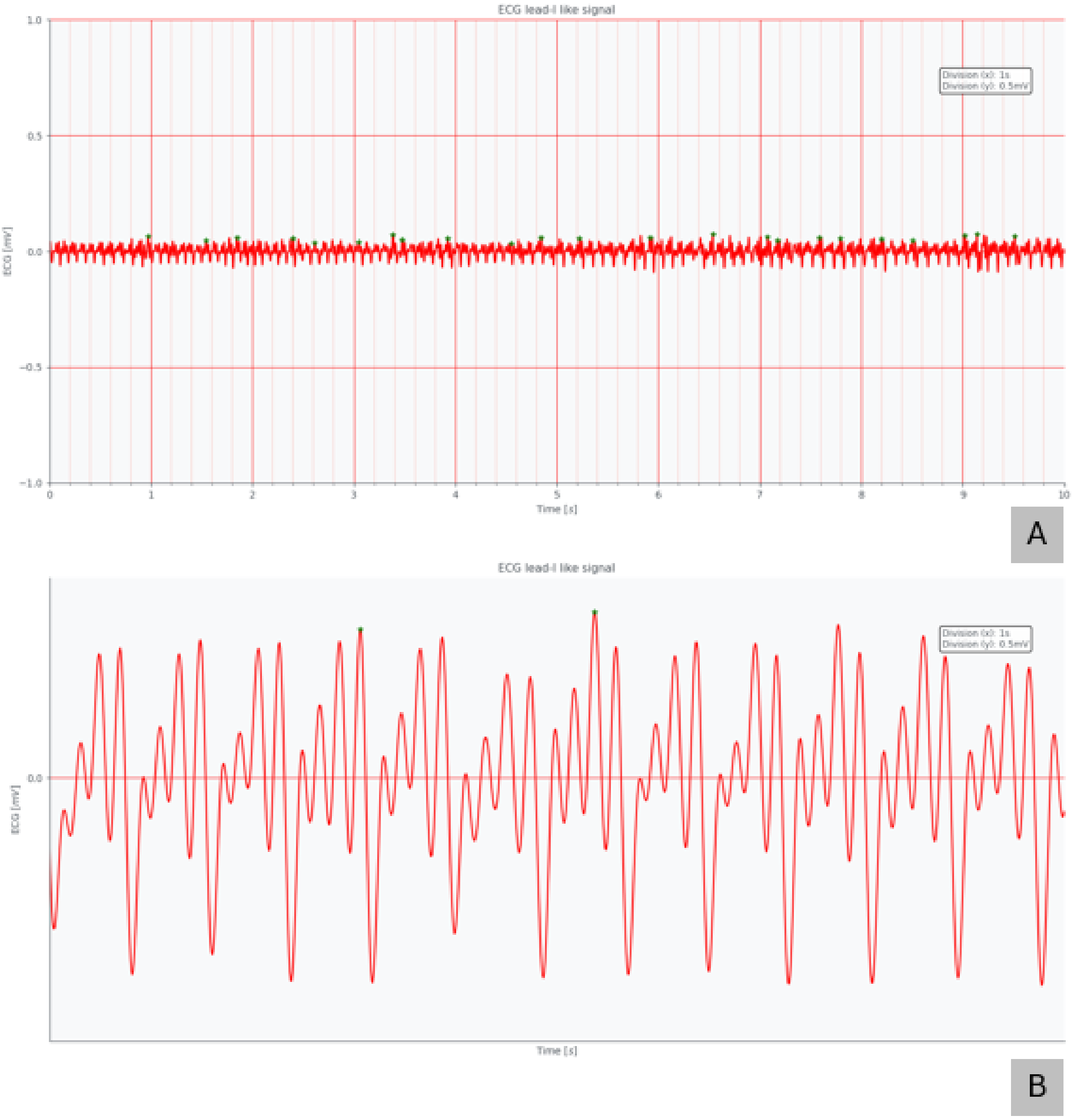


Figure E.3: ECG signal of participant 3.

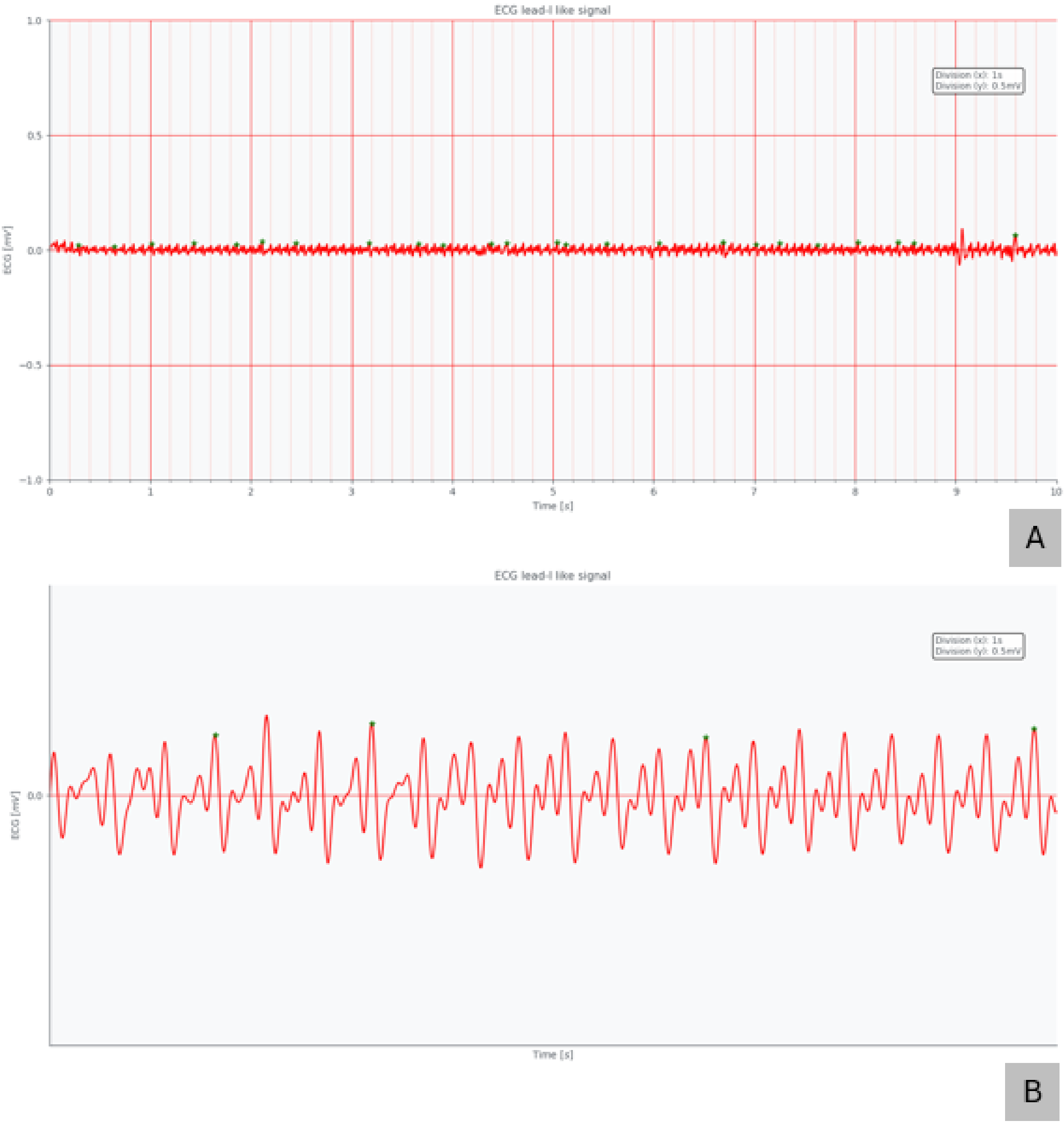


Figure E.4: ECG signal of participant 4.

F

PARTICIPANT COMFORT QUESTIONNAIRE RESULTS

Table F.1: Participants' responses concerning the comfort level of the EEG cap

ID	**Comfort level during the placement of the cap**	**Comfort level of the electrodes**	**Comfort level of the cap (fabric and securing mechanism)**	**Feedback**
P1	3	1	6	-
P2	7	7	7	-
P3	6	7	7	-
P4	6	1	5	The fastening mechanism initially caused discomfort in the neck.
P5	7	7	7	-
P6	6	5	4	-

Table F.2: Participants' responses concerning the comfort level of the ECG equipment

ID	**Comfort level during the placement of the electrodes**	**Comfort level during the execution of the activity**	**Comfort level during the removal of the electrodes**	**Feedback**
P1	7	7	4	-
P2	7	7	7	-
P3	7	7	7	-
P4	7	7	7	-
P5	7	7	7	-
P6	5	7	3	-

Table F.3: Participants' responses concerning the comfort level of the VR headset

ID	**Comfort level during the placement of the VR headset**	**Comfort level during the execution of the activity**	**Comfort level during the removal of the VR headset**	**Feedback**
P1	2	4	7	-
P2	7	7	7	-
P3	6	7	7	Sometimes a bit blurry
P4	3	7	7	-
P5	7	7	7	Difficult to adjust the VR headset when wearing the EEG cap
P6	4	7	6	-

Table F.4: Participants' responses concerning the comfort level of the EEG-ECG-VR system

ID	**Comfort level**	**Weight of the system**	**Mobility level while wearing the system**	**Ease of performing the tasks**
P1	3	7	7	6
P2	7	7	7	7
P3	7	5	6	6
P4	6	1	7	7
P5	7	5	7	7
P6	5	5	6	6

G

N200 AND P300 ANALYSIS DURING VR TASKS

Table G.1: First VR task analysis (looking activity): Baseline, Activity, and Real Results for EEG Biomarkers (N200 and P300).

Participant	**Baseline [µV]**	**Activity [µV]**		**Real Result [µV]**	
	Mean	N200	P300	N200	P300
P1	0,0080	0,6859	-1,1856	0,6779	-1,1936
		-1,5411	1,9018	-1,5491	1,8938
		2,3688	-1,5955	2,3608	-1,6035
P2	-0,0119	1,3331	-0,3394	1,3450	-0,3275
		-2,9597	2,5232	-2,9478	2,5351
		1,4166	-1,1461	1,4285	-1,1342
P3	0,0077	-3,8024	-0,4986	-3,8101	-0,5063
		2,1183	-0,2165	2,1106	-0,2242
		1,1119	1,6055	1,1042	1,5978
P4	-0,0024	0,9035	1,3020	0,9059	1,3044
		-1,9723	0,8550	-1,9699	0,8574
		0,9605	0,0927	0,9629	0,0951
P5	-0,0011	-1,8485	-1,9081	-1,8474	-1,9070
		1,8312	2,9789	1,8323	2,9800
		-1,5428	-2,1852	-1,5417	-2,1841
P6	0,0105	0,1771	-1,1443	0,1666	-1,1548
		-2,0885	1,5054	-2,0990	1,4949
		0,6696	-0,0203	0,6591	-0,0308
P7	0,0061	2,2635	0,1400	2,2574	0,1339
		-0,7536	-1,8220	-0,7597	-1,8281
		-0,1758	2,2830	-0,1819	2,2769
P8	-0,0213	-2,9017	4,7194	-2,8804	4,7407
		1,4458	0,6347	1,4671	0,6560
		-0,0560	-2,3749	-0,0347	-2,3536
P9	-0,0063	0,4254	-2,0504	0,4317	-2,0441
		-0,4262	1,8961	-0,4199	1,9024
		0,4588	-0,2766	0,4651	-0,2703
P10	-0,0032	-1,2155	0,9627	-1,2123	0,9659
		-0,4422	2,2521	-0,4390	2,2553
		0,2986	-1,3049	0,3018	-1,3017
P11	-0,0138	-0,9305	0,1859	-0,9167	0,1997
		-0,8931	0,6393	-0,8793	0,6531
		0,9370	0,1819	0,9508	0,1957
P12	0,0034	-0,7428	-0,5080	-0,7462	-0,5114
		0,0680	-0,8142	0,0646	-0,8176
		0,3915	1,4941	0,3881	1,4907
P13	0,0086	-0,0837	3,9964	-0,0923	3,9878
		-0,7491	-3,2545	-0,7577	-3,2631
		-0,0637	1,6385	-0,0723	1,6299
P14	-0,0033	0,1997	-2,6366	0,2030	-2,6333
		-0,3514	0,9012	-0,3481	0,9045
		1,8400	-0,9663	1,8433	-0,9630
P15	0,0145	-1,7074	0,8451	-1,7219	0,8306
		2,2936	-0,9530	2,2791	-0,9675
		-0,4047	-0,2885	-0,4192	-0,3030

Table G.2: Second VR task analysis (approach activity): Baseline, Activity, and Real Results for EEG Biomarkers (N200 and P300).

Participant	**Baseline [µV]**	**Activity [µV]**		**Real Result [µV]**	
	Mean	N200	P300	N200	P300
P1	0.008	-1,6183	0,265869	-1,6263	0,2579
		0,7275	0,9485	0,7195	0,9405
		1,1856	-1,39059	1,1776	-1,3986
P2	-0.0119	-0,2195	1,3211	-0,2076	1,3330
		-2,7901	-1,1039	-2,7782	-1,0920
		3,6334	0,7087	3,6453	0,7206
P3	0.0077	0,4124	-1,9520	0,4047	-1,9597
		-0,0167	-0,1041	-0,0244	-0,1118
		1,0819	2,5840	1,0742	2,5763
P4	-0.0024	0,5423	1,0774	0,5447	1,0798
		-2,8438	0,5951	-2,8414	0,5975
		2,8584	-0,6041	2,8608	-0,6017
P5	-0.0011	-3,7708	-0,7507	-3,7697	-0,7496
		2,5818	2,5851	2,5829	2,5862
		-0,1758	-2,3564	-0,1747	-2,3553
P6	0.0105	-1,1416	-1,2697	-1,1521	-1,2802
		-1,0539	0,4010	-1,0644	0,3905
		1,9110	-0,1210	1,9005	-0,1315
P7	0.0061	-1,0013	-1,7846	-1,0074	-1,7907
		2,3050	-0,0138	2,2989	-0,0199
		-2,7794	2,0122	-2,7855	2,0061
P8	-0.0213	-4,1222	1,1219	-4,1009	1,1432
		1,2299	-1,8005	1,2512	-1,7792
		0,5763	1,2761	0,5976	1,2974
P9	-0.0063	1,3440	-2,5607	1,3503	-2,5544
		0,1326	2,0686	0,1389	2,0749
		-1,7705	1,1428	-1,7642	1,1491
P10	-0.0032	-2,5767	0,8920	-2,5735	0,8952
		0,6217	0,6021	0,6249	0,6053
		0,6784	0,1929	0,6816	0,1961
P11	-0.0138	1,0519	-2,1043	1,0657	-2,0905
		-3,2169	3,0432	-3,2031	3,0570
		1,4423	0,0728	1,4561	0,0866
P12	0.0034	0,6037	-0,6416	0,6003	-0,6450
		-0,3045	-0,3607	-0,3079	-0,3641
		-0,4688	0,7072	-0,4722	0,7038
P13	0.0086	1,5533	2,0277	1,5447	2,0191
		-1,6795	-1,6999	-1,6881	-1,7085
		1,6498	0,3460	1,6412	0,3374
P14	-0.0033	3,3744	-1,7990	3,3777	-1,7957
		-2,5269	1,3357	-2,5236	1,3390
		1,5019	-0,4754	1,5052	-0,4721
P15	0.0145	1,3776	-2,0287	1,3631	-2,0432
		0,5297	-1,1176	0,5152	-1,1321
		-0,4696	2,4782	-0,4841	2,4637

Table G.3: Third VR task analysis (grabbing activity): Baseline, Activity, and Real Results for EEG Biomarkers (N200 and P300).

Participant	**Baseline [µV]**	**Activity [µV]**		**Real Result [µV]**	
	Mean	N200	P300	N200	P300
P1	0.008	-0,7194	-0,4424	-0,7274	-0,4504
		1,4349	-0,4045	1,4269	-0,4125
		0,8638	-0,4687	0,8558	-0,4767
P2	-0.0119	1,2119	1,8711	1,2238	1,8830
		-2,7542	-0,2491	-2,7423	-0,2372
		1,1108	-0,8553	1,1227	-0,8434
P3	0.0077	-3,9360	0,2166	-3,9437	0,2089
		2,0045	0,3764	1,9968	0,3687
		0,5939	1,0997	0,5862	1,0920
P4	-0.0024	0,1645	0,5510	0,1669	0,5534
		-1,4597	0,8617	-1,4573	0,8641
		0,7374	-0,7823	0,7398	-0,7799
P5	-0.0011	0,1063	-0,2723	0,1074	-0,2712
		-0,8988	2,9849	-0,8977	2,9860
		1,5736	0,6341	1,5747	0,6352
P6	0.0105	-0,8524	0,3245	-0,8629	0,3140
		-1,2559	0,1277	-1,2664	0,1172
		0,9544	1,0642	0,9439	1,0537
P7	0.0061	0,9662	-1,9687	0,9601	-1,9748
		0,5302	-0,1895	0,5241	-0,1956
		-0,9649	1,8362	-0,9710	1,8301
P8	-0.0213	-0,7130	0,8699	-0,6917	0,8912
		1,0771	-0,8712	1,0984	-0,8499
		-0,4486	0,4187	-0,4273	0,4400
P9	-0.0063	2,3988	-2,0618	2,4051	-2,0555
		-1,3262	-0,8667	-1,3199	-0,8604
		0,3485	3,1865	0,3548	3,1928
P10	-0.0032	-3,1433	-0,6959	-3,1401	-0,6927
		0,2916	1,8017	0,2948	1,8049
		0,8625	1,2363	0,8657	1,2395
P11	-0.0138	0,9173	-0,5991	0,9311	-0,5853
		-3,0918	1,2237	-3,0780	1,2375
		1,8535	0,6271	1,8673	0,6409
P12	0.0034	-1,6567	2,2104	-1,6601	2,2070
		0,0390	-3,5894	0,0356	-3,5928
		1,6743	4,1146	1,6709	4,1112
P13	0.0086	-0,3398	1,3688	-0,3484	1,3602
		-0,4830	-2,8911	-0,4916	-2,8997
		1,3473	3,8037	1,3387	3,7951
P14	-0.0033	0,2432	-2,5975	0,2465	-2,5942
		0,1045	0,8287	0,1078	0,8320
		2,3229	0,0403	2,3262	0,0436
P15	0.0145	-1,0069	0,3556	-1,0214	0,3411
		1,4998	-2,4301	1,4853	-2,4446
		0,3534	2,3111	0,3389	2,2966

Table G.4: Fourth VR task analysis (grabbing and eating activity): Baseline, Activity, and Real Results for EEG Biomarkers (N200 and P300).

Participant	**Baseline [µV]**	**Activity [µV]**		**Real Result [µV]**	
	Mean	N200	P300	N200	P300
P1	0,0080	-2,8901	-1,4740	-2,8981	-1,4820
		2,8612	2,5830	2,8532	2,5750
		-1,0745	-2,6784	-1,0825	-2,6864
P2	-0,0119	0,3332	-1,0761	0,3451	-1,0642
		-2,0816	4,2596	-2,0697	4,2715
		0,8980	-0,4455	0,9099	-0,4336
P3	0,0077	-0,9227	0,1470	-0,9304	0,1393
		-1,4831	0,3566	-1,4908	0,3489
		4,1682	0,7012	4,1605	0,6935
P4	-0,0024	-0,4041	0,8811	-0,4017	0,8835
		-3,0256	0,1835	-3,0232	0,1859
		3,3861	-0,8829	3,3885	-0,8805
P5	-0,0011	-0,8329	-1,6405	-0,8318	-1,6394
		-0,5486	3,2141	-0,5475	3,2152
		1,0655	0,3492	1,0666	0,3503
P6	0,0105	-3,0600	-1,9047	-3,0705	-1,9152
		0,1502	2,3416	0,1397	2,3311
		0,1084	-1,7174	0,0979	-1,7279
P7	0,0061	2,7587	0,3835	2,7526	0,3774
		0,5816	-2,0372	0,5755	-2,0433
		-0,6935	1,4753	-0,6996	1,4692
P8	-0,0213	-4,0417	-0,4644	-4,0204	-0,4431
		1,5488	1,9932	1,5701	2,0145
		0,5598	-0,5958	0,5811	-0,5745
P9	-0,0063	0,6982	-1,4008	0,7045	-1,3945
		1,3230	-1,2641	1,3293	-1,2578
		-2,3096	3,1399	-2,3033	3,1462
P10	-0,0032	2,0891	-2,4104	2,0923	-2,4072
		-2,9899	3,8879	-2,9867	3,8911
		0,4265	-1,5658	0,4297	-1,5626
P11	-0,0138	0,4280	-1,4667	0,4418	-1,4529
		-1,9372	3,7970	-1,9234	3,8108
		2,1612	-1,5364	2,1750	-1,5226
P12	0,0034	-1,0919	-2,1105	-1,0953	-2,1139
		0,4064	-0,1355	0,4030	-0,1389
		0,8284	2,6821	0,8250	2,6787
P13	0,0086	0,8918	1,6815	0,8832	1,6729
		1,2539	-1,8064	1,2453	-1,8150
		-2,3612	0,8245	-2,3698	0,8159
P14	-0,0033	-0,2421	-2,2063	-0,2388	-2,2030
		-0,4007	3,1488	-0,3974	3,1521
		1,9175	-2,5472	1,9208	-2,5439
P15	0,0145	-0,9319	3,0108	-0,9464	2,9963
		0,2366	-3,4398	0,2221	-3,4543
		1,5318	1,3619	1,5173	1,3474

H

DETAILED RESULTS OF EEG ANALYSIS FOR HABITUATION ASSESSMENT

Table H.1: C3 Activation: Baseline, Activity, and Real Results for 15 Participants

C3	**Baseline [µV]**	**Activity [µV]**			**Real Results [µV]**		
Participant	**Mean**	1st Apple	2nd Apple	3rd Apple	1st Apple	2nd Apple	3rd Apple
P1	0.0080	0.7301	-1.8245	-1.4960	0.7221	-1.8325	-1.5040
		-0.4579	2.6649	1.0826	-0.4659	2.6569	1.0746
		-0.6577	-1.0574	-0.2554	-0.6657	-1.0654	-0.2634
P2	-0.0119	2.0414	-0.2457	-0.6157	2.0533	-0.2338	-0.6038
		-1.8674	-0.5636	-0.5587	-1.8555	-0.5517	-0.5468
		-0.1030	2.0222	0.4487	-0.0911	2.0341	0.4606
P3	0.0077	-1.5474	-3.1953	-2.7385	-1.5551	-3.2030	-2.7462
		0.9792	5.0032	0.9653	0.9715	4.9955	0.9576
		-0.9527	-4.9679	0.6085	-0.9604	-4.9756	0.6008
P4	-0.0024	-2.3262	-0.4196	0.3500	-2.3238	-0.4172	0.3524
		2.6156	-0.9906	0.9198	2.6180	-0.9882	0.9222
		-1.4190	1.3721	-0.8037	-1.4166	1.3745	-0.8013
P5	-0.0011	-1.9907	2.6872	0.1636	-1.9896	2.6883	0.1647
		1.4999	-3.2767	-0.1523	1.5010	-3.2756	-0.1512
		-2.4434	0.9861	-1.0002	-2.4423	0.9872	-0.9991
P6	0.0105	-0.5522	0.3525	-2.2897	-0.5627	0.3420	-2.3002
		0.3218	2.2534	2.6703	0.3113	2.2429	2.6598
		0.3261	-3.4529	-2.0856	0.3156	-3.4634	-2.0961
P7	0.0061	-0.2947	-1.7343	-2.0540	-0.3008	-1.7404	-2.0601
		-1.0983	1.3329	0.5726	-1.1044	1.3268	0.5665
		2.2976	0.4258	1.7991	2.2915	0.4197	1.7930
P8	-0.0213	1.6869	0.5710	1.5140	1.7082	0.5923	1.5353
		-0.2343	-1.5470	-0.2892	-0.2130	-1.5257	-0.2679
		-1.4334	1.5398	0.4571	-1.4121	1.5611	0.4784
P9	-0.0063	-0.1090	0.0445	0.0871	-0.1027	0.0508	0.0934
		-2.5312	1.1053	0.0294	-2.5249	1.1116	0.0357
		4.2495	-2.6981	-1.0837	4.2558	-2.6918	-1.0774
P10	-0.0032	-0.4485	1.5574	0.7798	-0.4453	1.5606	0.7830
		0.6035	-1.2863	-1.3881	0.6067	-1.2831	-1.3849
		-1.2829	0.5933	1.8565	-1.2797	0.5965	1.8597
P11	-0.0138	-2.3078	0.6232	-0.1311	-2.2940	0.6370	-0.1173
		-0.1530	-0.2850	-1.2978	-0.1392	-0.2712	-1.2840
		1.0769	0.2253	1.7007	1.0907	0.2391	1.7145
P12	0.0034	0.7809	3.2599	0.1934	0.7775	3.2565	0.1900
		1.0341	-4.8445	0.8075	1.0307	-4.8479	0.8041
		-3.8199	2.3742	-0.2993	-3.8233	2.3708	-0.3027
P13	0.0086	-1.0658	-2.0907	-3.5741	-1.0744	-2.0993	-3.5827
		2.8306	2.2986	2.1218	2.8220	2.2900	2.1132
		-2.9750	-0.6499	-0.3337	-2.9836	-0.6585	-0.3423
P14	-0.0033	3.3176	2.3800	1.5031	3.3209	2.3833	1.5064
		-0.5659	-1.5533	0.4882	-0.5626	-1.5500	0.4915
		-2.9888	-0.8924	-2.7322	-2.9855	-0.8891	-2.7289
P15	0.0145	-1.6668	0.6675	2.6173	-1.6813	0.6530	2.6028
		3.5245	0.7117	-2.7784	3.5100	0.6972	-2.7930
		-2.7156	-0.8059	0.6667	-2.7301	-0.8204	0.6522

Table H.2: C4 Activation: Baseline, Activity, and Real Results for 15 Participants

C4	**Baseline [µV]**	**Activity [µV]**			**Real Results [µV]**		
Participant	**Mean**	1st Apple	2nd Apple	3rd Apple	1st Apple	2nd Apple	3rd Apple
P1	0.0080	1.8259	-1.8642	0.2227	1.8179	-1.8722	0.2147
		-0.5827	0.3172	1.6132	-0.5907	0.3092	1.6052
		0.45955	1.53392	-1.79468	0.4516	1.5259	-1.8027
P2	-0.0119	1.59274	-2.12893	-1.257	1.6046	-2.1170	-1.2451
		-1.04561	2.12521	2.42847	-1.0337	2.1371	2.4404
		-0.66459	-0.86737	-2.09084	-0.6527	-0.8555	-2.0789
P3	0.0077	-1.35675	-0.507175	-0.743713	-1.3645	-0.5149	-0.7514
		-1.00877	1.47479	0.375613	-1.0165	1.4671	0.3679
		2.64073	0.136724	0.08860	2.6330	0.1290	0.0809
P4	-0.0024	0.82093	0.80302	-1.87689	0.8233	0.8054	-1.8745
		0.122881	0.375002	-1.02334	0.1253	0.3774	-1.0209
		-1.74612	-1.62915	1.40472	-1.7437	-1.6268	1.4071
P5	-0.0011	-4.10385	-1.71949	-1.70688	-4.1028	-1.7184	-1.7058
		5.55577	-0.356393	2.99543	5.5569	-0.3553	2.9965
		-1.01387	1.68294	-3.81507	-1.0128	1.6840	-3.8140
P6	0.0105	-1.42385	-0.20986	0.397478	-1.4344	-0.2204	0.3870
		0.42441	-0.25956	0.17856	0.4139	-0.2701	0.1681
		0.45700	-0.46293	-3.00689	0.4465	-0.4734	-3.0174
P7	0.0061	0.52026	1.27259	0.76489	0.5142	1.2665	0.7588
		-0.49870	-2.50732	-1.62975	-0.5048	-2.5134	-1.6359
		0.27581	2.09265	1.32209	0.2697	2.0866	1.3160
P8	-0.0213	1.1688	0.29294	1.89933	1.1901	0.3142	1.9206
		-0.32716	-0.63422	0.40407	-0.3059	-0.6129	0.4254
		-0.75007	1.02836	-0.30216	-0.7288	1.0497	-0.2809
P9	-0.0063	0.72812	-3.52929	-0.80288	0.7344	-3.5230	-0.7966
		-0.64950	2.16363	-1.05294	-0.6432	2.1699	-1.0466
		-0.11632	1.02442	0.36826	-0.1100	1.0307	0.3746
P10	-0.0032	3.55323	-3.06654	0.597417	3.5564	-3.0633	0.6006
		0.42649	2.6822	-1.76324	0.4297	2.6854	-1.7600
		-3.90659	-2.27687	1.94641	-3.9034	-2.2737	1.9496
P11	-0.0138	-0.73979	-0.73033	0.36482	-0.7260	-0.7165	0.3786
		-1.13338	-0.75751	-0.95343	-1.1196	-0.7437	-0.9396
		2.20702	-0.38363	1.70021	2.2208	-0.3698	1.7140
P12	0.0034	-0.00401	0.68369	-2.48488	-0.0074	0.6803	-2.4883
		-0.07763	0.67991	3.0712	-0.0810	0.6765	3.0678
		1.01624	-2.19057	-0.24329	1.0128	-2.1940	-0.2467
P13	0.0086	-3.33813	-0.1244	0.82236	-3.3467	-0.1330	0.8138
		1.94581	0.66080	-1.33287	1.9372	0.6522	-1.3415
		-1.39248	-0.44229	0.30202	-1.4011	-0.4509	0.2934
P14	-0.0033	-0.87188	2.59979	-0.05241	-0.8686	2.6031	-0.0491
		-0.57987	-3.14484	0.63129	-0.5832	-3.1415	0.6346
		-0.34558	1.81834	0.07026	-0.3423	1.8216	0.0736
P15	0.0145	0.49720	-0.07907	-0.57017	0.4827	-0.0936	-0.5847
		2.8297	-0.15151	-2.45251	-2.8443	-0.1660	-2.4670
		2.31239	1.01058	4.38599	2.2979	0.9961	4.3715

I

PARTICIPANT COMPARISON AND HABITUATION EFFECTS ON CEREBRAL ACTIVITY

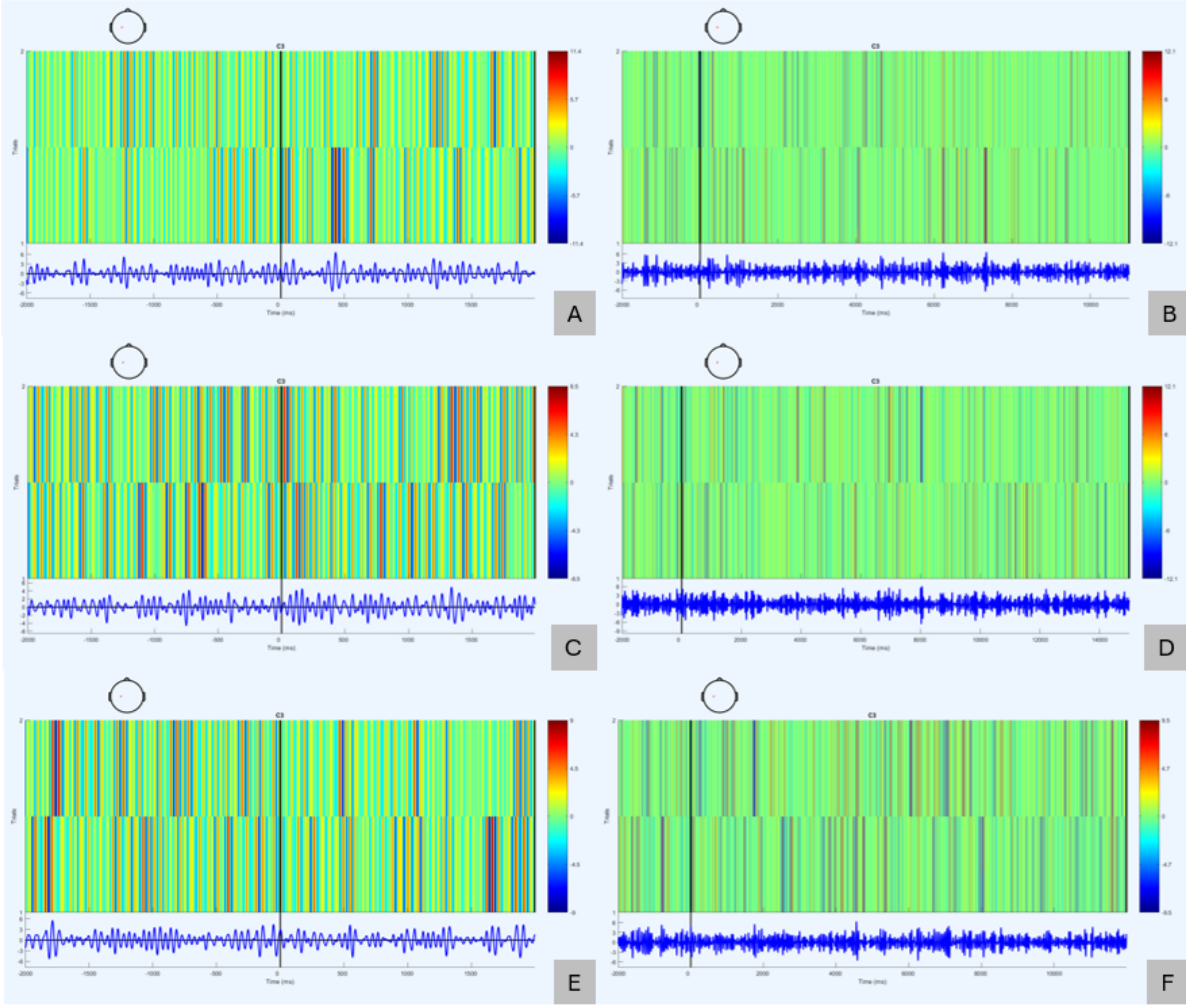


Figure I.1: Cerebral activity at electrode C3 for Participants 2, 10, and 11 during baseline (A, C and E) and task execution (B, D and F).

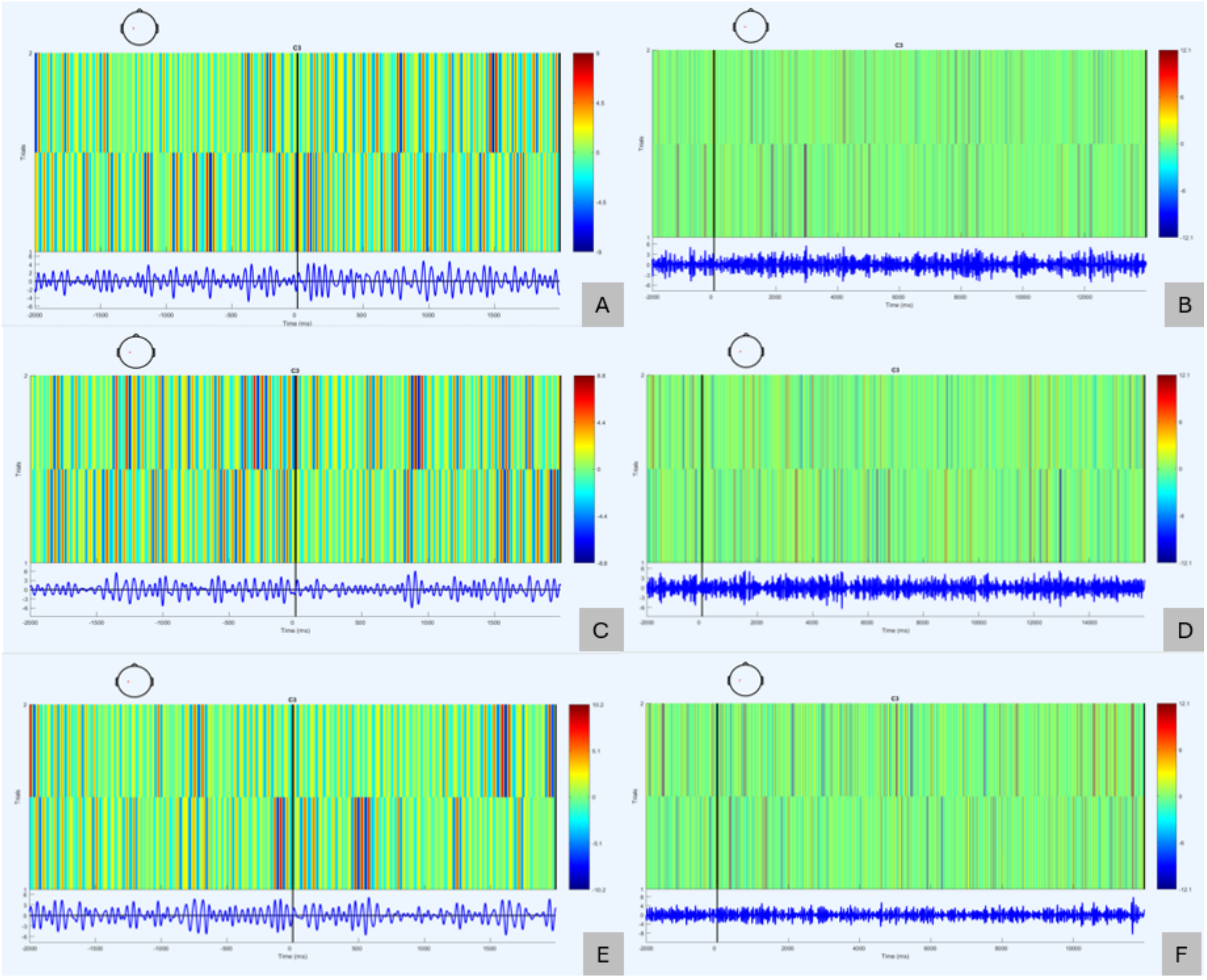


Figure I.2: Cerebral activity at electrode C3 for Participants 13, 14, and 15 during baseline (A, C and E) and task execution (B, D and F).

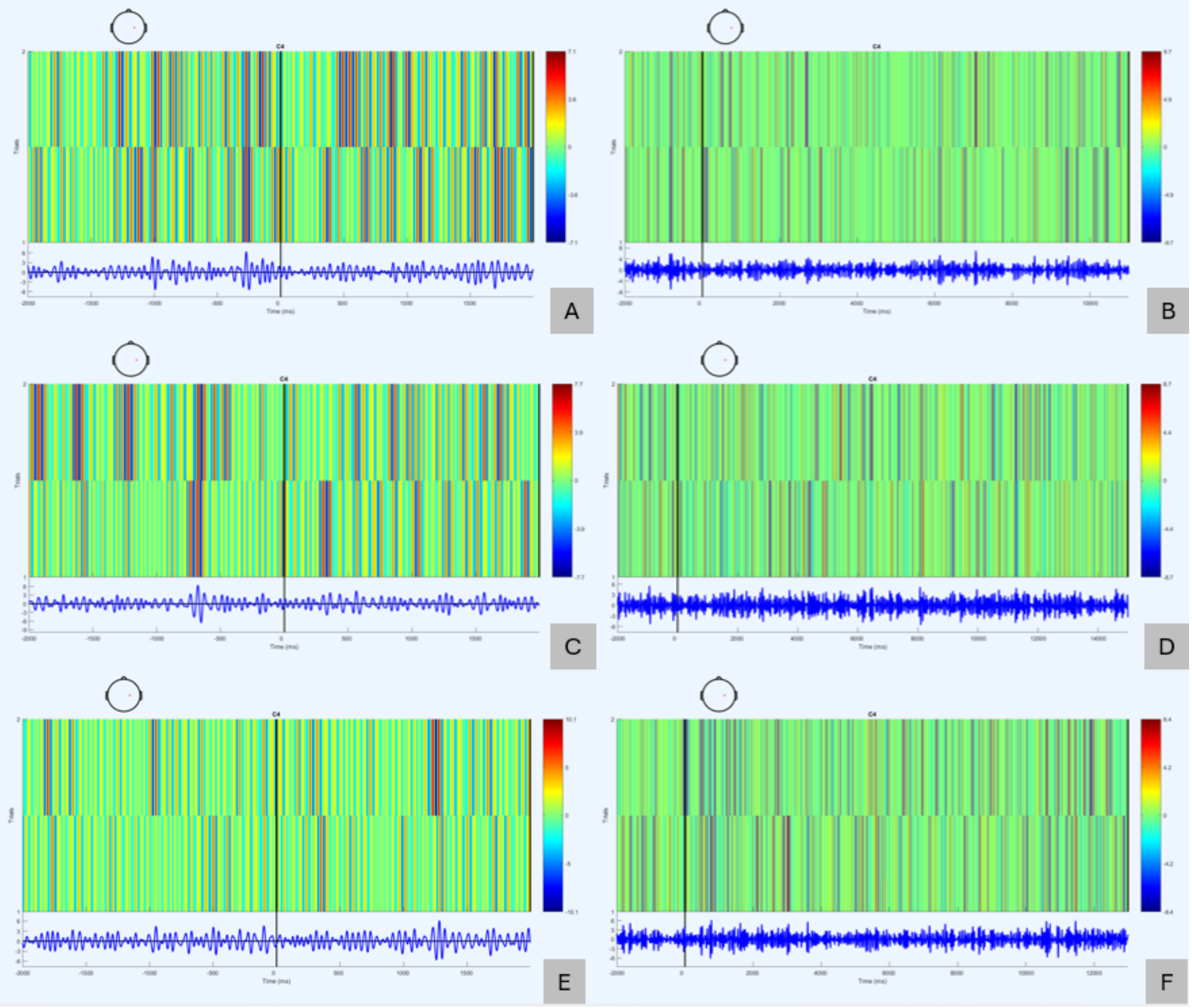


Figure I.3: Cerebral activity at electrode C4 for Participants 2, 3, and 4 during baseline (A, C and E) and task execution (B, D and F).

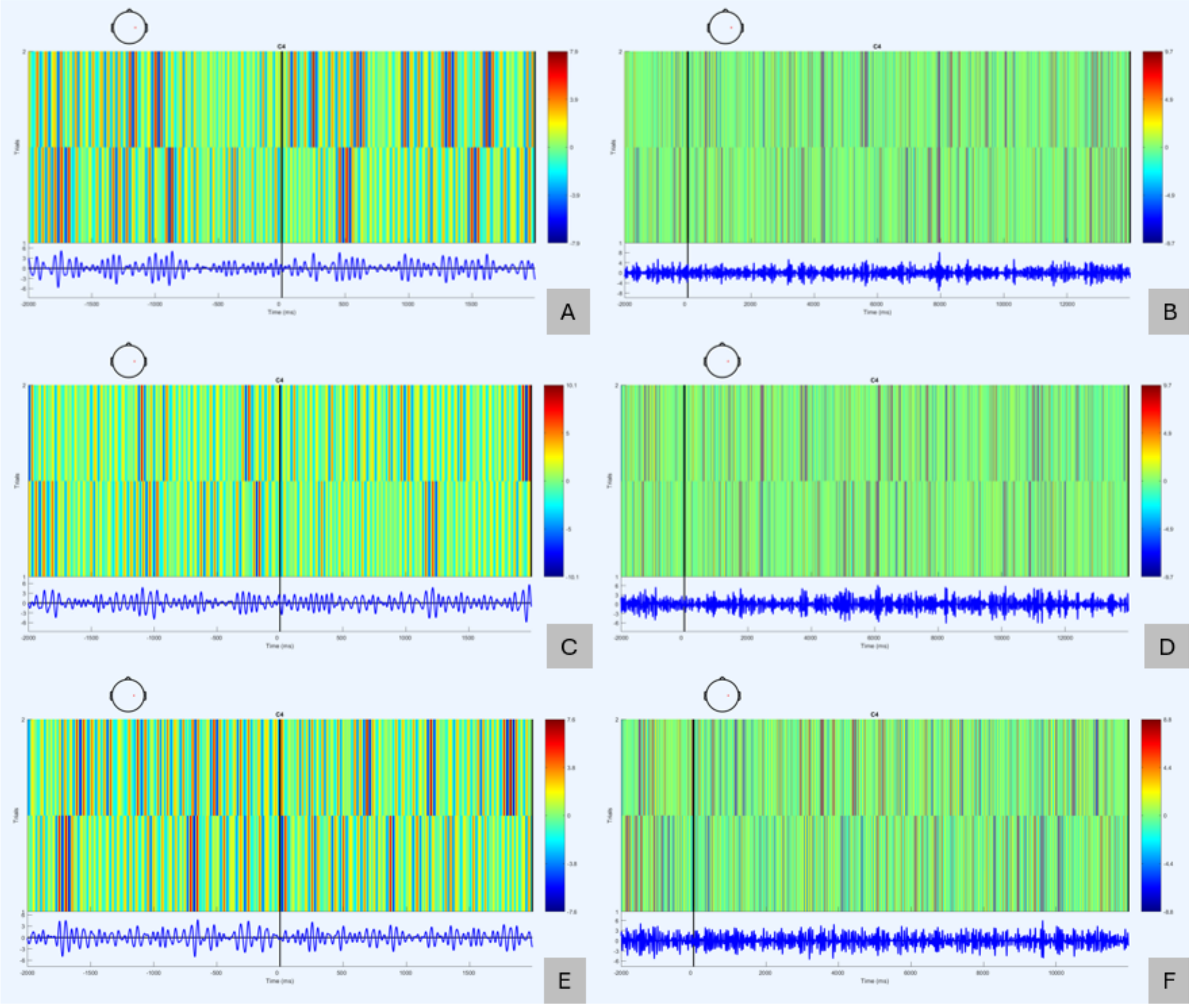


Figure I.4: Cerebral activity at electrode C4 for Participants 6, 13, and 15 during baseline (A, C and E) and task execution (B, D and F).

J

TASKS AND MARKERS CONDUCTED FOR THE INITIAL TESTING PHASE

Table J.1: Description of tasks and their corresponding marker types used during the experimental protocol (without VR).

Task	Type of marker
Task explanation audio	Stimulus
Beginning of blinking 3 times, closing the eyes for 5 seconds and repeating the process for 1 minute	Response start
Task end	Response end
Task explanation audio	Stimulus
Beginning of guided relaxation audio for 1 minute	Response start
Task end	Response end
Task explanation audio	Stimulus
Beginning of reading and memorizing a list of 10 words for 1 minute	Response start
Task end	Response end
Task explanation audio	Stimulus
Beginning of repeating the list of words	Response start
Task end	Response end
Task explanation audio	Stimulus
Beginning of watching a video and grabbing an object	Response start
Task end	Response end

Table J.2: Description of tasks and their corresponding marker types used during the experimental protocol (with VR).

Task	**Type of marker**
Task explanation audio	Stimulus
Looking for objects inside virtual environment	Response start
Task end	Response end
Task explanation audio	Stimulus
Getting closer to objects inside virtual environment	Response start
Task end	Response end
Task explanation audio	Stimulus
Grabbing objects inside virtual environment	Response start
Task end	Response end
Task explanation audio	Stimulus
Grabbing objects and bringing them to the mouth inside virtual environment	Response start
Task end	Response end
Task explanation audio	Stimulus
Looking to objects inside virtual environment	Response start
Task end	Response end
Task explanation audio	Stimulus
Looking around inside virtual environment	Response start
Task end	Response end

K

DISTINCTION IN INFORMATION PROCESSING BETWEEN REAL SCENARIOS AND VR ENVIRONMENTS

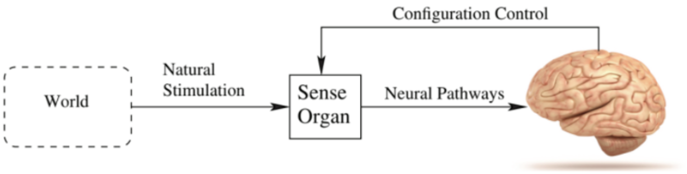


Figure K.1: Framework for receiving and processing typical stimuli [90].

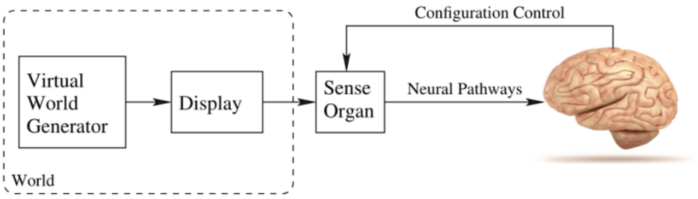


Figure K.2: Framework for receiving and processing VR stimuli [90].

L

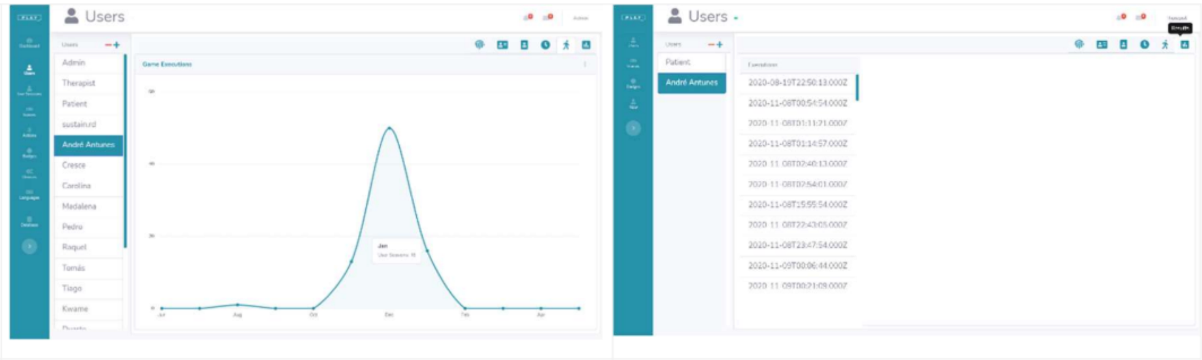
Brainwave Bands, Frequencies, Cognitive and Affective Correlates, and Neurofeedback Training Target Bands and States

Table L.1: Brainwave bands, frequencies, cognitive/affective correlates, and NF training target bands and states [9, 103].

Brain frequency band	**Cognitive/affective correlates of brainwave frequency bands**	**NF training targets to achieve calm and attentive brain states**
Delta (D) [1-4 Hz]	Sleep, deep meditation, complex problem solving, unawareness	-
Theta (T) [4-8 Hz]	Sleep, deep meditation, creativity, unconsciousness, anxiety	-
Alpha (A) [8-12 Hz]	Calmness, relaxation, mediation (border between theta and alpha may be related to musical creativity and performance)	Increase activity in alpha band, increase (A/T) ratio, decrease activity in high beta band
Sigma (S) [12-15 Hz]	Relaxed yet focused attention	Decrease (T/B) ratio, increase activity in SMR/beta
Beta (B) [15-30 Hz]	High engagement, focused attention	Decreased (T/B) ratio, increase activity in SMR/beta
Gamma (G) [>30 Hz]	Learning, cognitive processing, problem solving tasks, brain activity	-

M

PLAY PLATFORM DASHBOARD



2020-08-19T22:50:13.000Z
2020-11-08T00:54:54.000Z
2020-11-08T01:11:21.000Z
2020-11-08T01:14:57.000Z
2020-11-08T02:40:13.000Z
2020-11-08T02:54:01.000Z
2020-11-08T15:55:54.000Z
2020-11-08T22:43:05.000Z
2020-11-08T23:47:54.000Z
2020-11-09T00:06:44.000Z
2020-11-09T00:21:09.000Z

Figure M.1: Patient Progress Dashboard of the Platform.

N

Trigger Marking in the ECG Signal

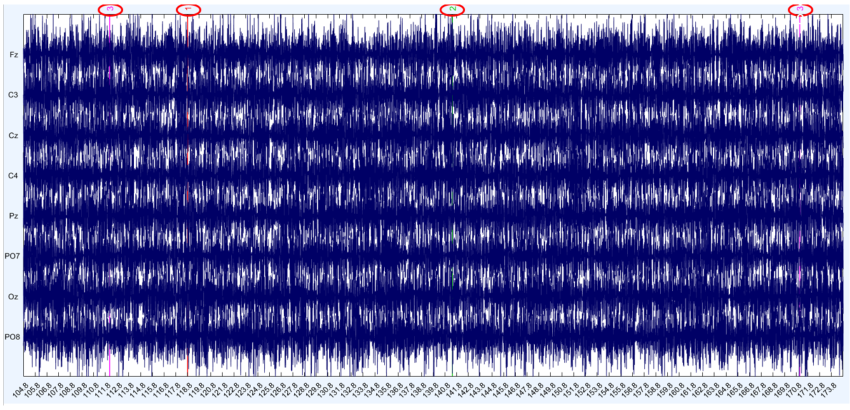


Figure N.1: EEG signal displaying vertical trigger markers.

O

ECG Function Output Plots

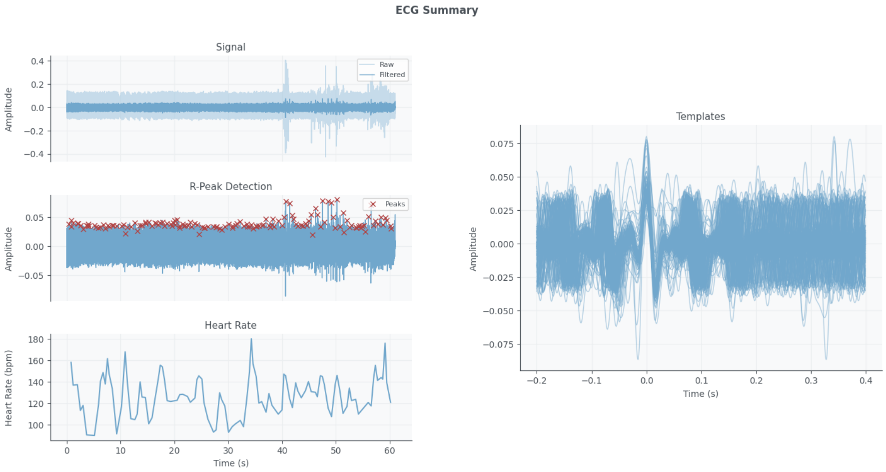


Figure O.1: Plots generated by the ecg() function. Signal: data before and after filtering; R-peak detection: identification of all R-peaks in the signal; Heart rate: representation of the entire signal; Templates: layering of the signal measured between R peaks.