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Expectations and Beliefs in Immersive Virtual Reality Environments: Managing of Body Perception

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1. Introduction

Chronic low back pain is a widespread musculoskeletal condition that represents a global problem both in terms of years lived with disability and healthcare costs. The Global Burden of Disease Study 2013 evaluated “years lived with disability” (YLDs: the prevalence multiplied by a disability-weighting factor) for a broad range of diseases and injuries in 188 countries, finding that the greatest cause of YLDs around the world is chronic low back pain (Rice et al., 2016; Treede et al., 2019). Pain is currently defined as an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage (Raja et al., 2020) and as for chronic pain it is necessary to add to the aforementioned definition a duration of at least 3 months (Treede et al., 2019). Thus, pain is recognized not only as simple physical measure but also as a psychological concept. The experience of pain is distinguished from mere noxious stimulation (Raja et al., 2020). Although pain is already defined as a subjective experience, this is even more true for chronic pain where it lacks the acute warning function of physiological nociception. Evidence related to the relationship between chronic low back pain and psychological elements such as personality traits, beliefs and expectations regarding the illness, point out the importance that personal experience plays in improving or worsening the symptoms of the disease. The inner psychological states play a significant role in maintaining chronic pain perception through negative expectations about one's own health state. These are well represented by erroneous convictions aimed to avoid pain, called fear-avoidance beliefs. They are the origin of an irrational fear of physical movement due to a feeling of excessive vulnerability of one's own body, named kinesiophobia, that in turn leads to a reduction in movement. These kinds of inner experiences about the state of an individual’s health are well documented in musculoskeletal conditions and particularly for chronic low back pain (Eklund et al., 2019). The available evidence demonstrates how people exposed to a greater levels of fear, negative beliefs and expectations about their health, experiment pain exacerbation and a reduction of movement capacity (Cuervo et al., 2020) leading, ultimately to disability and a lower quality of life. Therefore, in view of its significant psychological component, chronic pain can be modulated by modifying people’s personal experiences, attempting to modify what they expect and think about their general health condition. Expectations and beliefs (e.g., positive or negative about symptoms relief), quality of relations (e.g., the relationship of trust with the healthcare professional) and the features of the objects and of the spaces in the healthcare setting, are all elements that make up the context in which the cure is administered (Benedetti, 2013). All these elements, called contextual factors, act as facilitators of the placebo and nocebo effect through conscious and unconscious psychophysiological responses. For example, neurophysiological pain education (Tegner et al., 2018) is a strategy utilised to make people that suffer from chronic low back pain aware of their maladaptive illness beliefs, so as to alter maladaptive pain cognition and reconceptualize convictions about pain. This strategy, being based on verbal education about biological causes of pain, utilises an elaboration process that acts on a consciousness level. Something similar could be used in people with chronic low back pain where kinesiophobic traits could be reduced through interventions aimed at increasing the perception of the individual motion capacities. Since the creation of the personal pain experience is strongly influenced by contextual factors, inducing changes in the factors responsible for the expectations may be useful for the treatment of low back pain. However, the possibility to handle the alteration of contextual factors is not always easy in reality. In this sense, the use of immersive virtual reality (IVR) allows for control of environmental features in a simpler way than reality through the use of ad-hoc created environments. In the medical field, IVR has been up to now primarily used to distract patients from painful procedures. A wide scientific literature indeed, took care of investigating the IVR use in people with cancer (Fabi et al., 2022), for those who report burns (Faber et al., 2013) and for surgery training (Mao et al., 2021). Considering the above, our research question is whether the use of IVR can represent a useful tool for modulating both an individual's / patient's movement capacity and pain experience. The hypothesis is that through the modulation of users' perception, performed through purpose-constructed virtual spaces, it is possible to increase the first and lower the second.

To do this we built a project divided by:

A first general section shown in chapter 1 deepens the role of the context as a trigger of placebo and nocebo effects. To investigate the psychobiological functioning such as beliefs through which (musculoskeletal) pain is maintained. To present some operating mechanisms shared by painless and pain experience. Moreover, an overview of the opportunities and limitations offered by immersive virtual reality (IVR) will be described.

A study shown in chapter 2 investigates the real and perceived positions of lower limbs in a virtual environment under fatiguing and non-fatiguing conditions.

A study on the visual cues experienced in two different IVR environments to evaluate the modifiability degree of the virtual spaces and their plausibility is discussed in chapter 3.

A study reported in chapter 4 investigates the role of positive expectations in improving motor capacity through the administration of an IVR environment of a visual-haptic illusion and positive verbal stimuli.

Finally, a concluding chapter will discuss future developments of low back pain treatment.

1.1 The context, the placebo and the nocebo effects and the related psychobiological mechanisms: a brief overview

The SQUIRE 2.0 publication guidelines recently included the context as “the key features of the environment in which the work is immersed and which are interpreted as meaningful to the success, failure and unexpected consequences of the intervention(s), as well as the relationship of these to the stakeholders (e.g. improvement team, clinicians, patients, families, etc)” (Ogrinc et al., 2016). Context is not simply the background of treatment delivery. It interacts, influences, modifies, facilitates or constrains the intervention and its effectiveness (Coles et al., 2020). One of the first and greatest examples of the power of context to benefit patients is the studies of (Levine et al., 1981; Levine & Gordon, 1984). These authors found that a hidden intravenous injection of 6-8 mg of morphine obtained the same effect of an open intravenous infusion of saline solution. This means that the effectiveness of the pain relief is due to the expectation of the patient that the painful experience will disappear as a consequence of “the injection”. Moreover, this expectation is so strong that, at least within a certain pharmacological dosage, it can theoretically replace a powerful medication such as morphine. Actually**,** the context is considered as the whole internal and external world experienced by a person (Benedetti et al., 2011; Wager & Atlas, 2015). Just think of how our behaviours are aligned with the environment in which we find ourselves. Being in an unknown environment generates different psychophysiological activations to being in a comfortable place such as our own bedroom. Likewise, when feeling unwell, waiting for the visit of the general practitioner in a cosy waiting room rather than in a chaotic one results in a different psychophysical state. Hence, the scientists that investigate the role played by context in human health are always more inclined to consider it as composed of not only the external features of an environment but also as the internal psychological states. Among these, there are the more stable as the personality traits, to those more ephemeral as for example the belief regarding the re-occurrence of an event that happened shortly before. (Benedetti, 2013) defines the situation around the therapy as the "psychosocial context" that surrounds the delivery of the treatment. This author points out how each health care situation is composed of rituals, words and meaning that contribute to shaping the brains of patients. A broad scientific literature gives great importance to the type of context experienced in healthcare situations because depending on whether it is positive or negative might trigger placebo or nocebo effects, thereby improving or worsening the symptoms reported by the patients. Placebo and nocebo effects are psychobiological phenomena since they involve real changes in brain activations as a result of an administration of an inert substance or more generally of a sham treatment (Price et al., 2008). The healthcare condition in which these phenomena are most evident, and investigated by the scientific community is pain, primarily because it is a subjective condition strongly modulated by psychological and social factors. It has been discovered that the brain pathways in which placebo and nocebo effects act are the same as those activated by drugs. Opioids and cannabinoids represent the antinociceptive systems found as endogenous analgesic mediators capable of causing placebo responses (Grevert et al., 1983; Levine & Gordon, 1984; Lipman et al., 1990). Hence the elements that compose the context, otherwise called contextual factors (Rossettini et al., 2018), work as trigger stimuli, and, thanks to psychobiological mechanisms such as expectation (L. Colloca & Miller, 2011a), reward (de la Fuente-Fernández, 2009), anxiety reduction (Benedetti et al., 2011) and learning (L. Colloca & Miller, 2011b) cause placebo and nocebo effects. Positive expectations for stimuli generally considered adverse, can generate a reduction in anxiety, allowing us to perceive less pain. When this occurs, dopamine-mediated reward mechanisms come into play and tend to stabilise the search of those behaviours that lead to positive outcomes such as pain relief. Even learning is central to placebo and nocebo effect. Just consider the association between the features of a drug (e.g., colour, smell) with the benefit its taking provides. Continual repetitions of these associations lead to classical conditioning where the taste or the colour of the pill become the conditioned stimulus that can create an unconditioned stimulus, namely, a reduction in perceived levels of pain. In line with this idea of the role played by context to influence the general state of human health, (Koban et al., 2021) propose the "self-in-context models". The authors suggest them as tools for a better comprehension of diseases in which the western clinical practice achieved poor progress in treatment development, such as obesity, psychiatric illnesses, sleep disorders and chronic pain. They highlight that what these diseases share are the changes in brain systems that handle the way in which we conceptualise ourselves and our representations of the world. Giving in this sense a prominent role to the context in which an occurrence (e.g. a medical condition) is experienced.

1.1.1 What contextual factors are and how they work

Balint (*1955*) was one of the first to highlight the importance of context, defining it as the whole atmosphere that surrounds a treatment. Recently, contextual factors were defined as all of the elements that constitute a context, whether they have "physical" features or not (Carlino, Frisaldi, et al., 2014). Their importance is relevant because clinical settings are spaces frequented by people subject to fear related to their health state and where therefore, given the salience of the experience of illness, it is easy to be negatively impressed (Carlino & Benedetti, 2016). In this sense, it is safe to assume the great power played by contextual factors that can be divided in three categories: internal, external and relational. Internal contextual factors are represented by the world made of psychological states as beliefs, memories and expectancies but also by personality traits and biological features such as genetics. External contextual factors are the physical characteristics of environments and of the objects inside them. Among these, we find for instance the physical properties of the therapy such as the taste or smell of a pill, the characteristics of the medical equipment or of the place in which the treatment is delivered. With regard to the relational contextual factors, a good example is the type of communication utilised by the healthcare professional. A positive doctor-patient relationship is developed through reassuring communication, both verbal by the use of words aimed at empathising, and non-verbal through gestures aimed at comforting (Rossettini et al., 2018). In a clinical setting, the presence of positive contextual factors puts the patients in a positive mindset toward the therapy they are receiving and this, in turn, increases the possibility that placebo responses happen. Placebo is a good partner in a clinical setting since it is able to increase the effectiveness of the treatment. In the same way, even if opposite, the nocebo is a bad companion in a healthcare ambiance because it determines the exacerbation of the symptoms reported by the patient. Contextual factors are indeed those elements responsible for context building and more precisely the presence of positive contextual factors leads to the creation of a positive context and so to placebo effects. In the same way, negative contextual factors determine a negative context causing nocebo effects. Among the contextual factors defined as "internal", the most representative are expectations and learning mechanisms (L. Colloca et al., 2008; L. Colloca & Miller, 2011b). As regards the first, the author who built the theoretical framework mostly utilised to investigate the role of expectations in relation to the placebo effect is (Kirsch, 1985, 1997). He postulates the existence of "outcome expectancies", namely expectation forms relative to the occurrence of stimuli or events. Between them, he further divided between those relative to the appearance of external stimuli or events (such as to see a known general practitioner), called stimulus expectancies, and those relating to the manifestation of internal non-volitional experiences (such as pain relief), called response expectancies. Moreover, parallel to outcome expectancies, Kirsch theorised also the existence of “self-efficacy expectancies” i.e. expectations about an individual’s ability to perform a behavior. For example, someone with a high self-efficacy expectancy regards their own capacity to tolerate pain may tolerate hard physical activity despite already experiencing mild pain. The other element considered as a relevant internal contextual factor is learning. Classical conditioning represents the main theoretical framework to explain how placebo effects work. As a result of the association between the unconditioned stimulus (drug) with the neutral stimulus (a drug’s physical features such as smell or colour), the latter becomes a conditioned stimulus. In this way, the mere physical characteristics of the drug (conditioned stimulus) elicit the appearance of the conditioned response, namely the symptomatology relief. In addition to classical conditioning, social learning theory is also useful to understand the placebo responses, since learning does not occur only through direct experience. According to observational learning, the acquisition of new knowledge or behaviours happen also through the observation of others. (L. Colloca & Benedetti, 2009) demonstrated that a group that underwent a procedure of observational learning received the same benefit, in terms of analgesia, as that tested with classical conditioning. Moreover, within the theoretical framework of learning, it has been included also the reward mechanism (Schultz, 2016). The reward hypothesis (de la Fuente-Fernández, 2009) with regard to the placebo effect relies on the patient’s expectation of a reward. This is because the reward mechanism based on dopaminergic release occurs not only when a reward is received, but also when a stimulus (e.g., seeing a doctor) predicts a pleasant future event (e.g., pain relief) (Benedetti et al., 2011). Thus, in a way, it may be argued that expectations, whether they be conscious, such as those related to self-efficacy, or unconscious, such as those triggered by classical conditioning, underlie many forms of the placebo effect. With regards to external contextual factors, increasing numbers of scientific papers are interested in investigating the role played by the clinical environments in which treatments are delivered (Anderson et al., 2018; Bates, 2018; Grignoli, 2021).Evidence-based health care design has been widely accepted as a model to improve the physical features of the clinical environments (Ulrich et al., 2008). Gentle sounds such as a gentle breeze, singing birds or ocean waves can be important low-risk nonpharmacological elements to improve the perception of well-being and lower stress levels in patients (Iyendo, 2017). In a study by (Bukh et al., 2015) on people with arthritis that received intravenous therapy, the authors found that the patients attached great importance to the characteristics of the spaces in which the treatment was delivered such as smell and light, colors and tidiness. A safe atmosphere and comfortable furniture also proved to be important elements for a better care experience. As concern relational contextual factors, they are attributable to the interpersonal cues present in patient-practitioner communication (Rossettini et al., 2018). This may be verbal and non-verbal and as reported by a growing body of studies (Benedetti, 2013; Walsh et al., 2019; Wu et al., 2020) it is important that it conveys positive messages related to empathy and compassion for the patient's experience. For the World Health Organisation, a good patient-practitioner relationship is an important element through which clinical outcomes such as treatment adherence occur (World Health Organization, 2003). For a good adherence to the treatment indeed, the patient's trust in the practitioner plays a key role (Howick et al., 2018).

1.1.2 The role of context in motor performance

Beyond the reality of clinical practice, even the outcomes of movement in people without pain are affected by context (Carlino et al., 2016). This is because placebo and nocebo responses, as they are outcomes of the interaction between an organism and its environment, occur regardless of the presence or otherwise of a medical condition. A good example of this can be considered the improved performance achieved by sportspersons (Carlino, Piedimonte, et al., 2014) when they are driven by positive contextual factors such as internal (e.g., high motivation levels) (Almagro et al., 2020) or relational (for instance a coach you trust) (Jowett, 2017) ones. For example in a study of (McKay et al., 2012) a group of athletes was asked to complete a questionnaire telling them that it evaluated the capacity to perform well under pressure when in fact assessed personality aspects. Once completed, one group was told that they obtained a high score, from which they could conclude that they were able to maintain performance in stressful situations (experimental group), while the other group did not receive information about their results (control group). Before and after the questionnaire both groups carried out baseball throws in low and high pressure conditions. They showed the same outcome in the launches before completing the questionnaire, while after having completed it the group that expected to perform better under pressure obtained better results in the more stressful condition than the control one. This study highlights the effectiveness of a general expectancy in ameliorating, even in specific tasks, motor performance (Fiorio, 2018). Instead, regarding the role of anxiety in the execution of a physical performance there is still much debate and two models have been proposed: (i) the distraction model and (ii) the execution focus model. Both consider anxiety as a pejorative element of motor performance. The distraction model claims that anxiety shifts attention toward irrelevant environmental stimuli making them threatening. In this way there would remain less attention available for the correct movement execution (Eysenck et al., 2007; Wilson, 2008). On the other hand, the execution focus model argues that limited attention cannot explain a negative performance. It sustains that anxiety, shifting internally the attentional focus in an attempt to check explicitly the movements, affects the performance. This bad result would occur because the expert practioners are used to automatically execute movements without needing to monitor them consciously (Beilock & Carr, 2001; Lam et al., 2009; Masters, 1992). The close link between context and actors that perceive and act within it is well highlighted by the embodied approach that has its roots in ecological psychology (Lobo et al., 2018). This model highlights how the perceived information is the result of the interaction among persons and environment and not merely something processed thanks to their own sensorial channels. For instance, a good example of how information is constructed in the person-environment relationship is the different way in which a distance may be perceived. It could appear greater for a person with walking difficulties or a hill could appear steeper to someone with fatigue than for a trained or acclimatised person (Proffitt, 2006). This approach therefore makes evident the weight played by internal contextual factors, not only regarding the psychophysiological responses to environments or events (placebo and nocebo) but going so far as to affect an individual's very construction of reality. Thus, placebo and nocebo effects, as context-related psychobiological responses, can extend above and beyond clinical settings since they are triggered by ever-present human psychobiological mechanisms.

1.1.3 The role of beliefs in chronic pain

Despite the high levels of efficacy achieved by Western medicine, for example in vaccination and antibiotics, there remain areas that benefited less from similar discoveries, such as psychiatric and sleep disorders, obesity and chronic pain. According to Koban et al. (2021) the ventromedial prefrontal cortex and the related default mode network help to create self-in-context models (i.e. personal representations). They deal with the formation of narratives about the self and one's world by providing control over behaviours and peripheral physiology. For these authors, the lack of treatments' efficacy for the above mentioned medical conditions may be due to the fact that they share changes in the functions of brain systems relative to the personal representation of the self and the surrounding world. As far as chronic pain is concerned, it has been seen that the way in which people conceptualize themselves and their bodies has a lot of relevance in the type of experience they have of pain. A reciprocal relationship of chronic pain with psychopathological experiences such as depression and anxiety symptoms is already well established, both in clinical and research fields (de Heer et al., 2014; Fonseca-Rodrigues et al., 2021; Vadivelu et al., 2017). A constant experience of pain exposes people to strong and unpleasant emotions that can lead to depression and symptoms of anxiety. When these psychological symptoms worsen and become predominant in the daily routine, people even experience an increase of pain problems (Gorczyca et al., 2013). In case of sickness, high levels of anxiety and depression correlate with pain problems and in turn pain problems may lead to feelings of worry and mood lowering with clinical relevance. With regards to musculoskeletal pain, high levels of depression and negative beliefs that the pain will be permanent both contribute to augment the disability, suggesting as the transition from acute to chronic pain is more attributable to emotional and cognitive factors than medical conditions (Casey et al., 2008).

There are two basic ways to deal with (chronic) pain: (i) active coping strategies and (ii) passive coping strategies (Gorczyca et al., 2013). Coping is defined as a set of internal resources, made by thoughts and activities, to deal with stressful events (Folkman & Moskowitz, 2004). It is different from defence mechanisms mainly because coping is composed of consciousness modes to act rather than unconsciousness defence mechanisms. In the first category (i) people endeavour to function despite the pain or attempt to distract themselves so that they do not feel it. These people think that their condition, despite everything, is not so serious. Instead, in the second category (ii) there are those who delegate the control of the pain to external agents and manifest catastrophizing beliefs about their condition. These people can be summarised as those who perceive themself powerless and fragile (Jensen et al., 1991).

The Common Sense of Model of Self- Regulation (CSM) is a framework that explores the inner experience lived by patients, the meanings and the interpretation of the disease and the symptoms that they have about their state of health. Information included in such a model become patients aware of their condition and their emotional responses to it, their perception of threats, of possible treatment action and how they create feedback to check the efficacy of the actions planned and threat progression (Leventhal et al., 2016). Essentially, CSM is a way to investigate a patient's representations of the sickness, but in addition to the methods used by an individual to deal with a disease or a difficult pain situation, should be added the social and relational contribution provided by the environment in which the person lives. For example, advice offered by not only friends and relatives, but also the wider society and preexisting beliefs can turn out to be wrong or dangerous. This aspect is very important if you think that a wide variety of research highlights how what people believe and does about their musculoskeletal pain is predictive of its duration and of the disability it will cause (Campbell et al., 2013; Leventhal et al., 2016; Picavet, 2002; Quicke et al., 2017).

Beliefs can be (i) irrational, (ii) contradictory, (iii) explicit and (iiii) implicit (Caneiro et al., 2021). An example of (i) irrational belief is the conviction that a movement could severely damage the sore body part. (ii) Beliefs can be contradictory. Just think of someone that wants to strengthen their articulation but at the same time thinks that an active exercise could be dangerous for the joint. (iii) Beliefs are explicit when patients know what they think, i.e. when their behaviours, e.g. the treatments to follow, are driven by something that they believe consciously. In contrast, (iiii) beliefs are implicit when there is a lack of awareness about behaviours carried out to protect the body from activities considered dangerous. Often patients avoid a movement, and when asked them about it, they are initially surprised and after time refer to an injury of twenty years before and that Some of the wrong beliefs about the way to face musculoskeletal diseases are transmitted to the patients by the own clinicians. For instance the excess use of radiographic images risks creating misunderstandig about the cause of the situation lived by the patient. In turn, excessive inspections may lead to unnecessary interventions such as surgery, creating in the patient problematic attitudes towards the disease such as catastrophism and fear avoidance behaviours (Darlow et al., 2017).

Human beings perceive, act and think about their own self and the world around through the network of meanings in part inherited genetically but for most acquired by the context in which they grew up. The first relations, especially those lived inside the family, work as implicit/unconsciousness elements to build this reading card. Nevertheless, subsequent social experiences, for instance in the field of school and interpersonal relationships, or the news to which we all are often exposed, contribute to increase and to complexify our personal frame of reference. This continuous process goes hand in hand with cerebral plasticity i.e. the physical modification of our brain following the storage of knowledge and learning. Even though cerebral plasticity is one of the best tools human beings have to keep up to date (Mateos-Aparicio & Rodríguez-Moreno, 2019), it may be a double-edged sword. A good example is indeed central sensitisation which like a manifestation of the remarkable plasticity of the somatosensory nervous system (Latremoliere &

Woolf, 2009) can augment the perceived pain, contributing to chronicling it. Often, chronic pain can be the result of an increased sensitivity of the central nervous system toward nociceptive stimuli called central sensitisation (Nijs et al., 2021). The possibility to experience pain represents a protective factor, which allows an individual to avoid similar experiences in the future. It is precisely in this perspective that we should observe the phenomenon of central sensitisation. It is a consequence of brain plasticity which aims to protect the body injury area from dangerous stimuli. This occurs through the recruitment of previously subthreshold synapses in the somatosensory cortex to nociceptive neurons (Latremoliere & Woolf, 2009). A similar result can be caused by negative self-in-context models (Koban et al., 2021). In other words, negative and unhelpful beliefs and expectations about the self or of the treatment can be dangerous. Just think of problems derived by fear avoidance beliefs in people with back pain (Rainville et al., 2011). But fortunately beliefs are dynamic states of mind, able to be modified. Just for this reason it is important to underline that clinical guidelines suggest that changing erroneous beliefs represents the first line of treatment for all patients with musculoskeletal diseases (I. Lin et al., 2020).

1.1.3.1 The role of Fear-avoidance beliefs and Kinesiophobia as key elements for the maintaining of pain

Lethem and colleagues were the first in 1983 to propose a relationship between pain and fear in chronic low back pain (Lethem et al., 1983). They hypothesised that after an injury two opposite reactions are possible: (i) confrontation, where there is a gradual return to normal activities as pain decreases and (ii) avoidance, where the fear of pain leads to an increasein the perception of pain and disability. The authors outline how, despite the opposition of these responses, people often present a combination of the two.

Currently, the fear-avoidance beliefs model (FABs) is widely taken into account to attempt to shed some light on chronic musculoskeletal diseases, (Gatchel et al., 2016), and among them, this model is particulary utilised to explain how psychological factors affect chronic low back pain and chronic neck pain (Bordeleau et al., 2022; Wertli et al., 2014). Researchers and clinicians agree to define fear-avoidance beliefs as negative and unhelpful convictions and emotions (often relative to the back) derived from a fear of pain or of its exacerbation (Rainville et al., 2011). These kinds of inner experiences often lead to kinesiophobia, literally from the latin ‘fear of movement’. People with kinesiophobia indeed experience an irrational fear of physical movement due to a feeling of excessive vulnerability of the body, or of an individual body part (Darlow et al., 2015; Gregg et al., 2015). A good example of kinesiophobic behaviour concerning a specific movement is that of lifting objects, since there is a deep-rooted belief that lifting objects with the spine flexed can be dangerous and cause low back pain (Knechtle et al., 2021). A reduction of movement associated with kinesiophobia was found both in research (Thomas & France, 2007) and in the clinical field (Larsson et al., 2016). From 51 to 72% of patients with chronic pain present kinesiophobia (Bränström & Fahlström, 2008; Lundberg et al., 2006) and unlike other phobias, people who experience kinesiophobia are not aware of their inner experience relative to fear of movement, believing the avoidance of movement a sensible and justified reaction (Lethem et al., 1983; Trinderup et al., 2018). While movement restriction or avoidance can be considered a good strategy when trauma is in the acute phase, evidence suggests that such protective behaviours risks leading to further pain and disability. This kind of belief, endured over time, can reinforce protective movement strategies, which in turn have been associated with rigid motor behaviour, increased muscle co-contraction, and mechanical loading on spinal tissues (C. J. Colloca & Hinrichs, 2005; Granata & Marras, 2000). Progressively, once musculosckeletal disease is present, these protective movement strategies determine a decrease in movement, further aggravating pain (Knechtle et al., 2021) and triggering a loop where catastrophic convictions about one's health lead to disability. One efficient method to cope with fear avoidance beliefs and kinesiophobia is a reality-based education of the diagnosis and prognosis to prevent distorted and catastrophic views (Watson et al., 2019). On the other hand, physical exercise is also considered a useful approach to handle the irrational fear of movement (Bordeleau et al., 2022).

1.2 Low back pain: a Brief Overview

Musculoskeletal pain is defined as pain that strikes bones, ligaments, muscles, tendons and nerves (El-Tallawy et al., 2021). To the World Health Organization (WHO), musculoskeletal diseases represent the greatest contributors to worldwide disability, with about 1.7 billion people experiencing them (*Musculoskeletal Health*, s.d.) Moreover, chronic low back pain is the greatest cause of years lived with disability (YLDs) worldwide, followed by depressive disorder and other musculoskeletal conditions such as osteoarthritis and chronic neck pain (Treede et al., 2019). In the United States, low back pain is such a common problem that it affects 80% of people at a some point of their life (Patrick et al., 2014), representing one of the main causes of activity limitation and absence from work (Lidgren, s.d.; Wynne-Jones et al., 2014). A third of those who experienced back pain report persistent pain within a year of an acute episode (Chou et al., 2007). But low back pain is a symptom and not a specific medical condition, its causes can thus be diverse and only 15% of patients receive a specific diagnosis of their low back pain (Bartleson, 2001). This means that for the remaining 85% the causes of this kind of pain remains unclear (Hoy et al., 2010). It is also because of its spread and diagnostic uncertainty that treatments proposed by several healthcare professionals are various (G. L. Moseley, 2017). Those with a more medical approach are aimed at locating and intervention on the source of pain (e.g. discectomy, a facet joint block, lumbar rhizotomy) (Y et al., 2004). Physiotherapists are interested in treating the (chronic low) back pain with an approach aimed at mobilising the trunk muscles, thereby altering the motor strategy used by the patients primarily through physical exercises (Shipton, 2018). On the other hand, psychologists work on incremental acceptance and lower catastrophism traits through cognitive behavioural therapy and mindful-based stress reduction (Petrucci et al., 2021). The fact that the incidence of back pain is highest in people around 40 and decreases in older age (Mody & Brooks, 2012) could be interpreted as a phenomenon related to the increase in responsibilities of this age, highlighting the role of psychosocial factors in the maintenance of this musculoskeletal condition.

1.2.1 The negative body representation hypothesis behind the chronic low back pain

The disconnect between pain and tissue problems is a well known matter for those who deal with musculoskeletal diseases in particular regarding back pain, and especially given the numbers of people experiencing it. Starting from this perspective, it could be interesting to observe back pain, especially chronic back pain, deeping the role of mental representations about the body. The idea of mental representation derived from neural pathways is widely applied to investigate pain precisely because of its subjective nature. Beginning with representations most overarching, such as those aimed at link physical and mental health through personal narratives about the self and the self inside the world (Koban et al., 2021), and continuing with those more specific like those relative to explicit and implicit body image (Longo, 2015). To move from a mere somatosensation to a rich somatoperception, the ‘body matrix’ hypothesis has been proposed by Moseley and collegues (G. L. Moseley et al., 2012). It suggests an integration of somatotopic representations coming from the somatosensory cortex with those peripersonal and body-centred spatial coming from the post-parietal cortex, to construct the representation of the person’s body and that of the space around it. In the last few decades, many works focused on the relationship between the disturbance of these representations and chronic pain (Mansour et al., 2014; G. L. Moseley et al., 2012; G. L. Moseley & Flor, 2012; Wand et al., 2011). Jane Bowering and colleagues produced a study on the recognition of pictures of left/right trunk positions amongst four groups. These groups were composed of (i) healthy participants, (ii) people with current pain, (iii) people with a history of back pain and (iiii) people with both a history of and current back pain. Results showed that the last group performed worse than the others, suggesting that an initial experience of back pain could induce vulnerability in the cortical body maps, modifying them if another episode of pain happens (Bowering et al., 2014). Not only the representation of the motor domain turns out to be affected by chronic pain but the representation of the tactile domain too (Catley et al., 2014). A magnetic resonance imaging study evaluated the responses to tactile stimulus on chronic low back pain patients with Waddel signs dividing the sample in two groups: (i) those reporting 4-5 Waddel signs (WS-H) and (ii) those reporting one or zero Waddel signs (WS-L). All patients received an intense tactile stimulation on the lower back with a dedicated plate to not affect the imaging quality. Results showed an increased activation of the right posterior (retrosplenial) cingulate, extrastriate cortex and left posterior parietal lobe in the WS-L versus WS-H. The greatest activation of cingulate and parietal cortices of the WS-L patients suggests a wider involvement of cognitive-emotional resources to handle pain compared to those with higher numbers of Waddel signs (WS-H) (Lloyd et al., 2008). Alterations in specific areas or cortical networks should not be interpreted as the direct cause of problems such as chronic pain. Rather, they also should be seen as the results of cumulative effects of bad self representations, e.g. catastrophic thoughts (Koban et al., 2021).

1.2.2 The “operating mechanisms” that painless and pain motor experience share

Just as placebo and nocebo effects occur also beyond clinical realities, it is possible to identify brain mechanisms provided to a better individual-environment interaction which work is found also in everyday life experiences. I refer to the hypothesis of the bayesian brain, to what concerns functional and structural connection between motor and emotional cortex areas and the surprise mechanisms (wow-effect) and its consequences.

1.2.2.1 The Bayesian brain

The Bayes' theorem is a statistical theory that describes the probability that an event will occur based on prior knowledge of conditions about that event (Joyce, 2021). In the last decades this theory has been applied to human perception to indicate how choices or behaviours can be the result of a probabilistic brain computation aimed at reducing the uncertain information coming from an individual's own sensory channels (Kording, 2014). Although it is not entirely clear how this mathematical theory is practically applied on brain functioning (Rahnev, 2019), its application to the field of perception is promising. We generally tend to think of the brain as an organ that receives sensorial stimulus, whose processing then results in perception (e.g. tactile or visual), but the bayesian brain hypothesis strongly questions this assumption. The Bayesian brain hypothesis is based on the premise that our senses are continuously exposed to a huge amount of information, both coming from our own body and the world around us. Such a constant stream would require a lot of energy to be handled and transformed into something coherent, and so for the purpose of adaptation the brain utilises a probabilistic approach to manage it (Knill & Pouget, 2004). According to this model the brain is a predictive machine that generates top-down predictions about what will happen, called 'priors'. The comparison between priors and the bottom-up sensory afferences results in 'prediction error' that is the difference between what was expected and what really took place (Friston, 2005). To have a reliable life experience, it is necessary to minimise the prediction error and this can be done in two possible ways: through perceptual inference and active inference. The perceptual inference allows the calibration of priors according to sensorial information, through this process 'posteriors' are generated, that are refreshed priors so as to be a more accurate representation of what the future holds. On the contrary, active inference gives more importance to priors, namely to what is expected than to sensorial afferences (Friston, 2009) highlighting the role of expectations in perception. The bayesian brain theory suggests that the world as it is experienced (including both cognitive and emotional experiences) is not a true representation of reality, but is continuously subjected to redefinition thanks to the updating of priors in the brain. This aspect is relevant and matches with the previously discussed ideas about the power of 'personal narratives' (i.e., the self-in-context models, unhelpful beliefs and expectations) in influencing the health state in conditions such as musculoskeletal chronic pain.

1.2.2.2 The Limbic-Motor interface

Scientific literature broadly reports the role played by the amygdaloid complex to modulate the emotions related to the appropriate context behaviours (Adolphs, 2010). However, even if emotions are often considered as triggers for human motions, less is known about the mutual influence between the limbic system (mainly represented by the amygdaloid complex) and the premotor and motor cortex.

First studies that investigated the anatomical connectivity between the limbic system and the cortical motor-related areas demonstrated through tract-tracing methods the existence of a motor-limbic interface in rats, cats and monkeys (Llamas et al., 1977).

In humans, the existence of pathways connecting the amygdala- to motor-related areas, is more recently described by Grezes and colleagues through a probabilistic tractography study (Grèzes et al., 2014) that pointed out how a direct amygdala-motor pathway could influence complex motor behaviours. This is particularly interesting considering the importance of the context in which the motor performance is executed as an ‘emotion mediator’ (Wager & Atlas, 2015) and given that action planning requires information for the accuracy of the movements, both from the effector of the action and from the surrounding environment.

Limbic and sensorimotor pathways connectivity in humans has been investigated by (Rizzo et al., 2018) in a tractography study. Their research further reinforced the idea of the existence of a motor-limbic interface involved in the emotional modulation of complex functions such as spatial perception and movement computation.

In view of all this, it could be interesting to consider the emotional-motor connection to implement rehabilitation methods and/or learning of new motor strategies that hinges on emotional aspects to motivate and promote the recovery of patients with musculoskeletal disabilities.

1.2.2.3 The surprise or “Wow Effect”

Surprise is commonly defined as a basic emotion derived from something unexpected taking place. The cognitive-evolutionary model of surprise (Reisenzein et al., 2019) sustains that human beings possess implicit and well-organised schemas (or beliefs) by which they act, think, and perceive their surroundings and their internal world. This model proposes that the surprise mechanism is innate and works beyond the level of consciousness since it is a hardwired information-processing device provided by evolution to detect and update expected stimuli. Another model to examine surprise is the metacognitive explanation-based (MEB) theory (Foster & Keane, 2015, 2019) which looks as surprise as a tool to make sense and to learn more so as to solve the feeling of the unexpected. In this regard, the higher the impact of the inexplicable, the higher the possibility to memorise the event. Recently, (Grassi & Bartels, 2021) proposed an effect derived from surprise, called the “Wow” effect. They highlight how surprise is the consequence of the abrupt contradiction of our expectations derived by the senses. The authors utilise this model to describe in detail the mechanisms by which magic tricks take place, discussing both the brain areas involved and the role played by context in their genesis and functioning. Authors further suggest how the violation of expectations leads human beings to believe in the existence of magic, thus highlighting the importance and the assurance we attach to our senses and the difficulty inherent in disagreeing with them.

All these theories consider the new information (i.e., unexpected events) as something that modifies the equilibrium of the system (e.g., beliefs or previous knowledge also called ‘priors’) and that must be integrated into a new reading of reality. In this consideration, the wow-effect (Grassi & Bartels, 2021), considered as a consequence of a surprise emotion derived by the occurrence of unexpected events, could involve the amygdaloid complex activation to detect contingencies stimuli. Thus, the creation of an illusion able to cause a wow-effect as a consequence of strong emotion of surprise might trigger the quick learning of new motor patterns.

1.3 An overview of Immersive Virtual Reality (IVR) and its applications

Immersive virtual reality (IVR) is primarily described as a computer-generated environment where users experience the perception of being surrounded by a digital scenario (Slater, 2018). The revolutionary aspect of the IVR consists in the fact that the real world, together with most of its features, becomes reproducible. The possibility for users to be engaged in a variety of environments makes it possible to experience situations otherwise difficult to experience, such as exposure to dangerous situations or to scientific hypotheses that would be difficult to perform in reality. As early as 1965, Sutherland was the first to imagine transforming the screen into “a room within which the computer can control the existence of matter” (Sutherland, 1965), thus laying the foundations to imagine the creation of digital environments with similar properties to the real ones. Nowdays, thanks to its versatility, IVR finds applications in many scientific disciplines that use it for different purposes. Recently, IVR systems have been recognized as a useful tool and utilised in education

(Srikong & Wannapiroon, 2020), surgery (Fida et al., 2018), treatment of psychological disorders (Freeman et al., 2017) and rehabilitation from injury (Tieri et al., 2018), all of which demonstrates its wide versatility.

1.3.1 The importance of immersion and presence

Two important and useful concepts to consider in the IVR world are those of immersion and presence. The first is determined by the IVR system's capacity to offer good sensorimotor contingencies for perception; the greater the quality of the IVR system’s technological quality, the higher the resultant immersion. An IVR system is generally composed of a tracking system and a set of visual, haptic and audible feedback. The immersion level is proportional to the capacity of the system to offer to the users an experience in line with what they expect were they to perform the same actions in the IVR as in reality. The immersion level is not only characterised by the extent to which the IVR system supports action execution in terms of a movement’s credibility, but also by the qualities of the outputs used to show them, such as the overall extent of tracking (e.g., how much body is tracked and if there is latency to this tracking) and the visual properties of digital recreations (e.g., how much they appear reliable for illumination, geometrical and physical features). The sense of presence represents the feeling of experiencing something realistic and it is determined by the place illusion (PI) i.e. the sensation of being in a real place and by the plausibility illusion (PSi) relative to the fact that the scenario being depicted is actually occurring (Slater, 2009). Sensorimotor contingencies are important elements for a realistic experience inside immersive virtual worlds. They represent the right coupling between movements and perception. For instance, moving the head to the left we expect to see something different than when we move it downward (O’Regan & Noë, 2001). Surprisingly, contrary to the sensorimotor contingencies, the accuracy of what appears in the display in terms of image resolution appears not to be a critical factor to experiencing a high level of presence (Sanchez-Vives & Slater, 2005). As suggested by the gestalt approach to the vision (Wagemans et al., 2012), probably this is due to a general tendency to organise and simplify complex images into something unified. Just think of the ease with which two dots and one line are enough to have the perception to be in front of a face (Tsao & Livingstone, 2008).

1.3.2 The use of virtual reality in patients with chronic low back pain

Recently, the idea of utilising IVR as a useful tool to treat musculoskeletal diseases and utilise it to reduce pain and increase joint mobility in people suffering of chronic pain has been growing (Kantha et al., 2023; H.-T. Lin et al., 2019). As regards chronic low back pain, three different working mechanisms were identified: (i) distraction, (ii) neuromodulation and (iii) graded exposure therapy (Tack, 2021). The mechanism of distraction (i) is based both on the gate control theory of pain (Melzack & Wall, 1965) which takes into account the role of attention in the perception of pain, and also on the fact that seeing a virtual representation of one's healthy body (i.e., the virtual avatar) can have analgesic effects (Martini et al., 2014). With regards to neuromodulation (ii), the incongruence often highlighted between somatic and pain perception in chronic musculoskeletal patients (L. G. Moseley, 2008) evidences an effect due both to cortical plasticity (G. L. Moseley & Flor, 2012) and negative beliefs (Rainville et al., 2011) about the own's health state. Virtual environments appropriately created either to facilitate movements or to contrast the fear of movements thanks to specific illusions, have potential to be successful tools in rehabilitation. Both in terms of cortical reorganisation (Won et al., 2015) and also in terms of a reduction of inner negative states (Gulsen et al., 2022). Graded exposure therapy (iii) relies on activities exposure that combines frightened movements with positive reinforcers(Leonhardt et al., 2017). Its usefulness in immersive virtual reality spaces is represented by the possibility to reproduce movements related to real life activities (Alemanno et al., 2019)), breaking the disability cycle of kinesiophobia and movement avoidance.

1.4 References

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2. Real and Perceived Feet Orientation Under Fatiguing and Non-Fatiguing Conditions in an Immersive Virtual Reality Environment

2.1 Abstract

Lower limbs position sense is a complex yet poorly understood mechanism, influenced by many factors. Hence, we investigated the position sense of lower limbs through feet orientation with the use of Immersive Virtual Reality (IVR). Participants had to indicate how they perceived the real orientation of their feet by orientating a virtual representation of the feet that was shown in an IVR scenario. We calculated the angle between the two virtual feet (α-VR) after a high-knee step-in-place task. Simultaneously, we recorded the real angle between the two feet (α-R) (T1). Hence, we assessed if the acute fatigue impacted the position sense. The same procedure was repeated after inducing muscle fatigue (T2) and after 10 minutes from T2 (T3). Finally, we also recorded the time needed to confirm the perceived position before and after the acute fatigue protocol. Thirty healthy adults (27.5 ± 3.8: 57% female, 43% male) were immersed in an IVR scenario with a representation of two feet. We found a mean difference between α-VR and α-R of 20.89° [95% CI: 14.67°, 27.10°] in T1, 16.76° [9.57°, 23.94°] in T2, and 16.34° [10.00°, 22.68°] in T3. Participants spent 12.59, 17.50 and 17.95 seconds confirming the perceived position of their feet at T1, T2, T3, respectively. Participants indicated their feet as forwarding parallel though divergent, showing a mismatch in the perceived position of feet. Fatigue seemed not to have an impact on position sense but delayed the time to accomplish this task.

2.2 Introduction

Position sense is the ability to perceive the location of different parts of our body in space, even in absence of vision. It relays on the integration of the information retrieved from the 'postural schema' and the 'body model', which are a result of complex bottom-up and top-down mechanisms, respectively (Ganea & Longo, 2017). Bottom-up mechanisms depend on different types of peripheral afferent signals such as mechanoreceptors from joints signalling flexion or extension movements and from muscles spindles signalling contraction and lengthening, but also stretch-sensitive receptors from the skin (Longo et al., 2010; Proske & Gandevia, 2012). Together they are called 'proprioceptive afferent signals'. Their integration and elaboration with the efferent signals from the motor system specifying movements, provide information about joint angles, leading to the ‘postural schema’. This scheme contains the angular orientation of our body segments in space. On the other hand, the top-down mechanisms lead to the ‘body model’, an inner body representation that contains information about the length and shape of body segments, information not available through any afferent signal (Longo & Haggard, 2010a). The integration of the ‘postural schema’ and the ‘body model’ provides the ‘position sense’. Despite the important role that the ‘body model’ has in the position sense, little is known about its specific nature (Longo et al., 2010).

Given the multifactorial nature of the position sense processing, its assessment is not easy due to the impossibility to access a single information but only the final output which is the body segments’ location and orientation (position) referred by the person. Many authors have assessed the distance between the actual and judged locations, defined as “localisation error”, of a single landmark (Longo, 2015), others instead have been able to entirely map the ‘body model’ representations of limbs assessing the distance between the judged locations of two adjacent landmarks (Longo & Haggard, 2010b). However, there are still many sources that can affect the position sense output, such as misperceptions of joint angles or the indirect use of vision that can help to build spatial references related to the body (Nieto-Guisado et al., 2022; Radziun & Ehrsson, 2018). Experiments with visual sensory-deficit participants or with prism spectacles induced a conflict in position sense tasks (Mon-Williams et al., 1997; Rossetti et al., 1995; Stenneken, Prinz, Bosbach, et al., 2006; Stenneken, Prinz, Cole, et al., 2006). It is thought that visual information, when available, can bypass the afferent signals of the body and lead the brain to integrate automatically that information even if not congruent (Touzalin-Chretien et al., 2010).

Moreover, in several conditions the position sense has been studied to be altered or affected, such as ageing (Ferlinc et al., 2019; Herter et al., 2014), central (Ateş & Ünlüer, 2020; Rand, 2018) and peripheral (Goldberg et al., 2008; Li et al., 2019) nervous system injuries, movement, and (Abbruzzese et al., 2014) musculoskeletal disorders (Mohammadi et al., 2013; Röijezon et al., 2015a), and fatigue (Proske, 2019; Vafadar et al., 2012; Verschueren et al., 2020). In particular, fatigue seems to be associated with neuromuscular control changes that lead to proprioceptive and executive function deficits, joint instability, and musculoskeletal injuries (Abd-Elfattah et al., 2015; Steib et al., 2013). Possible mechanisms are thought to be linked to acute workload, perturbation of feedback loops or signal processing (Jahjah et al., 2018; Johnston et al., 2018), but further research is needed. Similarly, the connection between fatigue and position sense is still unclear due to the difficulty in assessing quantitatively to what extent each factor entailed in the proprioception can influence position sense (Proske, 2019; Romero-Franco & Jiménez-Reyes, 2017).

A possible solution to isolate afferent sensory signals, such as visual bodily and spatial cues, and assess position sense is Immersive Virtual Reality (IVR). The investigator, through IVR, can reduce external stimuli by immersing the person into an ad hoc created scenario partially devoid of visual cues (Fogg, 2002; Valori et al., 2020; Witmer & Singer, 1998), where vision cannot help to build any self-body or space reference. For instance, Valori et al. implemented the IVR to investigate the extent to which the presence or absence of visual cues aids proprioceptive afferent signals accuracy across lifespan (Valori et al., 2020). Similarly, Bayramova et al. studied the accuracy in reproducing a rotation angle in a self-rotation task in IVR, and the memory aspect of the task, reporting that position sense is more accurate when vision and proprioception are optimally integrated (Bayramova et al., 2021). Moreover, by displaying a virtual user interface, the participants can synchronously and subjectively quantify their position sense without relying on visual bodily or spatial cues. The reported strengths of IVR, together with its versatility, highlight a new role of this technology in this research framework (Sanchez-Vives & Slater, 2005; Valori et al., 2020). Relying on these premises, we posited whether the real orientation of the lower limbs can differ from the perceived one, measuring this possible variability inside an IVR environment deprived of visual references. Considering the preliminary findings on the effect of visual sensory inputs on position sense, we expected a discrepancy between the actual and the perceived orientation of the lower limbs. Furthermore, we hypothesised that this parameter, along with the time to process it, might change under acute fatigue conditions, as a result of a reduction in the accuracy of position sense. Hence, the main aims of this study are (1) to assess the position sense of the lower limbs by quantifying the difference between the real and the perceived orientation of feet, and the time required to confirm it, and (2) to investigate how fatigue can influence these parameters in healthy people by immersing them in an ad hoc virtual environment devoid of visuospatial contextual factors.

2.3 Methods

2.3.1 Trial Design

A pre-post trial study was performed at the Rehabilitation and Engineering Laboratory (REHElab) at the campus of Savona, Department of Neuroscience, Rehabilitation, Ophthalmology, Genetic and Maternal and Child Health (DINOGMI) of the University of Genova. The study was conducted per the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee for University Research (CERA: Comitato Etico per la Ricerca di Ateneo), University of Genoa (approval date: 10/06/2020; CERA2020.06).

2.3.2 Participants

People without diseases (18 ≤ age ≤ 50) were considered eligible to partake in this study if they did not report any acute injuries or musculoskeletal and/or neurological disorders in the last six months. Moreover, people in cure under psychotropic drugs, those who have taken non-steroidal anti-inflammatory drugs and corticosteroids in the previous 48 hours before the experimental session, and those unable to understand the tasks were not allowed to join the study. Participants were also excluded if they had drunk caffeinated or alcoholic beverages six hours before the beginning of the session. The use of spectacles or contact lenses was allowed, and all participants had to sign the informed consent.

Participants were informed that the trial would be performed barefoot wearing comfortable sports clothing and provided with all the information and explanation about the aims, the phases, the instrumentations, and the risks of the experimental trial. Each doubt and curiosity was answered. The possibility of interrupting participation in the study at any moment was also explained. The signing of the informed consent was mandatory.

2.3.3 Interventions

The HTC VIVE Pro IVR system was adopted for the trial. The apparatus was installed into a 7x5 room, with no reflective surfaces and the possibility to avoid any exposure to natural lighting. The system setting included a Vive PRO Head-mounted display (HMD), two Vive controllers (2018), and two SteamVR 1.0 “Lighthouse” base stations. The choice to use a simple setup (HMD+2 controller) was made for two main reasons. Firstly, since our experiment was aimed at the study of proprioception, we wanted to minimise the invasiveness of the set-up, especially for the lower limbs. Secondly, the dimensions of rather cumbersome sensors (Vive Trackers 2018, Ø=10 cm) (HTC Vive, 2018), and the difficulties of a stable and repeatable positioning on the instep, raised some concerns about the accuracy of the measurements obtainable from additional devices.

The two lighthouses were connected through a 'sync cable', 5m apart from each other, and fixed to the ceiling at the height of h= 3 m, with an inclination of 40° to it. This system uses a robust full-room tracking technology, and it records the position and orientation of all the trackable components across a 2,5 x 2,5 m space (recording area) (Sansone et al., 2021). More specifically, the tracked position and orientation are updated primarily through inertial measurement units (Niehorster et al., 2017). The lighthouses limit and correct the intrinsic "drift" error of the inertial measurements by providing additional kinematic data. The system extrapolates positional and orientation values from a set of photodetectors located on the trackable device illuminated by the lighthouses, which emits an IR synchronisation blink followed by two IR pulses, sweeping the tracking area repeatedly, from left to right and then from top to bottom. By knowing the angular velocity of the device, and the time between the blink and the detection of the laser pulse, the system determines the directions in which each photodetector is located. The directions of four non-coplanar photodetectors are the basis to solve the so-called perspective-n-point (PnP) problem (Maciejewski et al., 2020) and improve the accuracy of the tracking.

The trial is divided in various phases settled into different virtual scenarios 1) Welcome Scenario; 2) Adaptation Scenario; 3) Stepping Scenario; 4) Fatiguing Scenario 5) Measuring Scenario. During the virtual simulation, the investigator stayed close to the participants to guide them throughout the experiment.

The participants were instructed to move towards the centre of the recording area, outlined by a 60 x 60 cm scaled tile with 12 parallel lines, distanced 5 cm from each, marked on its surface (Figure 1). Subsequently, they wear the HMD and two controllers (one for each hand) to interact with the virtual world. Hence, the participants were immersed into the 'Welcome Scenario', a white virtual environment without any spatial references, and with a virtual disclaimer reading "Welcome to the body perception test. In this period, feel free to get accustomed to the virtual world. Follow the directions of the researcher and press START to begin" (Figure 3A).

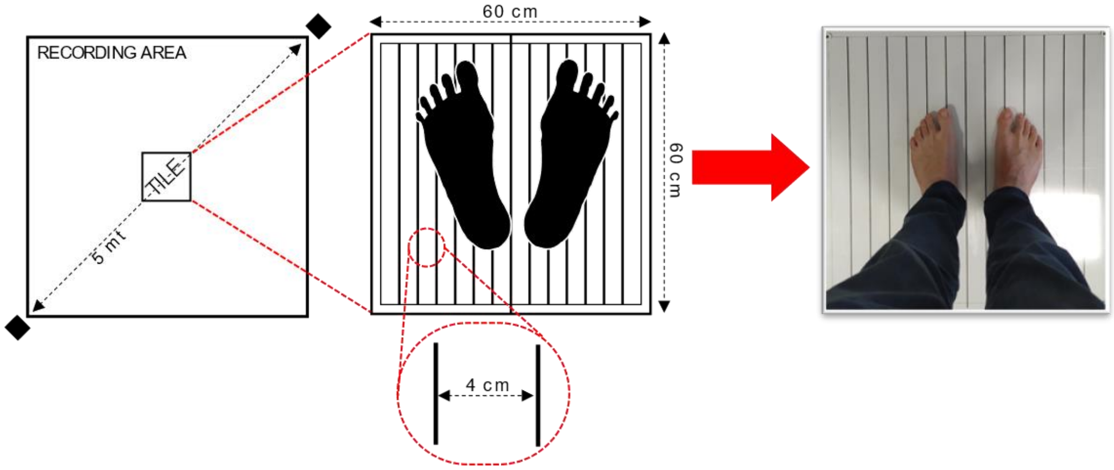

Figure 1 – “Recording area”; Fig 1a shows the tile on which participants were asked to get on; Fig 2a shows the same tile but with a participant on it

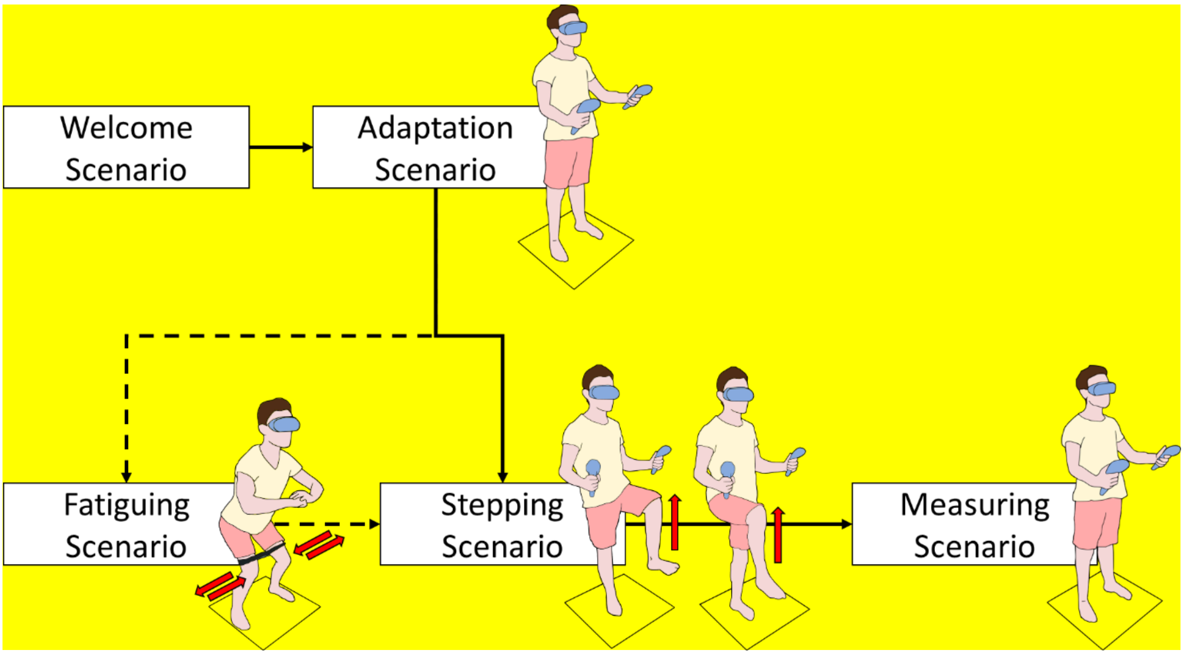

Figure 2 – Workflow of the experimental protocol across the different virtual scenarios

Under these circumstances, the participants' capability of reading the text was assessed to ensure the right positioning of the HMD. After that, by pressing the trigger button of the controllers, the next phase of the experiment started. The participants were transferred into the ‘Adaptation Scenario’. In this scenario, the participants were asked to orientate two feet icons, represented by two arrows for each foot respectively, towards specific-coloured zones, by the simultaneous use of the two controllers (Figure 3B). Here, they were free to experience and become confident with the use of the controllers. More specifically, the system registered the finger position on the touchpad and calculates the angle of the vector identified by the centre of the touch surface and the point of contact.

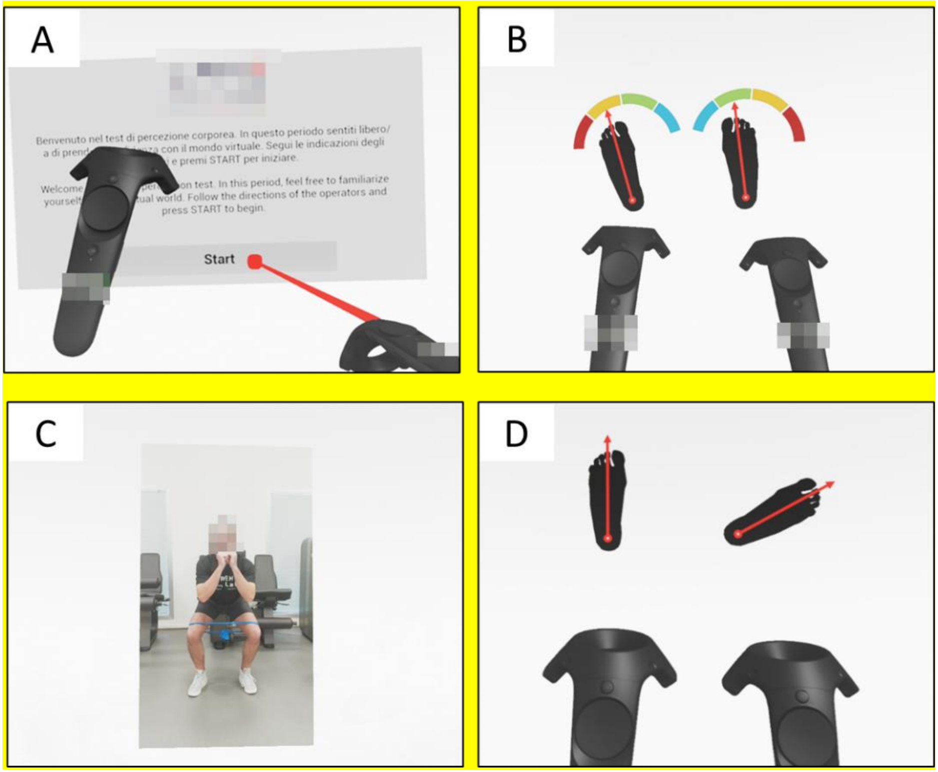

Figure 3 – First person view of the different scenarios of the virtual application: A) Welcome Scenario; B) Adaptation Scenario; C) Fatiguing Scenario; D) Measuring Scenario

Once they were familiarised with the controls, the experimental trial started with the ‘Stepping Scenario’ and the ‘Measuring Scenario’. In the ‘Stepping Scenario’, after an acoustic signal, participants had to perform a high-knee step-in-place task while staring at a black point displayed in front of them in the virtual environment. This point was used as an external attention focus to help them to hold their balance. After a second acoustic signal, the black point disappeared, and the participants had to stop in the reached position without moving further their feet, and then the ‘Measuring Scenario’ appeared. The time between the two acoustic signals was randomly defined between 10s and 15s to avoid any participant’s possible conditionings. In the ‘Measuring Scenario’ (Figure 3D), the participants saw the virtual feet icons in front of them, as seen in the ‘Adaptation Scenario’, but without the coloured dial to avoid influencing their assessments. Participants had to indicate their perceived feet’ orientation through the touchpad of the controllers.

When the participants pressed both controllers' triggers simultaneously, the program recorded the angle between the two feet (α-VR) icons and the time to confirm it, as the time spent with the finger on the touchpad. Once acquiring α-VR, they were instructed to maintain their feet still to let the investigator record the actual feet angle (α-R). This angle was obtained by considering the intersection of the straight lines that linked the II metatarsal axis to the calcaneal tuberosity of each foot on the tile surface (Figure 4).

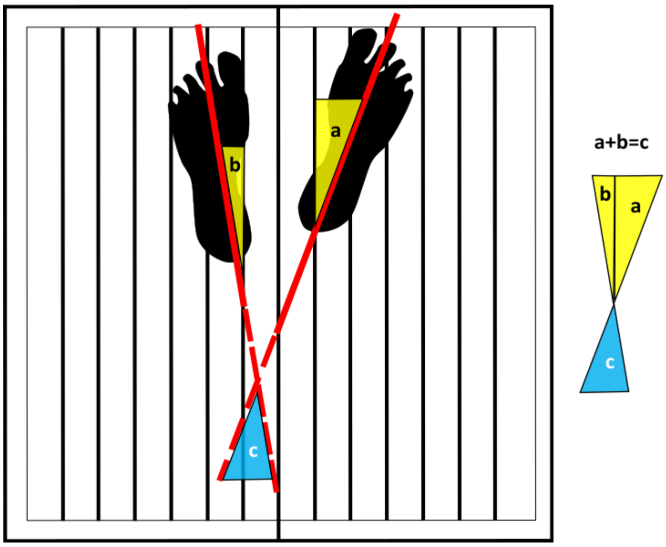

Figure 4 – The figure shows the technique used to calculate the actual feet angle; *angle a* represents the angle between the axis that connects the II metatarsal axis to the calcaneal tuberosity of the right foot and the first perpendicular line on the tile, same for the *angle b* but for the left foot. Their addition provides the *angle c*, which is the angle between the median axis of the two feet.

After acquiring α-VR and α-R measures by pressing the trigger button of the controllers, participants started the fatiguing protocols in the 'Fatiguing Scenario'. It consisted of a 90° squat exercise with an elastic band surrounding both knees aiming at straining the hip's external rotator muscles. During the descent phase of the squat, the hip and knee joints flexed (approximately 90°) while the ankle joint are dorsiflexing. Conversely, the hip and knee joints extended during the ascending phase, and the ankle joint plantarflexed. Once the lowest phase of the squat was reached, the participants had to rotate the hips externally and internally for a set of 15 repetitions. In this virtual scenario, participants were instructed to follow a recorded video inside the VR that showed a physiotherapist that kept on performing the movement set repeatedly (Fatiguing Scenario Figure 3C), which also allowed them to control the speed of the movements. Each set of exercises was followed by a 10s rest period, where the video was stopped and in which participants were asked to rate their perceived exertion on the Borg CR-10 scale (Ferguson, 2014; Lamb et al., 1999). The number of movements in each set was identical for all (15 repetitions), but the total number of sets performed by each participant depended on their fatigue assessment.

Thus, the participant continued with the fatiguing protocol until one of the following stop-conditions was met: they reported a Borg scale rate of 10 or could no longer fully extra-rotate their legs for three consecutive movements. Meanwhile, the investigator controlled the correct execution of the task while motivating the participants to carry on doing the exercise. This last point helped moderate the mental fatigue associated with participants' motivation (Marcora et al. 2009). Once one of the stop conditions was met, the participants could press the trigger button of the controllers, and they performed the stepping and measuring scenarios again. After taking the second measurement, participants removed the HMD and recovered from the fatiguing protocol for 10 minutes. After this recovery time, participants were immersed again into the 'Stepping Scenario' and, consequently, the 'Measuring Scenario' and the third measurement were taken. This last measurement was taken to make a comparison with the baseline. The duration of each experiment depended on the fatiguing protocol and participants' resistance. However, it required a maximum of 45 minutes.

2.3.4 Statistical Methods

A priori analysis was run with G*Power 3.1 to calculate the sample size. Based on 3x2 Mixed ANOVA, a sample of 30 participants per group (VR and R) was determined to accept a power of 95%, a significant level of 0.05, and an effect size of 0.4 (Cohen, 1992). Descriptive statistics were performed, including means and standard deviations. Software statistics SPSS 26.0 (IBM SPSS Statistics, Version 26.0, 2019, Armonk, NY, USA) and Stata 17 were used to run the analysis.

2.3.4.1 Primary Outcome – Feet Angular Differences Between the Real and the Perceived Orientation

The primary outcome of this study was the differences computed from the angles included between the virtual feet (α-VR group) and the real feet (α-R group) before (T1), immediately after (T2) and after 10 min from (T3) the fatiguing protocol. Data followed a normal distribution after inspections of q-q plots. A 3x2 Mixed ANOVA was used to detect statistical interaction at T1, T2 and T3 (times) between α-VR and α-R (groups). There were no outliers, as assessed by boxplots. Testing the homogeneity of variance (Levene's test) was unnecessary since the two groups' sample size was equal. Greenhouse's test of sphericity indicated that the assumption of sphericity was not violated for the two-way interaction, p = 0.89. The magnitude of the results of times and groups in the differences between α-VR and α-R was calculated through Cohen's d and mean differences (MDs) with their 95% interval confidence (95% IC).

2.3.4.2 Secondary Outcome – Time to Confirm the Perceived Orientation at the Virtual Reality Task

The secondary outcome of this study was the time to confirm the perceived orientation at the virtual reality task before (T1), immediately after (T2), and after 10 min (T3) the fatiguing protocol. In this case, data did not follow a normal distribution after inspections of q-q plots as they were positively skewed. Johnson's corrected t-test (stata function 'johnson') for skewed data were used to compute MDs and 95% CI across times.

2.4 Results

2.4.1 Descriptive Analysis

Thirty Italian participants were recruited for this study. Among them, 17 (57%) identified themselves as female and 13 as male (43%). The mean age was 27.5 ± 3.8, and the mean BMI was 21.9 ± 2.4.

2.4.2 Primary Outcome – Feet Angular Differences Between the Real and the Perceived Orientation

Table 1 reports α-VR and α-R and their mean differences. There was no statistical interaction between time (within-subject factor) and groups (between-subject factors) in determining the differences between α-VR and α-R (p = 0.26). Time did not show an effect in the estimation of the differences between α-VR and α-R. Precisely, T1 VS T2 has a 95% CI that ranged from -5.20° to 1.87°, T1 VS T3 from -5.03° to 0.49°, and T2 VS T3 from -4.70° to 3.48°. Conversely, an effect was found between the groups in the estimation of the differences between α-VR and α-R. Precisely, an effect was found between α-VR and α-R at T1 (MD = 20.89, 95% CI [14.67°, 27.10°]), at T2 (16.76, [9.57°, 23.94°]) and T3 (16.43°, [10.00°, 22.68°]) (Table 1).

Table 1. Angles obtained for α-VR and α-R at the three different times

Time	α-VR (N=30) [deg]	α-R (N=30) [deg]	Mean Difference (95% CI) [deg]	Effect Size (d)
T1	0.81 ± 14.35	21.70 ± 9.11	20.89 [14.67, 27.10]	1.74 [0.90, 2.58]
T2	4.54 ± 16.94	21.30 ± 9.96	16.76 [9.57, 23.94]	1.21 [0.43, 1.97]
T3	5.36 ± 14.78	21.70 ± 9.11	16.34 [10.00, 22.68]	1.33 [0.54, 2.12]

Legend: α-VR, angles included between the feet in virtual reality; α-R, angles included between the real orientation of the feet; T1, measure before the fatiguing protocol; T2, measure immediately after the fatiguing protocol; T3, measure after 10 minutes from the fatiguing protocol; CI, confidence interval.

2.4.3 Secondary Outcome – Time to Confirm the Perceived Orientation at the Virtual Reality Task

The mean and the SD of the seconds used to define the feet orientation in VR are reported in Table 2, together with their mean differences and 95% CI. An effect was found between T2 and T1 (MD= 5.10 95% CI [2.82, 7.39]) and T3 and T1 (4.97 [1.64, 8.30]), but not with T3 and T2 (0.13 [-3.40, 3.14]) (Table 2).

Table 2. Seconds to confirm the position at the three different times

Time	Seconds	Time	Seconds	Time	Seconds
T2	20.01 ± 9.57	T3	19.88 ± 10.88	T3	19.88 ± 10.88
T1	14.91± 8.02	T1	14.91± 8.02	T2	20.01 ± 9.57
	Mean Difference (95% CI)		**Mean Difference (95% CI)**		**Mean Difference (95% CI)**
	5.10 [2.82; 7.39]		4.97 [1.64; 8.30]		0.13 [-3.40; 3.14]

Legend: T1, measure before the fatiguing protocol; T2, measure immediately after the fatiguing protocol; T3, measure after 10 minutes from the fatiguing protocol; CI, confidence interval.

2.5 Discussion

The present study investigated the position sense of lower limbs in a perceptually deprived virtual environment. Specifically, it assessed the differences between the participants' perceived and real orientation of feet in space, the time needed to confirm it, and to what extent this difference might be affected by a fatiguing task. Our first hypothesis was the existence of a discrepancy between the actual and the perceived orientation of the lower limbs. Our results seemed to confirm that the perceived position of the feet generally differs from the actual one, as participants tended to perceive their feet in a parallel forward orientation, no matter where the real position was. The participants had an externally oriented real position of the feet, on average. Secondly, we were expecting this parameter, along with the time to process it, to change under acute fatigue conditions, as a result of a reduction in the accuracy of position sense. Nevertheless, neither before nor after the fatiguing protocol, participants' tendency to perceive their feet in a parallel forward orientation changed, but the time needed to confirm the orientation seemed delayed.

With our protocol we have been able to study only the position sense output through feet orientation in the total absence of any visual bodily or spatial cues. Therefore, we cannot know how the lower limbs 'postural schema' or 'body model' behaved but based on this phenomenon we can bring to the forefront several hypotheses that are discussed hereafter. Participants had no visual cues since they were immersed in an IVR scenario devoid of any spatial cues. Assuming that they actually reached the acute fatigue condition, as they reached the Borg scale rate of 10 or could no longer continue the exercise in the fatigue protocol, we were expecting a decrease in proprioception afferent signals (Abdelkader et al., 2020; Larson & Brown, 2018). Nevertheless, there was no change in the final position sense output across the three different times, as all the participants indicated their feet to be in a parallel forward orientation, despite they were generally divergent. According to the predictive processing theory, the brain generates inferences by comparing and integrating personal beliefs, cultural influences, and expected inputs with afferent multi-sensory stimulations. Upon these, it selects the best functional action to answer to an environmental output (Beierholm et al., 2009; Körding et al., 2007; Magnotti et al., 2013; Rohe & Noppeney, 2015; Wozny et al., 2008). Since the brain cannot directly access the position of the limbs, it can only make inferences upon sensory afferent inputs and 'body representation' data (Samad et al., 2015). Hence, the uncertainty becomes higher and higher when data from sensory inputs are fewer, like when there are no visual bodily and spatial cues, and the proprioception information is reduced since the participant cannot move. Both conditions were created in the present study. Von Castell et al. (2021) studied the integration of visual and postural eye-height information in a similar virtual reality context. They affirmed that observers, upon receiving incongruent perceptual information, calibrate visual eye-height information relying on an internalised rather than a flexibly updated posture (von Castell et al., 2021). Accordingly, other authors suggested that the visual experience of the body might play a role in shaping the ‘body model’ (Longo et al., 2010; Kimmel, 2013; Lagopoulos, 2019; Spurgas, 2005). Moreover, it might be possible that environmental and cultural factors influence the ‘body representations’, both ‘postural schema’ and ‘body model’, contributing to modelling a stereotyped picture of ourselves, just like they can influence emotions (Immordino-Yang et al., 2016; Kitayama et al., 2006). Furthermore, repeated exposure to anatomical content through different media sources (e.g., websites, books, etc.) might play a role (e.g., cultivation theory: (Gerbner et al., 2002); social learning theory: (Brown, 2002).

Likely, the brain, under the circumstance of our study, relies on cultural and cognitive components (i.e. personal and cultural beliefs, expectations, previous experiences) that bring to identify the feet' orientation closer to the body's midline (Paillard & Brouchon, 1968; Wann & Ibrahim, 1992; Wozny et al., 2008b). However, the exploration of this hypothesis needs further studies and more precise fatigue protocols, perhaps also investigating different populations with different cultural backgrounds (van Elk et al., 2013; Gerbner et al., 2002; Brown, 2002). Then, a possible reason behind the results of the study is that the participants relied mostly on their ‘body model’ representation with the feet interiorly represented as parallel. It is known that the ‘body model’ representations of the hand, as well as the leg, are distorted (Longo & Haggard, 2010b; Stone et al., 2018). Stone et al. (2018) described a distortion of the ‘body model’ representation for the leg highlighting how participants overestimated their lower limbs' width by about 10%, particularly relative to their ankles, which were perceived as significantly more ‘swollen’ than their knees and thighs (Stone et al., 2018). All these experiments are characterised by perceptual tasks performed without seeing the bones and the joints, as in the present study. Hence, also a possible distorted representation of the tibiotarsal joint can be found.

As far as the muscular fatigue effects on position sense, although many researchers state that fatigue discharges muscle spindles and alters proprioception and therefore position sense (Gear, 2011; Myers et al., 1999; Röijezon et al., 2015b; Vuillerme et al., 2002), our participants' position sense performance did not get worse after the exercise session. It could be that in this study scenario, intended as an IVR environment, the fatigue was not sufficient to affect the integration of ‘postural schema’ and ‘body model’ and so the position sense got unaltered. Another possible explanation could be that our fatiguing task was focussed on extra rotators of the hip and so we could not get a general acute fatigue effect, which in literature is sustained to affect position sense compared to local fatigue (Abd-Elfattah et al., 2015). Therefore, the fatigue protocol proposed needs to be taken cautiously as it might not be the most suitable one. Despite this, we found that all participants during the fatiguing session reached the same results obtained in the baseline but with a more extensive lapse of time to confirm the orientation. The exercise may have induced an overload of local information, caused by fatigue, and a bigger computational effort required by the brain. This may represent an obstacle to motor learning since the cognitive effort, expressed in the time required to construct the position sense, becomes higher (Batson, 2013; Eddy et al., 2015). This temporal shift hypothesis is in line with the results of (Vuillerme et al., 2002), who observed that ankle fatigue increases attentional demand in regulating static postural control in healthy adults (Bisson et al., 2014; Harkins et al., 2005; Hatami Bahmanbegloo et al., 2021; Jo et al., 2022).

This study presents a few limitations that need to be addressed. The current data preclude any conclusions regarding the validity of our assessment methods for α-VR and α-R, thereby limiting the interpretation of our results. For what concern the estimated virtual orientation of the feet, this parameter is linked to the perceptive sensitivity and representation capacity of each participant and for this reason it is intrinsically variable. Future studies in a larger population could use the methodology proposed in this work to compare the estimated virtual orientation against a set of predefined real angles of the feet, extracting normative values for the error related to the position sense of the lower limbs. As for the assessment of the real orientation of the feet, we could not explore the reliability of this specific methodology, since we did not have a proper gold standard for data comparison. Nonetheless, we adopted a series of strategies to reduce the measurement error and standardise the procedure as much as possible: (1) we used specific bone landmarks to clearly identify the reference vector for the measurement of the angle of the feet; (2) the assessment and the landmarks identification were always performed by the same operator; (3) we used a fine point ink pen (0.7 mm) to draw the lines on the scaled tile. Considering the sensitivity of the goniometer used during our experimental sessions, and the width of the drawn lines we can estimate a standard deviation of the measurements of about ± 2 degrees. This error can be reduced with the implementation of more advanced (and expensive) solutions integrating VR and optoelectronic motion capture systems. Another limitation of our study is that we focussed our analysis solely on the position sense output derived from the orientation of the feet, without exploring broader concepts related to the "body representations" such as the "postural schema," which investigates the angular configuration of all the lower limbs' joints, and the "body model". Future research should also focus on these representations adopting, possibly, a higher quality design (e.g., randomised controlled trial to test fatigue effects). Moreover, the fatigue protocol adopted presents some criticalities, as it has not been validated and the exercise proposed might have tired only the hip extra rotator muscles without inducing a general acute fatigue condition. Hence, this may have affected the fatigue effects, limiting the interpretability and the magnitude of our results. However, the strength of this study is the use of a new measurement system (i.e., IVR) to assess position sense, in absence of any visual-spatial cues, not affected by the experimenter.

2.6 Conclusion

People without diseases in the absence of a direct vision of their body and environmental cues, tend to sense their feet as forwarding parallel even though they are divergent. Moreover, muscle fatigue does not affect the task, but it delays the time to accomplish it. IVR represents an interesting and easy-to-use tool to perform tasks intended to study position sense due to its ability to modify the impact of visual bodily and spatial cues. Future studies should test the hypothesis of this work and better investigate the position sense and the effect of fatigue, adopting physiological measurements like electromyography. Moreover, it would be important to see any possible changes in our results on clinical conditions where the elaboration of body representations is hindered by damage of the central nervous system and high fatigability (e.g., multiple sclerosis, myasthenia gravis, fibromyalgia, stroke).

2.7 Declarations

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The authors have no relevant financial or non-financial interests to disclose.

Conflicts of interest/Competing interests

The authors report no conflicts of interest. All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

Ethical approval

Ethical approval was obtained from the Ethics Committee for University Research (CERA: Comitato Etico per la Ricerca di Ateneo), University of Genova (approval date: 14/06/2020; CERA2020.12).

Consent to participate

The participants signed informed consent before participation.

Consent for publication

The participants signed informed consent for publication.

Availability of data and materials

Data are available upon reasonable request to the corresponding author.

Authors' Contributions

All authors made substantial contributions to the conception and design, data acquisition, or analysis and interpretation of data. All authors participated in drafting the article or revising it critically for important intellectual content. All authors gave final approval of the version to be published. All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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3. The Effect of Context on Eye-Height Estimation in Immersive Virtual Reality: a Cross-Sectional Study

3.1 Abstract

Eye-height spatial perception provides a reference to scale the surrounding environment. It is the result of the integration of visual and postural information. When these stimuli are discordant, the perceived spatial parameters are distorted. Previous studies in immersive virtual reality (IVR) showed that spatial perception is influenced by the visual context of the environment. Hence, this study explored how manipulating the context in IVR affects individuals' eye-height estimation. Two groups of twenty participants each were immersed in two different IVR environments, represented by a closed room (Wall - W) and an open field (No Wall - NW). Under these two different conditions, participants had to adjust their virtual perspective, estimating their eye height. We calculated the perceived visual offset as the difference between virtual and real eye height, to assess whether the scenarios and the presence of virtual shoes (Feet, No Feet) influenced participants' estimates at three initial offsets (+100 cm, +0 cm, -100 cm). We found a mean difference between the visual offsets registered in those trials that started with 100 cm and 0 cm offsets (17.24 cm [8.78; 25.69]) and between 100 cm and -100 cm offsets (22.35 cm [15.65; 29.05]). Furthermore, a noticeable mean difference was found between the visual offsets recorded in group W, depending on the presence or absence of the virtual shoes (Feet VS No Feet: -6.12 [-10.29, -1.95]). These findings describe that different contexts influenced eye-height perception.

3.2 Introduction

3.2.1 Background

One's self-perception of 'eye height' is fundamental for interacting with the world, as it provides a reliable reference to scale the surrounding environment (Lee, 1980; Leyrer et al., 2015b; Ooi et al., 2001; Warren, 2019; Whitehead, 1981; Wraga, 1999). The eye height can be obtained in real-time from (i) visual (i.e., accommodation, convergence, binocular disparity and motion parallax) and (ii) postural sources, based on proprioceptive and vestibular information (Leyrer et al., 2015b; Mittelstaedt, 1998). In the real world these stimuli are often tightly coupled. However, the same cannot be said when it comes to a virtual environment, where visual and postural informed heights are often contradictory (Dixon et al., 2000; Leyrer et al., 2011, 2015a, 2015a; Messing & Durgin, 2005; von Castell et al., 2021).

When visual and postural eye height cues are consistent with each other, the perceived size of surrounding objects and egocentric distances remains constant. Conversely, when this perceptual information is discordant, the perceived spatial parameters are distorted (von Castell et al., 2021). Moreover, in virtual environments, other visual information might be involved in the evaluation of spatial parameters. Several studies demonstrated that visual cues are related to the accuracy of spatial perception (Kunnapas, 1968; Loyola, 2018), depending on the presence of multifactorial aspects such as lightening (Tai, 2012), texture (Sinai et al., 1998;Thomas et al., 2002), perspective (Surdick et al., 1997), and architectural or environmental spatial cues (Asjad et al., 2018; Loyola, 2018; Luria et al., 1967; von Castell et al., 2014). Similarly, the presence of visual body-related representations in virtual environments (i.e., the presence of virtual limbs) affects the estimation of affordances, and object sizes by providing a direct reference to scale the world (Asjad et al., 2018; Jun et al., 2015; Leyrer et al., 2011; Linkenauger et al., 2013; Mohler et al., 2010).

The key feature of virtual reality is the possibility to create realistic simulations in which users behave as if they are really into an altered experience (Gonzalez-Franco & Lanier, 2017; Slater, 2009) (Gonzalez-Franco & Lanier, 2017; Slater, 2009). Therefore, it is essential to evaluate the perceptual limits within which it is possible to manipulate users' perception without hindering the plausibility of their actions. In this regard, only a limited number of studies have explored the perceptual accuracy of estimating one's eye height in virtual environments.

3.2.2 Objectives

Relying on the above premises, we hypothesised that modifying the characteristics of the virtual scenario (e.g., presence of visual-spatial references and body representations) would reflect into variations in the perceived eye height. Hence, this study aims to explore systematically how manipulating the context in virtual environments affects individuals' eye height estimation.

3.3 Methods

3.3.1 Research design and ethical approval

We conducted a cross-sectional study with the aim of exploring how manipulating a different context in virtual reality affects individuals' eye height estimation. This study was conducted at the REHELab laboratory of the Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Sciences (DINOGMI), University of Genova, Campus of Savona (Italy). It was conducted according to the criteria set by the declaration of Helsinki and received ethics approval by the Ethics Committee for University Research (ref. CERA2020.23, CERA: Comitato Etico per la Ricerca di Ateneo, University of Genova, Genova, Italy) and reported following the STROBE guidelines (Cuschieri, 2019).

3.3.1.1 Participants

To be enrolled in the study, participants had to: i) sign a detailed informed consent form, i) be between 18 and 65 years old, ii) have no neurological conditions and/or movement disabilities and have iii) normal or corrected-to-normal visual acuity, as eyeglasses could be comfortably worn inside the virtual reality system. Participants' sociodemographic characteristics, including age, height, weight, and gender, were collected upon their arrival at the laboratory.

3.3.1.2 Virtual reality system

For this study we adopted the HTC Vive Pro Virtual Reality System (Sansone et al., 2021). The experiments were set in a 7 × 5 m room, with neither reflective surfaces nor natural lighting exposure. Two Vive Base stations 1.0 lighthouses were used to track a full-body motion over an area of 2.4 x 2.4 m. The two lighthouses were fixed to the ceiling at the height of 3 m with a forward inclination of (45±1)° positioned along the diagonal direction of the tracking facing towards its centre. The system configuration also included a head-mounted display (HMD), two Vive controllers, and two Vive trackers 2.0 (2018). The HMD of the Vive Pro is characterised by two AMOLED lenses, a resolution of 1440 × 1600 pixels per eye, a refresh rate of 90 Hz, and a 110° field of view. The position and orientation of the trackable elements in the space (i.e., HMD, the controllers and the trackers) are registered through a combination of inertial and outside-in tracking (Borges et al., 2018). The experimental setup (Figure 1) involved the participant wearing the HMD while holding the controllers with both hands. The position and orientation of the feet were registered in real-time with the two trackers placed on the forefoot.

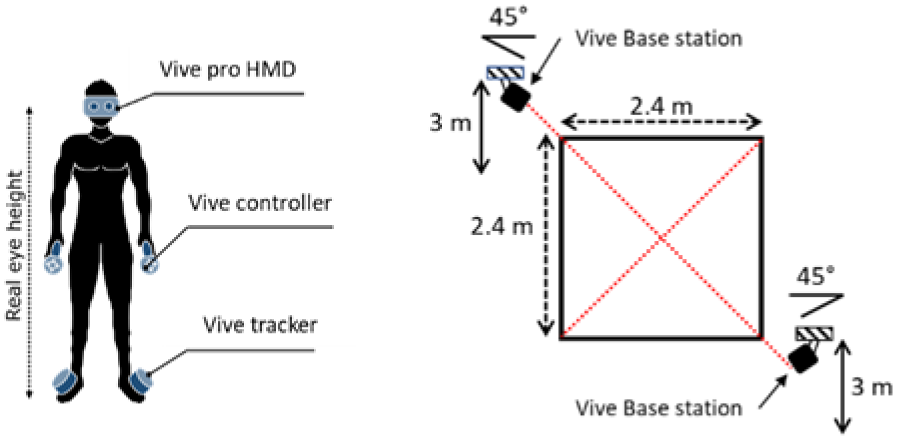

Figure 1 Experimental setup

3.3.2 Experimental procedure

Participants were assigned to one of two possible groups using a sealed envelope randomisation system managed by a third person not involved in the study. The first group (wall scenario “W”; Figure 2A) was immersed in closed virtual scenario, a 4x4x4m room delimited by a white ceiling, four grey walls, and an asphalt-textured floor, with well-defined spatial cues (i.e., limits of the room). The scenario was illuminated by an invisible point light source positioned at its center. The edges between the different surfaces were the only definite spatial references, as the surfaces were overlaid only with a fine-grained texture. We decided to use this texture as it did not give any hint about the virtual eye height as the case of bricks or piles on the walls. The second group was immersed in a virtual open space (no wall scenario (NW); Figure 2B) characterised by a grey plane surrounded by distant natural elements (i.e., mountains, hills, woods) which prevented the participant from seeing the horizon and having any definite spatial references. This scenario was illuminated by the preset sunlight. Moreover, a virtual representation of the subject feet wearing shoes (Fig. 2C) was implemented in both groups in the scenarios and it was displayed as reported below. The shoes were scaled according to the real participants’ shoe size. The natural environments were created using the Unreal Engine 4.25 pre-loaded assets and the “temperate

Vegetation: Spruce Forest" (Project Nature, 2019) package from the Epic Games content shop. The 3D model of the shoes was downloaded from Turbosquid under editorial license (TurboSquid, 2012).

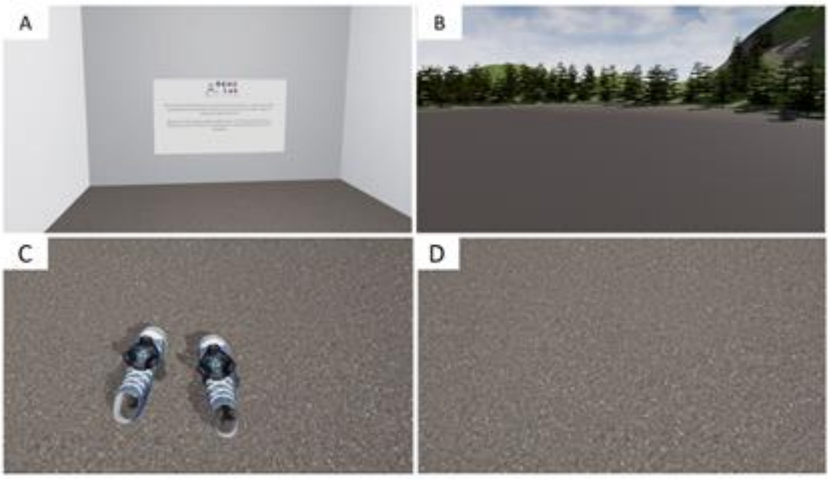

Fig. 2 Characteristics of the virtual environments: A) Enclosed space B) Open space C) Virtual Shoes Representations D) No Virtual Shoes representations

Upon the arrival of each participant, the randomisation was disclosed to the experimenter who set up the virtual simulation for the study. Participants from both groups were asked to wear the virtual reality apparatus and to position themselves upright in the centre of the playing area with parallel feet, spaced at a width equal to that of the shoulders. The Interpupillary distance (IPD) of the HMD lenses were adapted to the participant's facial conformation. The experiment started with an adaptation session, where the main functionalities, and the actions for interacting inside the virtual world were explained. Participants were then instructed to the main experimental task of giving an estimate of their real eye height (measured as the height of the HMD) by adjusting the perceived virtual eye height using the triggers behind the VIVE controllers (every click represented a variation of ±1 cm). Specifically, they were asked to maintain the upright stance and use any visual cue at their disposal from the virtual environment or from the presence of body representation (i.e., virtual models of shoes and controllers). Afterwards, participants performed a perceptual calibration to construct a perspective reference of their eye heights. They observed a small 7x10x14 cm black box located at 120 cm on the floor in front of them for one minute, both in the real environment (by momentarily removing the HMD) and in the simulated one, as shown in Figure 3.

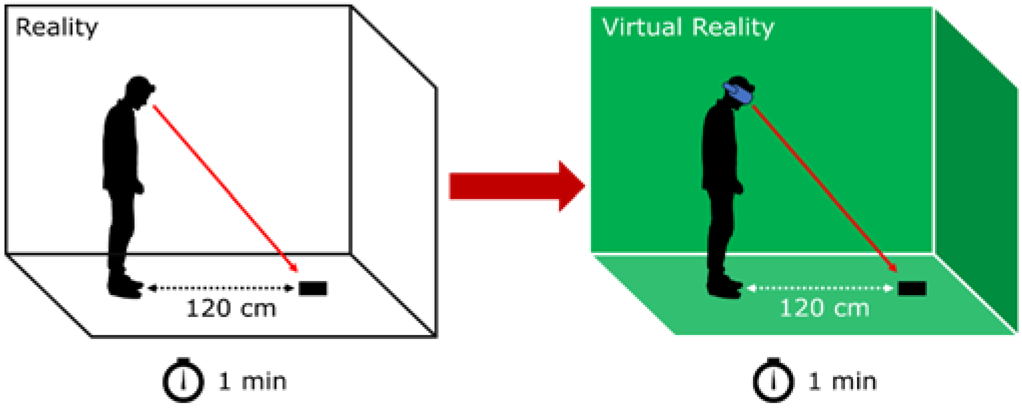

Fig. 3 Calibration process

Subsequently, the main task was performed across a series of six experimental trials characterised by different initial conditions: three initial offsets from the actual eye height (+100cm, +0cm, -100cm); and the presence or not of the abovementioned virtual shoes (Feet, No Feet) for the virtual body representation. Therefore, by matching the different offset (+100, +0, -100 cm) and the presence or not of the shoes (Feet, No Feet), six different trials per group were carried out. The order of the trials was random and no information regarding the predefined initial offsets was disclosed during the initial explanation of the study. To consider one of the possible learning effects between repeated measurements, at the beginning of every trial, the participants' virtual perspective was rotated randomly at 0°, 90°, 180°, and 270° resulting in pointing towards one of the four different grey-scaled walls in the enclosed environment, or towards a different landscape in the open environment. The overall protocol is schematically reported in Figure 4.

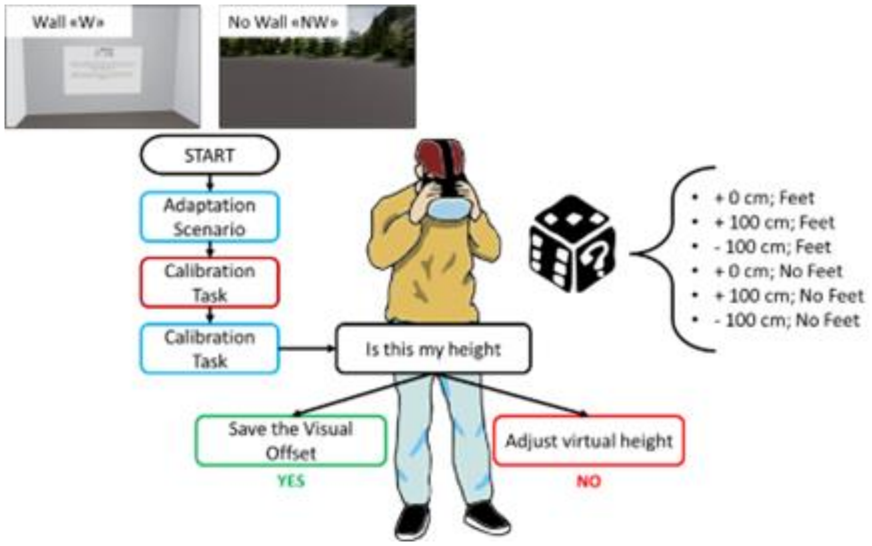

Fig 4 Experimental protocol

3.3.3 Primary Outcome

The primary outcome was the visual offset value registered during the various experiments and calculated as the difference between virtual and real eye height. A positive and a negative visual offset value represented respectively an underestimation, and an overestimation of the virtual eye height, respectively (Figure 5).

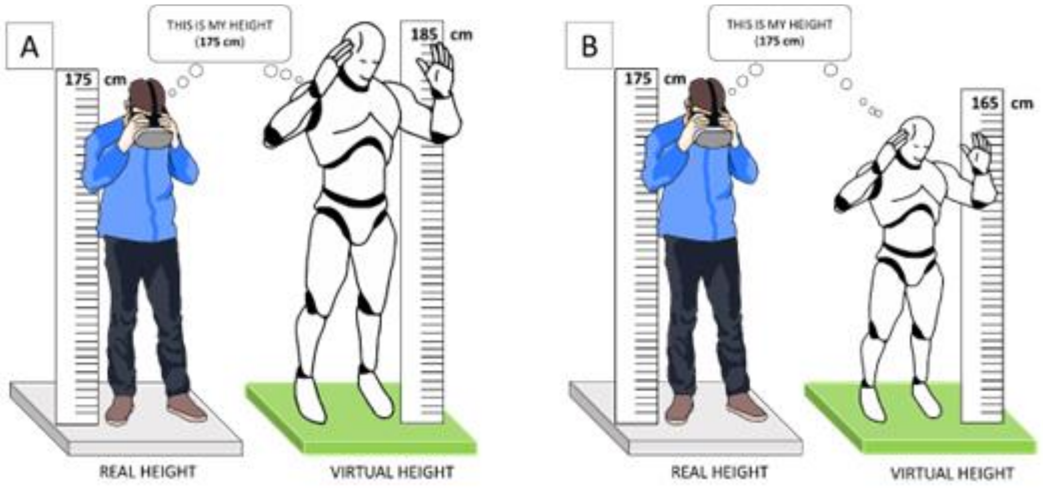

Fig. 5 A) Underestimation of the observer virtual height with a positive visual offset B) Overestimation of the observer virtual height with a negative visual offset

The data acquisition software was implemented through blueprint visual scripting. The visual offset variable was initialised at the beginning of every trial and updated at every click of the trigger pressed by the participant inside the main Level Blueprint. Consequently, this value was added as local offset between the "SceneRoot" and the "VRorigin" components of the MotionControllerPawn blueprint included in the VR sample project of Unreal Engine 4.25. The same offset was added also between the "SceneRoot" component and the mesh of the Virtual Shoes. In this way the virtual eye height was the result of the original eye height of the observer with the addition of the visual offset value, and the virtual shoes were always displayed at the floor level. A screenshot of the visual script can be found in the Supplementary Data and the full Unreal Engine Project of the virtual application is available from the authors on reasonable request.

3.3.4 Sample size and statistical analysis

A priori analysis was run with G*Power (v3.1.9.7) to calculate the sample size. Based on an 2 (between factors: W, NW) x 2 (within factors: feet, no feet) x 3 (within factors: three different onsets) mixed-method ANOVA, a sample of *n* = 20 participants per group was determined to accept a power of 99%, a significant level of 0.01, and an effect size of 0.3 (Cohen, 1992) extrapolated from the results obtained by Asjad (Asjad et al., 2018). The calculations accounted for a 15% dropout in the sample.

The statistical analysis was performed using MATLAB (*MATLAB*, 2022), SPSS (*IBM SPSS Statistics*, 2022) and JAMOVI statistics software (*jamovi*, 2021). Descriptive statistics of the population socio-demographic data and the primary outcome were reported means and standard deviations. A descriptive statistics were computed using mean and standard deviation (SD) for continuous variables (i.e., age, height, and weight) and absolute and percentages frequencies for categorical ones (gender they identified with). The normality of the data was visually investigated through the inspection of the Q-Q plots (Supplementary Data). As data followed a normal distribution, a 2x2x3 Mixed Method ANOVA was used to detect possible significant variations between the presence of spatial references (between factor: groups W vs. NW) and the presence of virtual body representations (first within factor: Feet vs. No Feet) across the three possible initial offsets (second within factor: 0 cm vs. +100 cm vs. -100 cm). Levene's test identified no violations of the assumption of homogeneity of variance. Mauchly's test of sphericity was unnecessary for the first within factor (Feet or No Feet) since the sphericity is always satisfied with only two levels and indicated no violation of the assumption for the second within factor (initial offset, p=0.278). The Huynh-Feldt correction was considered for the two-way interaction between the two within factors since it violated the sphericity assumption. Post-hoc analysis with a t-test was conducted with a Bonferroni correction, with a p-value ≤ 0.025. The results are presented as estimated marginal means with their 95% confidence intervals, and the magnitude of their effects was reported using mean difference estimates with their 95% confidence intervals and Cohen’s d.

3.4 Results

3.4.1 Participants

A total of 44 participants were considered eligible and participated in the study. Results from four participants were excluded from the analysis due to technical problems during the data acquisition process. Demographic data from the remaining 40 participants grouped by the different allocation groups are presented in Table 1. The complete dataset is reported in the Supplementary Data.

Population Characteristics	**Wall (W)** **n=20**	**No Wall (NW)** **n=20**
N	**20**	**20**
Age (y) (mean(SD))	**24 (4)**	**24 (3)**
Male / Female (N(%))	**7 (35%) /13 (65%)**	**16 (80%) /4 (20%)**
Height [cm] (mean(SD))	**169 (10)**	**179 (11)**
Weight [Kg] (mean(SD))	**62 (10)**	**72 (8)**

Tab. 1 Descriptive characteristics of the population grouped by intervention group. (SD)

3.4.2 Primary outcome - Visual offset between virtual and real eye height

Overall, we found a mean visual offset of 16.00 cm [12.20, 19.70]. The marginal means for visual offset measured across the two groups, W and NW, were respectively 11.10 cm [1.34, 20.90] and

20.80 cm [11.03, 30.60]. The mean difference between the two groups was 9.69 cm [-4.12, 23.50] (Table 2).

Spatial References	Mean [cm]	95% Confidence [cm]	Mean Difference [cm]	95% Confidence [cm]	d
NW	20.80	[11.03; 30.60]	9.69	[-4.12; 23.50]	0.46
W	11.10	[1.34; 20.90]			

Tab. 2 Estimated marginal means and mean difference– Spatial References

The estimated marginal means of the visual offset related to the representation of the virtual shoes were 14.50 cm [7.37, 21.70] and 17.40 cm [10.41, 24.30] depending on whether or not the virtual shoes were displayed in the virtual environment. The mean difference between the two conditions was estimated in 2.84 cm [-0.11; 5.79] (Table 3). The visual offset varied across the three initial offsets (Figure 6), with a value of 11.91 cm [6.00, 17.80], 29.15 cm [20.25, 38.00], 6.80 cm [-2.59, 16.20] starting respectively at 0 cm, 100 cm, and -100 cm (Table 4). In this case, the mean differences were 17.24 cm [8.78, 25.69] between the visual offsets registered with a +100 cm and 0 cm initial offsets, 22.35 cm [15.65, 29.05] between those registered with a +100 cm and -100 cm, and 5.11 cm [-2.69; 12.92] between those registered with a -100 cm and 0 cm initial offsets.

Body Representations	Mean [cm]	95% Confidence [cm]	Mean Difference [cm]	95% Confidence [cm]	d
Feet	14.50	[7.37; 21.70]	2.84 cm	[-0.11; 5.79]	0.63
No Feet	17.40	[10.41; 24.30]			

Tab. 3 Estimated marginal means and mean difference – Body Representations

Initial Offset	Mean [cm]	95% Confidence [cm]	Initial Offsets [cm]	Mean difference [cm]	95% Confidence [cm]	d
+100	11.91	[6.00; 17.80]	0	17.24	[8.78; 25.69]	1.42
0	29.15	[20.25; 38.00]	-100	5.11	[-2.69; 12.92]	
-100	6.80	[-2.59; 16.20]	-100	22.35	[15.65; 29.05]	

Tab. 4 Estimated marginal means and mean differences – Initial Offsets

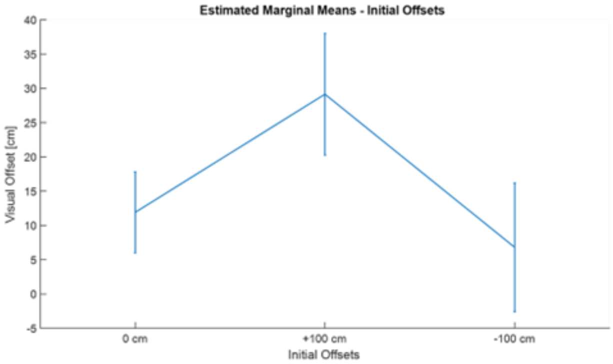

Fig. 6 Estimated marginal means: Initial Offsets

The main results obtained by the two-way interaction between the different statistical factors are synthetically reported in Table 5 and Figure 7. The statistical analysis highlighted a mean difference of -6.12 cm [-10.29, -1.95] between the visual offsets registered in the wall scenario, with and without the presence of the virtual shoes.

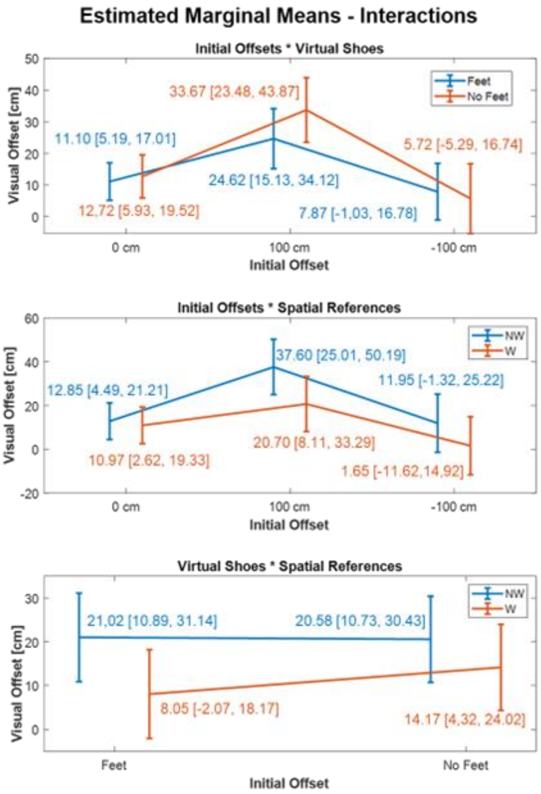

Fig. 7 Estimated marginal means – Interactions

Factor	**Comparison**	**Mean difference [cm]**	**95% Confidence [cm]**	**d**
Initial Offsets*Virtual Shoes				
Feet,+0 cm	**Feet,+100 cm**	**-13.53**	**[-21.403; -5.647]**	**0.49**
Feet,+100 cm	**Feet, -100 cm**	**16.75**	**[9.907 23.593]**	
No Feet,+0 cm	**No Feet, +100 cm**	**-20.95**	**[-32.177; -9.723]**	
No Feet,+100 cm	**No Feet, -100 cm**	**27.95**	**[16.487; 39.413]**	
Initial Offsets*Spatial References				

NW +0 cm	**NW +100 cm**	**-24.75**	**[-36.70, -12.795**	**0.45**
NW +100 xm	**NW -100 cm**	**25.65**	**[16.17. 35.13]**	
W +100 cm	**W -100 cm**	**19.05**	**[9.57, 28.53]**	
Virtual Shoes*Spatial References				
W, Feet	**W, No Feet**	**-6.12**	**[-10.29, -1.95]**	**0.73**

Tab. 5 Mean differences of the two-way interactions between the statistical factors

3.5 Discussion

3.5.1 Key findings and interpretation

In this study, we evaluated if individuals' eye height estimation varied by changing the surrounding virtual reality context. More specifically, we assessed whether the presence of spatial visual references (Wall and No wall) and virtual representations of shoes (Feet, No Feet) influenced the perceptual precision of the participants at different initial visual offsets (+100 cm, +0 cm, -100 cm). Overall, our results showed a tendency to underestimate the virtual eye height, as indicated by the positive values of the registered visual offset, no matter the context. Distances underestimation in virtual environments has been extensively documented. Users exploring virtual environments tend to underestimate distances among objects and spatial displacements (Foreman et al., 2004; Hayashibe, 2002; Witmer & Kline, 1998; Witmer & Sadowski, 1998). For instance, Witmer and Sadowski (Witmer & Sadowski, 1998) reported that participants asked to blindly walk towards a target after viewing it in real and in a virtual simulation, would respectively underestimate the walked distance by 8% to 15%, respectively.

Considering the presence of definite spatial references in the virtual environment, it has been suggested that the availability of such visual cues improves the level of accuracy in the estimates of egocentric dimensions (Asjad et al., 2018; Loyola, 2018; Zhang et al., 2021). A study by Zhang and colleagues (Zhang et al., 2021), highlighted that the surrounding context (virtual indoor or virtual outdoor) affects the outcome of a midpoint estimation task. In the aforementioned work, the participants were asked to evaluate the intermediate distance between them, and a target positioned on the ground at a variable distance from 4 to 7.8 m. The authors found larger midpoint underestimations in the virtual outdoor environment, compared with those in the virtual indoor environment. In our study we did not find a strong main effect related to the presence of spatial information, however, our results were partially in agreement with the work of Zhang, as pointed out by the two-way interaction between the presence of the virtual shoes and the presence of definite spatial references. More specifically we found that, when the virtual shoes were displayed, individuals assigned to the W group were more precise in the estimation task compared to those drafted in the NW group. Considering the similarities and differences between the two studies, it is possible to argue that the effect of the spatial context was clear only when an external reference was presented, either as a target on the floor (Zhang et al., 2021) or, in our case, as a pair of shoes. These results are in agreement with the concept of "embodied perception", which emphasises the importance of taking into account both visual and body-based information when studying distance perception (Josa et al., 2019). That is, an external reference frame might influence distance estimation in the surrounding space.

Following the same principles, previous studies pointed out that the availability of body-based information can potentially affect spatial perception in virtual environments (Asjad et al., 2018; Jun et al., 2015; Leyrer et al., 2011; Linkenauger et al., 2013; Mohler et al., 2010). Body-related information can potentially provide two types of perceptive cues. First, any information related to the body position might be used to establish a reference frame, especially in those situations where the perceptive stimuli are ambiguous. Moreover, body awareness provides a metric to scale the surrounding space. The body visualisation provides reliable spatial cues through a familiar size comparison or visual-motor feedback obtained during the movement. This theoretical background was extensively explored by Mohler and colleagues (Mohler et al., 2010), who have found that seeing a fully articulated and traced virtual representation of one's body affects the estimation of absolute egocentric distances in surrounding locations up to 6 m away.

Also in this case, based on the statistical interaction explained above, our results are partially in line with the literature, but still fail to detect a strong main effect of the presence of virtual shoes on the estimation of the participants' eye height. A possible explanation to the fact that these factors are highlighted by their interaction and not in their singularity, can be found in the impossibility of controlling the strategy by which each individual estimated their eye height. Having given no indication on how to perform the experiment, participants could choose any reference available to complete the task. That is, each person may have paid more attention to the space under their feet (i.e., presence of virtual shoes), or they may have looked for visual cues in the surrounding area (i.e., presence of spatial references), globally reducing the contributions of each individual factor.

Interestingly, our analysis revealed a difference in participants' eye height estimation between the different initial visual offset values set for each experimental trial. Participants were less accurate in their estimation when the experimental trial started at +100 cm, suggesting a greater capacity to handle the perception of own height when the floor was presented widely inside the one's body borders. Contextually, there is evidences that the brain creates internal representations of the visual space, based on previous events, actions and outcomes experienced in the surrounding environment (Clark, 2001; Coello & Cartaud, 2021). According to this, the perceptual visual space has been categorised across the years, in different ways as a function of the distance from the observer (Daum & Hecht, 2009). For instance, Cutting and Vishton (Cutting & Vishton, 1995) subdivided the visual space into three concentric regions: the personal space (limited to 2 m), the action space (up to a radius of 30 m), and the vista space (beyond about 30 m). In line with previous works that reported how distance perception decreases with the distance from the observer (Daum & Hecht, 2009; Naceri et al., 2011), our results suggest a greater perceptual precision when the initial visual offset was set at 0 cm and –100 cm. This evidence might underline a deeper neurophysiological process related to the perceptual integration and the activity of the so-called multimodal neurons (Murata et al., 2016). This type of neurons, found in the ventral intraparietal area, the premotor cortex and the putamen, has been shown to be sensitive both to tactile stimulation of different body segments and to visual stimuli located in their vicinity. According to this, it is possible to speculate that setting the initial visual offset inside the personal space might have contributed to a better sensory integration through the activity of these multimodal neurons responding to the view of a virtual floor inside what is commonly perceived as the own body volume. However this assertion, goes beyond the scope of the present work and should be confirmed by future neurophysiological and imaging studies.

3.5.2 Limitations

Our results should be considered in the light of some limitations which should be addressed in future research. As previously stated, we were not able to control the perceptual strategy adopted by the participants to recognise their own eye height, as they were left free to use any visual cue at their disposal during the experimental trials. We decided to opt for this choice not to limit the virtual experience by making the simulation as realistic as possible. Therefore, our results must be considered as the result of a global effect that mediates all the different factors that may have influenced the visual perception of the virtual scenario. Later studies could start from the data presented here and differentiate between the contribution of spatial and body visual cues on the estimation of eye height in virtual reality. In this regard, an interesting possibility is offered by the modern eye tracking feature implemented in the most recent immersive VR systems (i.e., VIVE Pro EYE, Oculus Quest 2). This technology would allow to identify the attentive focus of the participants during the observation of the virtual environment and, consequently, to understand their individual perceptual strategies. Another important limitation is related to the design of the study. To maintain a feasible dimensionality of the sample, we decided to randomise our population into two groups according to the statistical factors related to the spatial references in the virtual scenario. Hence, our results regarding the presence of virtual shoes, the different values of the initial visual offsets, and how these aspects affect the estimation of eye height might not be generalisable. For this reason, future studies should consider exploring these elements as separate between factors with a proper randomisation method. Finally, despite considering a perceptual calibration procedure, we acknowledge the lack of an objective measure to estimate an individual baseline error for each participant. This measure would have allowed an unbiased evaluation of how the estimate of eye height in virtual reality changes in relation to the context of the virtual environment.

3.5.3 Conclusions

Taken together, our work offers a systematic analysis of eye height estimation can be easily modified by exploiting the surrounding context in virtual reality. The present findings join a branch of research evidence that has been expanding in recent years and that describes spatial perception as the result of a complex multifactorial process that considers visual and bodily information. Our results should be used in future research to create more realistic and engaging experiences in application fields where the use of virtual reality technology is expanding, such as rehabilitation therapy.

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4. Positive Expectations led to Motor Improvement: an Immersive Virtual Reality Pilot Study

4.1 Abstract

This pilot study tested the feasibility of an experimental protocol that evaluated the effect of different positive expectations (verbal and visual-haptic) on anterior trunk flexion. Thirty-six participants were assigned to 3 groups (G0, G+ and G++) that received a sham manoeuvre while immersed in Immersive Virtual Reality (IVR). In G0, the manouvre was paired with by neutral verbal statement. In G+ and G++ the manouvre was paired with a positive verbal statement, but only G++ received a visual-haptic illusion. The illusion consisted of lifting a movable tile placed in front of the participants, using its height to raise the floor level in virtual reality. In this way, participants experienced the perception of touching the floor, through the tactile and the virtual visual afference. The distance between fingertips and the floor was measured before, immediately after, and after 5 minutes from the different manouvres. A major difference in anterior trunk flexion was found for G++ compared to the other groups, although it was only significant compared to G0. This result highlighted the feasibility of the present study for future research on people with mobility limitations (e.g., low back pain or kinesiophobia) and the potential role of a visual-haptic illusion in modifying the performance of trunk flexion.

4.2 Introduction

Human motion is the result of the interaction between the musculoskeletal apparatus and the central and peripheral nervous systems (Roy et al., 2017). They all cooperate via a complex integration of sensory-motor, emotional and cognitive inputs as a result of top-down and bottom-up processes (Taylor et al., 2010) to induce a flexible adaptation of human motor responses to the everyday environment (Pearson, 2000; Vingerhoets & Harrington, 2017).

The context into which the movement is set is characterised by internal (e.g., psycho-biological aspects like personality traits and genetics) and external factors (e.g., physical and social aspects of the environment). These factors together with previous individual experiences, social interactions, beliefs, and internal states play a key role in influencing physiological and behavioural responses (e.g., motor performance) as a result of an internal inferential process (Benedetti, 2013; Carlino et al., 2014; Testa & Rossettini, 2016; Wager & Atlas, 2015) that recently has been interpreted as predictive processing (de Bruin & Michael, 2017; Gadsby & Hohwy, 2021). This theoretical framework aimed at minimising the predictive error on the incoming external and internal stimuli (de Bruin & Michael, 2017; Gadsby & Hohwy, 2021) by continuing to compare the expected inputs (i.e., expectations) with the afferent multi-sensory stimulations (Friston, 2005) to interact with the environment with the best possible motor performance. In order to reduce the above-mentioned prediction error two opposite models were conceptualised: (i) the "Active Inference Model" and (ii) the "Perceptual Inference Model" (Friston, 2009; Friston et al., 2012; Seth & Friston, 2016). The (i) "Active Inference Model" gives greater importance to the so-called "Priors" (i.e., the previous consolidated view of the situation) compared them to the ongoing sensory inputs. In this condition, the incoming information is actively modulated to match the priors in the most accurate way. Conversely, (ii) the "Perceptual Inference Model" gives more weight to the afferent multi-sensory information than to the priors. The latter are modulated to match the afferent information and generating "Posteriors" (i.e., an updated view of the situation) used to interpret future events. Moreover, it has been adopted to broaden the understanding of pain and the placebo effect (Ongaro & Kaptchuk, 2019).

Immersive Virtual Reality (IVR) represents a promising approach that can tap into the aforementioned models by modifying the context in a way that is not predictable by the person immersed in this virtual environment, inducing modifications in their afferent information and expectations by modifying the temporal and spatial references as well as the shape of body segments (Nishigami et al., 2019). In the last few years, these advantages of the IVR have been explored in pain treatment and placebo effect as an intriguing solution (Alemanno et al., 2019). However, little is known about its possibility to enhance individuals' motor performance as a response to the new context into which they are immersed.

In line with what mentioned above, this pilot study aims to explore how changes in a priori information regarding the expectation of one's movement (priors) can affect motor strategy and motor outcomes (posteriors). In particular, this study aims at exploring if a sham treatment, associated with a verbal manipulation and a visual-haptic illusion created in IVR, coul change the amount of forward flexion in a sample of healthy people. We expect that a positive modification in participant's expectations of their capabilities of movement will induce a motor strategy to increase flexibility when bending forwards.

4.3 Methods

4.3.1 Participants

Participants were recruited from a convenience sample of healthy people. To be eligible they had to meet the following inclusion criteria: (a) no previous neurological, vestibular, rheumatic and musculoskeletal diseases. Moreover, participants should not have reported low back pain in the previous six months with repercussions on daily activities, work (e.g., absenteeism), or that forced them to start any medical or physiotherapy care. (b) Age between 18 and 55 years old, and (c) the ability to reach at least a distance of 25 cm from the floor, measured by the Fingertip-to-Floor Test (Perret et al., 2001). This last inclusion criterion was necessary as for the maximum height reachable from the movable panel as explained in paragraph – *Immersive Virtual Reality (IVR) system and virtual scenario* and in figure 3. Informed consent was presented in a written form and obtained from all participants before the experiment.

4.3.2 Interventions

4.3.2.1 Experimental Protocol

To cover the real purpose of this study, consisting of the administering of positive expectations induced by different verbal and perceptive stimuli aiming to improve trunk flexion through an IVR manipulation, a fictitious clarification of the study was provided to all participants once they arrived at the laboratory:

"The goal of this study is to evaluate whether Virtual Reality can be used as a tool to measure in real-time, changes in the mobility of the spinal column. We will take the measurements both with a manual instrument and with virtual reality, to see how much difference there is between the accuracy of these two measurements."

The real aim of the study was disclosed to each participant only at the end of the experimental session.

All participants performed a series of anterior trunk flexions standardised with the protocol as described below. Moreover, the entire experimental protocol was performed on a rigid step of 7 cm. This solution allows for increasing the distance from the floor so that also the participants who easily reached the floor without the step could be included in the study. Starting from a standing stance position with the feet together, the participants had to bend forward, maintaining the elbows and the knees extended, with the palms of the hands together, reaching a target represented by a black "X" mark located to a distance of 20 cm from the tip of the toes, positioned along a line painted on the floor. Each anterior trunk flexion was accompanied by the experimenter's indications about its execution in both modality and timing ("go down slowly - bend as much as you can - stay – up").

Following these directives, the participants executed 30 warming-up flexions before the experiment start. The first 15 were utilised as exclusion criteria to make sure that the participant did not reach the floor, and the last 15, executed immediately before the beginning of the study, to adjust for the eventual mobility gain related to the continuous repetitions of the task (Boyce & Brosky, 2008).

Subsequently, each participant performed 4 trials Baseline, Intervention, After-Effect, and Follow-Up according to the specific allocation group: (i) Neutral Expectation Group (G0), (ii) Positive verbal Expectation Group (G+), and (iii) Visual-Haptic illusion + Positive verbal Expectation (G++). Each trial was executed consequently. The 4 trials were performed in the immersive virtual simulation (see technical characteristics of the system at *Immersive Virtual Reality (IVR) system and virtual scenario*) toward 4 different floor panels of the tracking area, positioned orthogonally to each other, as displayed in Figure.1.

Each group performed the experimental task (5 anterior trunk flexions) toward each tile shown in figure 1. A sham physiotherapy manoeuvre, consisting of four pressures of 40 N for 10 sec. each in four bony sites not directly involved in the back movement (left and right posterior-superior iliac spine, and left and right medial margin of the spina scapulae) were executed in all groups before performing the experimental task towards the "Intervention" tile paired with a verbal stimulus as described hereafter. The physiotherapy sham manoeuvre was executed and standardised with an algometer Wagner Force OneTM Digital Force Gage (Wagner, Greenwich 2020, USA).

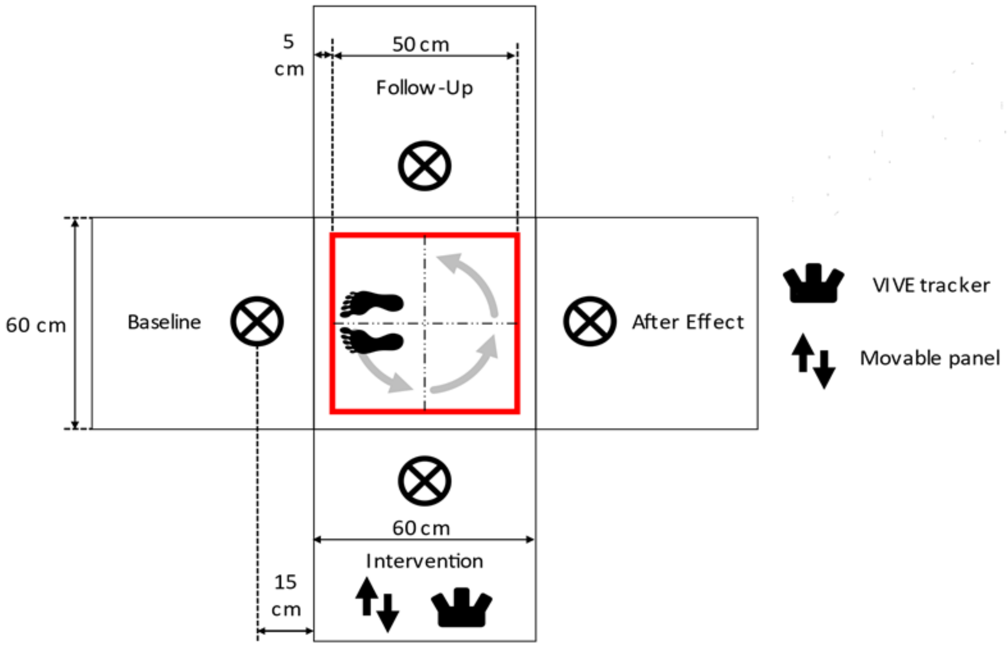

Figure 1: Tracking area in which the study was performed

The sham physiotherapy manoeuvre took place for all groups inside the red square (Figure 1), with the experimenter positioned behind the participant. In group G0, the execution of the sham physiotherapy manoeuvre was paired with a neutral verbal statement regarding its effectiveness and stated by the experimenter immediately after the end of the manouvre. On the contrary, the groups G+ and G++ received a positive verbal stimulus regarding its efficacy. Only in the group G++, after the sham manoeuvre and the positive verbal stimulus, the tile toward which the experimental task has been performed was raised unbeknownst to the participants making them believe that they succeeded in touching the floor (figure 2). Regardless of the groups, all the sham physiotherapy manoeuvres were conducted by a Ph.D. student in Neurosciences who was trained by specialised physiotherapists to apply the pressures on the anatomical marks. To cover the noise coming from the tile elevation, the same lounge music was played in the background through the earphones of the head-mounted display of the VR system, for the whole duration of the study and for all the groups with the purpose to standardise the intervention.

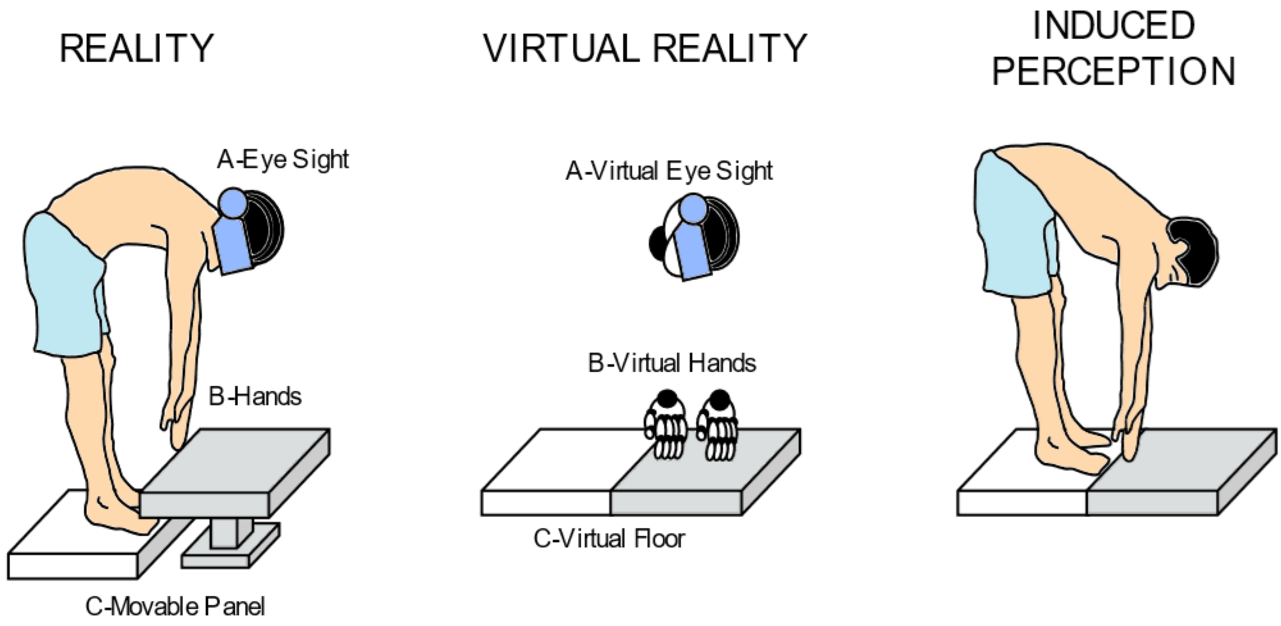

Figure 2: Participant's perception of the trunk flexion during the visual-haptic illusion in virtual reality (G++ group)

The different experimental protocol in the virtual environment of each group is thoroughly reported below.

Neutral Expectation Group (G0)

Baseline:

Participants executed five forward flexions. The level of the virtual floor was maintained at the same level as the real one. The last flexion was measured by a tape measure.

Intervention

Immediately after the Baseline, participants received a sham physiotherapy manoeuvre accompanied by the following verbal stimulus: *"Now I am going to apply this tool (*Wagner digital Algometer*) on different points of your back after which we will resume the measurement, both with the manual method and with virtual reality."* Subsequently, participants executed 5 forward flexions. The level of the virtual floor was maintained at the same level as the real one.

After-Effect

Immediately after the intervention, participants performed 5 forward flexions. The level of the virtual floor was maintained at the same level as the real one. The last flexion was measured by a tape measure.

Follow-Up

After a 5 minutes break, participants performed 5 forward flexions. The level of the floor was maintained at the same level as the real one. The last flexion was measured by a tape measure.

Positive verbal Expectation Group (G+)

Baseline:

Participants executed 5 forward flexions. The level of the floor was maintained at the same level as the real one. The last flexion was measured by a tape measure.

Intervention:

Participants received a sham physiotherapy manoeuvre accompanied by the following verbal stimulus:

"Through this manoeuvre I will treat the main trigger points that reduce the flexibility of the spine and by stimulating them your mobility will increase and you will be able to bend forward more."

Subsequently, they executed 5 forward flexions with the level of the virtual floor maintained at the same level as the real one.

After-Effect

Immediately after the intervention, participants performed 5 forward flexions. The level of the virtual floor was maintained at the same level as the real one. The last flexion was measured by a tape measure.

Follow-Up

After a 5 minutes break, participants performed 5 forward flexions. The level of the floor was maintained at the same level as the real one. The last flexion was measured by a tape measure.

Visual-haptic illusion + Positive verbal Expectation Group (G++)

Baseline:

Participants executed 5 forward flexions. The level of the floor was maintained at the same level as the real one. The last flexion was measured by a tape measure.

Intervention:

Participants received the same verbal stimulus and the same sham physiotherapy maneuver as in the previous group (G+). Subsequently, participants performed 5 forward flexions with the tile in front of the participants lifted and the virtual floor maintained at ground level.

After-Effect

Immediately after the intervention, the level of the virtual floor was re-settled at the same level as the real one and the participants performed five forward flexions. The last flexion was measured by a tape measure.

Follow-Up

After a 5 minutes break, participants performed 5 forward flexions. The level of the floor was maintained at the same level as the real one. The last flexion was measured by a tape measure.

Immersive Virtual Reality (IVR) system and virtual scenario

The immersive environment was delivered through the HTC Vive Pro system. This system is based on a full-body tracking technology (SteamVR tracking) able to register synchronously the position and orientation of different trackable elements and translate this information into the virtual scenario for realistic visual-haptic feedback. The implemented apparatus was calibrated over a 2,5 x 2,5 m and included a Vive PRO Head-mounted display (HMD), two SteamVR 1.0 Lighthouse base stations, and three Vive trackers 2.0 (Valve, Washington, United States, 2018). The HMD was connected to a PC in wireless configuration and participants' movements were recorded through two Vive trackers positioned with velcro straps on the back of their hands. The virtual scenario (represented in Figure 3) in which the participants performed the experiment was a 1:1 reconstruction of the laboratory designed in Unreal Engine 4.25.4.

Figure 3: Real laboratory and its virtual reconstruction

In this environment, the virtual point of view of the user was adjusted according to the registered height position of the third VIVE tracker positioned over a movable panel on the floor. A schematic representation of the experimental setup is reported in Figure 4.

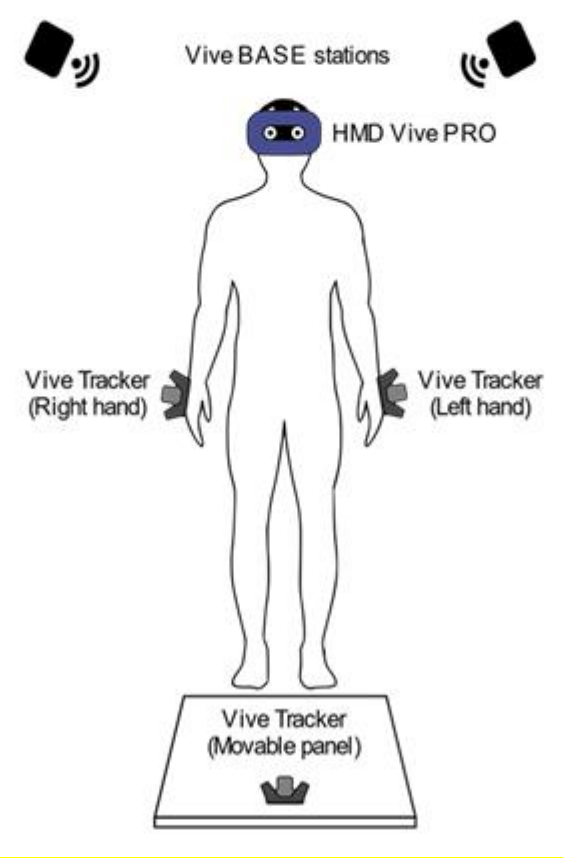

Figure 4: Experimental setup

4.3.3 Statistical Methods

Descriptive characteristics (age, BMI, gender they identified with) were carried out and reported as mean and standard deviation to extract the sample's main characteristics.

Mobility gain values were obtained by subtracting the distances from the floor reached in the after-effect and follow-up conditions from those obtained in the baseline, as reported below:

$$\Delta_{af/b} = x_b - x_{ae}$$

$$\Delta_{fu/b} = x_b - x_{fu}$$

Where the x is the distance reached from the floor and the subscripts *b*, *ae*, and *fu* represent the three experimental trials, namely, baseline, after-effect, and follow-up, respectively. $\Delta_{ae/b}, x_{ae}, x_b$, $\Delta_{fu/b}$, x_{fu}, x_b were reported as median (Q2) with the first quartile and third quartile

[Q1, Q3] as indexes of dispersion since data did not follow a normal distribution (Shapiro-Wilk tests, $p<0.05$).

As for the between-group analyses, they were performed using the Kruskal-Wallis H-Test to compare the mobility gain [cm] obtained during the after-effect and the follow-up in respect to the baseline. The post-hoc analyses were performed using pairwise Mann-Whitney U-Tests.

Within-group analyses were performed through the Friedman Test to detect differences in the distance reached from the floor in the three experimental trials (x_b , x_{ae}, x_{fu}) depending on their temporal execution. Post-hoc analyses were carried on using the Wilcoxon Signed-Rank Test.

The significance acceptance level for pairwise comparison was adjusted to 0.0125 using the Bonferroni Correction (Leon & Heo, 2005), with k representing the number of comparisons (k=3). Effect sizes were calculated as Cohen's d effect size (Cohen, 1988; Fritz et al., 2012). Following Cohen's guidelines, a value of d of 0.2 indicated a small effect, 0.5 represented a medium effect, and 0.8 characterized a large effect. That is, if the difference between the effects of two interventions was lower than 0.2 standard deviations, it was considered negligible (even in presence of statistical significance).

4.4 Results

A convenience sample of 58 eligible participants was considered for inclusion and screened for eligibility. Among them, 6 (10,3%) were enrolled to optimise and test the feasibility of the very first protocol of the study, 2 (3,4%) were excluded for difficulties related to experiences with an IVR environment, such as lack of air and dizziness, and 14 (24,1%) were excluded since they easily reached the floor during the 30 warming-up flexions.

Ultimately, thirty-six participants were considered eligible and included in the presented study. They were equally assigned to each experimental group (G0, G+, G++). Descriptive characteristics of the three experimental groups are presented in Table 1.

Table 1. Participants' descriptive analysis

Groups	G0	G+	G++
N	12	12	12
Age: Mean ± SD	26.2 ± 2.9	26.5 ± 5.0	25.5 ± 6.8
BMI: Mean ± SD	23.8 ± 3.9	24.9 ± 2.9	21.9 ± 1.8
Gender: F (%); M (%)	5(42); 7(58)	5(42); 7(58)	6(50); 6(50)

Legend: G0, neutral expectation group; G+, positive expectation group; G++, Visual-haptic illusion + Positive verbal Expectation Group; N, number; SD, Standard Deviation; BMI, Body Mass Index; M, Male; F, Female

Table 2 reports the medians [Q1, Q3] of the different parameters explored (i.e., $\Delta_{ae/b}, x_{ae}, x_b$, $\Delta_{fu/b}$, x_{fu}, x_b). Between-group analysis, using Kruskal-Wallis H-Tests, showed a statistically significant difference, in terms of mobility gain in relation to the baseline, between all the different groups in the after-effect ($\Delta_{ae/b}$) $\chi^2(2) = 9.083$, p=0.011, and in the follow-up ($\Delta_{fu/b}$) $\chi^2(2) = 6.987$, p=0.030. Post-hoc Mann-Whitney U-tests showed that $\Delta_{ae/b}$ and $\Delta_{fu/b}$ differ significantly only in the comparison between the G0 and G++ groups. $\Delta_{ae/b}$ and $\Delta_{fu/b}$ did not differ significantly in any other group comparison (Table 3).

Table 2. Participants' ability to bend forward throughout the trial under the different conditions

Parameters	G0 (N = 12) [cm] median [Q1, Q3]	G+ (N = 12) [cm] median [Q1, Q3]	G++(N = 12) [cm] median [Q1, Q3]
x_b	12.7 [8.5, 19.5]	13 [10.2, 16.7]	18.9 [17.2, 20.2]
x_{ae}	11.5 [7.2, 20.5]	10.75 [6.7, 15.2]	15.5 [12.2, 16.7]
x_{fu}	13 [8, 21]	12 [6, 16.7]	17 [14.2, 17.7]
$\Delta_{ae/b}$	0.8 [-0.7, 2]	2.2 [1, 3.5]	3.2 [2. 2,6]
$\Delta_{fu/b}$	0 [-1, 1.4]	0.7 [-0.2, 2.7]	1.7 [1.2, 3.2]

Legend: G0, neutral expectation group; G+, positive expectation group; G++, Visual-haptic illusion + Positive verbal Expectation Group; N, number; SD, Standard Deviation; BMI, Body Mass Index; M, Male; F, Female

Table 3. Between-group comparisons of the mobility gains obtained in the follow-up and the after-effect with respect to the baseline

Group comparison	**Dependent variable**	**Mann-Whitney U**	**Effect Size (d_{Cohen})**
	$\Delta_{ae/b}$		
G0 vs G++		U=24.0, p=0.015	1.37
G0 vs G+		U=41.5, p=0.231	0.77

G+ vs G++		U=43.5, p=0.297	0.71
	$\Delta_{fu/b}$		
G0 vs G++		U=27.0, p=0.027	1.25
G0 vs G+		U=49.0, p=0.546	0.56
G+ vs G++		U=49.0, p=0.549	0.56

Legend: G0, neutral expectation group; G+, positive expectation group; G++, Visual-haptic illusion + Positive verbal Expectation Group; : distance from the floor (baseline); , distance from the floor (after-effect); , distance from the floor (follow-up); , mobility gain at the after-effect respect to baseline; : mobility gain at the follow-up with respect to baseline.

Within-group analyses using Friedman Tests highlighted a statistically significant difference, in terms of distance reached from the floor, in the G+ and G++ groups depending on the temporal execution of the trials. [G0, χ 2 (2) = 2.2, p=0.336; G+, χ 2 (2) = 11.2, p =0.004; G++, χ 2 (2) = 19.5, p <0.001]. Post-hoc analyses using Wilcoxon Signed Ranks tests showed that $x_{ae}$was significantly lower than $x_b$for both the G+ and G++ groups. Only in the G++ group, x_{fu}differed significantly from both $x_b$and x_{ae}. (Table 4).

Table 4. Within-group comparisons of the distances reached in the 3 experimental trials for the 2 groups. G0 data are not reported because not statistically significance

Groups	**Comparisons**	**Wilcoxon Signed-rank test Z**	**Effect Size (d_{Cohen})**
G+ (N=12)			
	$x_{ae} - x_b$	Z = -2.809, p=0.015	1.06
	$x_{fu} - x_b$	Z = -2.011, p=0.132	0.71
	$x_{fu} - x_{ae}$	Z = -1.543, p=0.369	0.53
G++ (N=12)			
	$x_{ae} - x_b$	Z = -3.062, p=0.006	1.187
	$x_{fu} - x_b$	Z = -2.941, p=0.009	1.188
	$x_{fu} - x_{ae}$	Z = -2.403, p=0.048	0.874

Legend: N= number of participants per group; G+, positive expectation group; G++, Visual-haptic illusion + Positive verbal Expectation Group; : distance from the floor (baseline); , distance from the floor (after-effect); , distance from the floor (follow-up).

4.5 Discussion

The main finding of this pilot study is that the use of the IVR system is a feasible, safe, and well-tolerated instrument to modify healthy people's motor performance during a forward bending movement. Hereafter, we are discussing the preliminary results of this study, its future applications in research, and the possible improvements of the present protocol for forthcoming clinical trials. Our results showed that the verbal and the visual-haptic manipulation can modify the trunk flexion in a cohort of healthy individuals. Specifically, the results highlighted a direct proportionality between the nature of the intervention (i.e., verbal manipulation, visual-haptic illusion) received and their effect on mobility: the G0 group displayed less improvement compared to the G+ group, which, in turn, performed worse than the G++ in the trunk flexion task.

The role played by inducing positive expectations to increase the performance of motor tasks is in line with a broad array of previous studies (He et al., 2018; Hutchinson et al., 2008; McKay et al., 2012; Wulf et al., 2012; Wulf & Lewthwaite, 2009). Kirsch (Kirsch, 1985, 1997) suggested that the expectancies related to the occurrence of non-volitive responses, called response expectancies, and those related to the own self-efficacy, named self-efficacy expectancies, significantly contribute to the overall placebo and nocebo response.

According to his conceptualisation, it is possible to hypothesise that the presence of these two kinds of expectancies affected the magnitude of the improvement of the trunk flexion movement via a summative effect. G0 group with neutral expectancy reported the lowest mobility gain; G+ group, where the response expectancy was induced through an external verbal stimulus, provided by the experimenter, significantly improved trunk flexion. Finally, the G++ group, in addition to the verbal external stimulus, received the visual-haptic illusion. The latter is the most likely to induce the person to believe that they can successfully perform the requested task (i.e., touching the floor), increase their level of self-efficacy, namely, their beliefs about their capabilities to produce certain levels of performance. Hence, the improvement in the motor performance through the visual-haptic illusion may have tapped into the abovementioned self-efficacy expectancies.

Moreover, thanks to newly created expectancies of the movement, a modification of the “priors” induced by the “posteriors” (i.e., the updated view of the situation – specifically the possibility to touch the floor) ” (Friston, 2009; Friston et al., 2012; Seth & Friston, 2016) allows the participants to modify their interpretation of the ongoing stimuli. Hence, matching what was expected with the new situation (“posteriors”), induced a recalibration of the previous consolidated beliefs (“priors”), creating an improvement in participants’ motor performance, in line with the “Perceptual Inference Model” (Friston, 2009; Friston et al., 2012; Seth & Friston, 2016) of the brain predictive processing.

Moreover, this fast recalibration of the information might be elicited by the surprise or “wow effect” (Grassi & Bartels, 2021), induced as well by the unexpected possibility of touching the floor as a result of the visual-haptic illusion. Classically, surprise is considered as an emotion that occurs when there is a discrepancy between what is perceived and what is expected, and induces the recalibration of our beliefs, expectations, and behaviours, (Reisenzein, 2000; Reisenzein et al., 2019), inducing specific cortical activations (Sebastian et al., 2021) and cognitive responses (Gerten & Topolinski, 2019). The sense of surprise can also be interpreted through the framework of predictive processing (Reisenzein et al., 2019), in which the mismatch between expectations and incoming sensory information must be resolved. As suggested by the cognitive-evolutionary model of surprise (Reisenzein et al., 2019), the schemas that control perception and actions are continuously updated at an unconscious level through the comparing of the incoming information to those possessed (belief).

As a general limitation, this is a pilot study that serves as a feasibility study to support the design of following wider clinical investigations. Therefore, the presented findings should be appraised cautiously. Nevertheless, other researchers may find our paradigm, methodology, and results useful, and be inspired to further investigate ourfindings. If these findings will be confirmed in a larger sample, the use of immersive virtual reality for the creation of specific environments could be adopted to support and enhance sports training or rehabilitation treatments for example in case of chronic low back pain with kinesiophobia and related restriction of trunk mobility (Osumi et al., 2019). The researcher who assessed the distance between the fingertip and the floor by a tape measure knew to which group participants belonged to, inducing possible measurement bias. In order to reduce possible measurement biasses, it should be advisable the adoption of a laser metre firmly fixed to the fingers of the participants. Moreover, blinding the assessor and the statistician will reduce any possible detection biases that can arise from knowing to which group each participant belong to. Finally, we observed that the movement gain tends to reduce, repetition after repetition, but only the last repetition of the five trunk flexions performed by the participants was recorded. This generated an underestimation of the immediate effect of the intervention and the missing of the opportunity to describe the progressive return to the baseline performance, probably resulting from a violation of the new expectancy induced by the visual-haptic illusion. In this case, the adoption of the abovementioned laser metre would permit a reliable measure of each single forward flexion.

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5. Future perspectives on the use of immersive virtual reality combined with telemedicine for chronic low back pain sufferers.

Chronic low back pain is the most widespread musculoskeletal disease and represents a global health problem resulting in functional disability and lowered quality of life. Specifically, it affects one-fifth of adults in western countries, it is more diffused between female than male subjects and between people aged 40 to 80 years (Hoy et al., 2012). As regards treatments, the most used are exercises, manual therapy, psychological therapies, education and self-management Hayden et al., 2021; Ulger et al., 2017; Ferlito 2022; Du et al.,2017). However, there is a lack of indications to direct the choices of the healthcare professionals based on the phenotype of the patients (e.g. biological, psychological), and there is also little clarity in the way to proceed with treatment modifications according to patients outcomes (Mauck et al., 2022). This situation deals also with the fact that chronic pain has significantly subjective connotations whereby emotional, cognitive, behavioural and physiological factors influence each other, in ways that are often unclear. Immersive virtual reality allows us to act on some aspects of these elements. But it is necessary to underline that despite a growing body of literature about the use of virtual reality systems applied to acute and chronic pain, both in the clinical and research field, there is a lack of evidence on the understanding of how they impact on pain experiences (Trost et al., 2021). Although the underlying functioning mechanisms of virtual reality systems remain equivocal, the most well known are distraction, neuromodulation and graded exposure therapy (C. Tack, 2021). Beyond the usefulness of distraction in painful medical procedures such as in burns (Faber et al., 2013), literature often reveals that these three aspects need repeated sessions of virtual reality to bear fruit, for example in the field of musculoskeletal diseases (Thomas et al., 2016; Koo et al., 2018; Lin et al., 2019).

One of the most promising sectors in the healthcare system is telemedicine - defined as the practice of medicine via a remote electronic interface. Telemedicine can be experienced in a synchronous, asynchronous and remote monitoring way (Mechanic et al 2023). With the first, physicians provide information to the patients about tests or treatments in real-time. The asynchronous modality includes a check or a delivery of information by the physician to the patient after he/she stored their health state data (e.g. glycemic level). Finally, the remote monitoring method (Facilitated Virtual Visit-FVV) refers to a synchronous way. In this last modality the patient is in an equipped space (e.g. clinic) without the physician, located in another site, but supported by a tele-facilitator (e.g. nurse or medical assistant) (Kazi et al 2022; Mechanic et al., 2023). The main aim of telemedicine is to permit a wider range of population easier access to the health care system. Just think of the difficulties experienced by people that live in remote areas or those without the possibility to move independently (e.g. without a car or experiencing a disabling health condition). Moreover, a person monitored thanks to telemedicine often represents a better informed and more adherent patient with less probability to be hospitalised (Peters et al., 2021). Although the efficacy of telemedicine on national health system costs is still being debated (Evers et al., 2022; Clarke et al., 2018), it remains a promising and innovative tool in the field of medical assistance. In view of this situation, telemedicine represents a potentially useful instrument to apply to chronic low back pain. On the one hand, because of the global prominence of this musculoskeletal disease, and on the other because the impact of chronic patients are well known, both in terms of the healthcare system costs and in the low efficacy of proposed treatments. The innovation could be represented by unifying the potential shown by telemedicine with those of immersive virtual reality. The novelty may be not only utilising virtual reality as a more advanced and intuitive interface (Riva & Gamberini, 2000), but exploiting it for the creation of ad-hoc virtual environments in which medical data (e.g. kinematic) are stored. What would be required for sufferers of chronic low back pain would be to utilise the IVR system as an entertainment tool for constant but relatively short sessions periods (e.g. 20 minutes per day for 3 months). Patients could be offered different games where each of them have been designed to stress specific body regions, physical ability or psychological aspects. In addition to games aimed directly at alleviating symptoms, patients may benefit from the possibility that the performances required by the task can be personalised following the framework proposed by the adaptive training (Zahabi & Abdul Razak, 2020). This means that the rehabilitative tasks could be created with a consistent adaptive logic that permits their real-time adjustment according to the patient's features such as profile information or learning style. In this way the characteristics of the games/tasks proposed, such as difficulty level, could be alterered to better fit with the rehabilitation phase and the advancements obtained in that specific moment. Finally, thanks to telemedicine the doctor might monitor the physiological variations or/and the improvements of the patient. This would allow the design and production of a goal-oriented treatment able to produce a higher level of patient involvement that probably would have effects on their pain perception, on their perceived disability level and on the capacity to apply to daily life routine what was learned through the virtual spaces.

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