Multisensory Resizing Illusions as a Non-Pharmaceutical Treatment for Chronic Hand-Based Pain

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Abstract

Resizing illusions use augmented reality to alter the perceived size of a body part, typically combining visual and tactile inputs. These illusions have shown analgesic effects when applied to painful areas in people with chronic pain. This thesis explored the subjective experiences, neural underpinnings, and analgesic potential of resizing illusions through various sensory modalities, including visuotactile, unimodal visual, and visuo-auditory presentations.

Before inviting participants with chronic pain to take part in illusory resizing projects, Chapter 2 examined barriers and facilitators to involvement in non-pharmaceutical research for people with chronic pain. Findings revealed that addressing participant distrust and improving accessibility could improve the chances of people wanting to take part and their comfort levels when participating. Chapter 3 introduced hand-based resizing illusions in participants without chronic pain and used electroencephalography (EEG) to assess the associated neural underpinnings. Gamma-band oscillations related to multisensory integration were found during visuotactile illusions and theta-band oscillations indicative of increased cognitive load were found during incongruent illusory presentations. Chapter 4 assessed whether non-naturalistic auditory input enhances visual presentation of resizing illusions. Results showed that auditory input increased subjective experiences but was less effective than visuotactile conditions. Chapter 5 explored somatosensory steady state responses in participants without chronic pain, finding no significant differences between illusory and non-illusory conditions. Chapter 6 used the same approach as Chapter 5 for participants with chronic hand pain, and whilst finding no changes in somatosensory representations, showed meaningful pain reductions following illusory resizing for several participants. These findings extend previous research on illusory analgesia and suggest resizing illusions could offer a non-pharmaceutical treatment for chronic primary and secondary pain conditions.

The studies presented within this thesis highlight the potential of resizing illusions to be used both as a tool for understanding multisensory integration and as a potential non-pharmaceutical treatment for chronic hand-based pain.

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Author's Declaration

I, Kirralise Jaida Hansford, declare that this thesis is a presentation of origional work, carried out under the supervision of Dr Catherine Preston, Professor Daniel Baker, and Dr Kirsten McKenzie, and that I am the sole author. This work has not previously been presented for a degree ot other qualification at this University (University of York, UK) or elsewhere. All sources are acknowledged as references. All the studies containted within this thesis were conducted in accordance with the ethical standards of the Department of Psychology at the University of York. The research carried out in Chapters 3, 5, and 6 were supported by a Pain Relief Foundation John Miles PhD Studentship grant awarded to Dr Catherine Preston. Data in chapter 2 was collected in collaboration with Anna Crossland, and data in Chapters 5 and 6 were collected in collaboration with Shasha Wei. The work presented in chapters 3 and 4 have been published in the following articles:

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Primary Supervisor's Statement

I am listed as a co-author on the papers that comprise Chapters 2, 3, 4, 5 and 6 of this thesis:

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In these papers, the work was primarily that of Kirralise Hansford. Kirralise collected and analysed all of the data, wrote the first draft of the paper and did the majority of the editing and revising of the manuscripts. I assisted with providing advice, guidance and editing in my capacity as supervisor.

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1 Chapter 1: Introduction

1.1 Overview

1.1.1 A Background to Chronic Hand-Based Pain

Chronic pain is classified by the National Institute for Health and Care Excellence (NICE) as pain that lasts for more than 3 months (NICE, 2021), and is described by the International Association for the Study of Pain (IASP) as an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage. Chronic pain is a leading cause of disability globally (Vos et al., 2017). The three main types of chronic pain are back pain, headache, and joint pain (BMJ, 2018). Joint pain concerns pain felt in several joints across the body, with arthritis being one of the most common chronic pain disorders, diagnosed in 8-16% of the population across Europe and the US (BMJ, 2018). Arthritis and joint pain conditions often affect the hands, meaning that tasks such as tool use and self care can become very difficult. Finding an appropriate treatment for hand-based chronic pain, therefore, would not only address one of the main types of chronic pain, but would contribute to a greater quality of life for those affected. Chronic hand-based pain can come in many forms, such as pain from arthritis, osteoarthritis, carpal tunnel syndrome, ganglion cysts, tendon problems, repetitive strain injuries, or from a sports injury. The hand is composed of 3 major types of bone: phalanges, metacarpals, and carpal bones (Hopkins-Medicine, 2021). Each finger has three phalanges: distal, middle, and proximal, in addition to two phalanges in the thumb. The middle part of the hand is composed of metacarpal bones and the wrist of carpal bones. This section will first discuss what is termed as chronic primary or secondary pain and then will comment on the origins and prevalence of specific hand-based pain conditions, leading to a rationale for investigating hand-based pain disorders.

Hand-based chronic pain conditions can be termed as primary pain conditions, where the root cause of the pain has no clear underlying condition, or can be termed as secondary pain conditions, where the pain appears to be due to an observable injury or disease (NICE, 2021). Hand-based chronic pain can come from primary pain conditions such as fibromyalgia (chronic widespread pain), complex regional pain syndrome, chronic primary headache / orofacial pain, chronic primary visceral pain, and chronic primary musculoskeletal pain. Hand-based chronic pain can also arise from secondary pain conditions, such as forms of arthritis, carpal tunnel syndrome, and tendon issues in addition to repetitive strain or sports injuries.

Hand-based pain is particularly apparent in conditions such as arthritis and osteoarthritis (OA), where joint inflammation can occur in multiple parts of the hand. OA is one of the most common forms of arthritis (Hopkins-Medicine, 2021) and can be caused by either normal use of the hand or can develop after insult or injury. OA is characterised by cartilage degeneration within the joints of the hand, and is a leading cause of disability, particularly in older individuals (Guccione et al., 1994). Individuals with osteoarthritis typically experience pain in three key areas: the base of the thumb, the end joint closest to the fingertip, or the middle joint of a finger. In December 2018, when data on the prevalence of arthritis was last reported, 1 in 6 people in the UK were reported as experiencing arthritis (NHS, 2018), which is supported by a Versus Arthritis recent report stating that over 10 million people (just over 1 in 6) in the UK have OA (Arthritis, 2023).

Other hand-based pain conditions include carpal tunnel syndrome, which is a condition where the median nerve is compressed as it passes through the carpal tunnel within the wrist. The median nerve provides sensory and motor functions to the thumb and middle three fingers, and therefore compression of this nerve can impact overall hand function and can cause pain or numbness (Hopkins-Medicine, 2021). Another hand-based pain condition is ganglion cysts which, for no apparent reason, can develop on the front or back of the hand as soft, fluid-filled noncancerous cysts. As these cysts grow, they can become painful and can interfere with normal hand and wrist functionality.

Tendon problems can also cause pain in the hand in the form of tendonitis, inflammation of a tendon, or tenosynovitis, inflammation of the lining of the tendon sheath (Hopkins-Medicine, 2021). Common tendon disorders include lateral and medial epicondylitis, where pain can stem from elbow or forearm and progress into the wrist and palm due to damage to the tendons that bend the wrist either away or towards the palm. The most common type of tenosynovitis is DeQuervain's tenosynovitis (Hopkins-Medicine, 2021), which is characterised by swelling of the tendon sheath in the thumb. Another common form of tenosynovitis is trigger finger / thumb, where the tendon sheath becomes inflamed and thickens, preventing a smooth extension or flex of the finger or thumb.

With hand-based chronic pain coming from many different sources and affecting such a large proportion of the population, the medical, social, and economic costs of hand-based pain disorders cannot be overstated.

1.1.2 Chronic Pain Contextualised

Chronic pain does not exist in isolation. Individuals who experience chronic pain very often experience other health issues due to high rates of comorbidity, with around 26% of the chronic pain population reporting 2 or more comorbid physical conditions (Dominick et al., 2012). Alongside experiencing other conditions such as anxiety (Arnold et al., 2019; Gracely et al., 2012), depression (Walitt et al., 2015), and sleep disturbances (Nicholson and Verma, 2004), these being the most common co-morbidities with chronic pain, societal context also plays a role in our understanding of life with chronic pain. Health-related stigma concerns attitudes held towards people with specific health conditions, such as chronic pain. This stigma can lead to discrimination in workplaces and at home, and can leave the patient feeling shame and guilt regarding their condition (Scambler, 2009). Additionally, individuals with stigmatised health conditions tend to avoid treatment, have poor treatment outcomes, decreased social opportunities, difficulty in obtaining employment, and a decreased overall quality of life (Perugino, 2022). The absence of a clear medical diagnosis for several types of chronic pain, alongside there being a lack of concordance between structural damage and experiences of pain, contribute to chronic pain often receiving stigmatisation (Perugino, 2022).Health-related stigma associated with chronic pain, whilst not being a specific focus within the research within this thesis, is important in shaping our understanding of the additional pressures that people living with chronic pain face in wider society.

In addition to health-related stigmatisation being a societal concern for those living with chronic pain, there are two other societal / medical concerns that are highlighted alongside chronic pain; obesity and long-COVID. Obesity is defined as a person who is very overweight and has a large proportion of body fat (NHS, 2019). 1 in 4 adults in the UK fall into this description, with obesity estimated to cost the UK healthcare system £6.5 billion per year (DHSCMC, 2023). Long-COVID is defined as COVID-19 symptoms that last weeks or months after the infection has gone (NHS, 2022). These symptoms include, extreme tiredness, chest pain, difficulty sleeping, depression, anxiety, joint pain, and problems with memory and concentration, which have striking similarities with chronic pain symptoms and comorbidities. With the obesity epidemic and the increasing number of people suffering with long-COVID, despite not being the focus of the work within the thesis, it is vital to consider chronic pain within these wider societal and medical contexts to gain a holistic understanding of the pressure chronic pain conditions present to wider society, and those living with the conditions.

Referring first to obesity, there appears to be a relationship between chronic pain and obesity, both of which are conditions that place a large strain on the healthcare system. If this relationship does exist, then it is important to understand which is driving the other to alleviate strain on the healthcare system and provide a more holistic treatment approach to individuals suffering from obesity and chronic pain. Stone and Broderick (2012) found that obese individuals were 68% more likely to experience pain than healthy weight individuals. Additionally, a correlation has been found between body mass index (BMI) and prescription opioids, with a higher BMI correlating with a higher chance of being prescribed opioids for pain management (Stokes et al., 2020). Most of the literature on obesity and chronic pain use BMI as an index for obesity, however, it has some major limitations which could cloud the links seen between more obese people reporting more chronic pain issues. Notably, BMI cannot differentiate between fat and lean muscle mass, meaning that people with low body fat but high muscle mass could be classified as obese on the BMI scales, with similar issues presenting in the opposite direction for people with high body fat percentage being classified as having a healthy BMI (Emerson et al., 2021). This reliance on BMI as a measure could have impacted the findings of a correlation between chronic pain and obesity, as the understanding of what is meant by the term obese from a BMI measurement is likely different from the lay understanding of what an obese person is. It has however, been posited that an amplification of nociceptive processes in obese individuals could make them more susceptive to experiencing chronic pain (Stone and Broderick, 2012).

However, when using BMI in addition to anthropometric parameters of central adiposity and percent body fat, Emerson et al. (2021) found no difference when comparing pain scores to nociceptive stimuli between healthy weight and obese individuals with no current reports of chronic pain. Therefore, indicating that this relationship between obesity and chronic pain could lean more towards chronic pain causing an increased likelihood of developing obesity rather than obesity causing an increased likelihood of developing chronic pain. As such, the need to find a valid therapy for chronic pain conditions is brought to the foreground as reducing pain levels in chronic pain patients could also help to alleviate the obesity crisis and in turn put less strain on healthcare systems.

When looking at the broad impact of COVID-19 on pain levels, across several chronic pain conditions there has been reported increases in the pain levels across the entire body experienced by individuals due to lockdown effects (Fallon et al., 2021) and due to increases in overall anxiety levels (Kharko et al., 2020). There has, however, been a recent report of a decrease in pain levels amongst cancer pain sufferers when they had COVID-19, however this was only found in 3 patients and the neurological imaging and pathological findings were inconclusive (Hentsch et al., 2022). The impact of COVID-19 on chronic pain is not limited to the direct impact the pandemic had on individuals with chronic pain, but also the instance of individuals now living with long-COVID. Long-COVID shares several symptoms with that of many chronic pain conditions, such as; difficulty sleeping, depression, anxiety, joint pain, and problems with memory and concentration (NHS, 2022). Therefore, in addition to the heightened pain experienced by chronic pain sufferers during the pandemic, there are also more and more people suffering chronic pain-like symptoms due to long-COVID in need of appropriate therapeutic options to improve their pain levels.

1.1.3 Current Treatments for Chronic Hand-Based Pain

Current pharmaceutical interventions for chronic hand-based and pain conditions more generally have been reported as minimally effective. Examples include aggressive treatments of periodontitis, a chronic destructive inflammation of periodontal tissue (Detert et al., 2010) which has been attempted due to a proposed link between oral bacterial infections and the etiopathogenesis of rheumatoid arthritis. Therefore, treatment of periodontitis is aimed at preventing arthritis development in genetically susceptible individuals. However, no evidence has been found to support the aggressive treatment significantly ameliorating the risk of developing arthritis (Chen et al., 2013). On the other hand, intra-articular injections of Sodium Hyaluronate (HA) are one of the most effective pharmaceutical treatments for OA pain, with HA around 20% more effective than placebo at reducing pain (Altman, 2000), but the long-term effects of this treatment are undefined. Intra-articular injections of glucocorticoids or hyaluronic acid are often used to try and alleviate pain at the thumb base, but these are found to be no more effective than placebo at improving pain levels or functionality of the hand in general (Heyworth et al., 2008; Meenagh et al., 2004).

In addition to this, many of the drugs that are prescribed to deal with pain, such as antidepressants, antiepileptics, and opioids, result in around 60% of patients reporting showing no improvement in pain or reporting adverse effects (Dworkin et al., 2010). When looking at a recent multicentre research study into the use of Ketamine for pain alleviation in chronic pain, despite the positive finding of pain intensity decreasing significantly from baseline to a 12-month follow-up, 50% of patients reported experiencing adverse effects from the drug 1 week after administration, which continued for some patients throughout the follow-up period (Corriger et al., 2022). In addition to adverse side effects, opioids are extremely addictive which presents issues for the patients when trying to reduce their opioid use, as they experience withdrawal symptoms in addition to increases in pain. Non-steroidal anti-inflammatory drugs (NSAIDs) are the most frequently prescribed medications for OA (Altman, 2000), but resistance / intolerance to NSAIDs is very common, leading individuals to surgical interventions for their pain. Due to these evidenced issues with prescribing pharmaceutical / drug treatments for chronic hand-based pain, it comes as no surprise that the current draft of the NICE guidelines (GID-NG10068) advises against using pharmaceutical treatments for chronic pain conditions.

Surgical interventions for osteoarthritis, however, are typically only offered to patients over the age of 60 years (Perrot and Menkes, 1996) meaning those experiencing pain at a younger age are far more limited in pain relief options. However, surgery itself is not a magic fix for chronic pain conditions. A systematic review conducted in 2012 found that regarding OA surgeries, up to 23% of patients reported unfavourable pain outcomes after hip surgery along with up to 34% of patients reporting the same unfavourable outcomes after knee replacement surgery (Beswick et al., 2012). An alternate intervention for chronic pain is the use of transcranial direct current stimulation (tDCS). tDCS is a neuromodulation technique that is used to modulate cortical excitability across brain areas thought to be involved in chronic pain conditions such as fibromyalgia. A systematic review of the effectiveness of tDCS however, found that whilst tDCS is a safe intervention that has the potential to lower pain intensity in fibromyalgia, only a small-to-moderate effect was found when assessing subjective ratings of pain intensity, with a percentage change in pain ratings after undergoing tDCS of 17% (Lloyd et al., 2020).

Due to the ineffective current pharmaceutical therapies, the issues discussed with prescribing drugs to aid in pain relief and the lack of a suitable surgical option for chronic pain patients, it is paramount to research into a non-pharmaceutical / non-surgical therapy for chronic hand-based pain conditions, which is the focus of the research within this thesis.

1.1.4 Uptake of Non-pharmaceutical Treatments for Chronic Pain

There are non-pharmaceutical treatments for chronic pain currently available, such as physical therapy (Cherkin et al., 1998; Ferreira et al., 2007; Hill et al., 2011), cognitive behavioural therapy (Keefe et al., 1991; Lamb et al., 2010; Wetherell et al., 2011), mindfulness (Cherkin et al., 2016), yoga (Sherman et al., 2011; Tilbrook et al., 2011; Wren et al., 2011), and chiropractic treatments (Cherkin et al., 1998). Virtual reality has also been explored as an avenue for chronic pain treatment, however, there are mixed findings regarding the efficacy of using virtual reality to reduce chronic pain (Wittkopf et al., 2020). Currently research has found that interactive virtual reality can reduce chronic pain for ankylosing spondylitis (Karahan et al., 2016) and for post-mastectomy pain (Aguirre-Carvajal and Marchant-Pérez, 2015), however evidence is limited for other chronic pain conditions. Affective touch is another interesting treatment avenue for chronic pain, described as gentle stroking of the skin to provide a pleasant sensation (Bjornsdotter et al., 2010). Affective touch activates a particular type of low threshold mechanosensory C-fibres to modulate pain (Liljencrantz et al., 2017) and can come in the form of slow stroking (between 1 and 10 cm/s (Bjornsdotter et al., 2010)) with a soft brush or with the hand. Affective touch has been found to reduce acute pain (Gursul et al., 2018; Habig et al., 2017; Liljencrantz et al., 2017; Mohr et al., 2018), and recent evidence from Lernia et al. (2020) found that it significantly reduced the severity of pain in chronic pain patients by 23% after 11 minutes of stimulation.

However, uptake of non-pharmaceutical methods is still outweighed by pharmaceutical treatment engagement, with the use of narcotics, muscle relaxants, benzodiazepines, and neuropathic agents significantly increasing from 1999-2000 compared to 2009-2010 for back and neck pain (one of the most common pain reasons for visiting a physician) (Mafi et al., 2013). Given the lack of side effects for many non-pharmaceutical methods compared to pharmaceutical treatments, it is surprising that there is a lack of uptake of these treatments. Research has been conducted regarding the possible barriers that exist for people concerning the uptake of non-pharmaceutical therapies for chronic pain, finding top-ranked barriers to be the high costs involved, in addition to transportation problems and low patient motivation (Becker et al., 2017). Looking specifically at an older patient sample, as older individuals are at a disproportionate risk of developing pain conditions (Blyth and Noguchi, 2017), top-rated barriers were found to be time conflicts with other healthcare appointments, concerns about the efficacy of non-pharmaceutical treatments compared to drug treatments, and again, concerns about transportation for these treatments, including worries about falling and not being able to travel alone (Austrian et al., 2005). The concern regarding the efficacy of non-pharmaceutical treatments was also present in finding from Simmonds et al. (2015), when assessing the barriers to multi-modal chronic pain care among veterans for non-cancer pain. Additionally, when investigating barriers to self-management of chronic pain among patients with comorbid depression, which makes up from $40-60\%$ of chronic pain patients (Surah et al., 2014), findings echoed the barriers mentioned previously, in addition to feeling a lack of support from friends and family relating to maintaining their treatment, along with the avoidance of activities for fear of pain exacerbation, the lack of tailoring of treatments to meet personal needs, and difficult patient-physician interactions (Bair et al., 2009).

Research focusing on the barriers to the uptake of non-pharmaceutical treatments already in circulation is vital, however, there appears to be no evidence of research looking into the barriers patients face at an earlier stage of the treatment development pipeline, regarding participating in research relating to future non-pharmaceutical treatments. It has been found that patient engagement in research can lead to improved credibility of results, and improvements in direct applications of the research to the patient sample (Domecq et al., 2014). Therefore, when looking to create novel non-pharmaceutical methods of pain intervention therapies, getting clinical populations involved at the research stage is extremely important, and has the potential to remove some of the aforementioned barriers to the uptake of the non-pharmaceutical treatments that are developed.

1.1.4.1 Future Research

There is limited research in general into barriers to patient involvement with research, and there is an apparent gap in the literature regarding barriers to participation specifically in non-pharmaceutical chronic pain research, with the research mentioned before focussing on uptake of treatments once they are available, rather than involvement of patients whilst treatments are being developed. Therefore, there arises a need to investigate barriers for chronic pain patients relating to participating in research on non-pharmaceutical treatments, investigating an earlier step in the treatment pipeline than previous research relating to barriers to engagement with non-pharmaceutical treatments.

1.2 Illusion Therapy

1.2.1 Theory Behind Illusion-Based Therapies

The basis of illusion-based therapies is rooted in the understanding that structural damage and perceived pain are not always concurrent. Evidence suggests that pain and sensitivity to noxious and non-noxious stimuli are not correlated with the extent of the structural damage seen, since there is often a lack of concordance between radiographic (physical damage) and symptomatic pain (Felson, 2005; Szebenyi et al., 2006). Even when research has highlighted avenues to reduce this lack of concordance, such as including the patellofemoral joint in chronic knee pain analyses, as this leads to a closer relationship between radiographic and symptomatic pain reports, there is still pain experienced that is not correlated with the structural damage at all, such as night pain, pain at rest, and pain when in use (Szebenyi et al., 2006). This links heavily to the unfavourable surgical outcomes mentioned previously, as the lack of improvement in pain after surgery could likely be that despite the presence of tissue damage as part of arthritis and chronic pain conditions in general, there is evidence to suggest that there are critical additional processes contributing to the pain being experienced. Therefore, surgery to remove the physical and structural damage might not be improving the pain experience overall, leading to the need for a therapy to treat the experience of pain rather than the structural damage.

The rubber hand illusion (RHI) centres on the theory underpinning this lack of concordance between radiographic and symptomatic pain. The RHI taps into the neural substrates of our sense of bodily self and highlights its apparent malleability (Armel and Ramachandran, 2003). This experimental paradigm involves the induction of a feeling of limb-ownership through synchronous tactile stimulation of a participant's hidden hand at the same time as tactile stimulation is given to a visible rubber hand (Botvinick and Cohen, 1998). This mismatch in incoming sensory data leads the participants to experience the illusion of assimilating the tactile and visual inputs to feel like the rubber hand is in fact their hand. This paradigm demonstrates that the brain resolves conflicting multisensory inputs via its best guess at what the cause of these inputs could be, leading to an illusion of ownership over the rubber hand. This highlights the malleability of our sense of bodily self when faced with conflicting sensory inputs. A Bayesian approach to the problem of contradictory incoming sensory evidence is based on a core aspect of predictive coding (Friston, 2008). This account denotes that the brain interprets incoming sensory data in a hierarchical generative model of the world (Limanowski and Blankenburg, 2015). Here, any mismatch between predicted and actual sensory inputs, such as the difference between peripheral signals and symptomatic pain, generates prediction errors. These prediction errors are minimised via updating high-level top-down expectations, called priors, so that in future the likelihood of experiencing prediction errors is minimised. A formal presentation of a Bayesian account of body ownership illusions, with reference specifically to the rubber hand illusion, comes from Kilteni et al. (2015) who provide an equation to mathematically formalise the concept of the nervous system needing to compute the probability of there being one hand compared to there being two hands in the rubber hand illusion, given available sensory inputs and prior knowledge. Under the Bayesian approach, it could therefore be posited that in chronic pain patients, there is a lack of an updating of priors, leading to constant mismatches between experienced and actual painful sensory inputs, resulting in chronic experiences of pain. Pain perception in chronic pain could also hinder capacity to adapt to changing sensory environments, becoming a maladaptive compensatory mechanisms to aberrant sensory predictive processing (Castejon, 2024). Additionally, it has been posited that individuals with chronic pain show a heightened prediction of pain when presented with harmless sensory inputs, due to an assumed link between pain and a harmless bodily sensation, whereby their mind infers pain as the most likely cause for the sensation (Hetchler, 2016).

The predictive coding account of multisensory illusory embodiment has been posited by Zeller et al. (2016), arguing that illusory embodiment occurs because of the brain downregulating conflicting bottom-up somatosensory information in preference of top-down predictions to resolve sensory ambiguity during bodily illusions. When additional incongruent somatosensory / visual information is presented to the perceiver which cannot be downregulated by top-down predictions about how sensory and visual inputs should correspond with each other, this leads to reduced subjective embodiment (Carey et al., 2019). When there is synchronous somatosensory / visual information presented, this leads to enhanced subjective embodiment.

In addition to the predictive coding account, central sensitisation has been proposed as an underlying mechanism of arthritic and chronic musculoskeletal pain (Arendt-Nielsen et al., 2010; Arendt-Nielsen and Graven-Nielsen, 2003). Central sensitisation is seen as an amplification of neural signalling within the central nervous system that elicits pain hypersensitivity through the facilitation that manifests at the end of a conditioning stimulus, which once triggered, remains autonomous for some time, or only requires a very low level of nociceptor input to sustain it (Woolf, 2011). This represents a condition where the input in one set of nociceptor sensory fibres amplifies subsequent responses to both non-nociceptive and nociceptive fibres, which influences one’s perception of painful and non-painful inputs. This means that pain experienced might not reflect the presence of a peripheral noxious stimulus. Central sensitisation leads to the central nervous system changing, distorting, or amplifying pain by increasing its duration and degree in a way that no longer reflects the peripheral input from the body. Under the influence of central sensitisation, it has been posited that pain could become the equivalent of an illusory perception (Woolf, 2011) where the sensation has the same quality as that evoked by a true noxious stimulus, but which occurs in the absence of one. Central sensitisation and predictive coding theories are not necessarily positioned in opposition to each other, but rather both contribute to our overall understanding of what could be the cause of chronic pain conditions and symptoms, and both indicate the suitability of illusion therapies for amelioration of chronic pain.

1.2.2 Previous Examples of Illusion-based Therapies

Illusion-based therapy has been previously used for pain conditions such as complex regional pain syndrome and phantom limb pain, both of which have been posited to have substantial cortical involvement. These pain conditions have been treated with mirror therapy, which involves positioning a mirror between the limbs so that the image of the non-affected limb gives an illusion of normal movement or appearance of the affected limb. Looking specifically at complex regional pain syndrome, McCabe et al. (2003) found evidence for immediate analgesic effects of mirror visual feedback therapy for those who had early complex regional pain syndrome, defined as less than 8 weeks of symptoms. McCabe et al. (2003) also found that for those experiencing pain for around a year, there was a reduction in stiffness of the affected limbs. This analgesic affect interestingly though, was not found in those with chronic complex regional pain syndrome.

Support for mirror therapies for chronic pain conditions, however, comes from phantom limb studies. Phantom limb pain occurs in around 90% of limb amputees and is thought to be based in a mismatch between visual feedback and proprioceptive representations of the affected body part (Melzack, 1990), similar to the mismatch in radiographic and symptomatic pain in the majority of chronic pain conditions mentioned previously. Mirror therapy has been found to be extremely effective for phantom limb pain, with reports of near 100% efficacy at reducing pain (Chan et al., 2007). Mental visualisation therapy, however, showed only 33% of participants experiencing a reduction in pain, and 67% reported a worsening of pain (Chan et al., 2007). This highlights that real-life visualisation of an illusory limb, such as in mirror therapies, is far superior to mental visualisation of a limb for treating chronic pain conditions, such as phantom limb pain and complex regional pain syndrome.

1.2.3 Multi-Modal Body Illusions for the Treatment of Chronic Hand-Based Pain

Looking specifically at hand-based chronic pain, the literature focusses on multi-modal body illusions. Multi-modal illusions typically consist of both tactile and visual inputs to the participant. These illusions are often delivered using an augmented reality system that presents real-time video capture of the hand, from the same position and perspective as if the hand were being viewed directly (Preston and Newport, 2011). This allows for the experimenter to deliver tactile manipulations, such as gently pulling or pushing the hand, whilst the participant views their hand either stretching or shrinking in the augmented image. This therapy was tested in 20 OA patients, where 85% reported at least 50% reduction of the reported pain in the affected hand area, and impressively, around 33% of patients reported temporary elimination of all pain (Preston and Newport, 2011).

These findings were replicated recently by Preston et al. (2020), with a larger sample size of 38 OA patients, wherein a 39.6% pain reduction was seen in stretching illusions and a 28.1% reduction was seen in shrinking illusions. Although no significant difference in overall pain reduction was seen between illusion types, the shrinking illusions did not improve perceived flexibility of the affected area, whist stretching illusions did. Therefore, stretching illusions were commented to have potentially more clinical importance than shrinking illusions, as there is more of a holistic therapeutic advantage, along with more patients reporting clinically relevant levels of pain reduction.

When assessing resizing illusions in participants without chronic pain, but who are exposed to an experimentally induced painful stimulus, such as heat, research has found that viewing magnified or minified reflections of one's hand does not appear to influence pain perception (Wittkopf et al., 2018). This therefore highlights that the cortical misrepresentations that appear to be present in chronic pain conditions could be what drives the resultant analgesia from resizing illusions, as when these misrepresentations are not present, such as in a sample of participants without chronic pain, the analgesia is not found.

1.2.4 Rationale for Uni-Modal Visual Body Illusions

Despite the analgesic effects seen in the multi-modal illusions previously mentioned (Preston et al., 2020; Preston and Newport, 2011), this sort of illusion is not very applicable as an ongoing treatment option for those living with chronic hand-base pain. This is because the implementation of the illusion requires large, cumbersome equipment and an experienced researcher to deliver the tactile inputs of the illusion. For the illusion to benefit people living with chronic pain, it needs to be accessible. Part of this accessibility means assessing if the multi-modal aspects of the illusion, notably the touch and the visual manipulation of hand / finger size, are required for the induction of analgesia, or if a uni-modal visual illusion would be able to elicit similar levels of analgesia.

When looking at the possibility of sufficient uni-modal visual illusions, synchronous visuotactile stimulation has been found not to be required to trigger subjective embodiment during bodily illusions. Looking first at full body illusions, visual capture alone has been found to elicit embodiment in both immersive virtual (Maselli and Slater, 2013) and physical environments (Carey et al., 2019). When moving to visual manipulations of a specific body part, embodiment has been reported when viewing an illusion of an elongated arm (Schaefer et al., 2007) and changes to embodied perception have also been reported from visual-only manipulations of the hand (McKenzie and Newport, 2015).

Furthermore, referring again to the rubber hand illusion as a theoretical basis for these hand-based illusions, Ferri et al. (2014) were able to demonstrate that tactile stimulation was not required to induce the illusion, positing that the expectation of tactile stimulation based on the visual stimulation alone was sufficient for the embodiment of the hand in the illusion.

1.2.4.1 Future Research

Given that embodiment can therefore be elicited by visual input alone, it is logical that the analgesia experienced by visuotactile illusions could also be experienced by visual-only illusions, creating an avenue for future research. This then highlights the possibility for illusion therapies to be delivered without such large, cumbersome equipment, and with chronic pain patients being able to deliver the illusion without the presence of a researcher.

1.2.5 Auditory Inputs During Resizing Illusions

Research into bodily resizing illusions typically focuses on the combination of visual and tactile inputs for multisensory integration. Multisensory integration is the combination of several sensory inputs to give a holistic experience of a stimulus. However, there is also evidence to support a facilitatory role of auditory input for visual manipulations. Studies have investigated the addition of auditory inputs during visual detection tasks, finding that the addition of auditory stimuli enhanced overall efficiency in difficult detection tasks (Frassinetti et al., 2002). It has also been found as an inverse effect, wherein the addition of visual cues to an auditory task improved detection of a low-intensity sound (Lovelace et al., 2003). There is also evidence supporting audio cues modulating tactile perception, which comes from a study by Zampini and Spence (2004), which found that increasing the overall volume and / or the amplitude of high frequency sounds, combined with the tactile input of biting a potato chip, increased the reported crispness of the chip.

The role of auditory input in multisensory interactions has also been found to influence body representations regarding perceptions of body size and length (Tajadura-Jiménez et al., 2012), along with altering perceived material properties (Senna et al., 2014) and weight (Tajadura-Jiménez et al., 2015) of the body. Looking specifically at visual, tactile, and auditory inputs in the rubber hand illusion, the illusion which underpins theoretical accounts of the subjective embodiment of resizing illusions, O'Mera (2014) found with the use of proprioceptive drift tasks that the addition of auditory inputs consistent with the visual and tactile inputs of stroking the hand, here they used the sound of sandpaper scratching the skin, heightened the illusory experience more than when white noise was added to the illusion. Proprioceptive drift tasks are often used as an index of body schema, which is the experience of one's body relating to action and interaction with the physical world. Radziun and Ehrsson (2018) also looked at the addition of ecologically relevant auditory inputs to the rubber hand illusion by using the sound of a surface being stroked with a paintbrush and used subjective questionnaires along with proprioceptive drift tasks and found that synchronous auditory cues made the illusion stronger compared to when using asynchronous auditory cues, in line with findings from O'Mera (2014).

The addition of auditory input in the studies mentioned thus far all include naturalistic auditory input, that being experimental auditory input that is consistent with the real-life auditory input that we are used to encountering in everyday life. However, Tajadura-Jiménez et al. (2017), looked at the influence of non-naturalistic auditory inputs, to see if this still resulted in changes to body perception. Here, they used changes in pitch, due to their associations with a change in height or size (Hubbard, 2018) whilst not typically being associated with bodily movement. They found that when participants closed their eyes and pulled their right index finger with their left hand with an accompanying rising pitch sound (700 – 1200Hz), they estimated the length of their index finger to be longer than when this pulling was accompanied with either a descending (700 – 200Hz) or constant (700Hz) tone and termed this the "Auditory Pinocchio" effect.

1.2.5.1 Future Research

Given previous findings that the addition of naturalistic auditory input in the rubber hand illusion (O'Mera, 2014) and the addition of non-naturalistic auditory input in resizing manipulations without visual inputs (Tajadura-Jiménez et al., 2017), it is plausible that the addition of auditory input could heighten illusory experience when using augmented reality to induce resizing illusions using visual and tactile inputs. Non-naturalistic auditory input would be favourable over naturalistic input for resizing illusions, as there is no clear naturalistic sound associated with one's finger / hand changing size. Furthermore, it is possible that this increase in illusory experience could result in chronic pain patients experiencing a greater reduction in pain. The addition of auditory input to visual resizing illusions would also allow for multisensory integration within an accessible form of the resizing illusion, removing the need for tactile inputs to give this multisensory component.

1.3 Methodological Approach and Overview

1.3.1 Neuroimaging

Various neuroimaging methods have been used to investigate multisensory brain mechanisms, such as those used when observing multisensory illusions. Parietal, temporal, and premotor responses are commonly observed in functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) studies which use both visual and somatosensory stimuli (Macaluso et al., 2001; Macaluso and Driver, 2001). Looking at electroencepholograpgy (EEG) studies, the parietal area specifically has been proposed as a processing site of integrated multimodal information (Kanayama et al., 2007). This is due to several studies demonstrating a relationship between gamma-band oscillations (at frequencies above 30Hz) and integration of multisensory processes across both audio and visual stimuli (Kaiser et al., 2005; Sakowitz, 2005; Senkowski et al., 2005).

Looking specifically at visuotactile stimulation, such as that used in multisensory hand-based illusions, power increases have been observed in the gamma band (40–50 Hz) in parietal regions 200–250ms into congruent visuotactile stimulation during the rubber hand illusion (Kanayama et al., 2007). This increase in gamma band activity in the congruent condition was later replicated and was found to exist in virtual reality environments (Kanayama et al., 2021). The researchers posited that the increased gamma-band activity is likely related to crossmodal promotion effects, which refer to presentations of both visual and tactile stimuli at the same location, which results in faster reaction times in a tactile discrimination task. However, there is much literature surrounding EEG studies looking at activity in this time course and frequency range which suggest a relation to more general cognitive processes, such as visual binding (Rodriguez et al., 1999; Tallon-Baudry et al., 1997), and memory performance (Gruber and Müller, 2006). Therefore, gamma-band activity could instead reflect general processes rather than being specific to multimodal integration. Kanayama et al. (2021) however, argue that since the gamma response in their study occurred after activation of the primary and secondary somatosensory areas (40–140ms), it is likely related to crossmodal promotion instead, reflecting an early stage of multimodal stimulus integration, which occurs subsequently to modality-isolated stimulus processing in somatosensory areas. Therefore, highlighting parietal regions as potential seats of multisensory integration.

Further research supporting the role of parietal regions within multisensory processing comes from Macaluso and Driver (2001) who used fMRI, and from Macaluso et al. (2001) who used PET imaging, both highlighting the temporo-parietal junction as a site involved with sustained spatial attention processing for visual and tactile stimuli. Furthermore, Ehrsson et al. (2004) used fMRI and the RHI to assess areas involved in body representation and multisensory integration and found premotor areas to be associated with body representation, with links extending into areas of the parietal cortex and cerebellum, in addition to finding activation in parietal areas related to integration of visual and tactile sensory inputs during the illusion. This is further supported by Kanayama et al. (2021) who observed activation over parietal electrode sites during visuotactile congruent conditions, but not incongruent conditions, indicating again the role of the parietal area in multisensory integration.

Interelectrode synchrony should also be considered when understanding the neural mechanisms behind visuotactile hand-based illusions. Kanayama et al. (2007) found increased interelectrode synchrony of gamma-band activity in congruent (illusion) conditions, but not in incongruent (non-illusion) conditions, indicating that the process of multimodal integration between visuotactile stimuli might not only be centred on parietal regions, but could also require neural synchronization (Kanayama et al., 2007).

EEG research has also pointed to the existence of EEG components related to multisensory integration within theta bands. Theta band (3–8 Hz) activity has been observed between 100 and 300ms post stimulus and is then found to be followed by gamma band activity (Kanayama et al., 2021). Whilst gamma band activity was observed around the parietal region and showed greater activity to spatially congruent visuotactile tasks, theta band activity was found around frontal sites and showed greater response to spatially incongruent visuotactile stimulation. When assessing theta activity between real and virtual reality environments, Kanayama et al. (2021) found significant differences in theta activity, wherein there were stronger activations in the real environment compared to the virtual reality environment. Therefore, positing that in virtual reality environments, visuotactile mismatch could be unresolved, meaning that the information would be unintegrated in both congruent and incongruent conditions. This leads to the theory that increases in theta power could be attributed to the cognitive load required to process incongruent visuotactile information.

Research further supporting the frontal location of this theta activity comes from Petkova et al. (2011), who using a full body ownership illusion and fMRI, found increased activity in the ventral premotor cortex which they linked to construction of ownership of the body, due to this activation being stronger when body parts were attached to a whole body than when they were viewed alone. This theory is also supported by Kanayama et al. (2017) estimating theta band activity to be located at the premotor area, which was subsequently expanded by the finding that theta band oscillations in frontal areas corresponded to error-related responses, cognitive load, and control processes, all elicited in frontal areas (Kanayama et al., 2021). Therefore, the current literature suggests strongly that theta oscillations linking to multisensory disintegration are located in frontal / premotor areas.

1.3.2 Why EEG?

Considering that the findings mentioned previously about the neural basis for multisensory integration have consisted of fMRI, PET, and EEG studies, it is important to discuss briefly why EEG is the modality chosen within this thesis to attempt to understand the neural mechanisms behind multisensory hand-based illusions.

Although fMRI and PET are useful techniques to understand the location of the neural activity involved in these illusions, these techniques lack precise temporal resolution, which is extremally useful to examine neural activity in direct response to the induction of the illusion and in clinical studies, has the potential to examine the temporal onset of the analgesic effects. EEG and magnetoencepholograpgy (MEG) offer superior temporal resolution to investigate and distinguish whether multi-modal integration is most linked to early sensory or later cognitive stages of information processing (Kanayama et al., 2007). An issue with MEG, however, is that since the technique relies on detecting very weak magnetic fields to capture brain activity, it is not possible to deliver the hand-based illusion, which requires metal equipment, in a MEG scanner, therefore resulting in EEG being the most appropriate neuroimaging technique to be used.

The techniques deployed in resizing illusion consist of stretching or shrinking a participant's hand / finger. These techniques therefore capitalise on the temporal benefit of EEG, since the induction of the stretching / shrinking illusion has clear temporal onset and given that the experience of the illusion can only occur in the few seconds that the finger / hand is being manipulated makes it possible to use EEG to pinpoint the neural evoked potentials in response to subjective illusory experience, over previously mentioned theta, and gamma band oscillations.

Another benefit of using EEG is that several previous studies that have looked at the neural basis for multisensory illusions have also used EEG, thereby making any findings from this research comparable to previous research, which increases the replicability and validity of findings in this area of research.

1.3.3 EEG Paradigms

There are several ways to use EEG to understand the neural underpinnings of resizing illusions. Techniques consist of continuous EEG recording whilst presenting different experimental conditions to participants, collecting event related potentials which measure brain responses that are the direct result of a specific sensory, cognitive, or motor events, and using sensory evoked potentials which are electrical potentials recorded from the central nervous system when a sensory organ is stimulated which are phase-locked to a stimulus (Vialatte et al., 2010). Additionally, it is possible to use steady state evoked potential which are repetitive sensory evoked potentials and consist of discrete frequency components that remain constant in their phase and amplitude over successive repetitions (Victor and Mast, 1991). Within this thesis, continuous EEG recording and steady state evoked potentials will be used to probe understanding of the neural underpinnings of resizing illusions.

Continuous EEG recording consists of sampling data from multiple sensors at multiple time points across several frequency bands during different experimental conditions. Due to the collection of data from multiple time points and sensors, during statistical analysis there arises the issue of correcting for multiple comparisons within traditional parametric statistical frameworks. Therefore, to solve the issue of multiple comparisons, a non-parametric framework is needed. Nonparametric tests were first proposed by Blair and Karniski (1993) for testing the difference between MEG and EEG waveforms at a particular sensor, and later a framework was created for topographies at particular timepoints (Achim, 2001; Galán et al., 1997; Karniski et al., 1994). Nonparametric cluster-based permutation analysis is proposed as a technique to solve the multiple comparisons issue for multisensory analyses statistically (Maris and Oostenveld, 2007). Here, a one-sample t test statistic and p-value are calculated for each sensor and timepoint, using a threshold, traditionally of $p < .05$, resulting in a list of clusters with significant elements being produced. The largest cluster is then stored, and a null distribution is built from random sets of permutations (typically 1000 sets) of the experimental condition labels. The original clusters are then compared to the null distribution and any clusters falling outside of the 95% confidence intervals are retained. This approach controls for the multiple comparisons issue at the cluster level and the permutation approach accounts for any correlational structure within the data.

Next, regarding steady state evoked potentials, there have been several studies on visual and auditory steady state evoked potentials (Vialatte et al., 2010), but few looking at somatosensory steady state evoked potentials. Initially electrical stimulation of peripheral nerves was used as a standard practice in somatosensory evoked potential research, but this technique was reported as uncomfortable and quite ineffective (Fox et al., 1987). Snyder (1992) developed a new practice of looking at somatosensory steady state evoked potentials using a vibratory technique consisting of variable modulation frequencies and found the greatest signal to noise ratio to be near 26 Hz. Since steady state amplitude modulated vibration is a continuous and phase-locked technique, which makes it very suitable for evoked potential recordings (Fox et al., 1987). There is, however, some disparity in the ideal frequency to be used. Whilst Synder found the optimal modulation frequency at around 26 Hz, Tobimatsu et al. (1999) found this to be closer to 21 Hz, with Tobimatsu et al. mentioning the differences in peak frequencies likely being attributed to differences in calculating signal to noise ratios and potentially missing modulation frequencies in Snyder's initial work.

The topographical representation of the somatosensory cortex has been found, in animals, to adapt dynamically depending on situational requirements and is shown to reflect a perceived rather than the actual location of a peripheral stimulus, such as a hand (Chen et al., 2003; Eysel, 2003). Modulation of the primary somatosensory cortex has also been found in humans undergoing an experimental manipulation of perceived body image. Schaefer et al. (2007), manipulated visual and somatosensory inputs to elicit an illusion of an elongated arm and using neuromagnetic source imaging found a corresponding modulation of the primary somatosensory area. Briefly, the more the subjects felt the subjective experience of an elongated arm, the more the cortical distance between the first and fifth digit decreased, showing the topographical representation of the somatosensory cortex being modulated by perceived location of a peripheral stimulus in humans. This in turn demonstrates that our understanding and interpretation of our body is not fixed and can be altered by manipulations of sensory, visual, or proprioceptive information, such as those manipulated in multisensory hand-based illusions. Specifically looking at stretching illusions, such as those found to reduce pain in OA (Preston and Newport, 2011), theories suggest that they directly impact the neural representations of the body, including the somatosensory cortex, and therefore are posited to potentially elicit detectable changes in steady state evoked potentials.

1.3.3.1 Future Research

The technique of continuous EEG recording is suitable for detecting differences between experimental conditions, and therefore is appropriate for research focusing on discerning the different neural signatures of multimodal and unimodal resizing illusions. Steady state evoked potentials are useful for assessing the changes in somatosensory representation between different conditions, and between participants with and without chronic pain undergoing resizing illusions. Changes in somatosensory representation have been evidenced using MEG (Schaefer et al., 2007), however there has not been research into the somatosensory changes in multisensory or unimodal hand-based illusions using EEG to look at steady state evoked potentials. Therefore, there is scope to investigate potential changes in somatosensory cortex representations during illusory finger stretching. In participants without chronic pain, EEG research would help to better understand the neural underpinnings of resizing illusions, and in participants with chronic pain, EEG will help to understand the differences between participants with and without chronic pain, in addition to improving understanding of the neural basis of the analgesic effects seen in previous multisensory illusions, since these illusions are thought to directly impact neural representations of the body, including the somatosensory cortex.

1.3.4 Behavioural Tasks

In addition to neuroimaging measures, behavioural tasks can be used to assess experiences of resizing illusions. Behavioural tasks allow insight into more objective measures of one's experience when undergoing different resizing illusion conditions.

Previously, a behavioural measure called 'proprioceptive drift' has been used to assess changes in the proprioceptively perceived position of a participant's hidden body part (Davies et al., 2013). Previous research assessing proprioceptive drift during the rubber hand illusion have produced conflicting results regarding the influence of the illusion on body schema and body image. Kammers et al. (2009) investigated the relationship between body schema and body image using the rubber hand illusion with a reaching proprioceptive drift task wherein participants were asked to reach with one hand to point to the tip of the index finger of the other hand in a single movement (body schema) or to verbally report when the experimenter's moving finger matched the felt location of their own finger (body image), finding that only body image measures regarding limb ownership were sensitive to distortion, finding no effect on body schema. In contrast, Newport et al. (2010) used augmented reality and a dot touch proprioceptive drift task with supernumerary limbs to assess body schema using a virtual version of the rubber hand illusion and found that distortions in body schema were apparent, evidenced through pointing errors in the dot touch task that were consistent with the remapped limb position. Therefore, procprioceptive drift can be used as a measure of illusory experience, but there is some disagreement in the field regarding how bodily illusions impact on our body image and body scheme. Using proprioceptive drift tasks alongside resizing illusions could ehnance our understanding of how body image and body schema interact under different presentations of bodily illusions.

1.3.5 Questionnaires and Rating Scales

Alongside behavioural tasks such as those assessing proprioceptive drift, questionnaires and rating scales can be used to gather data about a participant's subjecitve experience of a bodily illusion.

Previous research has often used questionnaires to assess illusory experience during bodily illusions (Kalckert and Ehrsson, 2012; Kilteni and Ehrsson, 2017; Matsumiya, 2021), with the typical presentation of the questionnaire giving a statement about the illusion and then a Likert or visual analogue scale for the participants to give their rating of agreement with the statement given. Visual analogue scales allow for more discrete measures of illusory experience than Likert scales, as they typically comprise a scale of 0 - 100 rather than a scale of -3 - +3 given with Likert scales. This added discretion in ratings means that the nuances of one's experience of the illusion can be gathered, meaning more descriptive conclusions regarding subjective experience can be made. However, it is sometimes the case that the level of detail that a visual analogue scale can give is not needed for the research question, and a Likert scale giving levels of agreement or disagreement with a statement is sufficient for gaining an understanding of how participants perceive an experience, such as when collecting data from a wide sample of participants about the experience of living with chronic pain. Both Likert and visual analogue scales will be used throughout this thesis to assess subjective experiences of resizing illusions, and of people's experiences of chronic pain conditions.

1.3.6 Focus Groups

To understand the experiences of people living with chronic pain, neuroimaging, behavioural, and questionnaire measures can only give so much detail. When personal experiences are transferred into quantitative data, the essence of someone's journey with their chronic pain often gets lost. Including qualitative methods allows for a much richer form of data collection, where participant's voices can be heard. Focus groups are one way in which life experiences can be collected as qualitative data. The benefits of focus groups with multiple participants compared to interviews with only one participant, is that those attending can feel support from their fellow participants that their thoughts and feelings are not experienced in isolation. Focus groups also allow for more qualitative data to be collected from more participants over a shorter time scale than one-on-one interviews. It is for these reasons that when considering how one lives with chronic pain, a focus group technique will be used within this thesis.

There are several different types of methods used for qualitative data collection. Interviews can use either structured, semi-structured, or unstructured approaches to qualitative data collection (Gill, 2008), whereby the transcript used as a basis for the interview differs depending on the level of structure wanted. Focus groups are most similar to semi-structured interviews (Gill, 2008), whereby there is often a transcript of questions or prompts, but the nature of having several participants attending the session allows for a natural flow of ideas and narrative. A large benefit of using focus groups compared to interviews is that focus groups allow for the generation of information on collective views, and can provide the meanings, both personal and group level, that lie behind those views. The nominal group technique (NGT) is a method often used in focus group research that allows for the integration of qualitative narrative and quantitative voting. A NGT focus group obtains the views of experts on a given topic to bring about group consensus (Harvey & Holmes, 2012). Within this thesis, the qualitative data collected will be through the use of NGT focus groups, so that participant's personal views can be heard, and a consensus can be reached regarding group views.

1.3.7 Research Philosophy

Open and reproducible research is important within any field of work. However, when research involves patient groups and can have an impact on treatment outcomes for these patient groups, the need for research to be open, reproducible, accessible, and replicable is vital. Patients give their time and energy when taking part in research, and if the basis of this research is not rooted in open research practices, then the researchers are doing a disservice to their participants.

With this research philosophy in mind, all work within this thesis has open data and code. The only data not made publicly available is that from the qualitative data in Chapter 2 which could identify participants. All work published from the research within this thesis is published open access, so that everyone, including patients, can access the findings. Lay summaries of work involving patients with chronic pain were created and disseminated to all interested participants, to aid accessibility of research findings (Project communication documents - Chapter 2: https://osf.io/98yph; Chapter 6: https://osf.io/k2smb). Chapters 4, 5, and 6, are all computationally reproducible, with links to open source code given alongside published manuscripts and preprints. All work within this thesis was pre-registered, and Chapter 5 underwent several rounds of peer-review on this pre-registration before data were collected.

It is hoped that the open research practices followed throughout this thesis give the best chance of this work being helpful to the understanding and implementation of non-pharmaceutical treatment approaches for chronic hand-based pain.

1.4 Summary

This introduction provides a basis for the subsequent experiments to be conducted within the thesis, with the background literature for potential future research applications discussed. The overall narrative is that chronic pain affects a large proportion of the population and adds pressure to the health care system, whilst current drug / surgical treatments appear ineffective. Therefore, there is rationale to investigate other forms of treatment to help this patient population, in addition to investigating patient experiences when taking part in research studies. Given the theoretical underpinnings of chronic pain, with the inclusion of predictive coding and central sensitisation accounts, there appears rationale to use resizing illusion therapies as a method for pain reduction. Research in this area has already been conducted and provides convincing accounts of the analgesic potential of such treatments in a multi-modal capacity, but the potential for using a unimodal visual therapy, or a visual-auditory therapy, is yet to be understood. In addition to investigating the experience of unimodal and visual-auditory illusion therapies, there is also a rationale for investigating the neural response when experiencing illusory resizing, to gain a further understanding of the neural mechanisms during these illusions in participants without chronic pain, and of those behind the associated analgesia in chronic pain patients. Should these experiments provide useful evidence for the application of these illusions for the treatment of chronic hand-based pain, this will directly address the issues mentioned surrounding ineffective current pain management treatments and provide an alternative therapy for the growing population of chronic pain sufferers.

1.5 Thesis Overview

The main objective of this thesis is to investigate and understand multisensory resizing illusions as a therapy for hand-based chronic pain using augmented reality, EEG, and behavioural measures.

Chapter 1 offers a general introduction that includes a background to chronic hand-based pain and the current treatments that are offered, before commenting on illusion therapies in general, leading to the rationale for multisensory resizing illusions to be used to provide analgesia. Previous research using unimodal-visual presentations of illusions is discussed along with the feasibility of using non-naturalistic auditory input within resizing illusions. Specific narrative is given regarding why EEG is the neuroimaging method of choice and details the specific EEG paradigms to be used to investigate the neural underpinnings of resizing illusions.

Chapter 2 reports the results of a two-phase study looking at the barriers and facilitators that exist for people with chronic pain conditions when taking part in research. Phase 1 involved online focus groups to generate barrier and facilitator items for thematic analysis, and Phase 2 used the themes generated within Phase 1 to assess wider agreement and disagreement with these themes in a larger sample of people with chronic pain conditions across the UK.

Chapter 3 recruited a sample of participants without chronic pain and used EEG to investigate the neural signatures of multimodal (visual & tactile), uni-modal visual, and incongruent visuo-tactile resizing illusions as well as using questionnaire reports to assess subjecitve illusory experience.

Chapter 4 presents a study using a sample without chronic pain and used non-naturalistic auditory input (a rising pitch tone) as an additional sensory input during visual and visuo-tactile presentations of resizing illusions. Subjective experience was measured using a self-report questionnaire and performance-based tasks were used to index more objective measures of illusory experience. Two performance-based tasks are used; a dot touch proprioceptive drift task indexing body schema, and a ruler judgement task indexing body image.

Chapter 5 reports the results of an EEG study using somatosensory steady state evoked potentials and vibrotactile stimulation (at 26Hz) of the index and middle fingers within participants without chronic pain when undergoing four different presentations of resizing illusions; multisensory (visual & tactile) resizing, unimodal visual resizing, a non-illusion condition with tactile input, and a non-illusion condition without tactile input. A subjective experience questionnaire was also given to assess illusory experience.

Chapter 6 presents the results of a study wherein participants with chronic hand-based pain underwent the same experimental conditions and used the same measures presented as within chapter 5, but with the addition of a visual analogue scale being used to give a pain rating before and after each condition.

Chapter 7 summarises the findings presented within this thesis and discusses clinical and theoretical applications, as well as suggesting avenues for future research.

2 Chapter 2: Understanding Barriers and Facilitators to Non-Pharmaceutical Chronic Pain Research Engagement

This chapter has been adapted from: Hansford, K.J., Crossland, A.E., Baker, D.H., Preston, C.E., McKenzie, K.J. 2024. Understanding barriers and facilitators to non-pharmaceutical chronic pain research engagement among people living with chronic pain in the UK: a two-phase mixed-methods approach. BMJ Open, 14(12), e089676. https://doi.org/10.1136/bmjopen-2024-089676[1]

2.1 Abstract

Chronic pain is increasingly treated with non-pharmaceutical methods; however, treatment engagement is still dominated by pharmaceutical methods. Research assessing the barriers to uptake of non-pharmaceutical treatments highlights transportation problems, concerns regarding treatment efficacy and lack of support. However, there has not been research one step earlier in the treatment development pipeline; assessing barriers to taking part in research that develops non-pharmaceutical chronic pain treatment methods. A two-phase approach was used to assess barriers and facilitators to research participation for people living with chronic pain. Online focus groups were run in phase 1, generating qualitative data, whilst phase 2 used the themes identified within phase 1 to assess agreement and disagreement in a wider sample of people with chronic pain across the UK. Phase 1 identified the largest barrier to be "Distrust", relating to a distrust of medical and research professionals, distrust of confidentiality assurances, and distrust that the research would have impact. The greatest facilitator identified was "Improved Accessibility", which related to the accessibility of the research environment, the type of research being conducted, and accessible advertisement of the research within trusted settings. Phase 2 found around 80% agreement with all facilitator themes and a mix of opinions regarding barrier themes, highlighting the individuality of barriers experienced when living with chronic pain. Addressing the barriers and implementing the facilitators identified here ensures that patient participants are comfortable and safe within research environments. Furthermore, this project provides recommendations for researchers to follow to help increase patient engagement in research studies.

2.2 Introduction

Chronic pain, defined as pain lasting for more than 3 months (Merskey, 1986; NICE, 2021), is increasingly treated with non-pharmaceutical methods (without drugs / surgery) due to evidence that pharmaceu-

[1] The author, Kirralise Hansford, collected the data for this experiment, analysed the results, and wrote the manuscript under the supervision of Dr Catherine Preston, Professor Daniel Baker, and Dr Kirsten McKenzie. The experiment was designed jointly with Dr Catherine Preston, Professor Daniel Baker, and Dr Kirsten McKenzie.

tical treatments alone can be unsafe and/or ineffective (Chou et al., 2009; Patel et al., 2023). However, use of pharmaceutical treatment is still prevalent, with 25% of people in the US relying solely on pharmaceutical methods for chronic pain management (Harris, 2023), 96% of people with chronic pain in the UK receiving an opioid analgesic between 2004 and 2009 (Hart et al., 2015), and despite NICE guidelines (GID-NG10068) advising against pharmaceutical chronic pain treatments, prescription rates for pain killers are reportedly unchanged for years (NHSBSA, 2020). Research concerning the lack of uptake of non-pharmaceutical treatments has found that barriers include high costs, transportation problems, low patient motivation, healthcare appointment time conflicts, and concerns about non-pharmaceutical treatment efficacy (Austrian et al., 2005; Bair et al., 2009; Becker et al., 2017; Simmonds et al., 2015). However, no investigation has yet explored barriers and facilitators for participants taking part in research into non-pharmaceutical treatments, which is vital for their successful development and uptake.

In 2018, national standards were set for patient engagement in research, highlighting the importance of including patients when designing novel treatments (NICE, 2018). Patient engagement can lead to improved credibility of results, and improvements in direct applications to patient samples (Domecq et al., 2014), therefore, understanding barriers and facilitators for patient involvement is paramount. Previous work has found barriers for patient involvement in chronic pain research and/or clinical trials to include practitioners' lack of knowledge about conditions, poor communication, lack of knowledge about the nature of clinical trials, concerns about adverse side effects, misgivings relating to being used as "guinea pigs", and distrust of the medical community (Shukla et al., 2020; Vogt et al., 2018). Research assessing facilitators for people with chronic pain taking part in research, has found motivators to be social engagement/enjoyment, pain improvement/advancement of science, to seek relief of pain (both short- and long-term), to try a different drug, to have their pain taken seriously, and to receive compensation for taking part (Start et al., 2024; Wasan et al., 2009).

This study therefore aimed to address the apparent gap in literature by assessing the barriers and facilitators to participation specifically in non-pharmaceutical research. Phase 1 used a nominal group technique (NGT), commonly used to assess barriers and facilitators within online focus groups. Following this, phase 2 extended upon previous methods by using an online questionnaire to assess agreement/disagreement with the barriers and facilitators identified within phase 1 in a much larger sample, to assess the generalisability of the facilitator and barrier themes to the wider UK population with chronic pain. For phase 1, our preregistered hypotheses were that (i) transportation problems and (ii) the concerns regarding the efficacy of non-pharmaceutical treatments, would arise as top-most barriers, but there were no directional hypotheses regarding facilitators. We had no directional hypotheses for phase 2.

2.3 Chapter Structure

This chapter details a study comprised of two phases, methods and results for phase 1 will be presented first (sections 2.4 and 2.5), then methods and results for phase 2 will be detailed (sections 2.6 and 2.7), with discussion of both phases included in the general discussion (section 2.8).

2.4 Phase 1 Methods

2.4.1 Preregistration

The preregistration for this study can be found on OSF at the following DOI: https://doi.org/10.17605/OSF.IO/37SNZ. Slight deviations from the preregistration consist of the following:

- Phase 1 sample size aim was 30 participants minimum, and although 36 participants were recruited for phase 1, only 29 were able to take part in a focus group session.

2.4.2 Participants

Thirty-six participants with chronic pain conditions (defined as any pain lasting or recurring for more than 3 months) were recruited from the UK through contact with UK-based chronic pain support groups and online advertisement to take part in an online focus group. 7 participants could not attend their focus group or a subsequent session, leaving a final sample size of 29 participants (83% Female, 17% Male; Age = 20 − 78 years, M = 44.3 years). Demographic information for phase 1 participants can be seen in Table 2.1. A list of the chronic pain conditions within this sample can be seen in Appendix A, Table A1.

Table 2.1: Ethnicity and Highest Education Level Achieved for Phase 1 Participants.

Ethnicity	Ethnicity_Freq	Education_Level	Education_Freq
White	79%	Undergraduate Degree	31%
Asian or Asian British	7%	College (A-level equivalent)	31%
Mixed/Multiple Ethnic Groups	7%	Masters Degree	17%
Black, Black British, Caribbean, or African	3%	Postgraduate PhD or MD	17%
Other Ethnic Group	3%	Primary School	3%
		Secondary School	0%

Ethical approval for this research was gained from the Department of Psychology, University of York (ethics application code 950), in line with the Declaration of Helsinki.

2.4.3 Data Collecion

A Nominal Group Technique (NGT) was used to assess barriers and facilitators to participation in non-pharmaceutical chronic pain research. An overview of the NGT has been reported by Harvey and Holmes (2012), who recommend using face-to-face focus groups to obtain views of experts on a given topic and bring about group consensus. Here, the experts were people with lived experience of chronic pain. It is recommended that focus groups for the NGT are to be run with between 5-9 participants (Elliott and Shewchuk, 2002), however due to participant drop out, groups were run with between 2-7 participants. All focus groups were conducted online using Zoom video conferencing software (Zoom Video Communications, Inc., San Jose, CA, USA), version 5.17.7.

Participants were provided with a brief background to the study, and an explanation of key terms and procedures. Distinctions were made between pharmaceutical and non-pharmaceutical chronic pain treatments before the first question was presented to the group. Participants were asked about barriers to their participation in non-pharmaceutical chronic pain research; "What are some barriers to patients participating in research about chronic pain? In other words, why do some patients not want to participate or what makes it hard for them to participate?" along with a question regarding facilitators of participation in non-pharmaceutical chronic pain research; "What are some of the things that would make it more likely for patients to participate in chronic pain research? What makes it easier for patients to participate?" These questions were adapted from previous research using NGT to investigate barriers and facilitators to using non-pharmacological pain treatments and were presented in a random order for each group to remove ordering bias (Becker et al., 2017). After each question, participants were asked to silently write down as many responses to the question as possible in five minutes before the researcher asked each participant to say their responses aloud, or type using the chat function. The researcher wrote each response on an editable document (Google Forms, Google LLC, Mountain View, CA, USA) until each participant had all their answers recorded. Group discussion was encouraged to clarify any responses, and edit as necessary, in addition to consolidating any answers that the participants deemed to be identical or very similar.

Once the final list of answers was agreed upon, each participant was sent a link to the google form and anonymously voted on the most important (3 points), second most important (2 points), and third most important item (1 point). Researchers were blind to which response was given by which participant. The same process was completed for both the barriers and the facilitators question, after which the researchers tallied up the voting, giving the topmost barriers and facilitators for each focus group.

Phase 1 data from all focus groups can be seen at the following OSF page: https://osf.io/8y7rz/.

2.4.4 Data Analysis

To facilitate comparisons of items from each focus group across all sessions, researchers used thematic analysis through a deductive approach (Braun and Clarke, 2006) to categorise items into either facilitator or barrier themes based on a consensus of interpretation of the item meanings. A post-positivist approach was used for thematic analysis, to focus on the individual experiences of people living with chronic pain when considering taking part in non-pharmaceutical research (Kiger and Varpio, 2020). Through these approaches, three researchers (KH, AC, and CP) independently reviewed the raw data for familiarisation, before identifying patterns within the data set. They then created codes for each group of items, before placing these coded items into overarching themes within either the barrier or facilitator structure. An additional fourth researcher (KM) was included to facilitate discussion of theme review amongst the three researchers. Following this, 2 researchers (KH & CP) refined and defined the themes with the following agreements; Barrier themes percentage agreement: 87.03% (Berk, 1979; McDermott, 1988), Barrier themes Cohen's Kappa: 0.832 (strong agreement; McHugh (2012); near perfect agreement; Landis and Koch (1977)), Facilitator themes percentage agreement: 89% (Berk, 1979; McDermott, 1988), Facilitator themes Cohen's Kappa: 0.869 (strong agreement; McHugh (2012); near perfect agreement; Landis and Koch (1977)). This process resulted in the final list of themes agreed upon by all 4 researchers.

2.5 Phase 1 Results

From the 7 focus groups, 121 items were generated for barriers and 95 items were generated for facilitators. As a result of thematic analysis, 7 barrier themes were created and can be seen in Table 2.2: (1) Distrust; (2) Lack of Accessibility/Physical Practicalities; (3) Chronic Symptoms & Comorbidities, (4) Lack of Information, (5) Lack of Motivation, (6) Self-Identification/Eligibility, and (7) Cultural Barriers/Individual Differences. Table 2.3 shows the 5 facilitator themes that were created: (1) Improved Accessibility, (2) Positive Impact of Participation, (3) Detailed and Accessible Information, (4) Motivation, and (5) Safe Space.

Tables 2.2 and 2.3 show the themes identified, with the themes (and wherever relevant, subthemes) listed according to size, with the theme containing the most items listed first. All items from the focus groups are included within their associated theme, and the highest rated items by participants during the ranking section of the NGT are denoted with superscript text. Since items are collated across all focus groups, several themes contain more than one highest ranked item.

Table 2.2: Themes and subthemes for barrier items, with the topmost facilitators from a focus group indicated with a superscript “1st”, second topmost facilitators indicated with a “2nd”, and third topmost facilitators indicated with a “3rd”. Items which received votes but did not rank within the top 3 facilitators are indicated with an asterisk. Additional text has been added to some items based on the focus group recording that gives context to the item being raised and can be seen within square brackets.

Theme	Subtheme	Items
Distrust	Anonymity/	Anonymity (of participation)
	Confidentiality	Lack of trust of confidentiality of data
		Don’t want to share medical/personal information
	Impact of Research	Not knowing if the research will benefit me or others - 2nd
		Not being sensitized to the importance of such research - 2nd
		Implications for not taking pharmaceutical drugs*
		Lack of trust that it will lead to anything*
		Fear of toxicity/ side effects of treatments
		Poor understanding of how I can influence change/help the research
		Fear of addiction to pain treatments
		Don’t think research will make any difference
		A lack of seeing where the research can lead / not getting feedback
	Professionals / Setting	Lack of understanding about chronic pain - 1st
		Fear of scrutiny - 2nd
		Fear about what might be involved - 3rd
		Fear surrounding group situations - 3rd
		Previous negative experiences of taking part - 3rd
		Fear of the research process*
		Lack of trust of health professionals/researchers*
		Doctors not being interested in new or ongoing research*
		Distrust of medical professionals*
		Fear of judgment (friends, family, professionals)*
		Not wanting to talk about pain*
		General barriers to alternative treatments
		Concern of invalidation
		Fear of being judged
		Lack of belief about chronic pain
		Fear of judgement/stigma - people will think I am making the pain up, or not being able to relate
		Fear of sharing
		Judgement (for having chronic pain)
		Not wanting to talk about upsetting things
		Feelings of embarrassment
		Stigma around pain and disability
		Fear of invalidation of pain

		Invisibility of chronic pain
Lack of Accessibility/ Physical Practicalities	Travel	Travel
		Location of research studies (other locations/hard to travel to)
		Travel and pain that could get worse with travel
		Is it possible to travel to location?
		Winter - bad weather will stop people going out
		Travel issues
	Accessibility - Personal	Environments not conducive to research, particularly in public places/unknown environment - 3rd
		Accessibility of the research placement - 3rd
		Fear of losing control [of pain management] when participating (avoidance behaviours)
		Is venue accessible once there?
		Issues for attending in person
		Accessibility of research psychologically
		Lack of childcare
	Accessibility - Technological	Not having internet - 2nd
		Not having necessary equipment (e.g. laptop) - 3rd
		Lack of access to technology - 3rd
		Communication - visual and audio options (accessibility for those with additional needs and anyone with chronic pain)
		Access issues for technology
		Fearful of online tools
		Not having access to technology to participate
	Time	Not having time / cannot make dates offered - 3rd
		Limited time to take part - 3rd
		Being asked to participate at inappropriate times*
		Not having time to take part
		Lack of time
Chronic Symptoms & Comorbidities	Fatigue	Worry of future fatigue (as a consequence of taking part) - 1st
		Not having energy - 2nd
		Fatigue during research - 3rd
		Too much fatigue
to take part - 3rd		
		Not being able to commit to the research on the day [not enough energy]*
		Too much fatigue
	Psychological	Mental health issues - 3rd

	Symptoms	Psychological/social difficulties associated with pain (difficulty talking about psychological consequences) - 3rd In too much pain (physically/mentally)* Lowered mood reduces motivation to take part
	Physical Symptoms	Unpredictability of chronic pain (impact of pain on being able to participate due to fluctuation) - 1st Fear of increase in pain (in other areas) - 2nd Being too unwell - 3rd Being in too much pain to consider being involved in research - 3rd In too much pain (physically/mentally)* Being in too much pain to take part Pain preventing people taking part - how will I cope with participation? Worry pain will get worse Using hands to take part Taking part could exacerbate the pain
Lack of Information	Study Details	Not knowing research expectations (of you) - 3rd Not knowing what to expect Lack of information to know what to expect Lack of understanding about non-pharmaceutical treatments
	Recruitment/ Study Advertisement	Little or no awareness of research happening/Lack of advertising of research - 1st Not knowing about the research because it is not often spoken about - 1st Not being aware that research takes place/ not being mentioned in doctors' surgery - 1st Not knowing what research is out there - 2nd Unaware that there is anything beyond pharmaceutical - 2nd Researchers not reaching out into communities - 2nd Not knowing the research exists - 2nd Not knowing that there are non-pharmacological alternatives - 2nd Lack of information about how to participate / fear of unknown Lack of contact information to take part Don't want to take medication so avoid pain clinics etc [and therefore won't see advertisements] Not knowing where to find out about research studies
Lack of Incentivisation/ Motivation	Incentivisation/ Motivation	Lack of incentives to take part - 1st Doesn't help pain right now - 2nd Needing expenses for travel etc* Lack of financial renumeration

		Travel renumeration not coming before
		Compensation (must be worth it)
	Priority	Not a priority because of other pain - 1st
		Caring responsibilities being the focus - 2nd
		Burden: Not motivated to take extra responsibility - participation too much to do on top of pain management - 3rd
		Not a priority for managing time - 3rd
		Lack of motivation - 3rd
		Only focus on pain during crisis rather than prevention and management
		Lack of interest
Cultural Barriers/ Individual Differences		Lack of cultural understanding about experience of pain*
		Cultural differences in pain management/labelling*
		Not taking into account individual differences*
		Lack of culturally specific approaches in research
		Learning disabilities and sensory issues
		Lack of cultural specific approaches in research
Self-Identification/ Eligibility		Not feeling like you can take part if you don't have a diagnosis - 2nd
		Lack of diagnosis - 3rd
		Feel that pain is not bad enough, so feel that they should not attend*
		Not being 'poorly' enough to take part
		Denial
		Thinking pain is just a normal part of ageing

Table 2.3: Themes and subthemes for facilitator items, with the topmost facilitators from a focus group indicated with a "1st", second topmost facilitators indicated with a "2nd", and third topmost facilitators indicated with a "3rd". Items which received votes but did not rank within the top 3 facilitators are indicated with an asterisk.

Theme	Subtheme	Items
Improved Accessibility	Practical Accessibility	Extra support - 1st
		Accessibility to research - 3rd
		Easy access to venue/internet - make it a local venue that is easy to reach and access*
		Having accessible research*
		Accessibility of location
		Public transport available
		Childcare options (in person testing)
		Access to pain relief/management at an in-person session
		Making in person research physically accessibly
		Offering assistance with technology

	Timings	Flexibility in when to participate (around pain) - 2nd
		Sweet spot' of pain level at the time - 3rd
		Flexibility for time of involvement - 3rd
		Shorter focus groups (around one hour) / breaks if longer sessions*
		Having several options for times of sessions / out of hours testing*
		Out of hours participation*
		Give data when the participant is able*
		Several options of dates/times for sessions
		Can be done in my own time
		Flexibility of times for research
		One hour as maximum (depends upon individual needs)
	Participation Options	Having both online and in person option available - 1st
		Remote participation (online) - 2nd
		More ways to participate (especially online; Zoom/Google Forms/Survey Monkey) - 2nd
		Flexibility of methods of research (shorter and longer options) - 3rd
		Preference for zoom - 3rd
		Flexible options about how to participate (paper/computer/phone)*
		Option to have researchers come to you*
		Options of where to go for the research*
		Flexibility for unpredictability (range of times as well as formats for participation)
		Different formats available to participate (e.g. paper vs. talking)
		Having a range of contribution methods (paper, telephone)
	Communication/ Advertisement	Putting information in community and medical spaces - 1st
		Awareness of the opportunities/More advertising through trusted routes, e.g. NHS/GP surgery/ - 1st
		Hear about research from GP/ trusted person - 3rd
		Hearing about research in trusted setting*
		Calls for taking part being easy to find and available to a wide range of people*
		Research information needs to be accessible (understood)
		Better communication (visual & audio - accessibility)
		Availability in different languages
		Clear publicising of research
		Better advertising: Sharing social media posts / Word of Mouth (Facebook / Twitter)
		Advertising the research
		Advertising on social media
Positive Impact of Participation	Impact on Day	Improvement in pain - 2nd
		Knowing there are others who experience the issues - 2nd

		Feeling a part of the community (others experiencing same things) / loneliness - 3rd
		Understand how it might impact pain on the day
		Knowing it won't influence my current pain levels
		Participating in a group
	Impact After	Research could facilitate potential new methods - 2nd
		Knowing if research can have long term benefits - 3rd
		More information about the benefits of the research - 3rd
		Get feedback about the research outputs (results)/ accessible - 3rd
		Better understanding of how their contribution can help*
		If the research can improve personal wellbeing*
		Have an idea about the possible outcomes of the research*
		Getting feedback about outcomes and a thank you for taking part*
		Follow up about what happens with the research*
		Knowing if the research will have medical implications*
Detailed & Accessible Information	Eligibility	Being clear about diagnoses that are relevant - 3rd
		Being able to invite other participants to take part/ knowing people who have taken part
	Research	Very detailed information about what to expect - 1st
		Knowing research aims - 2nd
		Clarity about group or one on one sessions - 3rd
		More information about the research and benefits - 3rd
		Clarity of what to expect*
		Confidence that the research is well founded*
		More information about what is involved*
		Being clear as to what adjustments can be made for the research
		Clarity how to participate (online/offline)
		Having more information about what the research is based on
		More information needed regarding what the research involves, aims, rationale
		Understanding existing research
		Knowing what will happen on the day (reduce anxiety)
Increased Motivation		Financial compensation for your time for participation - 1st
		Incentive for taking part (financial/ other) - 1st
		Improvement in pain - 2nd
		Research needs to be interesting and relevant - 2nd
		Paying people properly for their time in research - 3rd
		Easier access to healthcare - 3rd
		Paying people properly for their time in research - 3rd
		Reimbursement of travel expenses*
		Having incentives for taking part

	Altruistic motivations (helping others) Wider acceptance of non-pharmacological interventions
Safe Space	Approachable researchers - 3rd Smaller focus groups more comfortable / discuss in safe space / anonymity - 3rd Non-clinical/ non-academic setting for the study* Having researchers with lived experience* Discussion between researcher and participant (individualised) prior to participation to cater for needs* Feeling like others (researchers/professionals) care Understanding there is help available Videos of people involved/ researchers Being able to have a companion during the research Having researchers who are understanding

2.6 Phase 2 Methods

2.6.1 Preregistration

The preregistration for this study can be found on OSF at the following DOI: https://doi.org/10.17605/OSF.IO/37SNZ. Slight deviations from the preregistration consist of the following:

- Phase 2 planned to ask participants to confirm the themes reached through thematic analysis in phase 1, however this was deemed impractical without adequate training on thematic analysis for participants.
- Phase 2 stated inclusion of data where only 100% of the survey was completed, however after phase 1 highlighted that fatigue can act as a barrier to taking part in research, this was revised to acceptance of data if 100% of either the barriers or facilitators questions were completed.

2.6.2 Participants

103 participants with chronic pain conditions (89% Female, 10% Male, 1% Prefer not to say; Age = 20 – 80 years, M = 46.6 years) and based within the UK, responded to the phase 2 online survey. Demographic information for these participants can be seen in Table 2.4. A list of the chronic pain conditions within this participant sample can be seen in Appendix A, Table A2.

Table 2.4: Ethnicity and Highest Education Level Achieved for Phase 2 Participants.

Ethnicity	Ethnicity_Freq	Education_Level	Education_Freq
White	96%	College (A-level equivalent)	30%
Mixed/Multiple Ethnic Groups	2%	Undergraduate Degree	29%
Black, Black British, Caribbean, or African	1%	Masters Degree	19%
Other Ethnic Group	1%	Secondary School	15%
		Postgraduate PhD or MD	5%
		Primary School	2%

2.6.3 Data collection

After running the focus groups, a questionnaire was created containing all themes regarding both barriers and facilitators to taking part in non-pharmacological chronic pain research. This was distributed online and through chronic pain support groups to facilitate assessment of wider agreement or disagreement with the themes identified from the focus groups. Participants were asked to assess their personal perspective regarding each theme and respond with their level of agreement or disagreement. The questionnaire was created using Qualtrics (Qualtrics, Provo, UT), and included Likert scales ranging from -3 indicating strong disagreement to +3 indicting strong agreement, and 0 indicating a neutral opinion of the theme. The 7 themes identified as barriers in phase 1 were presented, along with the 5 themes identified as facilitators. Each theme was stated using a title, followed by a short definition, which was created using the items listed within the theme from the focus groups. For example, the theme "Distrust" was followed by "…this is described as having distrust of the level of anonymity and confidentiality or having a distrust of medical or research professionals". After all barriers themes were presented, participants were asked if there were any other barriers that they experience that were not mentioned within the themes presented. The same was asked following presentation of all facilitator themes.

The Phase 2 questionnaire, phase 2 data, and respective analysis code can be seen at the following OSF page: https://osf.io/8y7rz/. Date of Birth and Qualitative data have been removed to prevent participant identification.

2.6.4 Data Analysis

Data were exported from Qualtrics and responses ranging from +1 to +3 were classified as indicative of agreement with the theme and were coded with an "A", whilst scores of -1 to -3 were indicative of disagreement with the theme and were coded with a "D", and finally, scores of 0 were indicative of a neutral stance regarding the theme and were coded with an "N". Percentages were calculated for overall agreement, disagreement, and neutral responses, in line with the preregistration. Further exploratory analyses were conducted regarding the level of agreement and disagreement within each theme. The free text sections included within the questionnaire asked if the participant was aware of any additional barriers or facilitators that were not included within the themes mentioned, allowing for further exploratory qualitative analyses. This qualitative analysis of phase 2 data involved assessing if any items fit within an existing theme, or within a potential new theme/subtheme.

2.7 Phase 2 Results

Percentage agreement, disagreement, and neutral responses relating to each barrier and facilitator theme were calculated across all participants and can be seen in Figure 2.1.

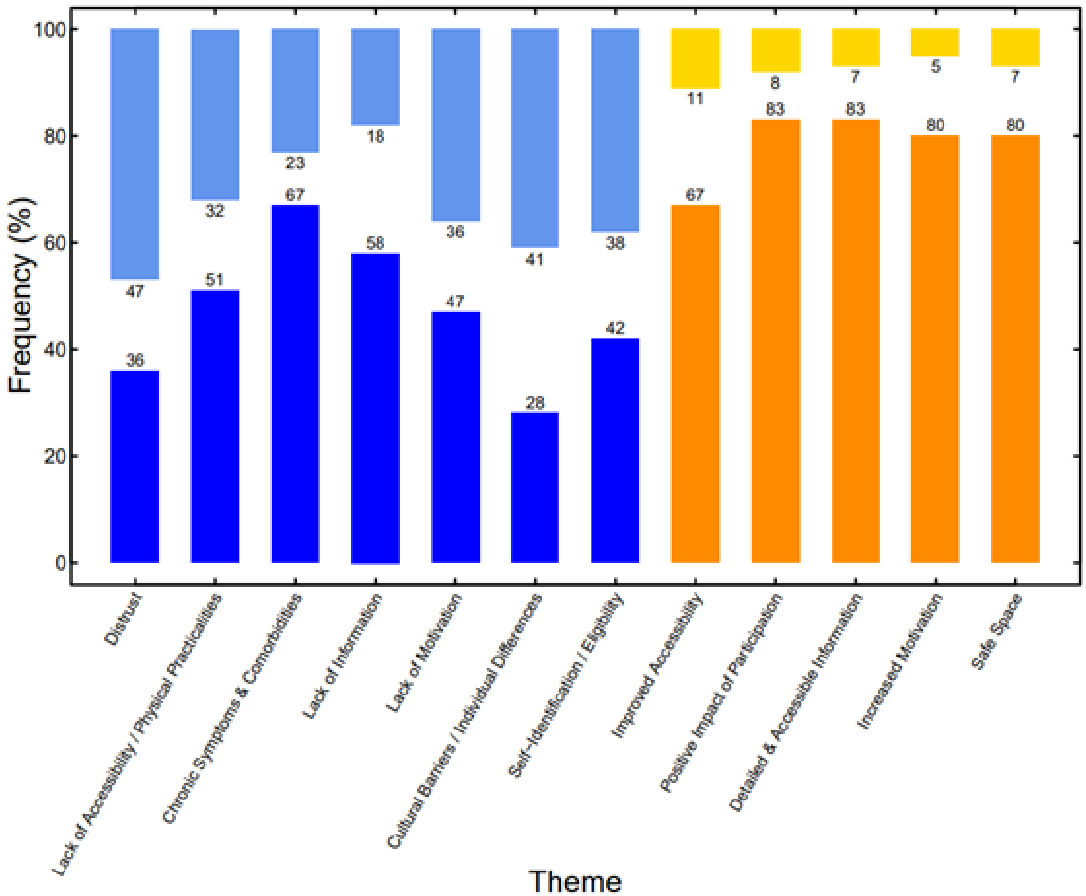

Figure 2.1: Percentage Agreement (bottom bars) and Percentage Disagreement (top bars) for each Barrier and Facilitator theme. Blue shaded bars represent Barriers whilst orange shaded bars represent Facilitators. The difference between the agreement and disagreement percentages gives the percentage of participants who gave a neutral response regarding their opinion of a theme.

Regarding agreement, the Barrier theme with the highest percentage was “Chronic Symptoms & Comorbidities”, closely followed by “Lack of Information”, with “Cultural Barriers/Individual Differences” getting the lowest level of agreement amongst the barrier themes. All facilitator themes achieved a similarly high level of agreement.

For disagreement, all themes had relatively low levels, apart from the barrier theme “Distrust”, where almost half of participants disagreed with this theme. This was followed by “Cultural Barriers/Individual Differences”, “Self-Identification/Eligibility” and “Lack of Motivation” having around 40% of participants disagreeing with these barrier themes. “Distrust” and “Cultural Barriers/Individual Differences” were the only two themes that showed more disagreement than agreement.

Exploratory analyses (Appendix A, Figure A1.1) showed a greater degree of variation (in terms of agreement/disagreement) with the phase 1 barrier themes, whereas there was moderate to strong agreement from phase 2 respondents with the facilitator themes identified in phase 1.

2.7.1 Analysis of Additional Barriers and Facilitators

Within the survey participants were asked to list any additional barriers/facilitators that they experience that differed to the ones mentioned. 22 participants mentioned additional barriers and 5 mentioned additional facilitators. Some participants mentioned more than 1 item within their responses. Following data familiarisation, two researchers (KH & DB) independently assessed whether these items comprised new themes or fit within an existing theme. Agreement between the two researchers was high for barriers items; Barrier theme allocation percentage agreement: 80% (Berk, 1979; McDermott, 1988), Cohen's Kappa: 0.789 (moderate agreement; McHugh, 2012; substantial agreement; Landis, 1977), and for facilitator items: Facilitator theme allocation percentage agreement: 84.61% (Berk, 1979; McDermott, 1988), Cohen's Kappa: 0.634 (moderate agreement; McHugh, 2012; substantial agreement; Landis, 1977). Both researchers agreed on the final allocation of items to existing themes.

Of the additional barrier responses, 8 could be placed within the "Lack of Information" theme, 6 within "Chronic Pain Symptoms & Comorbidities", 5 within "Self-Identification/Eligibility", 3 within "Distrust", and 4 within "Lack of Accessibility/Physical Practicalities". Importantly, within 2 responses the item "rarity of diagnosis" was mentioned, which whilst fitting under the theme "Self-Identification/Eligibility" could create a new subtheme pertaining to how common the diagnosis is, with less research likely available for those with rarer diagnoses.

Regarding facilitator responses, no new themes were identified, as 4 could be placed with the theme "Improved Accessibility" and 1 within "Positive Impact of Participation".

2.8 Discussion

This study assessed barriers and facilitators to non-pharmaceutical research participation for people with chronic pain. Although our hypothesised barriers "Transportation Problems", and "A lack of understanding of non-pharmaceutical treatments for chronic pain" were present, they were not found to be the largest, instead "Distrust" was the largest barrier theme identified, and "Improved Accessibility" was the largest facilitator theme. Overall, more people in phase 2 agreed than disagreed with each theme from phase 1, with two key exceptions: Barrier themes "Distrust" and "Cultural Barriers/Individual Differences". Exploratory analyses revealed larger variation within opinions for barrier themes whilst showing overall agreement across facilitator themes.

Phase 1 analysis found the topmost barrier to participation in non-pharmaceutical research to be a "lack of understanding about chronic pain" under the largest barrier theme "Distrust". This distrust of researchers' and medical professionals' understanding of the lived experience of chronic pain is unsurprising considering UK medical schools dedicate a median of only 13 hours to teaching pain medicine over 5 years, and only 4% have a dedicated pain science module (Shipton et al., 2018). Interestingly, phase 2 analyses highlighted that almost 50% of the wider sample disagreed with experiencing distrust, however, this is possibly due to a self-selection bias, as individuals who experience distrust of research are less likely to have taken part in our study. One further caveat is that phase 1 participants assessed barriers and facilitators for themselves and others living with chronic pain, whereas phase 2 participants only gave personal reflections. This difference likely explains the pattern of results seen, with phase 1 participants speaking to a distrust that others might have of researchers' and medical professionals' understanding of chronic pain.

Our finding that a lack of time is a barrier to participation was supported by the attrition data for phase 1, whereby 19% of participants recruited were unable to attend their focus group or a subsequent session. Although restrictive participation dates may not appear to be a barrier specific to those with chronic pain, the lack of control and unpredictability of chronic pain symptoms often results in participants needing to cancel participation at short notice (Crowe et al., 2017), therefore, this population group are likely disproportionately affected by this barrier. Further evidence for this barrier arose within our third largest barrier theme "Chronic Symptoms & Comorbidities", with phase 2 analysis finding this theme to have the highest overall agreement of barrier themes, with 67% of participants agreeing that it can prevent non-pharmaceutical research participation.

Considering the impact that research participation can have on individuals with chronic pain - from physical impact, time commitments, and psychological impacts - compensation and additional incentives must be given to participants. The facilitator theme "Increased Motivation" demonstrates that compensation can come from sources such as financial renumeration, pain improvement, travel reimbursement, and altruistic motivations. The facilitator theme "Positive Impact of Participation" highlights that feeling part of a community can also have long term benefits.

One of the most pressing barriers to participation, and arguably the easiest to fix, arose within the "Lack of Information" theme; people simply do not know research is happening. Participants mentioned that improving awareness of participation opportunities could come from advertising within community and medical spaces, such as the NHS, GP surgeries, and places of faith/worship. Participants highlighted that research advertisement should come through trusted routes, rather than unknown sources. The importance of accessible advertising, such as different formats (visual/audio) and different languages, was also emphasised.

The facilitator theme “Detailed and Accessible Information” received the highest level of agreement within phase 2, clearly reinforcing this need for inclusive research advertisement through trusted sources.

The barrier theme “Cultural Barriers/Individual Differences” received more disagreement than agreement within phase 2, likely due to the overrepresentation of white female participants in both samples. Nevertheless, a main concern within this theme related to learning disabilities and sensory issues, which is important to consider since research has demonstrated links between chronic pain and neurodivergence. Studies have highlighted links between joint hypermobility, which underlies several chronic pain conditions, and conditions such as Autism and ADHD (Csecs et al., 2022). Additionally, Fibromyalgia has been significantly associated with autistic traits (Ryan et al., 2022). Therefore, designing research studies which encompass learning and sensory accommodations is important to encourage participation from everyone with chronic pain. One barrier raised related to culturally mediated distinctions between experiencing chronic pain as a natural outcome of aging, or regarding chronic pain as pathological. However, since there were few items relating to this within our sample, it is important to consider conclusions based on this potential dichotomy as tentative and in need of replication in samples from more ethnically diverse populations. The barrier theme “Self-Identification/Eligibility” also raised concerns over knowing if you could take part without a specific diagnosis of a chronic pain condition, which is likely a further barrier for those from ethnically diverse backgrounds where diagnoses may not be as prevalent. Findings within this theme underscore the intersectional barriers that individuals with chronic pain from diverse backgrounds face when considering taking part in research, despite the relatively homogenous nature of our sample. A recommendation to facilitate participation from diverse backgrounds is to be clear what constitutes eligibility, showing a defined symptom profile (such as having lasting or reoccurring pain for more than 3 months; Merskey, 1986; NICE, 2021), rather than a list of diagnoses.

Another facilitator suggested was including researchers with lived experience of chronic pain. Although this may not always be possible to achieve within existing research groups, methods such as patient and public involvement in research, research co-production, or the inclusion of patient-experts within the research team can ensure that those with lived experience are included in the research process. Previous research assessing the barriers that patients with persistent pain face when acting as patient advocates, found a lack of financial compensation, and inflexible deadlines existed as barriers (Hartley & Penlington, 2023), which is directly supported by barrier items identified here relating to inflexible time and a lack of compensation, and maps directly to the facilitators found regarding a need for incentives, compensation, and flexibility within the research environment. This highlights that these concerns need to be considered when engaging with samples with chronic pain, either as participants or advocates.

Overall, despite the homogeneous nature of the sample in both phases, the data leads to several clear recommendations for improving non-pharmaceutical chronic pain research participation. When creating a research group, having approachable researchers and including people with lived experience is vital to address the distrust and fear that participants report experiencing when considering taking part. The environment in which research will be conducted must be accessible, comfortable, and ideally in a non-academic/non-clinical setting. Advertisement of participation opportunities should be in community spaces, through trusted communication routes and must include detailed and accessible information about the research aims and what is involved in taking part. Eligibility must detail specific symptom profiles to encourage participation from all ethnic groups, and researchers must be contactable to discuss accessibility requirements prior to participation. If participation could potentially increase pain, this must be made clear from the outset. During research sessions, accessible participation options including the use of public internet/computers, flexible timings/data input formats, and translation services must be given. Having the possibility of a friend or carer attending the research appointment should be accounted for and breaks must be offered to reduce fatigue. After participation, participants must be adequately compensated for their time and travel, and the longer-term benefits or implications of the research must be made clear. Finally, a lay summary of research findings should be offered to participants, to ensure they are aware the impact that their participation has had on research outputs.

2.9 Conclusions

This project addresses an apparent gap in our understanding of what prevents people with chronic pain conditions from taking part in non-pharmaceutical research. Across 2 distinct samples of participants, facilitators have been identified, and consolidated, and are recommended to be implemented in all applicable chronic pain research settings. Barriers and facilitators identified here are likely generalisable to both pharmaceutical and non-pharmaceutical projects, as there were limited items specifically related to non-pharmaceutical research identified during the focus groups. Considering these barriers and facilitators when developing research programmes for chronic pain treatment is likely to encourage involvement of individuals with chronic pain throughout the research process, and thus the likelihood of designing effective non-pharmaceutical therapies should be greatly increased.

3 Chapter 3: Distinct neural signatures of multimodal resizing illusions

This chapter has been adapted from: Hansford, K.J., Baker, D.H., McKenzie, K.J., Preston, C.E. 2023. Distinct neural signatures of multimodal resizing illusions. Neuropsychologia, 108622. https://doi.org/10.1016/j.neuropsychologia.2023.108622[2]

3.1 Abstract

Illusory body resizing typically uses multisensory integration to change the perceived size of a body part. Previous studies associate these multisensory body illusions with frontal theta oscillations and parietal gamma oscillations for dis-integration and integration of multisensory signals, respectively. However, recent studies also support illusory changes of embodiment from unimodal visual stimuli. This preregistered study (N = 48) investigated differences between multisensory visuo-tactile and unimodal visual resizing illusions using EEG, to gain a more comprehensive understanding of the neural underpinnings of resizing illusions in a healthy population. We hypothesised (1) stronger illusion in multisensory compared to unimodal, and unimodal compared to incongruent (dis-integration) conditions, (2) greater parietal gamma during multisensory compared to unimodal, and (3) greater frontal theta during incongruent compared to baseline (non-illusion) conditions. Subjective Illusory results partially support Hypothesis 1, showing a stronger illusion in multisensory compared to unimodal conditions, but finding no significant difference comparing unimodal to incongruent conditions. Results partially supported EEG hypotheses, finding increased parietal gamma activity comparing multisensory to unimodal visual conditions, happening at a later stage of the illusion when compared to previous rubber hand illusion EEG findings, whilst also finding increased parietal theta activity when comparing incongruent to non-illusion conditions. While results demonstrated that only 27% of participants experienced the stretching illusion with unimodal visual stimuli compared to 73% of participants experiencing the stretching illusion in the multisensory condition, further analysis suggested that those who experience visual-only illusions exhibit a different neural signature to those who do not, with activity focussed around frontal and parietal regions early on in the illusory manipulation, compared to activity focussed more over parietal regions and at a later point in the illusory manipulation for the full sample of participants. Our results replicate previous subjective experience findings and support the importance of multisensory integration for illusory changes in perceived body size, whilst adding to our understanding of the temporal onset of multisensory integration within resizing illusions, differing from that

[2]The author, Kirralise Hansford, collected the data for this experiment, analysed the results, and wrote the manuscript under the supervision of Dr Catherine Preston, Professor Daniel Baker, and Dr Kirsten McKenzie. The experiment was designed jointly with Dr Catherine Preston, Professor Daniel Baker, and Dr Kirsten McKenzie.

of rubber hand illusions.

3.2 Introduction

Illusory body resizing is a form of multisensory illusion, often using visual and tactile inputs, whereby a body part is resized using augmented reality or magnifying optics and can consist of stretching or shrinking manipulations (Preston et al., 2020; Preston and Newport, 2011; Stanton et al., 2018). Other sensory combinations such as visual and proprioceptive inputs can also be used to elicit resizing illusions (Banakou et al., 2013; Kilteni et al., 2012) and research has found that auditory signals alone can alter perceived tactile distances of the arm (Tajadura-Jiménez et al., 2015). Resizing illusions change how a body part looks and are used to try to induce changes to cortical representations and subjective embodiment of the newly sized body part (Gilpin et al., 2015; Haggard et al., 2013). Such illusory manipulations of the bodily self stem from studies using the rubber hand illusion (RHI). The RHI involves delivering tactile stimulation to a seen fake hand placed on top of a table at the same time and in the same place that tactile stimulation is given to the real hand which is hidden from view using a cloth, which elicits feelings of ownership over the fake hand. The integration of the multisensory (tactile and visual) inputs drives this illusory experience and taps into the neural substrates of our sense of bodily self, highlighting its apparent malleability (Botvinick and Cohen, 1998). Leading from these findings, further research has shown that embodiment can also occur during mirror illusions, such as those used in phantom limb studies (Chan et al., 2007), in which a mirror is placed adjacent to the patient's remaining limb, giving an illusion of the amputated limb still being there, and from multisensory resizing illusions involving both tactile and visual inputs within augmented reality manipulations, whereby an augmented reality system is used to show participants an augmented version of their hidden limbs through a live camera feed (Preston and Newport, 2011).

In addition to multisensory resizing illusions, embodiment has also been reported for unimodal visual resizing illusions such as when viewing an illusion of an elongated arm (Schaefer et al., 2007), while changes to embodied perception have also been reported from visual-only manipulations of the hand (McKenzie and Newport, 2015) and illusory experience has been successfully induced in the rubber hand illusion using visual-only stimulation (Ferri et al., 2014). Furthermore, visual capture alone has been found to elicit embodiment when participants see a virtual or fake/mannequin body egocentrically instead of their own body (Carey et al., 2019; Maselli and Slater, 2013). Interestingly, it has been found that some individuals are more susceptible than others to visual only manipulations, with some participants not experiencing embodiment at all (Carey et al., 2019). The subjective embodiment measures used in these studies have primarily consisted of self-report questionnaires, or objective proprioceptive drift measures, with limited research into the accompanying neural responses to such illusions. Where there has been research into neural responses of resizing illusions, this has only come from multisensory fMRI data (Ehrsson et al., 2005; Preston and Ehrsson, 2016). Therefore, it is unknown if similar levels of subjective illusory experience can be elicited by unimodal visual manipulations during resizing illusions, and we are not aware of the neural underpinnings of either multisensory or unimodal visual resizing illusions using other neuroimaging techniques.

Of the previous studies looking at EEG data and multimodal information processing, the parietal area specifically has been proposed as a multimodal integration processing site (Kanayama et al., 2007). This is due to studies demonstrating a relationship between gamma-band oscillations and integration of multisensory processes across both auditory and visual stimuli (Kaiser et al., 2005; Sakowitz, 2005; Senkowski et al., 2005). Looking specifically at visuotactile manipulations, such as those used in multisensory hand-based illusions (e.g., the rubber hand illusion), power increases have been observed in the gamma band (40-50 Hz) in parietal regions 200-250 ms into congruent visuotactile stimulation (Kanayama et al., 2007) in virtual and real-life environments (Kanayama et al., 2021). This is posited to reflect an early stage of multimodal stimulus integration, highlighting parietal regions as potential seats of multisensory integration. fMRI findings from Ehrsson et al. (2005) who delivered the rubber hand illusion in MRI scanners, and from Petkova et al. (2011), who used full body ownership illusions in an fMRI study, also support parietal involvement in multisensory integration, finding activity in the ventral premotor cortices, intraparietal cortices, and the cerebellum (Ehrsson et al., 2005) in addition to the bilateral ventral premotor cortex, the left intraparietal cortices and the left putamen (Petkova et al., 2011; Preston and Ehrsson, 2016).

Furthermore, ERP findings from Rao and Kayser (2017), also highlight the possibility of intraparietal areas mediating illusory body ownership during the RHI. Multisensory EEG research has also pointed to the existence of oscillatory components related to multisensory integration within theta bands. Theta band (3-8 Hz) activity has been observed between 100 and 300 ms post stimulus (Kanayama et al., 2021). Whilst gamma band activity is observed around the parietal region and shows greater activity to spatially congruent visuo-tactile tasks, theta band activity is found around frontal sites and shows greater response to spatially incongruent visuo-tactile stimulation. Increases in theta power have been attributed to the cognitive load required to process incongruent visuotactile information (Kanayama et al., 2021). Research further supporting the frontal location of theta activity comes from Petkova et al. (2011), who used a full body ownership illusion and fMRI, and found increased activity in the ventral premotor cortex linked to construction of ownership of the body, cognitive load, and control processes. Therefore, additional cognitive load is primarily thought to be reflected by increases in frontal theta, with aspects of body ownership during body-related illusions also being potentially reflected in frontal theta activity.

Therefore, this study aims to further develop our understanding of the neural underpinnings of multimodal integration by using EEG, in addition to subjective experience questionnaires, to enhance our understanding of the mechanisms behind resizing illusions. This will be achieved by investigating the neural signatures of multisensory and unimodal resizing illusions to determine whether the multi-modal aspects of the finger stretching/shrinking illusion used in previous augmented-reality illusions, notably the touch and the visual manipulation of hand/finger size, are required for induction of the illusory experience, or if a unimodal visual-only illusion is also able to elicit similar levels of illusory experience. Given the previous literature denoting the feasibility of unimodal visual illusions, the first hypothesis for the study is that (i) illusion strength will be greater in the multisensory (MS) condition compared to the unimodal visual (UV) condition, which will be greater than an incongruent control (IC) condition. Referring to the neural underpinnings of these illusions, the next hypothesis is that (ii) there will be stronger parietal gamma band activity (30-60 Hz) elicited during MS compared to UV conditions, and finally, to assess additional cognitive demands of the incongruent condition, (iii) there will be greater frontal theta activity (5 - 7 Hz) elicited during IC conditions compared to a non-illusion baseline condition.

3.3 Methods

3.3.1 Preregistration

The preregistration of this study can be found at the following OSF link: https://doi.org/10.17605/OSF.IO/TRP39.

3.3.2 Data/Code Availability Statement

Raw EEG data for each participant and the code used to analyse the data can be found at the following OSF link: https://osf.io/7wpqe/.

3.3.3 Participant Sample

3.3.3.1 Power Analysis and Sample Size

A priori power analysis using illusion data from a pilot study showed a minimum sample size of 26 participants was required (d = 0.67, power = .95, alpha = .05). Due to the small pilot study sample size (n = 9) and the current study using EEG, which was not used previously, in addition to the inherent ambiguity of power analyses and to account for participant drop out/attrition, the sample size of 26 participants was approximately doubled, with recruitment of 50 participants.

3.3.3.2 Participants

48 participants (83.5% Female. 14.5% Male, 2% Non-Binary; mean age = 21 years, age range = 18-29 years) completed the experiment (2 participants lost to drop out/attrition), with exclusion criteria being prior knowledge or expectations about the research, a history of neurological or psychiatric disorders, operations or procedures that could damage peripheral nerve pathways in the hands, a history of chronic pain conditions, history of drug or alcohol abuse, history of sleep disorders, history of epilepsy, having visual abnormalities that cannot be corrected optically (i.e. with glasses), or being under 18 years of age.

3.3.4 Materials

Participants were fitted with a 64-channel EEG cap (ANT Neuro Waveguard) with electrodes arranged according to the 10/20 system. EEG set up included use of conductive gel between the electrodes and the scalp to attempt to obtain impedance levels of <10 kΩ per electrode. Resizing illusions were delivered using an augmented-reality system (see Figure 3.1) that consisted of an area for the hand to be placed which contained a black felt base, LED lights mounted on either side and a 1920×1080 camera situated in the middle of the area, away from the participant's view. Above this area, there was a mirror placed below a 1920×1200 resolution screen, so that the footage from the camera was reflected by the mirror such that the participant could view live footage of their occluded hand. The manipulation of the live feed from the camera was implemented using MATLAB r2017a, wherein the participant's finger would stretch/shrink by 60 pixels during illusions lasting 2.4 s. This stretching or shrinking would be accompanied during the multisensory condition by the experimenter gently pushing or pulling on the participant's finger to induce immersive multisensory illusions. After manipulation, there was a 2.4 s habituation phase in which participants could view and move their augmented finger before the screen went dark, indicating that the next trial could start. Subjective illusion experience was collected via Qualtrics (Qualtrics, Provo, UT) on a Samsung Galaxy Tab A6 tablet. This was given to participants towards end of the experiment, wherein each trial was presented again, and subsequently participants were asked to recall the trial they had just experienced and previous trials that were similar, and then give a response on a Likert scale of -3 to $+3$, with -3 being strongly disagree and $+3$ being strongly agree with statements made. The questionnaire consisted of six statements, two relating to illusory experience: "It felt like my finger was really stretching"/"It felt like the hand I saw was part of my body", two relating to disownership: "It felt like the hand I saw no longer belonged to me"/"It felt like the hand I saw was no longer part of my body", and two were control statements: "It felt as if my hand had disappeared"/"It felt as if I might have had more than one right hand". The questionnaire was delivered 7 times, once after each trial.

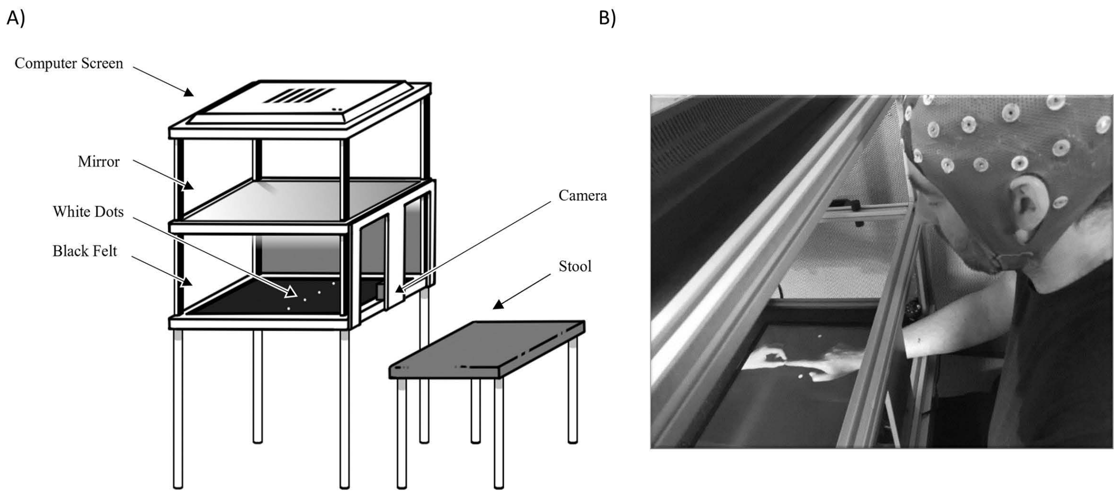

Figure 3.1: A) Schematic of Augmented Reality System. B) Image of Participant in EEG Cap Undergoing Resizing Illusion

3.3.5 Procedure

After EEG set up, participants were seated at the augmented-reality system and instructed to place their right hand, with their index finger outstretched, onto the felt. There were two white dots on the felt to guide where their hand should be placed. Participants were instructed to view their hand's image in the mirror (whilst their real hand was hidden from view) throughout the experiment. Participants completed 12 repetitions of 7 distinct conditions: 1, immersive multisensory (MS) stretching; 2, immersive multisensory (MS) shrinking; 3, unimodal visual (UV) stretching; 4, unimodal visual (UV) shrinking; 5, incongruent control (IC) stretching; 6, incongruent control (IC) shrinking; 7, non-illusion baseline. Multisensory conditions consisted of the experimenter pulling or pushing the participant's index finger as the participant viewed their hand stretching or shrinking in a congruent manner. Unimodal conditions consisted of the participants viewing their finger either stretch or shrink without any experimenter manipulation. Incongruent conditions consisted of the experimenter pushing or pulling the participant's index finger as the participant viewed their hand stretching or shrinking in an incongruent manner. Non-illusion conditions provided no visual or tactile manipulations of the finger. (An infographic of each condition can be seen in Figure 3.2, and a video of a participant undergoing multisensory stretching can be seen at the following link: https://osf.io/drbzc). Conditions were randomised via MATLAB r2017a, and the experimenter was unaware which condition would be presented on a given trial. The experimenter was then informed of whether to push or pull the finger or to apply no manipulation via audio cues delivered through Bluetooth earphones. 6 repetitions of the

7 conditions were presented, with a 5 s interval between each trial condition where the screen went blank so that the participants could not see their hand, before the next trial condition then started. This block of trials was followed by a break for the participant to stretch their hand and rest, and then there were another 6 repetitions of the 7 conditions were presented, again in a random order. There was then another break before each condition was presented once in a fixed order, after which the participant completed the subjective illusory experience questionnaire. EEG was recorded throughout as a continuous recording with conditions indicated by numbered triggers sent when the researcher pressed a button box to start the illusion for each trial.

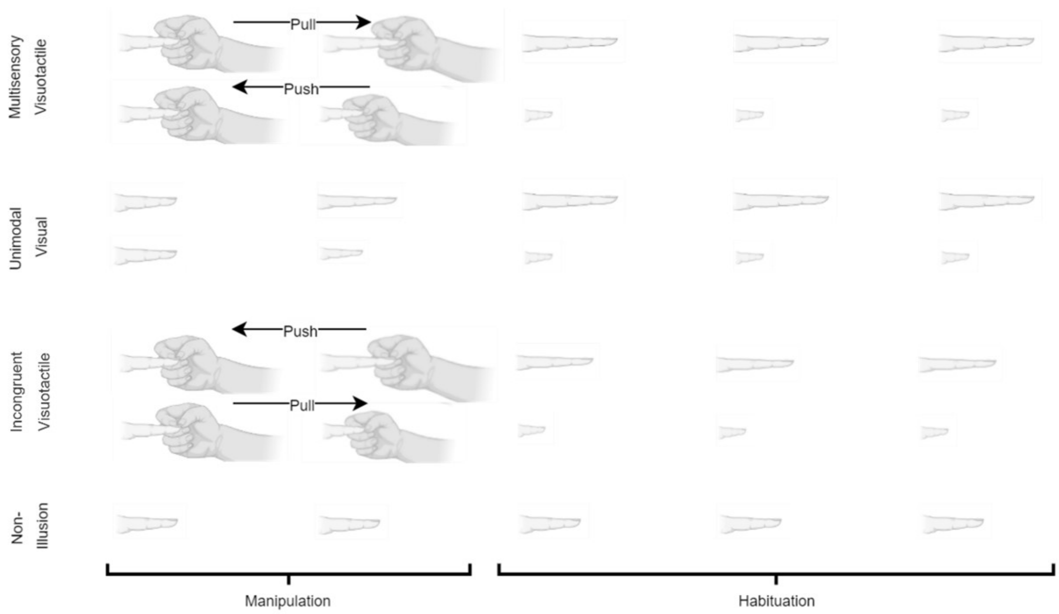

Figure 3.2: Infographic showing each of the conditions and the manipulations applied by the researcher.

3.3.6 Data processing

3.3.6.1 EEG Data Collection

EEG data were recorded continuously at 1 kHz using the ASALab software. 8-Bit digital triggers indicating trial onset and the end of the habituation period were sent from the stimulus computer to the EEG amplifier using a USB TTL module (Black Box Toolkit Ltd., UK). The whole head average was used as a reference for EEG data.

3.3.6.2 Questionnaire Data Collection

A Samsung Galaxy Tab A6 tablet was used to collect subjective illusory experience data via a questionnaire on Qualtrics (Qualtrics,Provo, UT), which the participants completed themselves, with a researcher present to answer any questions.

3.3.7 Data Analysis

3.3.7.1 EEG Data Analysis

To identify noisy data, we calculated the standard error over time (Luck et al., 2021) for each electrode for each participant (following application of a 50 Hz notch filter). Any electrode with a standard error in the top 5% of values (here, above a standard error of 1.5 V), or with a value of 0, were removed from the main analysis. Where a participant had over 50% of their electrodes over the 1.5 standard error threshold, their data were removed, resulting in a final sample of 47 participants (1 removed). The main EEG analysis was then conducted using Brainstorm (Tadel et al., 2011) where again a 50 Hz notch filter was applied to the raw data, and trials were epoched to 5 s at intervals of 1000ms. Time-frequency analysis (Morlet wavelets) across trials was completed for each condition for each participant, with central frequency at 1 Hz and time resolution (FWHM) at 3s. Data were grouped in frequency bands with the following ranges: Delta (2-4 Hz), Theta (5-7 Hz), Alpha (8-12 Hz), Beta (15-29 Hz), Gamma (30-60 Hz). Arithmetic averages were then computed for each condition across all participants, and then again over both MS conditions, both UV conditions and both IC conditions. A pre-stimulus baseline period of 1000ms was included, and activity here was subtracted from all subsequent timepoints, leaving 5 experimental timepoints: 0-0999ms, 1000-1999ms, 2000-2999ms, 3000-3999ms, and 4000-5000ms. Changes in magnitude were statistically assessed using non-parametric cluster-based permutation analysis (Maris and Oostenveld, 2007) implemented in MATLAB r2017a. Here, a one-sample T test statistic and p-value were calculated for each sensor/time point, using a threshold of $p < .05$, before a list of clusters with significant elements was produced. The largest cluster was then stored, and a null distribution was built from 1000 random sets of permutations of the group condition labels and signs. The clusters were then compared to the null distribution and any clusters falling outside of the 95% confidence intervals were retained. The electrode within the significant cluster with the greatest effect size was then used to plot activity over the time course of the experiment, to illustrate the effect seen.

3.3.7.2 Questionnaire Data Analysis

Raw data was exported from Qualtrics, and statistical analysis was completed in JASP (JASP Team, 2022). Scores for both illusion experience questions were averaged, along with both disownership questions and both control questions, resulting in 3 scores per trial per participant. Both MS conditions were then averaged, along with both IC and UV conditions, resulting in each participant giving 4 data points, one for MS, one for IC, one for UV and one for Baseline. Due to the nature of the Likert scale data not being continuous, a Friedman test was run to compare mean scores from each condition. Given significant findings, post-hoc Conover's tests were run, with Bonferroni correction for 6 comparisons at an initial alpha of 0.05.

3.3.8 Results

Control and disownership statement scores for all conditions showed negative mean results (as can be seen in Appendix B, Table B1), showing disagreement with all control and disownership statements, thereby showing confidence that the experimental results were not affected by experiences of disownership of the hand, or violations of the control statements. Hypothesis 1 predicted that reported illusion strength will be greater in the MS condition compared to the UV condition, which will be greater than an IC condition. Previous studies have identified illusion responders as those with illusion ratings $\geq +1$, such that they are reporting agreement with the illusion relevant questionnaire statements (Carey et al., 2019; Ehrsson et al., 2004; Kalckert and Ehrsson, 2012; Petkova and Ehrsson, 2009), therefore we also used this cut off in the current study. Of the total participants, 35 out of 48 participants (73%) scored $\geq +1$ on combined stretching illusion scores in the MS condition, with the average score across all participants showing an illusion score of 1 in the MS condition, therefore the whole sample was used for analysis. To test hypothesis 1, a Friedman test was conducted to determine whether illusion strength differed between MS, IC, UV and baseline conditions. Results, summarised in Figure 3.3, show a significant difference between conditions ($\chi^2(3) = 40.936$, $p < .001$; W= 0.29), with post hoc Conover tests showing significant comparisons after Bonferroni correction between baseline and MS conditions (T (138) = 5.10, $p < .001$), MS and IC conditions (T (138) = 3.38, p = .006), and MS and UV conditions (T (138) = 5.86, $p < .001$). However, note that the illusion strength was lower in the UV condition than the IC condition (T (138) = 2.49, p = .084), although not significantly lower, this is opposite to our hypothesis. There were no significant differences between baseline and IC conditions (T (138) = 1.73, p = .516), or between baseline and UV conditions (T (138) = 0.76, p = 1.0).

Using the average rating of $\geq +1$ showing that the participants had an experience of ownership. Of the total participants, 13 out of 48 participants (27%) scored $\geq +1$ on combined stretching illusion scores in the UV condition, showing an experience of the illusion in the UV stretching condition, and 5 out of 48 participants (10%) scored $\geq +1$ on combined shrinking illusion scores in the UV condition, showing an experience of the illusion in the UV Shrinking condition. When looking at UV stretching and UV shrinking scores, 5 out of 48 participants (10%) scored $\geq +1$ on combined illusion scores in the UV condition. Therefore, to assess differences in illusion strength when there is an effective illustration of the UV condition, exploratory analysis using a Friedman test was conducted on the 27% of participants who experienced an effective UV stretching condition, now termed the unimodal visual positive (UVP) sample, to determine whether illusion strength differed between MS, IC, UV and baseline stretching conditions. This exploratory analysis was not, however, conducted on the 10% who experienced an illusion in the UV shrinking condition or the combined 10% who experienced an illusion across both UV stretching and shrinking conditions, since the sample sizes would be too small that power to detect meaningful effects would be minimal.

Results, summarised in Figure 3.3, show a significant difference between conditions ($\chi^2(3) = 13.703$, p = .003; W = 0.351), with post-hoc Conover tests showing significant comparisons after Bonferroni correction between baseline and MS Stretch (T (36) = 3.40, p = .01). There were no significant differences between baseline and IC Stretch (T (36) = 1.27, p = 1.0), baseline and UV Stretch (T (36) = 2.61, p = .078), MS Stretch and IC Stretch (T (36) = 2.14, p = .24) or MS Stretch and UV Stretch (T (36) = 0.79, p = 1.0). Note that the illusion strength was not significantly higher in the UV condition than the IC condition in this group (T (36) = 1.35, p = 1.0).

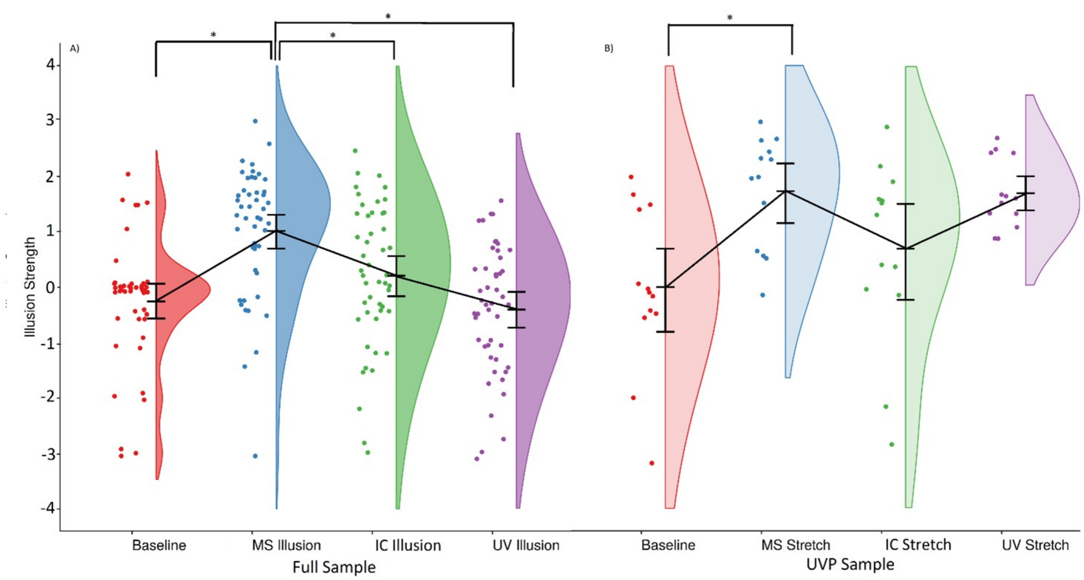

Figure 3.3: A) Illusion Strength in Each Averaged Illusion Condition for the Full Sample. B) Illusion Strength in Each Stretching Illusion Condition for the UVP Sample (27% of Participants). Error bars indicate 95% confidence intervals, *'s indicate significant comparisons.

We next assessed Hypothesis 2, that there will be stronger parietal gamma band activity elicited during MS compared to UV conditions. A significant cluster comparing these conditions was found in the gamma band (30-60 Hz) between 4000 and 5000ms (p = .008). The effect was strongest at electrode TP7, consistent with our prediction of a difference in parietal activity (see Figure 3.4).

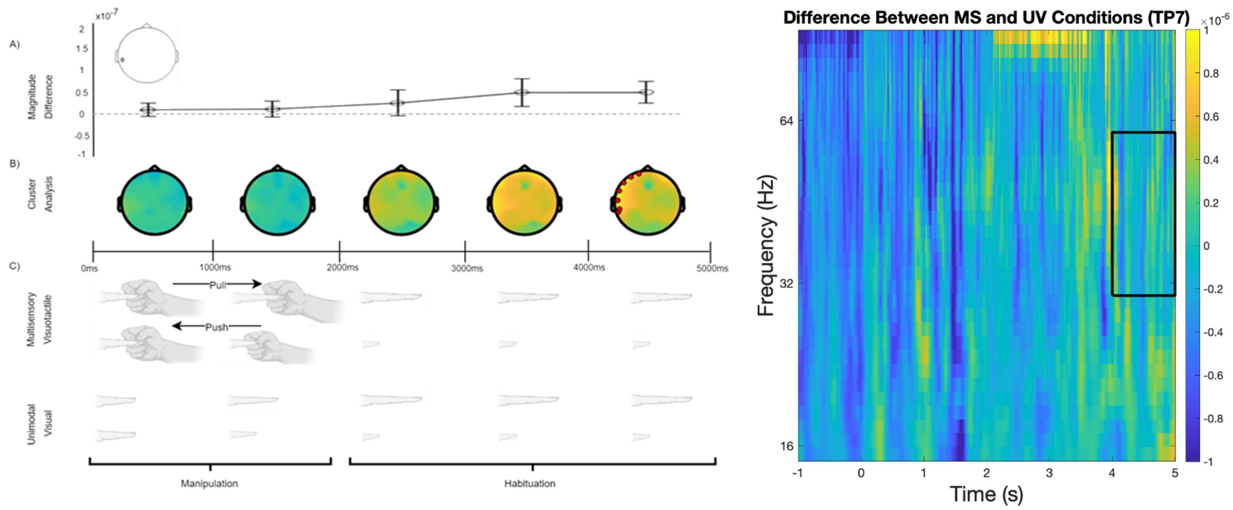

Figure 3.4: Comparison of gamma band activity between MS and UV conditions. The Magnitude Difference plot (a) shows time course of TP7 electrode, which was the significant electrode showing the largest effect size (d = 0.35). In panel (b), colour indicates the magnitude difference (blue: negative, yellow: positive), the significant cluster is highlighted by red dots. In panel (c), arrows denote the manipulation that the researcher's hand is applying to the finger. Panel (d) shows the full time-frequency plot, with the black rectangle indicating the gamma band and the time-window containing the significant cluster.

Due to the UV condition being present in this analysis, an exploratory analysis using the 27% of the sample who experienced an effective UV condition was also conducted. Here, three significant clusters were found in the gamma band between 0 and 1000ms ($p < .001$; $p = .015$; $p < .001$), again for comparing the MS and UV conditions. The difference was greatest over electrode F1, with clusters located in both frontal and parietal regions (see Figure 3.5).

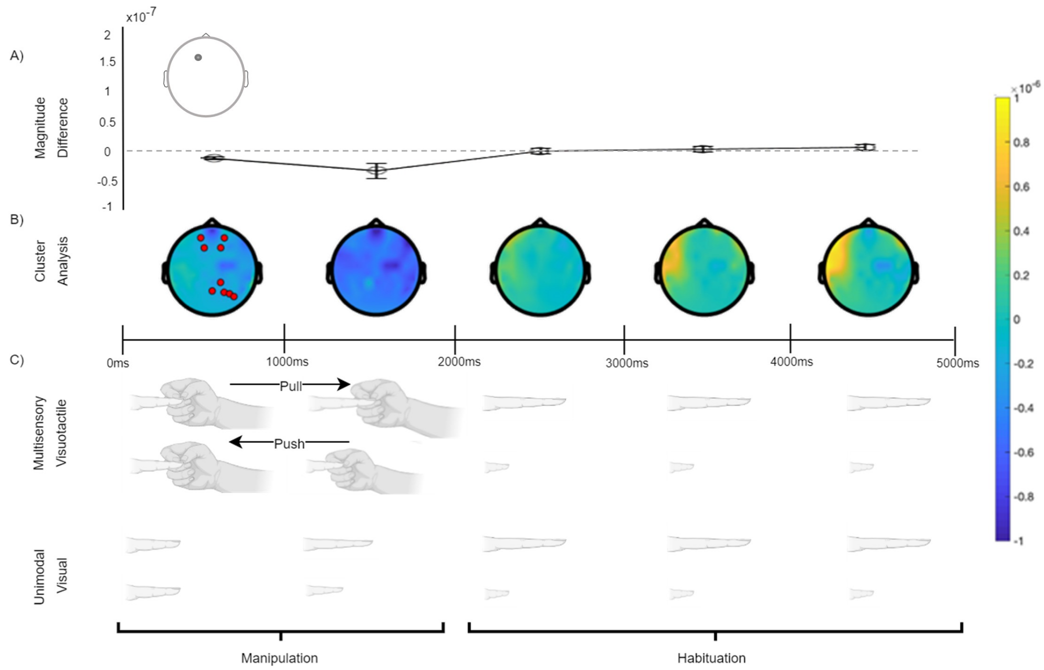

Figure 3.5: Comparison of gamma band activity between MS and UV conditions. The Magnitude Difference plot (a) shows time course of F1 electrode, which was the significant electrode showing the largest effect size (d = 0.91). In panel (b), colour indicates the magnitude difference (blue: negative, yellow: positive), and significant clusters are highlighted by red dots. In panel (c), arrows denote the manipulation that the researcher's hand is applying to the finger.

Finally, hypothesis 3 predicted that there would be greater frontal theta (5-7 Hz) activity elicited during IC conditions compared to a non-illusion baseline condition. A significant cluster was found in the theta band between 0 and 1000ms (p = .005) when comparing these two conditions. The difference was greatest over electrode M2, opposing our location prediction (see Figure 3.6).

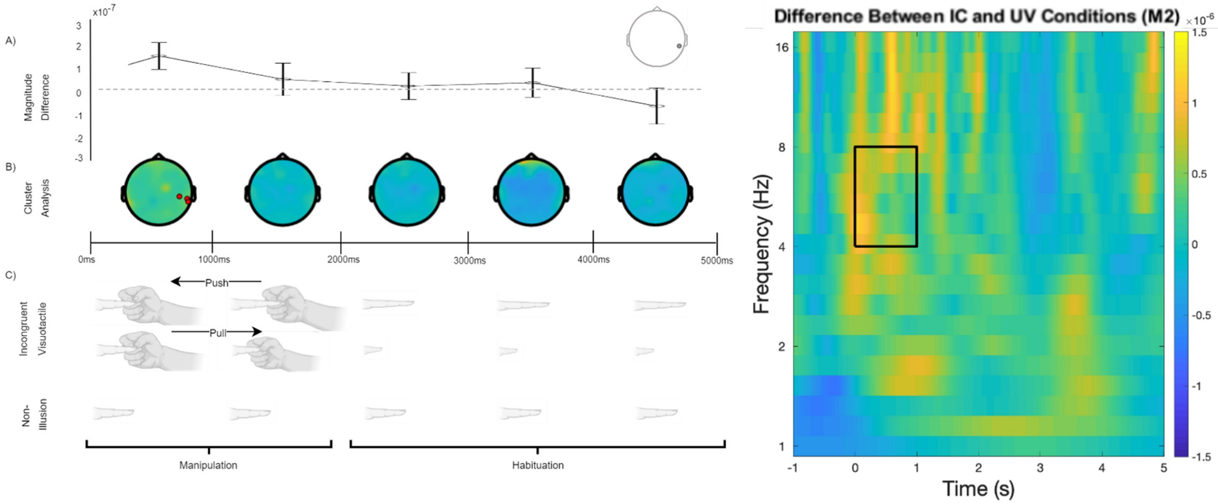

Figure 3.6: Comparison of theta band activity between IC and NI conditions. The Magnitude Difference plot (a) shows time course of M2 electrode, which was the significant electrode showing the largest effect size (d = 0.39). In panel (b), colour indicates the magnitude difference (blue: negative, yellow: positive), the significant cluster is highlighted by red dots. In panel (c), arrows denote the manipulation that the researcher's hand is applying to the finger. Panel (d) shows the full time-frequency plot, with the black rectangle indicating the theta band and the time-window containing the significant cluster.

3.3.9 Discussion

This study aimed to further develop our understanding of the neural underpinnings of multimodal integration by using EEG in addition to replicating previous findings regarding subjective experience of resizing illusions through using subjective experience questionnaires across multisensory visuotactile, unimodal visual, incongruent, and non-illusion conditions. Findings demonstrated that reported illusion strength of the newly resized finger was found to be significantly stronger in multisensory compared to incongruent and unimodal visual conditions, and exploratory analysis highlighted that when there was an effective experience of the unimodal condition, respective subjective embodiment surpassed that of the incongruent condition, but not significantly so. EEG analysis found increased gamma band activity in multisensory visuotactile compared to unimodal visual conditions, in line with previous findings, but found this to occur at a later time point than was previously found during rubber hand illusions. This increased gamma likely reflects multimodal stimulus integration effects, as the multimodal condition included visual and tactile manipulations, whereas the unimodal visual only included visual manipulations. Increased theta band activity was observed in the incongruent compared to the non-illusion condition, likely reflecting additional cognitive load requirements to integrate conflicting sensory inputs. This increase in theta band activity was located in the parietal region, contrasting previous findings of frontal theta activity in incongruent conditions.

Illusory experience data, as seen in Figure 3.3a, show a significant difference between conditions with a medium effect size (Lovakov and Agadullina, 2021), with an increase in subjective illusory experience in multisensory compared to unimodal conditions, as expected. Surprisingly, however, there was no difference in illusory experience between the unimodal and baseline condition, and the incongruent condition induced a stronger illusion than the unimodal condition, in contrast to our first hypothesis. This unexpected finding can be explained through two possible ideas. First, the incongruent condition might not have acted as an effective incongruent manipulation. This could be because during incongruent stretching, where the participant's finger stretched whilst the experimenter gently pushed the finger, this could instead act as a congruent multisensory condition, as the feeling of the experimenter pushing on the finger could feel as though the finger is pushing through a barrier, still giving a congruent stimulation effect. Exploratory analysis on disaggregated incongruent data supports this idea, as there was a significant difference between the incongruent stretching and incongruent shrinking conditions ($\chi^2(1) = 5.444$, $p = .02$; $W = 0.113$), with post-hoc Conover tests showing significant comparisons after Bonferroni correction between IC Stretch and IC Shrink ($p = .023$), with participants experiencing a mean illusion strength score of 0.40 in IC Stretch compared to a mean illusion strength score of 0.01 in IC Shrink. Participants would be expected to show illusion scores of around 0, showing no illusory experience for an effective demonstration of the incongruent condition. Therefore, the IC stretch condition (where the finger stretches visually but is compressed haptically) is likely to be a less appropriate control manipulation than the IC shrink condition (where the finger shrinks, but is stretched haptically). Additionally, as can be seen by the exploratory analysis for the effective unimodal condition, participants also experienced a stronger illusion with stretching compared to shrinking (27% reporting effective UV stretching compared to 10% reporting effective UV shrinking). This could be because we are more likely to experience across our lives our body stretching rather than shrinking, with regards to finger growing with age, therefore stretching illusions do not create an improbable scenario of our fingers shrinking, but rather act on the experienced situation of our fingers growing with age (Preston and Kirk, 2022). Secondly, as can be seen in Figure 3.3b, when participants do experience an effective unimodal visual condition, identified as scoring $\geq +1$ on combined stretching illusion scores in the UV condition, as was the case with almost a third of our participants within this exploratory analysis, the data show trends towards supporting our first hypothesis-that illusion strength would be greater in MS compared to UV, which would be greater than IC, with a slightly greater effect size than the full sample analysis. However, caution should be taken with this finding as it was exploratory analysis with a small sample size and did not show significant differences between MS and UV or UV and IC conditions, therefore replications of this finding with an adequately powered sample size based on effect sizes from this study are merited for confirmatory interpretations. Previous research has also found similar effects for visual only observation of a mannequin body, showing that 40% of participants experience subjective embodiment from visual-only observations

(Carey et al., 2019). Furthermore, McKenzie and Newport (2015) found variability in the degree to which people experienced visually-induced sensations, finding a correlation between somatoform dissociation and visually-induced sensations.

EEG data regarding multisensory integration can be seen in Figures 3.4 and 3.5. Findings show that for the total sample, a significant cluster is observed in the gamma band (30-60 Hz) within the final phase of the experiment, which extends to parietal regions and possibly indicates a later stage of multimodal stimulus integration, expanding on previous findings regarding earlier stages of integration (Kanayama et al., 2021, 2007). It is possible that we see differences in the temporal nature of multimodal stimulus integration for a few reasons. Firstly, this study used illusory finger resizing as a method of multisensory manipulation, whereas previous studies have used the rubber hand illusion (Hiramoto et al., 2017; Kanayama et al., 2021, 2007; Kanayama and Ohira, 2009), or visual and tactile discrimination tasks (Kanayama and Ohira, 2009). Therefore, the differences seen in the gamma-band concerning early and late-stage multimodal stimulus integration could be due to different aspects of multisensory integration that are indexed by these different multisensory manipulations. Specifically, the integration in the rubber hand illusion differs from the integration in resizing illusions, as the rubber hand illusion elicits congruent (or incongruent as in the IC conditions) tactile stimulation from the start of manipulation, whereas the resizing illusions elicit congruent tactile stimulation as the finger resizes, and then there is a habituation period for the participant to get used to this resized finger and therefore embody the longer finger, and this is where we see the later state of gamma activity relating to multimodal stimulus integration. Furthermore, in the present study, the gamma-band was classified as between 30 and 60 Hz, whilst the previous studies which have observed significant increases in early-stage gamma-band power, have done so in more specific frequency ranges of 40-50 Hz (Kanayama et al., 2007), 40-60 Hz (Kanayama and Ohira, 2009) and 25-35 Hz (Kanayama and Ohira, 2009). Additionally, Kanayama and Ohira (2009) found low-frequency gamma power reduction in congruent conditions, although non-significant, when dividing participants into groups based on depersonalisation tendencies. Hiramoto et al. (2017) suggested that reduction in low-frequency gamma could be modulated by individual differences. Our results also show individual differences in gamma activity, as seen in Figure 3.5 regarding the participant population who experienced an effective unimodal visual condition. Here, slightly decreased gamma activity was found in frontal and parietal regions, suggesting that those who experience visual-only resizing illusions demonstrate a different neural signature to those who do not. The significant clusters are in the manipulation phase, localised in both frontal and parietal regions. The difference in location of the significant clusters between the full sample and this subsample is likely due to the subsample experiencing an illusion in both multisensory and unimodal conditions, and therefore when looking at the difference in neural activity between the two conditions, this difference is seen at an early stage when there is the additional tactile input in the multisensory condition. Further analysis of the unimodal visual positive sample can be seen in Figures C1.1 - C1.3 in Appendix C. Caution should again be taken with the findings from this sub-sample of participants since this was exploratory analysis, therefore studies with larger sample sizes would be warranted to enhance understanding of the different neural signatures of this population of individuals.

EEG Data relating to multisensory dis-integration can be seen in Figure 3.6, which shows a significant cluster in the theta band (5-7 Hz) 0-1000ms after onset of the manipulation. Previous literature posits that increases in theta band power relate to an additional cognitive load required to process the incongruent visuo-tactile information, which is likely reflected here in the theta band activity difference between incongruent and non-illusion conditions. The increased theta band activity seen here is located around parietal sensors, ipsilateral to the tactile manipulation. This location contrasts with our hypothesis of increased frontal theta activity, however, this could be due to the aforementioned issue with the incongruent stretching condition, whereby the finger is visually stretched whilst the researcher pushes on the finger, which could have been interpreted as the finger pushing against a barrier and therefore still feeling like a multisensory condition. This could then explain the parietal location, as multisensory integration effects have been previously linked to parietal areas (Kanayama et al., 2007). Additionally, EEG is known to lack discrete spatial resolution (Srinivasan, 1999), and therefore caution should be taken with this theta finding, and the previous gamma findings, when discussing the location of significant clusters.

In addition to being a useful method to investigate the malleability of our bodily self, resizing illusions have also shown the potential to reduce pain in chronic pain conditions such as complex regional pain syndrome (CRPS) (Moseley et al., 2008), chronic back pain (Diers et al., 2013) and osteoarthritis (OA) of the hand (Preston and Newport, 2011) and knee (Stanton et al., 2018). Theories regarding this pain reduction are linked to the inaccurate size reports chronic pain patients often give to their affected limbs (Gilpin et al., 2015; Lewis et al., 2007; Moseley, 2005; Peltz et al., 2011; Stanton et al., 2018) and the resizing illusions ameliorating this discordance. Multisensory illusory resizing, however, requires the use of a large augmented-reality system as well as the presence of a researcher to deliver the manipulations, and is therefore, somewhat impractical as a treatment option. Given that unimodal visual illusions have been shown in our results to elicit subjective embodiment for 27% of participants, it is plausible that there could be accompanying analgesia for chronic pain patients undergoing this illusion. Recently, there has been evidence to suggest that visual-only illusory resizing of the hand and auditory-driven illusory resizing in complex regional pain syndrome can reduce pain levels (Lewis et al., 2021; Tajadura-Jiménez et al., 2017), however, previously the neural underpinnings of both multisensory and unimodal visual resizing illusions were not investigated in resizing illusions, meaning that inferences regarding possible analgesic effects of unimodal visual resizing illusions in chronic pain more widely could not be made. Here, we have shown evidence supporting multimodal stimulus integration in our EEG data and show a distinct neural signature for participants who experienced an effective unimodal visual condition, heightening our understanding of how these resizing illusions work in healthy participants, creating an avenue to further investigate this in chronic pain samples.

Taken together, our EEG findings support the previous literature regarding multisensory integration effects at gamma frequencies and advance our understanding of the neural underpinnings of hand-based illusory resizing, showing a later stage of multimodal integration within this illusory manipulation. Additionally, our findings support the previous literature surrounding additional cognitive load requirements within the theta bands, extending these findings specially to hand-based illusory resizing manipulations. Our findings therefore enhance our understanding of the neural underpinnings of resizing illusions, showing that there could be important differences between multisensory visuotactile manipulations in rubber hand illusions and resizing illusions, relating to the temporal onset of integration effects. Our findings also add to the narrow previous literature regarding individual differences in gamma band power in multisensory conditions, showing here that a subset of participants who experienced an effective unimodal visual condition show spatially and temporally different effects compared to the full sample of participants, when comparing multisensory and unimodal visual conditions. These findings, however, could be enhanced by research investigating whether these illusions produce changes to the somatosensory cortex of participants. Neuroimaging has previously been used in healthy populations undergoing resizing illusions, wherein modulation of the primary somatosensory cortex has been found using neuromagnetic source imaging during resizing illusions of the arm (Schaefer et al., 2007). Given the differences seen between illusory resizing manipulations in these data, it is possible to posit that there will also be somatosensory cortex changes during finger resizing. There is also scope to investigate the differences between healthy and chronic pain participants, to see if the discordance reported for chronic pain conditions between real and perceived limb size would affect their somatosensory representations during illusory finger resizing.

These findings not only enhance our understanding of the neural signatures of multisensory visuotactile, unimodal visual and incongruent resizing illusions in healthy participants, but also provide a foundation to explore the neural signatures of resizing illusions in chronic pain populations. Further research is required to investigate whether the discordance in perception of limb size seen in chronic pain populations could result in different neural signatures to a healthy population. If found, this could indicate neural differences between the conditions that resizing illusions could help ameliorate, or conversely could show no differences between the populations, indicating a possible placebo analgesic effect of resizing illusions. Regarding future research with chronic pain populations, our data show that almost a third of healthy participants experience subjective embodiment in a visual-only illusion, which is supported by previous research (Carey et al., 2019), however, it is not known if a similar proportion of individuals experiencing an effective unimodal visual condition would be seen in chronic pain populations, which therefore gives merit for future research into subjective embodiment during visual-only conditions for this population.

3.3.10 Conclusions

Overall, our findings support our EEG hypotheses in relation to activity increases in the gamma and theta bands, with both gamma and theta findings extending to parietal regions. These findings enhance our understanding of the neural signatures of visuotactile, visual only, and incongruent illusory resizing manipulations in healthy participants, by adding novel evidence regarding what happens in a different presentation of a multisensory visuotactile illusion. Findings also show partial support for the subjective illusory experience hypothesis and illustrate the importance of individual differences in illusory experience of the unimodal visual condition.

4 Chapter 4: Multisensory processing and proprioceptive plasticity during resizing illusions

This chapter has been adapted from: Hansford, K. J., Baker, D. H., McKenzie, K. J., & Preston, C. E. (2024). Multisensory processing and proprioceptive plasticity during resizing illusions. Experimental Brain Research, 1-12. https://doi.org/10.1007/s00221-023-06759-7[3]

4.1 Abstract

Bodily resizing illusions typically use visual and/or tactile inputs to produce a vivid experience of one's body changing size. Naturalistic auditory input (an input that reflects the natural sounds of a stimulus) has been used to increase illusory experience during the rubber hand illusion, whilst non-naturalistic auditory input can influence estimations of finger length. We aimed to use a non-naturalistic auditory input during a hand-based resizing illusion using augmented reality, to assess whether the addition of an auditory input would increase both subjective illusion strength and measures of performance-based tasks. Forty-four participants completed the following three conditions: no finger stretching, finger stretching without tactile feedback and finger stretching with tactile feedback. Half of the participants had an auditory input throughout all the conditions, whilst the other half did not. After each condition, the participants were given one of the following three performance tasks: stimulated (right) hand dot touch task, non-stimulated (left) hand dot touch task, and a ruler judgement task. Dot tasks involved participants reaching for the location of a virtual dot, whereas the ruler task concerned estimates of the participant's own finger on a ruler whilst the hand was hidden from view. After all trials, the participants completed a questionnaire capturing subjective illusion strength. The addition of auditory input increased subjective illusion strength for manipulations without tactile feedback but not those with tactile feedback. No facilitatory effects of audio were found for any performance task. We conclude that adding auditory input to illusory finger stretching increased subjective illusory experience in the absence of tactile feedback but did not affect performance-based measures.

4.2 Introduction

Resizing illusions can be delivered through either augmented reality or magnifying optics and typically use combined visual and tactile inputs to manipulate the size of a body part, making it appear either larger or smaller. These illusions, through changing the way a body part is perceived, are thought to

[3]The author, Kirralise Hansford, collected the data for this experiment, analysed the results, and wrote the manuscript under the supervision of Dr Catherine Preston, Professor Daniel Baker, and Dr Kirsten McKenzie. The experiment was designed jointly with Dr Catherine Preston, Professor Daniel Baker, and Dr Kirsten McKenzie.

exploit principles of multisensory processing to elicit modulations in the perceived size and shape of the body part (Preston et al., 2020; Preston and Newport, 2011; Stanton et al., 2018). In addition to visual and tactile illusions, the combination of visual and proprioceptive, or visual and motor inputs, has also been found to elicit body resizing illusions. Research demonstrates that proprioceptively aligning a child's avatar body with a participant's adult body can elicit a strong illusion of having a smaller child-sized body (Banakou et al., 2013). Further research also similarly shows that synchronous movements of an avatar with an elongated arm influence participants' judgements of arm length (Kilteni et al., 2012). Furthermore, tasks using combined visuotactile inputs have been compared to those employing unimodal visual inputs for finger-stretching illusions, with participants reporting greater subjective embodiment of the illusion during combined visuotactile stimulation than that during unimodal visual illusions (Hansford et al., 2023). Such findings serve to highlight the importance of multisensory processing for subjective embodiment during illusory changes in finger length.

Multisensory processing helps us to perceive a stimulus as a single coherent experience, despite comprising a combination of several different sensory inputs. This process is thought to be important for experiencing our body as our own, as has been demonstrated during the rubber hand illusion, whereby the simultaneous visual and tactile stimulation of a fake hand, at the same time and location as inputs applied to a participant's own visually occluded hand, can manipulate our understanding of what we experience to be part of our own body (Botvinick and Cohen, 1998). Theories explaining body ownership and multisensory body illusions focus primarily on tactile and proprioceptive inputs (Botvinick and Cohen, 1998; Tsakiris, 2010) as these senses are thought to be unique to bodily experience. Sensory inputs such as vision, which is understood to be weighed heavily in multisensory integration processes during body illusions (Makin et al., 2008), and audition, which is thought to be a more external sense, are experienced both in relation to our own body and to objects in the external world. However, more recent Bayesian accounts of body ownership suggest that the addition of other senses may also facilitate feelings of embodiment and vividness of body illusions (Kilteni et al., 2015). Studies have claimed additive effects of additional senses in multisensory integration concerning non-body events, a finding that the addition of auditory stimuli enhanced overall efficiency in difficult visual detection tasks (Frassinetti et al., 2002). This has also been demonstrated in the other direction, showing that visual cues can aid the detection of low-intensity sounds (Lovelace et al., 2003). In addition, there is evidence supporting the modulation of tactile perception via audio cues; a study by Zampini and Spence (2004) found that increasing the overall volume and/or the amplitude of high-frequency sounds, combined with the tactile input of biting a potato chip, increased the reported crispness of the chip.

Research examining multisensory processing relating to the body and body illusions has also begun to explore the importance of other senses; notably, the role of auditory inputs in multisensory interactions, which have been found to influence perceptions of body size and length (Tajadura-Jiménez et al., 2012), as well as altering perceived material properties (Senna et al., 2014) and the weight (Tajadura-Jiménez et al., 2015) of the body. Looking specifically at visual, tactile and auditory inputs within the rubber hand illusion (which is used as an experimental test for embodiment experienced in resizing illusions), O'Mera (2014) used proprioceptive drift tasks, which measure localisation bias after proprioceptive manipulations, and found that adding auditory inputs consistent with the visual and tactile inputs related to stroking the hand (in this instance, the sound of sandpaper scratching the skin) heightened the illusory experience more than when white noise was added to the illusion. This is further supported by the findings of Radziun and Ehrsson (2018), who also looked at the addition of ecologically relevant auditory inputs to the rubber hand illusion. Their study used the sound of a surface being stroked with a paintbrush, subjective questionnaires and proprioceptive drift tasks to demonstrate that synchronous auditory cues made the illusion stronger, compared to asynchronous auditory cues.

The addition of auditory inputs in the studies mentioned above involved naturalistic auditory inputs, i.e. experimental auditory input that was consistent with realistic auditory stimuli, such as we are used to encountering in everyday life. However, Tajadura-Jiménez et al. (2017) looked at the influence of non-naturalistic auditory inputs, to see whether this still resulted in changes to body perception. Here, they used changes in pitch, due to their associations with a change in height or size (Hubbard, 2018), and which are not typically associated with bodily movement. They found that when participants pulled their own right index finger with their left hand, with an accompanying rising pitch sound (700-1200 Hz) and an absence of any visual information, they estimated the length of their index finger to be longer than when this pulling was accompanied with either a descending (700-200 Hz) or constant (700 Hz) tone and coined this the 'auditory Pinocchio' effect (although they did not attempt to stretch participants' noses).

Given these previous findings involving naturalistic auditory inputs in the rubber hand illusion (O'Mera, 2014) and non-naturalistic auditory inputs in auditory-tactile resizing manipulations (Tajadura-Jiménez et al., 2017), it is plausible that the addition of non-naturalistic auditory inputs accompanying a visual input of a finger changing size through the use of augmented reality to induce visual and visual-tactile resizing illusions could increase the strength of the illusory experience. This prediction refers again to the notion that the inclusion of more senses provides a more holistic and vivid experience of an event (Kilteni et al., 2015).

Measuring the experience of illusory effects often consists of questionnaires given to participants after they have experienced an illusory condition to gain a subjective measure of their experience. However, more performance-based evidence can also be taken from behavioural measures of proprioceptive drift, which is defined as the change in proprioceptively perceived position of the participant's hidden body part (Davies et al., 2013). Previous studies assessing proprioceptive drift during the rubber hand illusion have produced conflicting results regarding the influence of the illusion on body schema. Body schema are representations of the body based on bottom-up sensory inputs that are needed for action, and are thought to be distinct from body image, which refers to a top-down body representation that is needed for perception (Paillard, 1999). Kammers et al. (2009) investigated the relationship between body schema and body image using the rubber hand illusion with a reaching proprioceptive drift task (action task), wherein participants were asked to reach with one hand to point to the tip of the index finger of the other hand in a single movement, to assess body schema. The participants were also asked to verbally report when the experimenter's moving finger matched the felt location of their own finger (perceptual task), to assess body image. Kammers et al. (2009) found that only the perceptual judgements regarding limb ownership were sensitive to distortion in the rubber hand illusion, concluding that action movements, and therefore body schema, were not affected. In contrast, Newport et al. (2010) used augmented reality and a dot touch proprioceptive drift task with supernumerary limbs to assess body schema using a virtual version of the rubber hand illusion and found that distortions in body schema were apparent, evidenced through pointing errors in the dot touch task that were consistent with the remapped limb position.

A point to note within this previous research is that the terms 'subjective' and 'performance task' can be used to refer to several concepts in relation to data regarding bodily experience. For the purposes of the current study, the term 'subjective self-reports' is used to refer to data collected from self-report questionnaires, whereas the term 'performance task' is taken to refer to data collected from proprioceptive plasticity and ruler judgement tasks, such as those used by Davies et al. (2013), Kammers et al. (2009) and Newport et al. (2010). Previous studies concerning the rubber hand illusion typically use proprioceptive drift to assess performance-based illusory experience; however in the current study, we are looking more broadly at proprioceptive plasticity. Proprioceptive plasticity refers to the changeable nature of proprioception that can be influenced by body illusions, but that is not specific to drift from one body part to another such as in the rubber hand illusion. Proprioceptive plasticity acts as a more general term regarding changes to proprioception. This is due to self-report tasks indexing personal, subjective, experience of resizing illusions, whereas proprioceptive drift and ruler judgement tasks index aspects which some researchers consider as more impartial, performance-based, data regarding the effects of resizing illusions on one's percept of their bodily experience.

Given previous research demonstrating additive effects on the overall illusion experience when including several different sensory inputs, and the recent evidence that additional auditory inputs can affect illusory experience in comparison to unimodal stimulation alone, we hypothesised that through using a between-subjects design wherein one group has non-naturalistic auditory input (one that is consistent with the visual and tactile manipulations of stretching a finger) during augmented-reality resizing illusions, whilst the other group has no auditory input, (1) illusion strength, measured via a subjective illusory experience questionnaire, will be heightened for (1a) visual and (1b) visuotactile manipulations within the audio group. In addition, we hypothesised (2) that the addition of auditory input will lead to stronger illusions as indexed by performance tasks, in line with the experience of a longer finger, as measured using a dot touch proprioceptive plasticity task that indexes body schema for (2a) visual and (2b) visuotactile manipulations. We also hypothesised that the addition of auditory input will increase judgements of finger length, measured using a ruler judgement task that indexes body image for (3a) visual and (3b) visuotactile manipulations. Our inclusion of two different proprioceptive plasticity tasks, a dot touch task and a ruler judgement task, aims to address the apparent discordance between the findings of Kammers et al. (2009) and Newport et al. (2010), relating to the effects of resizing illusions upon body image and body schema.

4.3 Methods

4.3.1 Preregistration

Pre-registration of this study can be found at the following OSF link: https://osf.io/6x4ce.

4.3.2 Participant Sample

4.3.2.1 Power Analysis and Sample Size

A priori power analysis using subjective illusion data and performance task dot touch data from a pilot study (N=10, https://osf.io/pb3ku) showed that a minimum sample size of 26 participants is required for hypothesis 1a regarding visuo-auditory/visuotactile-auditory manipulations (Cohen's d=1.02, power=0.80, =0.05, between-subjects design), and a sample of 22 participants is required for hypothesis 2 regarding the dot touch task (f=0.64, power=0.80, =0.05, between-subjects design). Due to the inherent ambiguity of effect size estimations used to determine sample sizes in power analysis, and to account for the additional ruler judgement task, the upper sample size of 26 participants was doubled to a sample size of 52 participants.

4.3.2.2 Participants

Fifty-two participants (44 females, 6 males, 2 non-binary; mean age = 19.3 years, age range = 18-24 years, sample population = students at the University of York) gave informed consent, were allocated randomly to either the audio group or the no-audio group, and completed the experiment. A between-subjects design was used to avoid any potential confounding or order effects of the illusions with auditory input. Exclusion criteria were detailed on the participant information sheet and included: prior knowledge or expectations about the research, a history of neurological or psychiatric disorders, any operations or procedures that could damage peripheral nerve pathways in the hands, a history of chronic pain conditions, a history of drug or alcohol abuse, a history of sleep disorders, a history of epilepsy, having visual abnormalities that cannot be corrected optically (i.e. with glasses) or being under 18 years of age. From these 52 participants, 8 scored above 50 (indicating experience of the illusion) on the subjective experience questionnaire item regarding feeling stretching of the finger within the baseline condition where no stretching took place. It was therefore determined that these eight participants did not complete the subjective illusory experience scale correctly, and they have therefore been removed from subsequent analyses, resulting in 44 participants being included in the final sample; 23 in the no-audio group and 21 in the audio group. Analysis of all the 52 participants' data was completed in line with the pre-registration for transparency and can be seen in Figures D1.1 - D1.3 in Appendix D.

4.3.3 Materials

The resizing illusions were delivered using an augmented-reality system (see Figure 4.1) that consisted of an area for the hands to be placed which contained a black felt base, LED lights mounted on either side and a 1920×1080 camera situated in the middle of the area, away from the participant's view. Above this area, there was a mirror placed below a 1920×1200 resolution screen, so that the footage from the camera was reflected by the mirror such that the participant could view live footage of their own occluded hands. The manipulation of the live feed from the camera was implemented using MATLAB r2017a, wherein the participant's finger would stretch by 60 pixels (2.1 cm) during illusions lasting 2.4s. This stretching was accompanied during the visuotactile/visuotactile-auditory conditions by the experimenter gently pulling on the participant's right index finger to provide tactile input and induce immersive multisensory illusions. In the audio group, the stretching manipulations in the visuotactile-auditory and the visual-auditory conditions were accompanied by a pure tone that increased linearly in frequency from 308 to 629 Hz. Trials during which no stretching took place were accompanied by a 440-Hz tone. Auditory input was delivered by two speakers located beneath the augmented reality system. This positioning of the speakers was to ensure that the location of the sound was aligned with the location of the resizing manipulations (based on feedback from the pilot study that suggested auditory input delivered further from the augmented-reality system created a disconnection between the different sensory inputs). After each condition, the participant's hands were occluded from view and the dot touch or ruler judgement tasks were presented (detailed in section

4.3.4 ‘Procedure’), until the experimenter pressed a button to indicate the start of the next trial. A blue rectangle was superimposed on the screen so that the participants knew where to reposition their hands to after each task. Subjective illusion experience data were collected via Qualtrics (Qualtrics, Provo, UT) on a Samsung Galaxy Tab A6 tablet. This was given to the participants after all experimental trials were presented, when each manipulation was presented again, without the subsequent tasks, and the participants were asked to recall the trial they had just experienced and previous trials that were similar, and then give a response on a visual analogue scale of 0 to 100, with 0 being strongly disagree, 50 being neutral and 100 being strongly agree, with written statements. The questionnaire consisted of six statements, two relating to illusory experience: ‘It felt like my finger was really stretching’/‘It felt like the hand I saw was part of my body,’ two relating to disownership: ‘It felt like the hand I saw no longer belonged to me’/‘It felt like the hand I saw was no longer part of my body,’ and two were control statements: ‘It felt as if my hand had disappeared’/‘It felt as if I might have had more than one right hand.’ The questionnaire was delivered three times, once after baseline manipulations, once after visuotactile/ visuotactile-auditory manipulations and finally once after unimodal visual/visual-auditory manipulations.

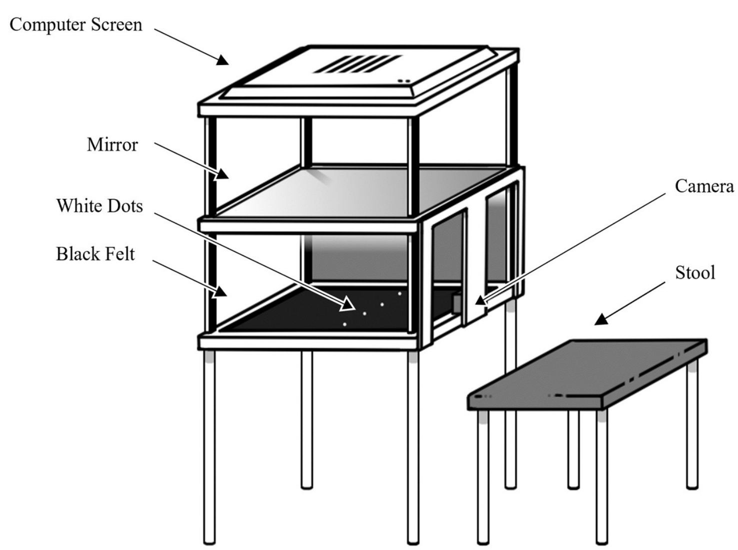

Figure 4.1: Schematic of Augmented Reality System.

4.3.4 Procedure

The participants were assigned to either the auditory group or the non-auditory group based on a randomised MATLAB output of the total number of participants split randomly and evenly into two groups.

They were then seated at the augmented-reality system and were instructed to place both of their hands onto the felt lining, with their index fingers outstretched. There were four white dots on the felt to guide where their hands should be placed, creating two hand spaces (one between each pair of dots), and arm rests were provided for comfort. The participants were instructed to view the image of their hands in the mirror (whilst their real hands were hidden from view) throughout the experiment. They viewed their hands whilst receiving baseline conditions in which no manipulations were applied (with a 440-Hz tone played for auditory group), stretching conditions in which they saw the index finger on their right-hand visually stretch (unimodal visual/visual-auditory conditions with accompanying 308-629 Hz sound for the auditory group) and stretching conditions in which they saw their index finger on their right hand stretch as a researcher gently pulled on the end of their finger simultaneously (visuotactile/visuotactile auditory conditions with accompanying 308−629 Hz sound for the auditory group). After viewing the manipulation of their right hand, the participants completed either a left-hand dot touch task, a right-hand dot touch task or a ruler judgement task. The dot touch tasks consisted of the participant's hands being occluded from view before a magenta dot appeared in front of either their right or left hand, and the participants were then asked to move their index finger in one smooth ballistic pointing movement to touch the dot. When the participants had completed this movement, they were asked to leave their finger in place for a few seconds whilst the experimenter pressed a button to record an image of the hand position through the camera. The participants then returned their hand to the indicated pre-trial position. The ruler judgement task consisted of the participant's hands being occluded from view before a 14-cm ruler, with 8 marks spaced 2 cm apart, was displayed to the right of the participant's right hand. The ruler changed in position and scale to avoid trial order bias. The start point of the scale ranged from 10 to 60 (in arbitrary units), and the vertical position of the ruler was jittered using a normal distribution with a mean of 0 and a standard deviation of 40 pixels. The participants were asked to verbally indicate the location on the ruler that corresponded with where they felt the tip of their right (stimulated) index finger was. The participants completed six repetitions of nine distinct conditions which can be seen in Figure 4.2. A video of a participant undergoing visuotactile stretching can be seen at the following link: https://osf.io/drbzc. Conditions were randomised via MATLAB r2017a, and the experimenter was unaware which condition would be presented on a given trial. The experimenter was informed whether to gently pull the index finger or to apply no manipulation via the presentation of a small blue rectangle on the screen, out of the participant's view. Six repetitions of the nine conditions were presented, followed by a break for the participant to remove their hands from the box and rest, and then the baseline, visuotactile/visuotactile-auditory and the unimodal visual/visual-auditory conditions were presented once in a random order, without any dot touch or ruler judgement tasks, after which the participant completed the subjective illusory experience questionnaire.

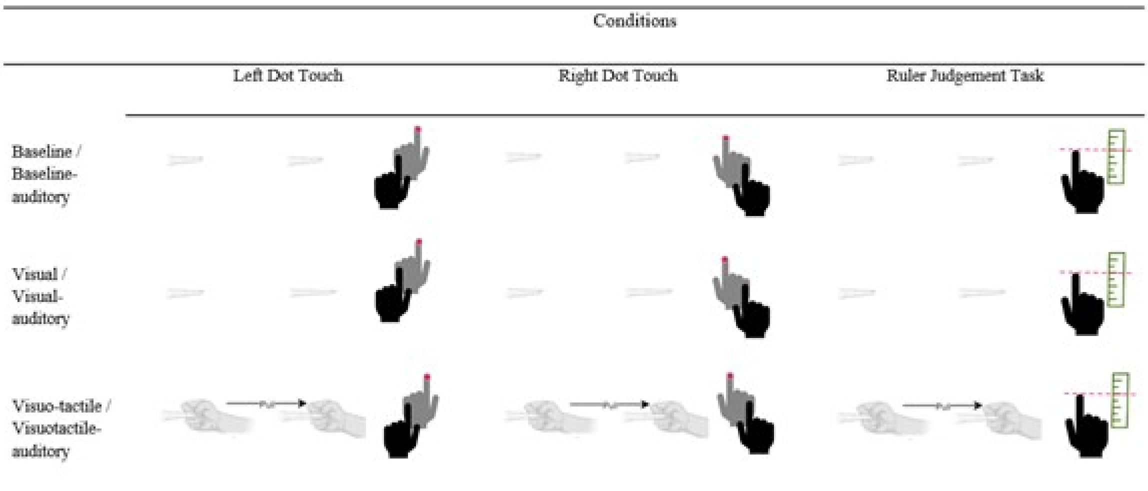

Figure 4.2: 9 Distinct conditions with associated tasks shown as infographics. The no-audio group experienced the condition without audio, whilst the audio group had auditory input during the resizing illusions (increasing pitch tone) and the baseline trials (constant tone). Performance-based tasks can be seen to the right of each condition under the respective column headers.

4.3.5 Analysis

Questionnaire data were exported from Qualtrics to a .csv file before being loaded into RStudio for analysis. For the dot touch and ruler judgement data, during each trial, a still image was taken of the location of the participant's hands within the augmented-reality system. Pre-processing was done algorithmically using image intensity data to estimate finger position; details of this can be seen in the code available on OSF at the following link: https://osf.io/b9s48/. For the dot touch data, the images were used to determine how far away the participant's finger was from the magenta dot, which was stored as an error rating for each trial and then averaged across the same trial types for each participant. This was completed for both left and right dot touch tasks. The ruler judgement data analysis consisted of using the still images with the superimposed ruler and the ruler ratings given verbally by the participant during the experimental task to check that the rating given was within the range of the ruler. If this was not true, as was the case with four participants, then their data for those trials were removed before statistical analysis (analyses with these participant's data included can be seen in Figure D1.3 in Appendix D, which shows no deviation from statistical narrative compared to the analyses with these outliers removed). For all the included trials, the differences between the given ruler ratings and the actual tips of the fingers on the still images were used to generate error values, which were then used for statistical analysis.

For statistical analysis of all data, a factorial ANOVA with a within-subjects factor of condition and a between-subjects factor of group were used for hypothesis testing in line with the pre-registration.

All data and code for analysis are available on the following OSF page (https://osf.io/b9s48/), which also contains resources to computationally reproduce this chapter, including all analyses, figures and statistical outputs, from the raw data.

4.4 Results

Pre-registration of the study did not account for removal of any participant data; however, eight participants scored above 50 (indicating experience of their finger stretching) in the baseline condition where no stretching was induced. Therefore, it was determined that these participants did not complete the subjective illusory experience scale correctly, and they have been removed from all analyses presented in these results. Full sample analyses (including all participants) can be found in Appendix D.

Hypothesis 1 predicted that adding a non-naturalistic auditory input to augmented reality resizing illusions, that is consistent with the visual and tactile manipulations of stretching a finger, would increase subjective illusion strength. We measured this via a subjective illusory experience questionnaire, for (1a) visual and (1b) visuotactile manipulations, with results shown in Figure 4.3. The analysis showed a statistically significant interaction between condition and group ($F(2, 84)=3.62$, $p=0.038$). Main effects analysis showed that both condition ($F(2, 84) = 202.31$, $p<0.001$) and group ($F(1, 42)=4.48$, $p=0.04$) had a significant effect on subjective illusory experience score. Since a significant interaction was found between condition and group, extending the pre-registered analyses, post hoc pairwise t tests with Holm correction for multiple comparisons found that the participants experienced a significantly stronger illusion in the VA condition (M = 61.3, SD = 29, SE = 6) compared to the V condition (M = 41, SD = 27.1, SE = 6) ($t(41) = 2.40$, $p = 0.021$, CI [−3.39, 29.29]) and found no difference in illusion strength when comparing the VT/VTA conditions ($t(40) = 0.23$, $p = 0.82$, CI [−8.56, 11.09]), indicating that the addition of non-naturalistic auditory input significantly affected subjective illusory experience in the unimodal visual condition, but had no effect on the combined visuotactile condition. In addition, the combination of visual and tactile inputs in the VT condition resulted in a significantly higher mean subjective illusion score ($t(42) = -2.92$, $p = 0.006$, CI [−39.13,−10.76]) (M = 82, SD = 17.3, SE = 4) than that in the visual-auditory conditions (M = 61.3, SD = 29, SE = 6).

Mean scores across the participants were above 50 (the neutral point of the scale) in all conditions for the second item on the subjective questionnaire, indicating experience of ownership of the seen hand in all conditions, whilst the mean scores for disownership and control statements were below 50, indicating no average disownership of the hand and no average violations of the control statements (results can be seen in Figures E1.1 - E1.3 in Appendix E).

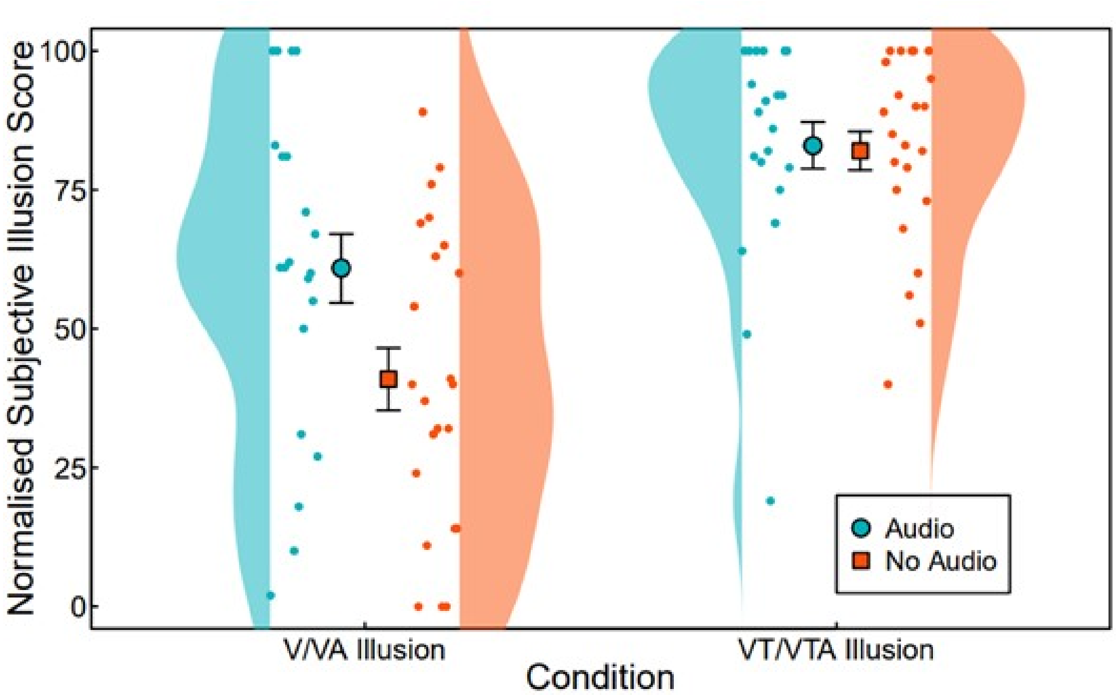

Figure 4.3: Normalised Subjective Illusory Experience Score for V/VA and VT/VTA conditions. Group is indicated by colour, with red showing the no audio group and blue showing the audio group. Error bars show the standard error of the mean, which is shown by the circle and square respectively. Y-axis shows subjective illusion scale data after normalisation through subtraction of each participant's baseline score from their V/VA and VT/VTA scores. Subjective illusion scale ranges from 0 indicating strongly disagreeing with the experience of finger stretching, 50 indicating a neutral opinion, and 100 indicating strongly agreeing with the experience of finger stretching.

Positive control analyses were run on the performance data to check that we were able to see an effect of the illusion with the dot touch and ruler judgement tasks. Positive control data plots can be seen in Figures F1.1 - F1.4 in Appendix F. For the right dot touch data, we found a significant effect of condition ($F(2, 84) = 31.25$, $p < 0.001$). Post hoc tests for multiple pairwise comparisons found that the participants placed their finger significantly lower than the dot in the V/VA condition ($p < 0.001, M = -0.89$, $SD = 1.27$, $SE = 0.19$, CI[-0.90, 0.6) and the VT/VTA condition ($p < 0.001$, $M = -1.07$, $SD = 1.19$, $SE = 0.18$, CI [-0.90, 0.60]) compared to the baseline condition ($M = -0.21$, $SD = 1.14$, $SE = 0.17$), indicating that an effect of the finger-stretching manipulation was indexed by this performance measure; the participants experienced their index finger as significantly longer under these manipulation conditions and this subsequently produced a measurable effect upon body schema. For the left dot touch data, we found a significant effect of condition ($F(2, 84) = 18.345$, $p<0.001$). Post hoc tests for multiple comparisons found that the participants placed their finger significantly lower than the dot in the V/VA condition ($p < 0.001$, M = -1.26, SD = 1.44, SE = 0.22, CI [-0.48, 1.27]) and the VT/VTA condition ($p = 0.009$, M = -0.89, SD = 1.29, SE = 0.19, CI [-0.43, 1.14]) compared to the baseline condition (M = -0.63, SD = 1.2, SE = 0.18). Finally, for the ruler judgement data, we found a significant effect of condition ($F(2, 84) = 11.5$, $p < 0.001$). Post hoc tests for multiple pairwise comparisons found that the participants judged their finger to be significantly longer in the V/VA condition ($p < 0.001$, M = -0.81, SD = 1.69, SE = 0.26, CI [-1.79, 0.23]) and the VT/VTA condition ($p = 0.006$, M = -0.91, SD = 0.28, SE = 0.28, CI[-1.99, 0.26]) compared to the baseline condition (M = -1.35, SD = 1.52, SE = 0.23).

We then addressed hypothesis 2 that the addition of auditory input would lead to stronger illusions as indexed by performance tasks in line with the experience of a longer finger, using a dot touch proprioceptive drift task as an index of body schema for (2a) visual and (2b) visuotactile manipulations (see Figure 4.4). Analysis of right dot touch data showed no significant interaction between condition and group ($F(1, 42) = 0.75$, $p = 0.391$), and the main effects showed no effect of condition ($F(1,42) = 2.11$, $p = 0.154$) or group ($F(1,42) = 0$, $p = 0.971$). Analysis of left dot touch data showed no significant interaction between condition and group ($F(1, 42) = 0.43$, $p = 0.516$), whilst the main effects showed no effect of group ($F(1,42) = 0.03$, $p = 0.858$) but did show an effect of condition ($F(1,41) = 11.09$, $p = 0.002$, CI [-0.65,-0.09]), with participants placing their finger significantly lower in the V/VA condition (M = -0.63, SD = 0.69, SE = 0.1) compared to the VT/VTA condition (M = -0.26, SD = 0.62, SE = 0.09), indicating that the participants experienced a longer finger in the V/VA condition compared to the VT/VTA condition.

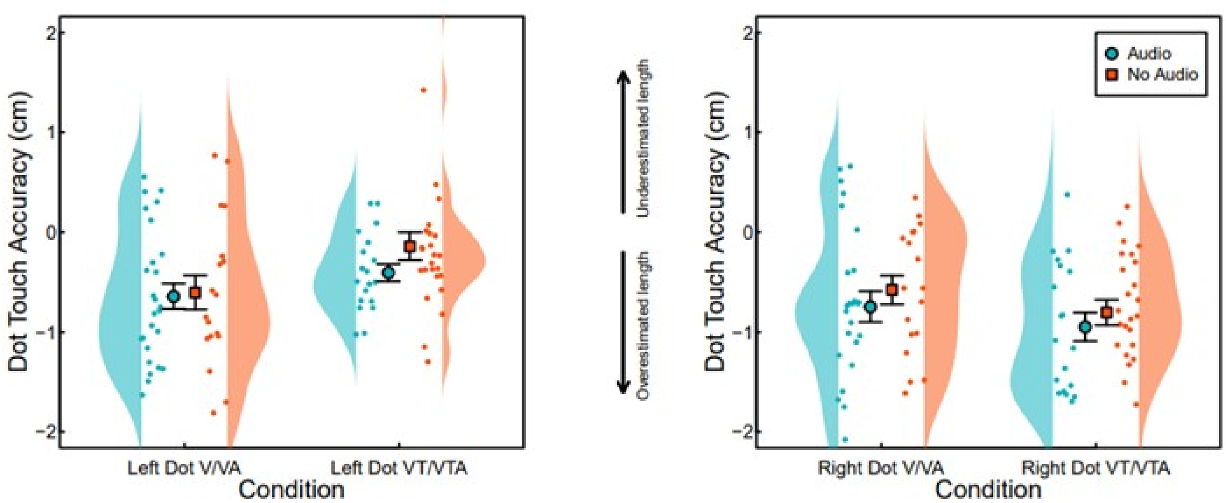

Figure 4.4: Dot Touch Data in centimetres for V/VA and VT/VTA conditions for both left and right hand data, relative to baseline judgements. Group is indicated by colour, with red showing the no audio group and blue showing the audio group. Arrows denote the direction of finger length estimation (downward arrow showing overestimation, upward arrow showing underestimation).

Finally, we assessed hypothesis 3 that the addition of auditory input would heighten ability, measured as differences between reported finger length and actual finger length, on a performance task using a ruler judgement task that indexes body image for (3a) visual and (3b) visuotactile manipulations (see Figure 4.5). The analysis showed no significant interaction between condition and group ($F(1, 42) = 0.334$, $p = 0.567$), and the main effects showed no effect of condition ($p = 0.336$) or group ($p = 0.639$).

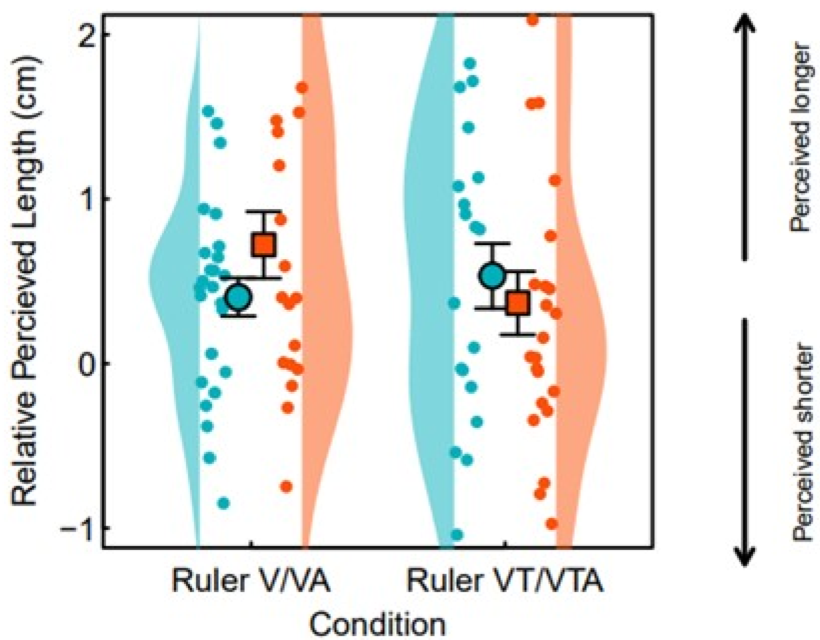

Figure 4.5: Ruler Judgement data in relative centimetres for V/VA and VT/VTA conditions. Group is indicated by colour, with red showing the no audio group and blue showing the audio group. Arrows denote direction of perceived finger length (downward arrow showing shorter perception, upward arrow showing longer perception).

In addition to analyses planned within our pre-registration, at the suggestion of a reviewer, exploratory correlation analyses were run to assess relationships between subjective illusion score and performance-based measures of resizing illusions.

We found no significant relationships between subjective illusion score and performance on any task, under any condition. Further details can be seen in Figure F1.5 in Appendix F.

4.5 Discussion

This study sought to understand what impact the addition of non-naturalistic auditory input would have on traditional visuotactile and unimodal visual hand-based resizing illusions. Our results showed that the addition of non-naturalistic auditory input, that was consistent with the resizing illusion, increased subjective experience of the illusion in the traditional unimodal visual condition, with participants experiencing a significantly stronger illusion in the visual-auditory condition as compared to the visual-only condition, supporting our first hypothesis. However, we found no facilitatory effects of auditory input for subjective experience of illusion strength within the combined visuotactile condition, or for either of the performance tasks, which was in opposition to our remaining hypotheses and served to highlight a potential discordance between the conscious subjective experience of resizing illusions compared to more unconscious performance-based responses. This discordance was reinforced by exploratory correlation analyses showing no significant relationships between subjective illusion scores and either performance-based task.

The subjective findings showed that participants in the audio group rated their experience of the illusion to be greater in the visual condition compared to the non-audio group, showing that the suggested effects of multisensory processing might be heightening the experience of a stimulus. There was, however, no difference between the audio group and the non-audio group in the visuotactile condition, likely due to ceiling effects, wherein the addition of auditory input to visuotactile input did not increase subjective experience of the illusion. The combination of visual and tactile inputs resulted in a significantly higher mean subjective illusion score than that in the visual-auditory conditions, demonstrating that the combination of two different senses produces differing levels of subjective experience of the illusion, with visuotactile surpassing that of visual-auditory manipulations. It is likely that this increased subjective experience within the visuotactile condition is due to the specific nature of the tactile and proprioceptive inputs, which are thought to be specific to the bodily experience, whereas senses such as vision and audition are experienced not only in relation to our body but also relating to objects in the external world (Botvinick and Cohen, 1998; Tsakiris, 2010). Therefore, it is plausible that including a sense that is integral to our bodily experience, such as a tactile input, would have a greater effect on body illusions in comparison to less embodied senses such as an auditory input. This is supported by Ernst and Banks (2002), who proposed the theory that sensory inputs are combined in a statistically optimal fashion based on their reliability in reflecting the accuracy of a given stimulus. In the current resizing illusions, Ernst and Banks' theory explains our findings of a greater illusory experience in the visuotactile condition compared to visual-auditory condition, since the tactile input was more task relevant and came from the same perceived spatial location as the visual input, resulting in the tactile input being upweighted, and therefore had a greater influence on the combined illusory percept, whereas the auditory input was comparatively downweighted. However, when there is an absence of a tactile input, such as in the visual-auditory condition, then the temporal synchrony of the auditory input and visual input serves to upweight the auditory input, allowing a greater influence on the combined percept within the resizing illusion.

Regarding performance findings, our positive control analyses showed that there was a significant difference between baseline and experimental conditions for left and right dot touch tasks, with participants accurately placing their finger on the dot in the baseline condition for the right dot task, and then touching around a centimetre too close to their own bodies in both experimental conditions due to the perceived elongation of the finger in the experimental conditions. For the left dot touch data, the participants were less accurate in their finger placement in the baseline condition, but still placed their finger significantly closer to their own bodies in both experimental conditions, indicating a perceived elongation of their finger in both right and left dot touch tasks. In addition, in the ruler judgement task, the participants reported the tip of their finger to be significantly further away in both experimental conditions compared to the baseline condition. This indicates that they experienced their finger as being longer in both experimental conditions when compared to the baseline non-illusion condition. These findings indicate success of the positive control analyses, showing that these performance tasks can highlight the differences between baseline and experimental conditions.

Referring to the confirmatory analyses regarding the dot touch data, our findings showed no significant effect of group or condition for the right dot touch task, and there was no effect of group for the left dot touch task, however there was an effect of condition, with participants placing their finger significantly closer to their bodies in the conditions without touch (V/VA) compared to the conditions with tactile input (VT/VTA). This finding of a significant effect of condition for the left dot touch data could be explained as a transference effect of stretching from the manipulated hand (right) to the non-manipulated hand (left). Petkova et al. (2011) found whilst using a full body illusion and fMRI evidence for a spread of ownership across connected body parts. Therefore, the resizing of the right hand could likely spread to the left unmanipulated hand, meaning participants felt as though this hand had also been resized, which is supported by the positive control analyses for the left dot touch task in which we found a significant effect of the illusion in the experimental conditions without manipulation of this hand. It is possible that the tactile inputs in the VT/VTA illusion could provide a grounding effect, wherein the participant's hand is grounded to the spatial location within the augmented-reality system, which does not occur for visual-only or visual audio manipulations. This is further supported by Ernst and Banks (2002) optimal integration model, with the tactile input providing a more accurate location estimate than the visual input alone, as the visual input is less reliable than the tactile input and is therefore downweighted in comparison to the tactile input which is upweighted within the combined percept. This spatial grounding in the tactile input conditions in conjunction with the transference effects mentioned previously could explain why we see a significant difference between experimental conditions in the left dot touch task. This is, however, speculative, and further research would be needed to assess the replicability of this effect. Finally, our ruler judgement data also showed no significant effect of condition or group, indicating that the addition of non-naturalistic auditory input showed no facilitatory effects for either performance task.

Exploratory correlation analyses found no significant relationships that survived Bonferroni corrections, thereby reinforcing the discordance observed between our confirmatory findings of a significant effect of group and condition for subjective measures, in comparison to that lack of significant effects for performance-based measures of resizing illusions. The data do, however, show trends towards relationships in the right dot touch and ruler judgement data in relation to subjective illusion score. It is possible that the current study was underpowered to find significant effects in correlation analyses since these analyses were exploratory; therefore, further research is needed to understand the relationship between subjective and performance-based measures of resizing illusions.

The rationale for including two performance tasks in the present study came from previous discordance in the literature with Kammers et al. (2009) finding an impact on body image, but not body schema, with the rubber hand illusion, whereas Newport et al. (2010) found distortions in body schema using the rubber hand illusion and supernumerary limbs. The use of differing measures of body representation in the previous literature often results in different findings, and this discordance between body image and body schema is one example of when this occurs regarding body illusions. Here, we see evidence for an impact of resizing illusions on both body image and body schema, as demonstrated by the positive control analyses, showing that resizing illusions affect one's percept of the body (body image) in addition to the control of the body in an external environment (body schema). The rubber hand illusion differs from the resizing illusion used here, in that the present manipulation does not attempt to relocate the hand, but rather attempts to alter the representation of the finger to be longer. Therefore, it could be that when changing an existing part of one's body, both body image and body schema are affected, whilst when attempting to create a new sensation of one's body in a different location, impact on body schema is dependent on the experimental manipulations being used. In addition, in the current study, we use an augmented-reality system that is similar to that used by Newport et al. (2010), and this system could be producing a more vivid illusion than the rubber hand illusion typically creates.

The increasing pitch tone that was used as the non-naturalistic auditory input in the current study was chosen as it closely reflected that used by Tajadura-Jiménez et al. (2017), who previously found increases in estimations of finger length when they were accompanied by an increasing pitch tone, compared to a decreasing or constant tone. However, in the current experiment, we cannot claim that the effect of an increase in subjective experience of the resizing illusion when this non-naturalistic auditory input is added is unique to a rising pitch tone. It is possible that other auditory inputs could elicit similar effects in increasing subjective experience. Examples might include naturalistic inputs, perhaps of the bones in the finger creaking as it is stretched, akin to the auditory inputs heard during chiropractic treatments, or an unrelated auditory input, such as a constant tone during the resizing conditions. It is also possible that the increasing pitch tone that was used in the current study could be manipulated to be presented in steps, rather than as a constant tone, to assess whether the same effects of increasing illusory experience are seen in different presentations of a rising pitch tone, or whether the addition of any tone at all would increase subjective illusory experience by directing attention towards the illusory manipulation. Nevertheless, the findings from the current study enhance our understanding of the role that auditory input can play in resizing illusions, and further research into the efficacy of alternate auditory inputs should be conducted to consolidate current findings.

Looking into the clinical applications of resizing illusions, it has been suggested that in individuals with chronic pain there may be a cortical misrepresentation of the body and its incoming somatosensory signals, including pain, along with perceptual size dysfunctions of affected limbs, which underpin their persistent pain (Boesch et al., 2016). Since resizing illusions are thought to change one's representation of their body parts, they have been used within chronic pain populations and have been found to reduce subjective pain ratings in participants with chronic pain conditions affecting the hands (Preston and Newport, 2011), back (Diers et al., 2013) and knees (Stanton et al., 2018). The findings from the present study serve to enhance our understanding of the conditions under which these manipulations can affect the personal experience of such illusions. Previously, we have demonstrated that around 30% of participants experience effective resizing illusions via a unimodal visual condition (Hansford et al., 2023). Here, we show that subjective illusion strength during the unimodal visual presentation of finger stretching can be increased through the addition of a simultaneous non-naturalistic auditory input. It is, therefore, possible that when using these resizing illusions for the treatment of chronic pain, it may be beneficial to include non-naturalistic auditory input to increase the subjective illusion strength for patients during the illusion, and consequently, potentially increase attenuation of pain. The unimodal visual condition has been suggested as the most accessible version of resizing illusions (Hansford et al., 2023) as it has the potential to be delivered via a mobile phone application without the need for a researcher to add tactile inputs to the illusion. The incorporation of auditory inputs would not require the presence of a researcher either and, therefore, is a potential method to utilise multisensory integrative processing effects during the unimodal visual application of these illusions to increase subjective illusion strength, which could in turn increase the analgesic effect of these illusions in a chronic pain sample. Future research should, therefore, assess whether the addition of an auditory input has a similar effect in enhancing the strength of these illusions in chronic pain patients, as has been demonstrated here in participants who do not experience chronic pain.

4.6 Conclusions

We found that the addition of non-naturalistic auditory input can increase the subjective illusion strength of resizing illusions administered via a visual input; however, we found no facilitatory effects of the auditory input for any performance measures of illusion strength. We address the previous discordance in the literature surrounding the impact of hand-based illusions on body image and body schema, showing that in a hand-based resizing illusion, the manipulation affects both representations of the bodily self. In addition, this study extends upon previous research finding additive effects of auditory inputs to tactile manipulations of finger resizing and highlights the potential for non-naturalistic auditory inputs to be included in resizing illusions used to treat chronic pain whilst inviting further research to assess the impact of non-naturalistic auditory inputs in chronic pain patient samples. In addition, our findings invite further research into the unique-ness of a rising pitch tone as the presentation of a non-naturalistic auditory input, to assess whether this alone causes an increase in subjective illusion strength. Finally, we highlight the differential effects of these resizing illusions on conscious subjective experience versus unconscious performance-based measures, further elucidating the mechanisms by which such manipulations can alter bodily experience.

5 Chapter 5: Illusory Finger Stretching and Somatosensory Responses

This chapter has been adapted from: Hansford, K.J., Baker, D.H., McKenzie, K.J., Preston, C.E. 2024. Illusory Finger Stretching and Somatosensory Responses, under review at PCI RR, Stage 2 Manuscript. https://osf.io/qky4n[4]

5.1 Abstract

Resizing illusions, delivered using augmented reality, resize a body part through either stretching or shrinking manipulations. These resizing illusions have been investigated in visuotactile, visual-only, and visuo-auditory presentations. However, the neural underpinnings of these resizing illusions remain undefined. This study sought to understand the neural mechanisms behind these illusions (n = 46), by using somatosensory steady state evoked potentials in addition to subjective self-report questionnaires, to enhance knowledge of what drives the subjective embodiment during resizing illusions. Since these Illusions have been shown to provide analgesic effects for individuals with chronic pain conditions, this study also aimed to provide an empirical basis for future investigations in chronic pain samples undergoing resizing illusions. Confirmatory results demonstrated significant differences in subjective experience between non-illusion and multisensory illusion conditions, whilst EEG data measuring somatosensory response across electrodes of interest (F1 & FC1) to 26Hz stimulation to the resized digit showed no significant effects of condition. Exploratory non-parametric SSEP analyses showed a significant effect of condition, with reduced amplitudes in illusory conditions compared to non-illusion conditions, however no significant differences arose in exploratory post hoc tests. These findings demonstrate no clear effect of resizing illusions on SSEP amplitudes for participants without chronic pain, but exploratory findings could hint at a potential sharpening of neural representations as a result of illusory stretching, thereby providing a basis for investigations of comparable subjective and steady state illusion responses in a chronic pain population, who are thought to have more diffuse neural representations of their affected body parts.

5.2 Introduction

Illusory finger stretching is a form of multisensory illusion, specifically a resizing illusion, which alters the subjective perceptual experience of the size of one's finger. Resizing illusions, through changing the way

[4]The author, Kirralise Hansford, collected the data for this experiment, analysed the results, and wrote the manuscript under the supervision of Dr Catherine Preston, Professor Daniel Baker, and Dr Kirsten McKenzie. The experiment was designed jointly with Dr Catherine Preston, Professor Daniel Baker, and Dr Kirsten McKenzie.

in which a body part is perceived, exploit principles of multisensory integration to elicit modulations in the perceived size and shape of the body (Preston et al., 2020; Preston and Newport, 2011; Stanton et al., 2018). Resizing illusions are based on the rubber hand illusion, in which touch is delivered to a visible fake hand at the same time and in the same place that touch is delivered to the hidden real hand. This manipulation elicits feelings of ownership over the fake hand through the integration of multisensory (tactile and visual) inputs highlighting the apparent malleability of bodily self (Botvinick and Cohen, 1998). Multisensory resizing illusions typically involve both tactile and visual inputs to the participant and can be delivered via an augmented reality system or through magnifying optics. Recent studies have also shown resizing illusions to be effectively administered through visual only, and visuo-auditory manipulations (Schaefer et al., 2007; Tajadura-Jiménez et al., 2017). However, multisensory visuotactile manipulations are reported as the most effective at inducing a strong experience of the illusion within an augmented reality system (Hansford et al., 2023).

The augmented reality system used to deliver these resizing illusions presents real-time video capture of the hand, from the same position and perspective as if the hand were being viewed directly (Preston and Newport, 2011). This allows the experimenter to deliver tactile manipulations, such as gently pulling or pushing the hand/finger, whilst the participant views their hand/finger either stretching or shrinking in the augmented image. Newport, Pearce and Preston (2010) found strong embodiment using a synchronous multisensory visuotactile illusion, which was replicated in our pilot data using the same experimental set up as the current study. The pilot data showed, although not significant, a numerically greater illusory experience during synchronous visuotactile manipulations compared to asynchronous (mismatching visuotactile manipulation) control conditions (Figure G1.1, Appendix G) for illusory finger resizing. When comparing multisensory visuotactile resizing illusions to unimodal visual resizing illusions, our recent work (Hansford et al., 2023) shows that multisensory illusions elicit significantly greater illusory experience compared to non-illusion and unimodal visual illusion conditions in healthy participants. We also showed, in exploratory analysis, that a subset of participants who experienced an illusion in the unimodal visual condition reported a stronger illusory experience in this condition than in an incongruent (mismatching visual and tactile inputs) control condition. This subset analysis, however, was of a small sample size, and was selected based on one of the measures analysed thus should be taken with caution, meaning further replication of the findings are needed. Furthermore, we have demonstrated that a visuo-auditory presentation of the finger resizing illusion, using non-naturalistic auditory input, provides a stronger illusory experience than a visual only presentation, but this does not surpass the illusion strength given by a visuo-tactile illusion (Hansford et al., 2024a).

Neuroimaging has previously been used in healthy populations experiencing resizing illusions, whereby modulation of the primary somatosensory cortex has been found using neuromagnetic source imaging during visual only resizing illusions of the arm (Schaefer et al., 2007). Briefly, the more the subjects felt the subjective experience of an elongated arm, the more the cortical distance between the first and fifth digit decreased, showing the topographical representation of the somatosensory cortex being modulated by perceived location of a stimulus. Specifically looking at stretching multisensory visuotactile illusions, which as mentioned are those that elicit the greatest illusion strength in a majority of participants, recent research suggests that these illusions impact the neural representations of the body and reflect early-stage multimodal stimulus integration through modulation of gamma band activity (Kanayama et al., 2021). We have recently also investigated this illusion in healthy participants using electroencephalography (EEG) and have found support for this previous research, finding significant increases in gamma band power, likely reflecting multimodal stimulus integration, in multisensory visuotactile compared to unimodal visual conditions during illusory resizing of a finger (Hansford et al., 2023). Previous research using rubber hand illusions found this multisensory integration effect in early-stage gamma band increases (Kanayama et al., 2021), whilst our recent findings show a later stage of multimodal stimulus integration when using illusory finger resizing manipulations (Hansford et al., 2023).

Looking specifically at research into somatosensory cortex modulation using steady-state evoked potentials (hereafter referred to as SSEPs), low-level somatosensory responses have been induced directly using vibrations of a known frequency applied to a body part. These generate a frequency-locked SSEP detectable at the scalp using EEG (Snyder, 1992; Tobimatsu et al., 1999), and are an index of the cortical response to a stimulus. This paradigm has been used with other sensory modalities to better understand the neural mechanisms underlying multisensory integration, with findings showing that presentation of temporally congruent auditory and visual stimuli significantly enhances the magnitude and inter-trial phase coherence of auditory and visual steady-state responses (Nozaradan et al., 2012). Research has also found evidence of enhanced steady-state responses for within-modality stimulation of auditory and visual stimuli in isolation (Giani et al., 2012), complementing Nozaradan et al.'s findings regarding visuo-auditory combination. Research using vibrotactile stimulation has found increases in steady-state response magnitude corresponding with the amplitude modulation rate of stimulation (Colon et al., 2012; Rees et al., 1986) suggesting an entrainment of oscillatory activity to temporal features of sensory stimulation (Timora and Budd, 2018). Given these findings, we anticipate that SSEPs might change during finger resizing illusions, due to the multisensory manipulations present, to give a potential index of changes in neural representations during the illusion.

Several studies have investigated the analgesic effect of these resizing illusions, as they have been shown to reduce chronic pain in conditions such as osteoarthritis (Preston et al., 2020; Preston and Newport, 2011;

Stanton et al., 2018), chronic back pain (Diers et al., 2013), and complex regional pain syndrome (Moseley et al., 2008). However, the understanding of how these illusions reduce pain is still undetermined. It has been suggested chronic pain involves cortical misrepresentations of the size of the affected body part (Boesch et al., 2016), however, it is unknown if resizing illusions affect this cortical misrepresentation, and if this is therefore what causes the reduction in pain. No study has yet used neuroimaging with a chronic pain population to determine the cortical activity correlated with this illusory analgesia. However, importantly, there has also not been research conducted using SSEPs in participants without chronic pain, to understand what the cortical representations of these resizing illusions are like without the impact of a chronic pain condition. Therefore, the aim of this study is to examine potential changes in the somatosensory cortex during illusory finger resizing in participants without chronic pain, using vibrotactile SSEPs, to use as a basis for later investigations in a sample of chronic pain participants. If we can identify a link between illusory resizing and somatosensory cortex changes, this will enhance our understanding of what is happening in the brain during these illusions and will act as a reference for comparison with neural representations in individuals with chronic pain conditions.

Using different sensory manipulations of finger resizing illusions, in addition to using an electromagnetic solenoid stimulator, this study aimed to investigate subjective illusory experience and somatosensory SSEP responses in participants without chronic pain, to better understand the experience of body ownership illusions from subjective experience and cortical representation perspectives. To test this, different finger resizing illusions consisting of multisensory (visuotactile) stretching (MS), unimodal-visual stretching (UV), a non-illusion control condition without tactile input (NI), and a non-illusion control condition with tactile input (NIT) were used to assess alternate aspects of illusory resizing manipulations and their related effects on somatosensory SSEP response. The inclusion of two control conditions (NI, NIT) was to assess whether localisation of cortical representations arise from resizing manipulations to the finger, or from tactile input given to the finger. The first hypothesis, acting as a positive control (1), was that there will be a greater illusory experience, measured via a subjective illusory experience questionnaire, in the (1a) MS condition compared to the NI condition and in the (1b) MS condition compared to the NIT condition. The main experimental hypothesis for this study was that (2) there will be a significant difference in somatosensory SSEP response across the electrodes of interest (F1 & FC1, see Appendix G Figure G1.2) when comparing across all conditions. Subsequent hypotheses were that there would be significant differences in SSEP response when comparing (2a) the MS condition to the NI condition, when comparing (2b) the UV condition to the NI condition, but (2c) that there would be no significant difference when comparing the NIT condition to the NI condition.

5.3 Methods

5.3.1 Sample Size

Overall, based on the power analyses in section 5.3.6, a total sample size of 46 participants were tested. This sample size adheres to the higher end of sample size estimates (Hypothesis 2 (5.3.6.2) showing 46 participants needed for post hoc tests 2a – 2c).

5.3.2 Participants

Ethical approval for this research was gained from the Department of Psychology, University of York (ethics application code 950), in line with the Declaration of Helsinki. All participants gave informed consent prior to the start of any experimental set up, and participants were instructed that they could withdraw their participation at any time during or after completion of the experiment. 46 participants were tested, with the participant's manipulated finger being randomly split between use of either the index or middle finger. However, 2 participant's data needed removal (>50% of electrodes requiring removal), and therefore 2 additional participants were tested to account for this missing data, both using the index finger as the manipulated digit, resulting in a final sample size of 46 participants (37 Female, 8 Male, 1 Prefer not say; Mean age = 20.3 years, age range = 18.3 – 32.7 years; 32 White, 11 Asian or Asian British, 3 Mixed or Multiple Ethnic Groups; Sample population = students at the University of York). 23 participants were tested using their index finger, the other half using their middle finger.

Sample inclusion / exclusion criteria:

Inclusion and exclusion criteria were determined using self-report responses relating to each item listed below:

- Inclusion Criteria: Right-handed, 18 years of age or over, no older than 75 years of age (include those aged 75 years).
- Exclusion Criteria: Prior knowledge or expectations about the research, a history of developmental, neurological or psychiatric disorders, history of drug or alcohol abuse, history of sleep disorders, history of epilepsy, having visual abnormalities that cannot be corrected optically (i.e. with glasses), or being under 18 years of age, or over 75 years of age. A history of chronic pain conditions, operations or procedures that could damage peripheral nerve pathways in the hands, current experiences of pain or more than 4 hours of consistent pain experienced in the preceding week.

Raw data exclusion criteria:

- Less than 100% of the experiment completed by a participant, more than 50% of electrodes for a single participant requiring removal from EEG data, or if both electrodes F1 and FC1 (electrodes of interest) required removal. More information about data removal can be found in section 5.3.4.1 'Preprocessing Steps'.

5.3.3 Experimental Procedure

All participants completed a demographic survey, asking their age, ethnicity, and sex, and were asked to complete the revised Waterloo Handedness Questionnaire (WHQr) (Elias et al., 1998). The WHQr self-reported handedness questionnaire consists of 36 questions. The questions are answered on a 5-level Likert scale to determine the degree of preferred hand use, with right always being +2, right usually being +1, equal use being 0, left usually being -1, and left always being -2. The sum of the total WHQr score was then used to categorise respondents as left-handed (score of -24 or lower), mixed handed (score of -23 to +23), or right-handed (score of +24 or higher). Only participants who were categorised as right-handed continued participation. Mean handedness score across participants was +57.91 (range = +29 to +71).

Participants were then set up with an appropriately sized 64-channel EEG cap with electrodes arranged according to the 10/20 system. The experimenter used conductive gel to make a conductive bridge between the electrodes and the scalp to attempt to obtain impedance levels of <10kΩ per electrode. Data were collected using an ANT Neuroscan system, sampling at 1kHz. The whole head average was used as a reference.

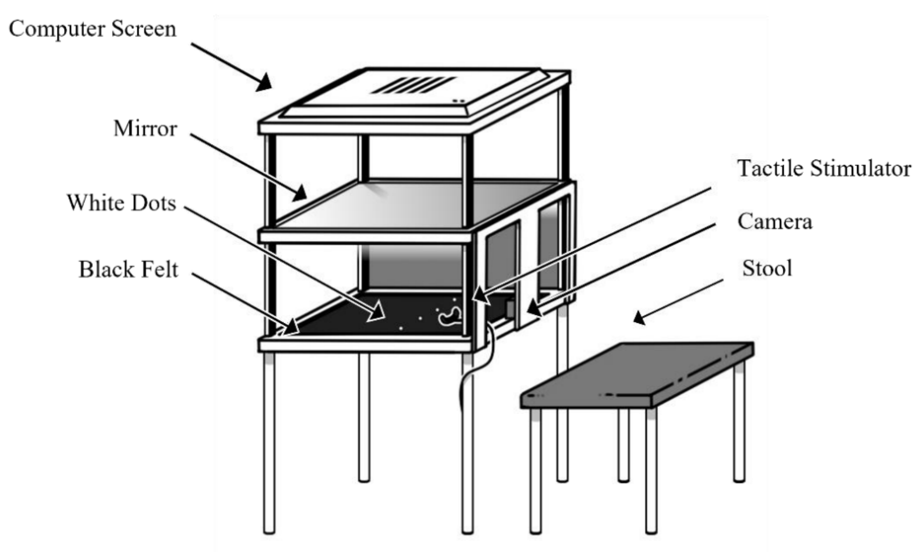

Figure 5.1: Schematic of Augmented Reality System with Tactile Stimulator.

Participants were then seated behind the augmented reality system (Figure 5.1) and instructed to place their hand onto the black felt fabric within the augmented reality system. Within the self-built system there was a 1920 x 1080-pixel Spedal Webcam Wide Angle Camera at the edge of the black felt on the side the participant sits, away from the participant's view. 26cms above the felt base, there was a mirror, which was placed 26cms below a screen with a resolution of 1920 x 1200 pixels, with a width of 52cms and a height of 32cms. The thickness of section on which the mirror sat was 2cms. This screen was 54cms from the base of the system, and the base of the system was 82cms from the ground. Participants were instructed to place either their right index or middle finger outstretched onto the felt. The decision of whether the participant used their index or middle finger was pseudo randomised (to give equal representation of each finger) via MATLAB prior to any participants taking part. There were two white dots for each hand on the felt and participants were instructed to place their hand between these two dots. Participants were instructed to view their hand's image in the mirror (whilst the real hand was hidden from view) throughout the experiment. The camera placed underneath the mirror on the felt base was used to deliver a live feed video of the participant's hands to the computer screen at the top of the augmented reality system, which showed in the mirror reflection to the participants. There was a delay of 170ms in the video processing pipeline from the camera image to the augmented video image.

Participants underwent 4 conditions: multisensory stretching (MS), unimodal-visual stretching (UV), a non-illusion control condition without tactile input (NI), and a non-illusion control condition with tactile input (NIT). There was vibrotactile stimulation to the finger in all conditions, but only tactile input of the researcher touching the participants finger in the MS and NIT conditions. Each trial lasted 2.4 seconds for the manipulation phase, where the finger was stretched by 60 pixels (2.1 centimetres) in UV and MS conditions, followed by a further 2.4 second habituation phase in which participants could view and move their (augmented) finger, whilst they keep the rest of their hand still, before the screen went dark, indicating that the next trial could start. The MS condition consisted of the researcher touching and pulling the participant's finger as the participant viewed their finger stretching in a congruent manner. The UV condition consisted of the participants viewing their finger stretch without any experimenter manipulation. The NI condition provided no visual or touching tactile manipulations to the finger, the image of their finger was visible and unchanged throughout. The NIT control condition involved no visual input of the finger stretching, again the image of their finger was visible but unchanged. Additionally, this condition included tactile input of the experimenter's hand touching the participant's finger, but without pulling. Visualisation of all conditions can be seen in Figure 5.2.

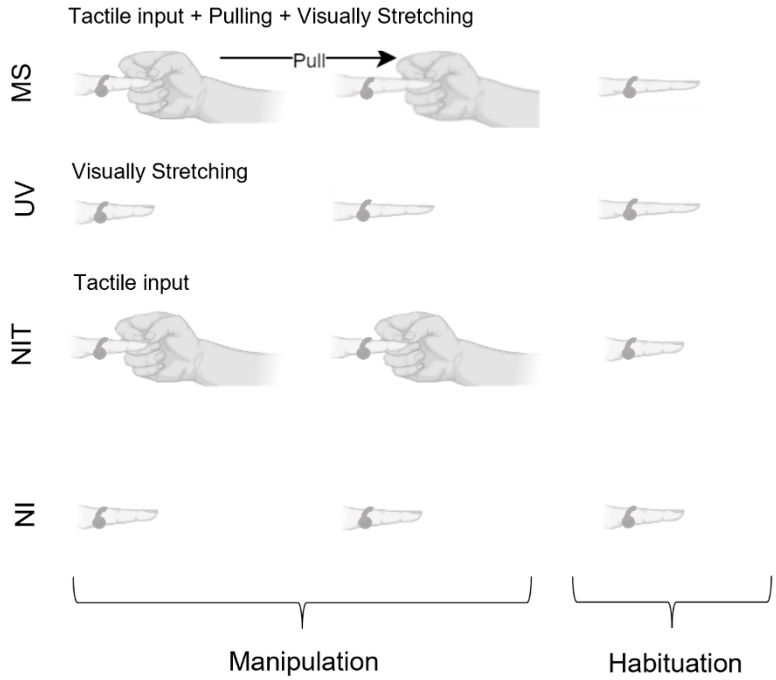

Figure 5.2: Infographic of Experimental Conditions. MS = Multisensory Stretching, UV = Unimodal Visual Stretching, NIT = Non-Illusion Tactile, NI = Non-Illusion. During the manipulation phase (2.4 seconds) the visual image of the finger is stretched in the MS and UV conditions, and/or the experimenter provides tactile input (touch) in the MS and NIT conditions. The tactile input in the MS condition is accompanied by pulling. During the habituation phase (2.4 seconds) participants are free to move their finger. The arrow denotes the direction of the experimenter's action. The vibrotactile stimulator is depicted on the finger in each phase of the experiment as vibrations are presented throughout.

The experimenter was seated opposite the participant, the other side of the augmented reality machine and touched the digit during MS and NIT conditions by holding onto the distal interphalangeal joint and gently touching (NIT) or pulling (MS) the finger whilst the participant kept their hand in place. Conditions were delivered across 4 blocks, with each block consisting of 24 trials of the same experimental condition, totalling 96 trials over all 4 blocks. The ordering of the blocks was randomised for each participant to prevent ordering effects. The experiment was programmed in, and the conditions randomised using MATLAB R2017a and the experimenter was informed of whether to pull the finger or to touch the finger via an indicative box displayed on the screen out of the participant's view. If the box was blue, this indicated a need to pull the finger, if it was white it indicated a need to touch the finger, if there was no box displayed then this indicated no tactile manipulation from the experimenter. The researcher used a button press to trigger the start of the manipulation, and started pulling the finger, when needed, synchronously within the 2.4 second manipulation phase. If the experimenter were to forget to pull the finger on a multisensory condition, or mistakenly pulled the finger in a control trial, then this would noted during the experiment, and that trial would be removed from analysis. Fortunately, no trials needed removal due to experimenter error. Vibrations were delivered to the participant's finger in all conditions using a miniature electromagnetic solenoid stimulator (Dancer Design Tactor; diameter 1.8mm) emitting vibrations produced by sending amplified 26Hz sine wave sound files, with stimulus intensity controlled by an amplifier (Dancer Design TactAmp). The tactor was driven at 50% of the maximum (i.e. a peak input voltage of 3V) using a 26Hz sine-wave, and delivered a peak force of 0.18N. The electromagnetic solenoid stimulator was attached to the participant's finger that was outstretched to receive the manipulations, between the knuckle and the first finger joint, using clear medical tape and gave continuous stimulation for the duration of each trial. Participants were encouraged to take a break between each of the blocks to stretch their hand. EEG was recorded throughout as a continuous recording with conditions denoted by numbered 8-bit digital at the start of each trial (USB-TTL Module, Black Box Toolkit Ltd.).

Finally, at the end of each block, the participant was asked to complete the subjective illusory experience questionnaire regarding a condition presented in a given block using a Samsung Galaxy Tab A6 tablet via a questionnaire on Qualtrics (Qualtrics, Provo, UT). The questionnaire consisted of six questions relating to the trials the participant had just experienced. Two statements related to illusory experience: "It felt like my finger was really stretching" / "It felt like the finger I saw was part of my body", two related to disownership: "It felt like the finger I saw no longer belonged to me" / "It felt like the finger I saw was no longer part of my body", and two were control questions: "It felt as if my finger had disappeared" / "It felt as if I might have had an extra finger" (all questions were directed towards the participants manipulated finger). Control questions were included to create an index for the illusion and disownership questions (more detail can be found in section 5.3.4.1 'Preprocessing steps'), whilst disownership questions were included to assess if the potential experience from the illusions resulted from a disownership of the body part, or from subjective embodiment of the body part (McCabe, 2011). A visual analogue scale from 0 – 100 was used for each statement, with 0 being strongly disagree, 50 being neutral and 100 being strongly agree.

Data collection was terminated when the full sample of participants had been tested. If a participant completed <100% of the experiment or if over 50% of electrodes needed removal, or if both electrode F1 and FC1 needed removal, then their data was not be included, and additional participants were recruited to replace any lost data.

5.3.4 Analysis Pipeline

5.3.4.1 Preprocessing Steps

EEG data were first converted using MATLAB and EEGlab from the ANT EEprobe .cnt format to EEGlab .set format. All subsequent analysis was then be conducted using the MNE-Python toolbox (Gramfort et al., 2013). A 50Hz notch filter was first applied to the raw EEG data for all electrodes, followed by calculation of the standard error across time for each electrode for each participant (Luck et al., 2021). Across the standard errors for all participants, the 5% of electrodes which showed the largest standard errors were used to create a standard error threshold. Any electrode with a standard error above this threshold, or with a value of 0, was removed from analysis. Where a participant had over 50% of their electrodes over the standard error threshold or with a value of 0, or if the electrodes requiring removal included either electrodes F1 or FC1 (electrodes of interest), then their data was removed. Primary analysis of the remaining EEG data then involved averaging the signal across the electrodes of interest (or using just electrode F1 or FC1 in case of electrode removal), and calculating the Fourier transform for each trial per participant. These amplitudes were then averaged across trials per condition to give overall results for each participant per condition. Statistical comparisons were then performed on the Fourier amplitudes at the stimulation frequency (26Hz), across conditions and participants. No additional filtering or denoising steps were applied to the EEG data, in line with Figueira et al.'s (2022) report that only a Fourier transform is typically needed for this type of EEG data.

Regarding questionnaire data, scores for both illusion experience questions were combined to give median scores, along with both disownership questions and both control questions, resulting in 3 median scores per condition per participant. The median control scores were used to create an index of the illusion and disownership scores by subtracting the median control score from the median illusion and median disownership scores, in line with previous research doing similarly (Kalckert and Ehrsson, 2012; Kilteni and Ehrsson, 2017; Matsumiya, 2021). The normalised (control indexed) data were used for analyses, with a new scale from -100 to +100 with 100 indicating strongly agree, 50 indicating a neutral opinion, and scores below 0 indicating strongly disagree with the statements on the questionnaire. 50 is maintained as a neutral opinion so that the normalised data still adhered to the thresholds that the participants were presented with during the experiment.

5.3.5 Planned Analyses

5.3.5.1 Hypothesis 1 (Positive Control)

(1 – Positive Control) There will be a greater illusory experience, measured via a subjective illusory experience questionnaire, in the (1a) MS condition compared to the NI condition and in the (1b) MS condition compared to the NIT condition.

The subjective illusory experience questionnaire was used as a positive control for the current study. Previous research has shown significantly greater illusion strength for MS conditions compared to non-illusion conditions (Carey et al., 2019; Hansford et al., 2023), which we attempted to replicate. Questionnaire data were be analysed using R (R Core Team, 2021). A one-way ANOVA would be run to compare the dependent variable of normalised (control indexed) illusion score from each independent condition. Given significant findings, post-hoc tests would be run, with Bonferroni correction for 2 comparisons (MS Vs NI, MS Vs NIT) at an initial alpha of 0.05.

5.3.5.2 Hypothesis 2

(2) There will be a significant difference in somatosensory SSEP response across the electrodes of interest (F1 & FC1). Subsequent hypotheses are that there will be a significant difference in SSEP response in (2a) the MS condition compared to the NI condition, and (2b) the UV condition compared to the NI condition, but (2c) that there will be no significant difference when comparing the NIT condition to the NI condition.

As mentioned in the EEG pre-processing steps in section 5.3.4.1, analysis of EEG data involved taking a Fourier transform for each waveform averaged across the electrodes of interest, to obtain the amplitude for each trial at the vibration frequency (26Hz). These amplitudes would then be averaged across trials to give overall results for each participant, before running a repeated measures one way ANOVA comparing somatosensory SSEP response from each experimental condition. The dependent variable would be SSEP amplitude in µV, whilst the independent variable would be the different manipulations given in each comparison condition. Given significant findings in the ANOVA, post hoc comparisons would be conducted at a new alpha of .016 (corrected for 3 comparisons (MS Vs NI, UV Vs NI, NIT Vs NI)). Based on the pilot data in Appendix G Figure G1.2, we expected to see activation most pronounced over mid-frontal distributions, covering F1 and FC1 electrodes and therefore these electrodes were selected as the electrodes of interest.

5.3.6 Power Analysis

5.3.6.1 Hypothesis 1 (Positive Control)

Effect sizes were determined by research from Hansford et al. (2023) using the subjective illusory experience questionnaire and comparing MS, UV, and incongruent finger-based resizing illusions to control conditions with no illusory resizing, using the same finger stretching illusions and the same equipment (n = 48), which show an effect size of $\eta^2 = .33$ (converted to Cohen's f = .70 and Cohen's d = 1.4). Additional effect size information comes from a visual capture study (n = 80) using a subjective embodiment questionnaire and visual and tactile manipulations to a mannequin body (Carey et al., 2019), showing an effect size of r = .64 (converted to Cohen's f = .83) when comparing embodiment scores from the questionnaire against control scores. An effect size of f = .70 was used for hypothesis 1 to adhere to the lower end of previous effect sizes.

Hypothesis 1: A priori power analysis using G*Power for the smallest effect size of interest (f = .70) showed that for a repeated measures, within factors one way ANOVA, with an effect size (f) of 0.70, alpha level of 0.05, power at 80% and 1 group with four measurements, 5 participants were needed.

Hypotheses 1a and 1b: A priori power analysis using G*Power shows that for a one-tailed difference between 2 means (pairwise) t test, with an effect size of dz = 1.4, alpha of 0.025, power at 80%, a total sample size of 7 participants was required.

5.3.6.2 Hypothesis 2

This was the first study to investigate illusory finger stretching using SSEPs, so appropriate effect size estimates were not available. We therefore conducted power calculations based on a smallest effect size of interest, in line with the recommendation of Lakens (2014). Here, we have chosen an effect size of d = 0.5 (a medium effect, see Cohen, 1988), since this is the smallest effect size we were interested in detecting, which we converted to a Cohen's f of 0.25 for Hypothesis 2's power analysis, and have maintained at 0.5 for the subsequent post hoc power analyses.

Hypothesis 2: A priori power analysis using G*Power showed that for a repeated measures, within factors one way ANOVA, with an effect size (f) of 0.25, alpha of 0.05, power at 80%, and 1 group with four measurements, a total sample size of 24 participants was needed.

Hypotheses 2a – 2c: A priori power analysis using G*Power shows that for a two-tailed difference between 2 means (pairwise) t test, with an effect size of dz = .5, alpha of 0.016 (corrected for multiple comparisons), power at 80%, a total sample size of 46 participants was needed.

5.3.7 Data and Code Availability

The stage 1 report given in principle acceptance for this study, with details regarding planned analyses and a Design Planner encompassing research questions, hypotheses, sampling and analysis plans and their resulting interpretations and observed outcomes can be seen at the following OSF page: https://osf.io/pfksu/. The current version of the stage 2 manuscript can be found at the following OSF page: https://osf.io/qky4n. Finally, all data and code to reproduce the analyses can be found at the following OSF page: https://osf.io/yhz6j/.

5.4 Results

Positive control analyses of the subjective illusion data can be seen in 5.3. A one-way ANOVA found a significant overall effect of condition with a large effect size (F(3,135), p = <0.001, $\eta p^2 = 0.229$). Post hoc t tests with Bonferroni corrections found significantly greater combined illusion score in the MS condition (Mean = 61.79, SD = 28.31) compared to the Non-Illusion (NI; Mean = 31.2, SD = 26.08, t = -5.67, $p.adj = < 0.001$, Cohen's d = -31) and Non Illusion Tactile (NIT; Mean = 37.41, SD = 20.59, t = -5.61, $p.adj = < 0.001$, Cohen's d = -24) conditions, thereby supporting hypotheses 1, 1a, and 1b and fulfilling the positive control checks.

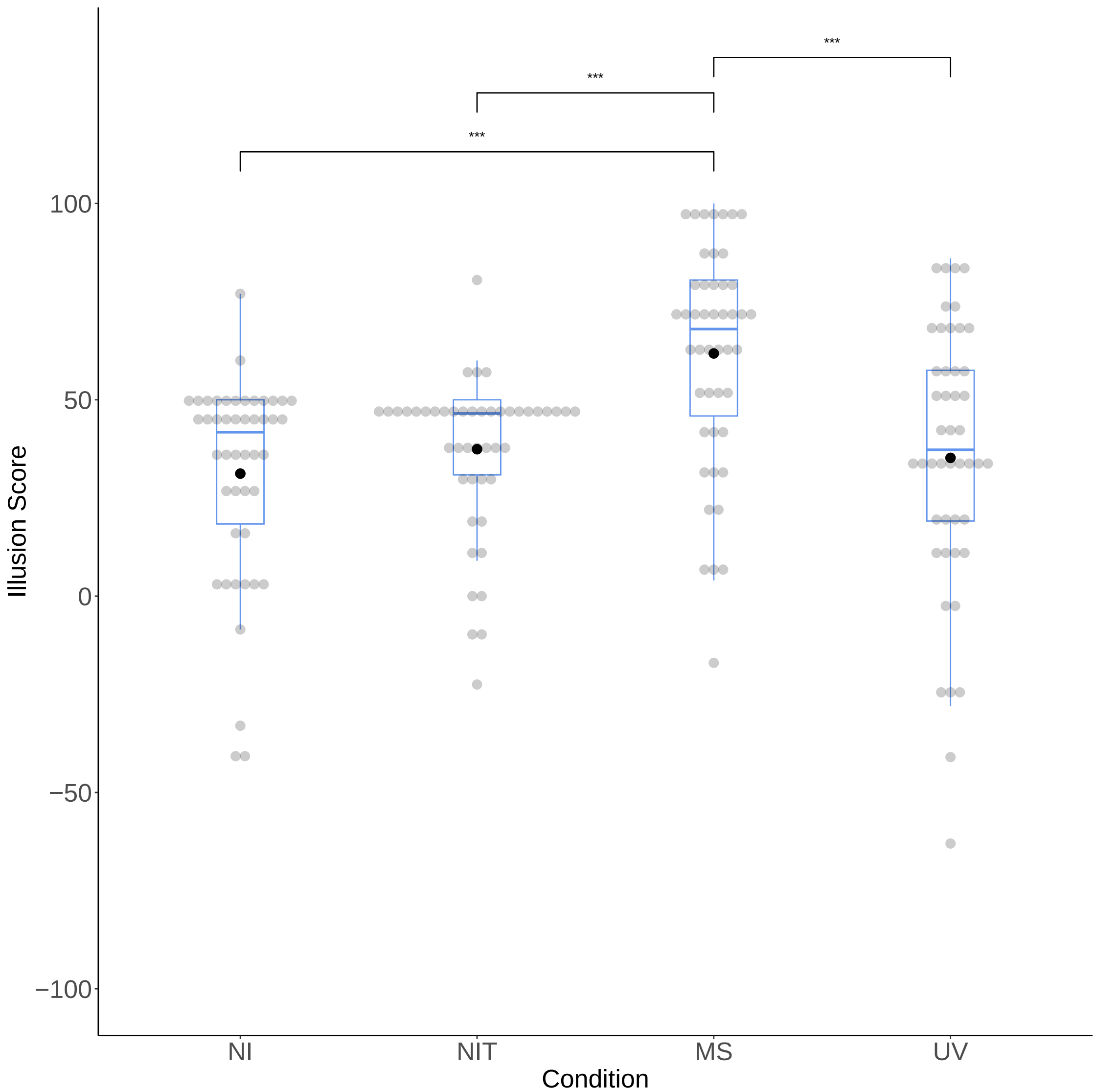

Figure 5.3: Combined Illusion Score Indexs Across Conditions (NI: Non-Illusion; NIT: Non-Illusion Tactile; MS: Multisensory; UV: Unimodal Visual). Scores below 50 indicate disagreement with experience of illusion statements, whilst scores above 50 indicate agreement. A continuous visual analogue scale was used in data collection, with agreement and disagreement statements located at each end of the scale. Box plots show means, medians and inter-quartile ranges of data. Medians are indicated with a horizontal line whilst means are indicated by a black dot. Box and wiskers show inter-quartile ranges. Data points are shown in grey jitter binned along the y-axis, grouped by condition.

Analyses of SSEP data can be seen in 5.4. The left panel confirms the presence of a clear steady-state signal at 26Hz, which was strongest over the fronto-central electrodes. A one-way ANOVA found no significant effect of condition with a small effect size (F(3,135), $p = 0.209$, $\eta p^2 = 0.033$), opposing Hypothesis 2. Post hoc t tests with Bonferroni corrections found no significant differences between SSEP amplitude when comparing the NI condition (Mean = 0.49, SD = 0.76) to the MS condition (Mean = 0.31, SD = 0.57, $t =$

1.7, $p.adj = 0.571$, Cohen's d = 0.18), or UV condition (Mean = 0.36, SD = 0.83, $t = 1.15$, $p.adj = 1.000$, Cohen's d = 0.13), meaning Hypotheses 2a and 2b were unsupported. There was no significant difference found when comparing the NI condition to the NIT condition (Mean = 0.29, SD = 0.35, $t = 2.02$, $p.adj = 0.298$, Cohen's d = 0.19), supporting Hypothesis 2c.

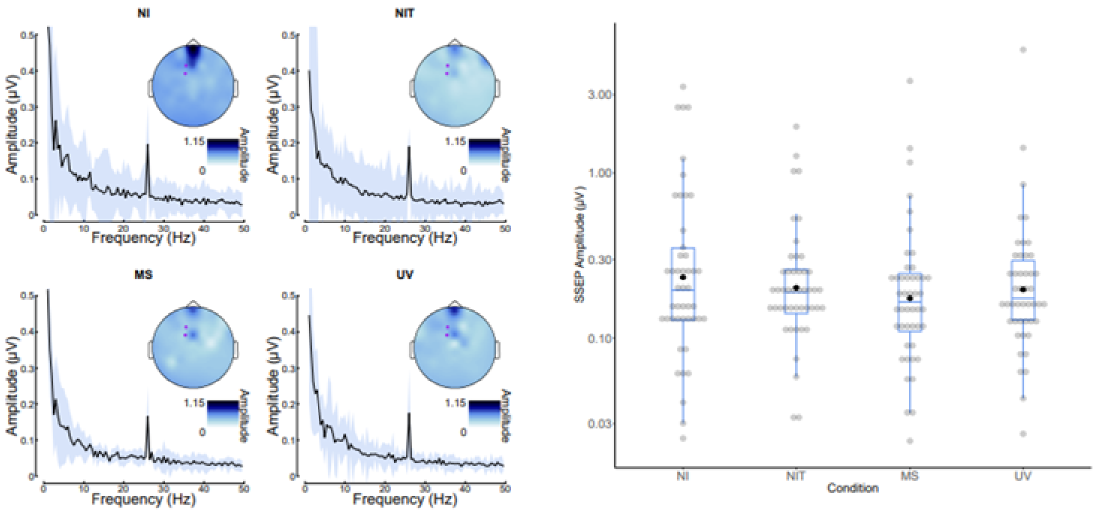

Figure 5.4: Left Panel: SSEP Amplitude Spectra Across Conditions (NI: Non-Illusion; NIT: Non-Illusion Tactile; MS: Multisensory; UV: Unimodal Visual) for electrodes of interest (F1 and FC1). Black line shows data average, shading shows ±1 standard error across participants (n=46). Right Panel: SSEP Amplitudes Across Conditions. Box plots show means, medians and inter-quartile ranges of data. Medians are indicated with a horizontal line whilst means are indicated by a black dot. Box and wiskers show inter-quartile ranges. Data points are shown in grey jitter binned along the y-axis, grouped by condition. A logorithmic scale is used for visual representation of data.

5.4.1 Exploratory Analyses

Since illusion data violated assumptions for parametric tests, an exploratory Friedman test was run and found a significant overall effect of condition with a moderate effect size ($\chi^2(3) = 42.05$, $p < .001$, Kendall's W = 0.305) and post hoc Wilcoxon tests with Holm corrections found significantly greater combined illusion score in the Multisensory Stretching (MS) condition (Median = 68, SD = 28.31) compared to the Non-Illusion (NI; Median = 41.75, SD = 26.08, $z = 103$, $p.adj < .001$, r = -29), Non Illusion Tactile (NIT; Median = 46.5, SD = 20.59, $z = 118$, $p.adj < .001$, r = -23.25) and UV conditions (Median = 37.25, SD = 34.37, $z = 903.5$, $p.adj < .001$, $r = 27.75$).

In addition to illusion data, disownership and control data were collected and therefore analyses on these datasets have also been run. Exploratory analysis of subjective disownership and control data can be seen in Figures H1.1 and H1.2 in Appendix H. A significant increase in disownership scores were found in the UV condition compared to all other conditions, and there were no significant comparisons found for control data. All statistical reporting can be seen in Appendix H.

EEG data also violated assumptions for parametric tests and therefore a Friedman test was also run and found a significant overall effect of condition with a small effect size ($\chi^2(3) = 8.17$, $p = .043$, Kendall's W = 0.059). However, post hoc Wilcoxon tests with Holm corrections found no significant differences between SSEP amplitude when comparing the NI condition (Median = 0.19, SD = 0.76) to the MS condition (Median = 0.17, SD = 0.57, z = 725, $p.adj$ = 0.131 , r = 0.05), or UV condition (Median = 0.17, SD = 0.83, z = 719, $p.adj$ = 0.131 , r = 0.03). There was no significant difference found when comparing the NI condition to the NIT condition (Median = 0.19, SD = 0.35, z = 686, $p.adj$ = 0.131 , r = 0.03).

Exploratory correlational analyses were conducted to assess the correlation between participant's subjective illusion score and their SSEP amplitude across electrodes of interest (F1 & FC1) for each condition to see if those who experienced a stronger feeling of the illusion had more reduced SSEP amplitudes, results showed no significant correlations and can be seen in Figure H1.3 in Appendix H.

5.5 Discussion

This study sought to understand both subjective and neural responses to resizing illusions in participants without chronic pain, to provide not only a greater understanding of how bodily illusions affect cortical representations, but also a basis for investigating differences in cortical representations between participants with and without chronic pain conditions when using resizing illusions for analgesic treatment. Subjective data replicated previous findings of greater subjective illusory experience in multisensory compared to non-illusion conditions, showing that the addition of vibrotactile stimulation does not appear to impact subjective experience of resizing illusions using augmented reality, since these effects replicate ones found previously without vibrotactile stimulation. EEG data showed no significant effect of condition when assessing SSEP amplitudes across the electrodes of interest (F1 & FC1) at 26Hz. Exploratory non-parametric analyses of SSEP amplitudes showed a significant effect of condition however, with a decreased median amplitude in the multisensory and unimodal visual conditions compared to the non-illusion condition. However, these differences did not reach statistical significant with exploratory post hoc tests. These findings, therefore, demonstrate that within exploratory analyses illusory resizing can lead to reductions in SSEP amplitude, but this finding would need to be replicated as a confirmatory analysis and a larger sample size would likely be needed to detect any significant differences in post hoc comparisons due to the small effect sizes found.

Whilst the subjective illusory experience data supported the positive control hypothesis of the multisensory condition providing greater illusory experience than either of the non-illusion conditions, exploratory analyses found that the unimodal-visual condition demonstrated a significantly reduced experience of the illusion compared to the multisensory condition. This reduction in illusory experience for the unimodal visual condition compared to the multisensory condition was also found in our previous work (Hansford et al., 2023), and similarly shows a more diverse range of responses compared to the multisensory condition. These findings reinforce the idea that not everyone experiences resizing illusions with only visual stimuli, and this should be considered when assessing the application of resizing illusions to chronic pain samples, as if subjective experience of the illusion is required for analgesic effects, then it is possible that not everyone will experience this from a unimodal visual presentation. Exploratory data looking at disownership of the digit during illusory resizing found significantly greater experiences of disownership in the unimodal visual condition compared to the multisensory, non-illusion, and non-illusion tactile conditions. This heightened disownership might explain the reduced illusory experience in the unimodal visual condition, as it could be that the presence of tactile input is needed during illusory resizing to ground the digit within the augmented reality system, otherwise feelings of disownership can arise.

Regarding SSEP data, the reduced amplitudes seen in the exploratory analyses could be explained through the somatosensory blurring / sharpening hypothesis (Haggard et al., 2013). This theory proposes that the somatosensory representation of a body part can be sharpened through improved tactile discrimination and acuity training. This sharpening is thought to represent increased organisation of the somatosensory area responding to the stimuli (Haggard et al., 2013). Tactile acuity can be increased through simply viewing an enlarged body part (Kennett et al., 2001). Therefore, it is likely that the enlarged digits created through illusory resizing are sharpening the somatosensory representations of the digits. The reduced amplitudes found during exploratory analyses in the illusory conditions compared to the non-illusion conditions therefore could demonstrate a neural representation of this somatosensory sharpening. However, since these differences were not found to be significant through confirmatory analyses or exploratory post hoc tests, it is likely that for people without chronic pain there are not clear changes in SSEP response during illusory resizing.

A possible explanation for the SSEP reductions found could be through the direction of attention to the digits in illusory conditions. However, previous research has found that attending to a specific vibrotactile stimulus can result in an increase, rather than a reduction, in SSEP amplitude (Giabbiconi et al., 2004). Furthermore, brain computer interfaces (BCIs) are used to intentionally modify a brain signal that can be detected by a computer to manipulate one's environment, and these are often based on increasing SSEP response amplitudes through directing attention (Muller-Putz et al., 2006). Therefore, it is unlikely that the reduction in SSEP amplitudes seen here are due to increased attention in tactile and illusory manipulation conditions. It is possible though, that if somatosensory sharpening is occurring, the reduction in amplitude associated with this could be confounded by this attentional effect, with somatosensory sharpening reducing amplitudes whilst attention is increasing the amplitudes, resulting in the small effect sizes we see in this dataset. Due to these small effect sizes, replication of these effects in larger samples might be better able to assess somatosensory sharpening or attentional effects, as here the sample size was only powered to detect at least medium effects.

Further exploratory analyses assessed correlations between subjective illusory experience and SSEP amplitude across electrodes of interest and found no significant correlations for any condition. These findings could indicate that subjective experience of the illusion is not required for there to be changes in cortical responses, although without clear support for changes in SSEP amplitudes found within the confirmatory analyses, this suggestion cannot be empirically justified. It is possible that SSEP amplitudes are too noisy to show such somatosensory changes, or that the sample needed to detect these effects would have to be larger than the one in the present study. However, when considering resizing illusions as a non-pharmaceutical method for pain reduction, a lack of correlation between SSEP amplitude and illusory experience could mean that patients do not need to subjectively experience resizing illusions for there to be the potential of illusory analgesia. Future research is needed to consolidate both this hypothesis and the exploratory correlational findings from the present study.

One of the main aims of the present study was to provide a basis for investigating somatosensory representations of illusory resizing in samples with hand-based chronic pain. Illusory resizing has been found to provide analgesic effects for hand-based chronic pain (Preston and Newport, 2011), however the neural underpinnings of this analgesia remain undefined. Since chronic pain is thought to create blurred somatosensory representations of the painful body part (Haggard et al., 2013), it is possible that when comparing the results seen here in participants without chronic pain to a sample of participants with chronic pain, the differences between amplitudes in the non-illusion and illusion conditions could be greater, due to more blurred initial representations of the painful digits. If somatosensory response changes are found in a sample with chronic pain, then these changes could underscore the analgesia experienced after illusory resizing, however if these changes are either not seen or do not align with pain reduction, then alternate mechanisms are likely behind illusory resizing analgesia. It is, however, possible that since there were no SSEP effects found through confirmatory analyses in the present study, that the impact of illusory resizing on SSEP responses could be too small to meaningfully detect in both population groups, especially since a patient group could have more varied and / or noisy data.

5.6 Conclusions

The present study enhances our understanding of whether there are cortical changes associated with illusory resizing in people without chronic pain and provides an empirical basis for later investigations of somatosensory response changes in a sample with chronic pain. The subjective data suggest that vibrotactile stimulation does not affect experience of resizing illusions, and therefore highlights the suitability of this method for eliciting somatosensory steady state evoked potentials in future investigations. Confirmatory analyses of SSEP data showed no clear effect of illusory resizing on SSEP amplitudes, however, trends toward supporting the somatosensory blurring / sharpening hypothesis were found within exploratory analyses whereby reduced amplitudes were seen in both illusory conditions compared to the non-illusion conditions. If similar reductions are observed in a sample with chronic hand-based pain, then it would be possible to assume that these neural response changes could be driving illusory analgesia.

6 Chapter 6: Illusory Finger Stretching and Somatosensory Responses in Participants with Chronic Hand-Based Pain

This chapter has been adapted from: Hansford, K.J., Baker, D.H., McKenzie, K.J., Preston, C.E. 2024. Illusory Finger Stretching and Somatosensory Responses in Participants with Chronic Hand-Based Pain, under review at PLOS ONE. Preprint: https://doi.org/10.31234/osf.io/ambwv. [5]

6.1 Abstract

Current pharmaceutical interventions for chronic pain are reported to be minimally effective, leading researchers to investigate non-pharmaceutical avenues for chronic pain treatment. One such avenue is resizing illusions delivered using augmented reality. These illusions resize the affected body part through stretching or shrinking manipulations and have been shown to give analgesic effects; however, the neural underpinnings of these illusions remain undefined. Steady-state evoked potentials (SSEPs) have been studied within populations without chronic pain undergoing hand-based resizing illusions, finding no convincing differences in SSEP amplitudes during illusory stretching. Here, we present comparable findings from a sample with chronic pain, who are thought to have blurred cortical representations of painful body parts, but again find no clear differences in SSEP amplitude during illusory stretching. However, no significant decreases in pain ratings were found following illusory resizing, and changes in SSEP amplitudes are thought to possibly reflect experiences of illusory analgesia. Despite a lack of illusory analgesia across the sample, several participants experienced clinically meaningful levels of pain reduction following illusory resizing, highlighting the potential of resizing illusions as an analgesia treatment avenue. Subjective illusory experience data showed significantly greater experiences of the illusion in the multisensory (visuotactile) condition compared to non-illusion conditions and a unimodal visual condition, replicating findings from participants without chronic hand-based pain. Exploratory analyses using subjective disownership data show that the multisensory condition did not elicit significant disownership experiences, demonstrating that the pain reductions seen in the multisensory condition do not arise from disownership of the limb, but more likely as a direct result of the illusory resizing manipulations.

[5] The author, Kirralise Hansford, collected the data for this experiment, analysed the results, and wrote the manuscript under the supervision of Dr Catherine Preston, Professor Daniel Baker, and Dr Kirsten McKenzie. The experiment was designed jointly with Dr Catherine Preston, Professor Daniel Baker, and Dr Kirsten McKenzie.

6.2 Introduction

Chronic pain is classified as pain that lasts or reoccurs for more than 3 months (Merskey, 1986; NICE, 2021), and is the leading cause of disability globally (Vos et al., 2017). Current pharmaceutical interventions for chronic pain conditions are minimally effective, with treatments having ill-defined long-term effects (Altman, 2000), and often being no more effective than placebo at reducing pain or improving functionality (Heyworth et al., 2008; Meenagh et al., 2004). Many drugs prescribed for pain result in around 60% of patients reporting no pain improvement or adverse effects (Corriger et al., 2022; Dworkin et al., 2010). Surgical interventions to reduce chronic pain can result in up to 34% of patients reporting unfavourable pain outcomes (Beswick et al., 2012). Due to current treatments being largely ineffective, there is a clear need to find a non-pharmaceutical and non-surgical option for chronic pain treatment.

Individuals who live with chronic pain could have a cortical misrepresentation of their body and its incoming somatosensory signals, including pain, along with perceptual size distortions of their affected limbs, which underpin their persistent pain (Boesch et al., 2016). There is often reported a lack of concordance between radiographic (physical damage) and symptomatic pain (Felson, 2005; Szebenyi et al., 2006). This highlights the likelihood of a cortical misrepresentation driving pain rather than structural damage, explaining why surgical interventions to treat structural elements of chronic pain could be ineffective. Theories underlying cortical misrepresentations include the predictive coding account (Friston, 2008) and the central sensitisation theory (Arendt-Nielsen et al., 2010; Arendt-Nielsen and Graven-Nielsen, 2003). Predictive coding posits that any mismatch between predicted and actual sensory inputs, such as the difference between peripheral signals and symptomatic pain, generates prediction errors. A lack of updating of top-down expectations in individuals with chronic pain, could lead to constant mismatches between symptomatic and radiographic sensory inputs. Central sensitisation theory, however, refers to the central nervous system changing, distorting, or amplifying pain in a way that no longer reflects the peripheral input from the body, leading to pain becoming an illusory perception (Woolf, 2011). Central sensitisation and predictive coding theories are not in opposition to each other, but rather both contribute to the overall understanding of potential causes of chronic pain conditions. Both theories support the suitability of illusion therapies for the amelioration of chronic pain, as bodily illusions can induce perceptual modulations of the painful body part, altering the patient's perception of their body and the pain related to it.

Illusory resizing is a bodily illusion which changes the way a body part is perceived, exploiting principles of multisensory integration to elicit modulations in the perceived size and shape of the body part (Preston et al., 2020; Preston and Newport, 2011; Stanton et al., 2018). Multisensory resizing illusions typically involve both tactile and visual inputs and can be delivered via an augmented reality system. Augmented reality can present real-time video capture of a hand, from the same position and perspective as if the hand were being viewed directly (Preston and Newport, 2011), allowing the experimenter to deliver tactile manipulations, such as gently pulling the hand / fingers, whilst the participant views their hand / fingers stretching in the augmented image. Newport et al. (2010) found strong embodiment using multisensory visuotactile illusions, and our recent work (Hansford et al., 2023) found that multisensory illusions elicited significantly greater illusory experience compared to non-illusion conditions. Regarding unimodal visual illusions, which consist of visual input of the finger stretching but without any tactile input, mixed results have been found with inconsistencies reported in illusory experience. Some participants show quite strong illusory experiences during unimodal visual presentations, whilst others report no experience of illusory stretching (Hansford et al., 2024c, 2023). Previous research has found a reduction in hand and knee pain in osteoarthritis (OA) patients using augmented reality to deliver multisensory resizing illusions (Preston et al., 2020; Preston and Newport, 2011; Stanton et al., 2018), therefore both multisensory and unimodal visual resizing illusions are delivered in the present study to assess if illusory experience is required for illusory analgesia.

There are two main theories underlying analgesic resizing illusions. Firstly, the somatosensory blurring hypothesis posits that the cortical representation of a painful body part is blurred, and viewing the body part sharpens this representation. This is supported through findings from participants without chronic pain, where visual analgesia has been found following experimentally induced pain (Haggard et al., 2013). The second theory stems from research by Gilpin et al. (2015), finding that participants with arthritis judge their affected hands to be smaller compared to individuals without the condition, suggesting a reduced cortical representation of their hands. Pain reductions have been found for participants with arthritis when using stretching resizing illusions (Preston and Newport, 2011), therefore, Gilpin et al. (2015) posit that increasing cortical representation of the hands through magnifying (stretching) could reduce pain. Both theories predict that cortical misrepresentations occur in the somatosensory cortex, with both theories predicting different neural changes regarding the experience of pain. Specifically, the somatosensory blurring hypothesis predicts a larger, more diffuse representation of the painful body part that would be reduced (sharpened) during resizing illusions, whereas the magnification theory predicts a shrunken representation of the painful body part that would be enlarged following illusory stretching.

Somatosensory cortex modulation has been investigated using steady-state evoked potentials (SSEPs), where low-level somatosensory responses can be induced directly using vibrations of a known frequency applied to a body part. These generate a frequency-locked steady-state evoked potential detectable at the scalp using EEG (Snyder, 1992; Tobimatsu et al., 1999), and are an index of the cortical response to a stimulus, therefore can potentially give an index of cortical response changes during illusory resizing.

Our previous work (Hansford et al., 2024c) despite finding slight steady-state response decreases when participants without chronic pain underwent resizing illusions, gave no convincing evidence of somatosensory sharpening in participants without chronic pain. Since people with chronic pain are thought to have cortical misrepresentations of their affected body parts, it is plausible that using the same paradigm as in our previous work, we might see greater differences in somatosensory response to illusory stretching in a population with chronic hand-based pain. SSEP responses can therefore be used to directly compare the somatosensory blurring hypothesis (Haggard et al., 2013) and the magnifying hypothesis (Gilpin et al., 2015), as an increased SSEP response following illusory resizing could indicate support for the magnification hypothesis, suggesting increased cortical representation of the painful body part, whereas a smaller SSEP response after illusory resizing could support the somatosensory blurring hypothesis, suggesting the cortical representation of the body part has become sharpened.

Using different sensory manipulations of finger resizing illusions, in addition to using an electromagnetic solenoid stimulator to elicit SSEPs, this study aimed to investigate subjective illusory experience and neural responses to resizing illusions in participants with chronic hand-based pain. To test this, different resizing illusions consisting of multisensory (visuotactile) stretching (MS), unimodal-visual stretching (UV), a non-illusion control condition without tactile input (NI), and a non-illusion control condition with tactile input (NIT) were used. Previous research has suggested that tactile input alone can reduce pain ratings (Mancini et al., 2014; Nahra and Plaghki, 2003), therefore this second control condition was used to test if the illusion itself delivered analgesia rather than the tactile or combined sensory inputs. The first hypothesis, acting as a positive control (1), was that there would be a greater illusory experience, measured via a subjective illusory experience questionnaire, in the MS condition compared to the NI and NIT conditions. The main experimental hypothesis was that (2) there would be a significant difference in SSEP response when comparing (2a) MS illusory resizing to the NI condition, when comparing (2b) UV illusory resizing to the NI condition, but no difference when comparing (2c) the NIT condition to the NI condition. The final hypothesis was that (3) there would be a reduction in pain, measured via a 21-point numeric rating scale, comparing before and after scores for (3a) MS and (3b) UV conditions, whilst we expected (3c) no reduction of pain following the NI condition, nor (3d) a reduction of pain following the NIT condition.

6.3 Methods

6.3.1 Sample Size

Based on power analyses in section 6.3.5, a sample size of 30 participants was aimed for to adhere to the higher end of sample size estimates (Hypothesis 2 (6.3.5.2)). However, due to scarcity of participants experiencing pain in either their right index or middle fingers (digits needed for the delivery of vibrotactile and illusory manipulations, see section 2.2 Sample inclusion / exclusion criteria), a final sample size of 21 participants (mean age = 48.8 years; age range = 19 – 73 years; sex = 22.7% male, 77.3% female; ethnicity = 95% white; chronic pain = 5 primary pain, 10 secondary pain, 2 mixed, 4 no diagnosis) were tested during an 8-month recruitment period.

6.3.2 Participants

Ethical approval was gained from the Department of Psychology, University of York (ethics application code 950), in line with the Declaration of Helsinki. Informed consent from each participant was gained prior to the start of any experimental set up, and participants were instructed that they could withdraw their participation at any time during or after completion of the experiment.

Sample inclusion / exclusion criteria:

Inclusion and exclusion criteria were determined using self-report responses relating to each item listed below: - Inclusion Criteria: Right-handed, over 18 years of age, must have ongoing or reoccurring pain in their right index or middle fingers (or their associated joints) for more than 3 months, hand-based pain present on day of testing. No formal diagnosis of a chronic pain condition is needed, as this has been found to be a barrier for participants taking part in non-pharmaceutical chronic pain research studies, especially for individuals from ethnic minorities (Hansford et al., 2024d).

- Exclusion Criteria: Prior knowledge or expectations about the research, a history of developmental, neurological or psychiatric disorders, history of drug or alcohol abuse, history of sleep disorders, history of epilepsy, visual abnormalities resulting in complete visual occlusion, being under 18 years of age, diagnosed with Complex Regional Pain Syndrome. No restrictions applied regarding any medication the participant might be taking. (Complex Regional Pain Syndrome is excluded as a chronic pain condition here, due to research showing increasing pain after stretching illusions (Moseley et al., 2006)).

Raw data exclusion criteria:

- Less than 100% of the experiment completed by a participant, more than 50% of electrodes for a single participant requiring removal from EEG data, or if both electrodes F1 and FC1 (electrodes of interest) require removal. More information about data removal can be found in section 6.3.4.1 ‘Preprocessing Steps’.

6.3.3 Experimental Procedure

All participants filled out a demographic survey, asking their age, sex, ethnicity, and any chronic pain condition diagnosis, and were asked to complete the revised Waterloo Handedness Questionnaire (WHQr) (Elias et al., 1998). The WHQr self-reported handedness questionnaire consisted of 36 questions. The questions were answered on a 5-level Likert scale to determine the degree of preferred hand use, with left always being -2, left usually being -1, equal use being 0, right usually being +1 and right always being +2. The sum of the total WHQr score was then used to categorise a respondent as left-handed (score of -24 or less), mixed handed (score of -23 to +23), or right-handed (score of +24 or higher). Only participants who were categorised as right-handed continued participation, with the exception of one participant who scored a result of mixed handed due to changes in hand use as a result of pain. Participants were asked their pain score on the day of testing for their digit in the most pain using a 21-point numeric rating scale (NRS) (0 = no pain at all; 20 = most severe pain imaginable). This 21-point scale has equivalent reliability to a more frequently used 11-point scale (Jensen and Karoly, 2011) and was chosen to aid comparability with previous studies which have used the 21-point NRS (Preston et al., 2020; Preston and Newport, 2011). Additionally, since the scale is different to a typical rating scale of 1-10 (which is commonplace in clinical settings), participants would be more likely to think about the answer they give, rather than giving a number they always use when asked to rate their pain on a scale of 1-10. Participants were only tested if their pain on the day was above 0 on the 21-point scale.

Participants were then set up with an appropriately sized 64-channel EEG cap with electrodes arranged according to the 10/20 system. The experimenter used conductive gel to make a conductive bridge between the electrodes and the scalp to attempt to obtain impedance levels of $<10k\Omega$ per electrode. Data were collected using an ANT Neuroscan system, sampling at 1kHz. The whole head average was used as a reference.

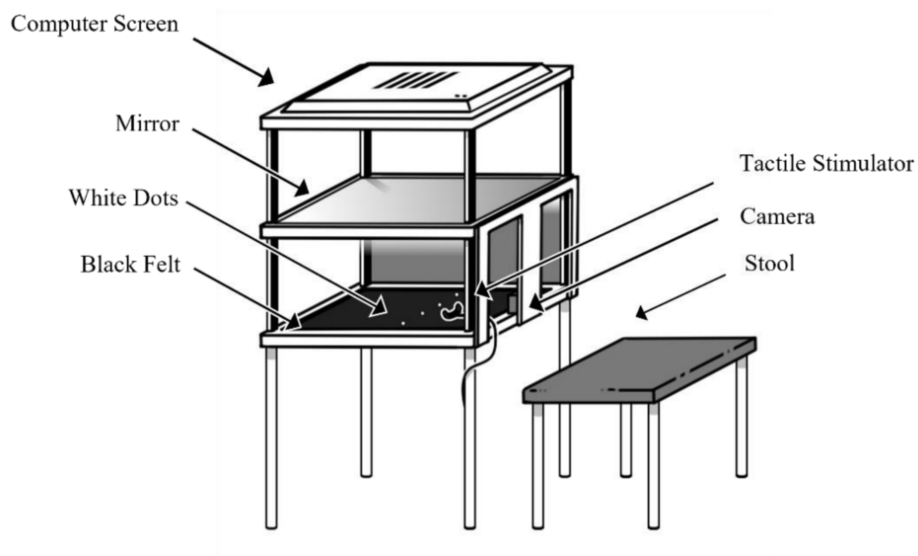

Figure 6.1: Schematic of Augmented Reality System with Tactile Stimulator.

Participants were then seated behind the augmented reality system (Figure 6.1) and instructed to place their hand onto the black felt fabric. Within the self-built system there was a 1920 x 1080-pixel Spedal Webcam Wide Angle Camera at the edge of the black felt on the side the participant sits, away from the participant's view. 26cm above the felt base, there was a mirror, which was placed 26cm below a screen with a resolution of 1920 x 1200 pixels, with a width of 52cm and a height of 32cm. The thickness of section on which the mirror sat was 2cm. This screen was 54cm from the base of the system, and the base of the system was 82cm from the ground. Participants were asked which digit (middle or index finger) was in the most pain and were asked to place this digit outstretched onto the felt. If both digits were equally painful, the digit that the participant chose as their preference was used. There were two white dots for each hand on the felt and participants were instructed to place their hand between these two dots. Participants were instructed to view their hand's image in the mirror (whilst the real hand was hidden from view) throughout the experiment. The camera placed underneath the mirror on the felt base was used to deliver a live feed video of the participant's hands to the computer screen at the top of the augmented reality system, which showed in the mirror reflection to the participants. There was a delay of 170ms in the video processing pipeline from the camera image to the augmented video image.

Participants underwent 4 conditions: multisensory stretching (MS), unimodal-visual stretching (UV), a non-illusion control condition without tactile input (NI), and a non-illusion control condition with tactile input (NIT). There was vibrotactile stimulation to the finger in all conditions, but only tactile input of the researcher touching the participants finger in the MS and NIT conditions. Each trial lasted 2.4 seconds for the manipulation phase, where the finger was stretched by 60 pixels (2.1 centimetres) in UV and MS conditions, followed by a further 2.4 second habituation phase in which participants could view and move their (augmented) finger, whilst they keep the rest of their hand still, before the screen went dark, indicating that the next trial could start. The MS condition consisted of the researcher touching and pulling the participant's finger as the participant viewed their finger stretching in a congruent manner. The UV condition consisted of the participants viewing their finger stretch without any experimenter manipulation. The NI condition provided no visual or touching tactile manipulations to the finger, the image of their finger was visible and unchanged throughout. The NIT control condition involved no visual input of the finger stretching, again the image of their finger was visible but unchanged. Additionally, this condition included tactile input of the experimenter's hand touching the participant's finger, but without pulling. Visualisation of all conditions can be seen in Figure 6.2.

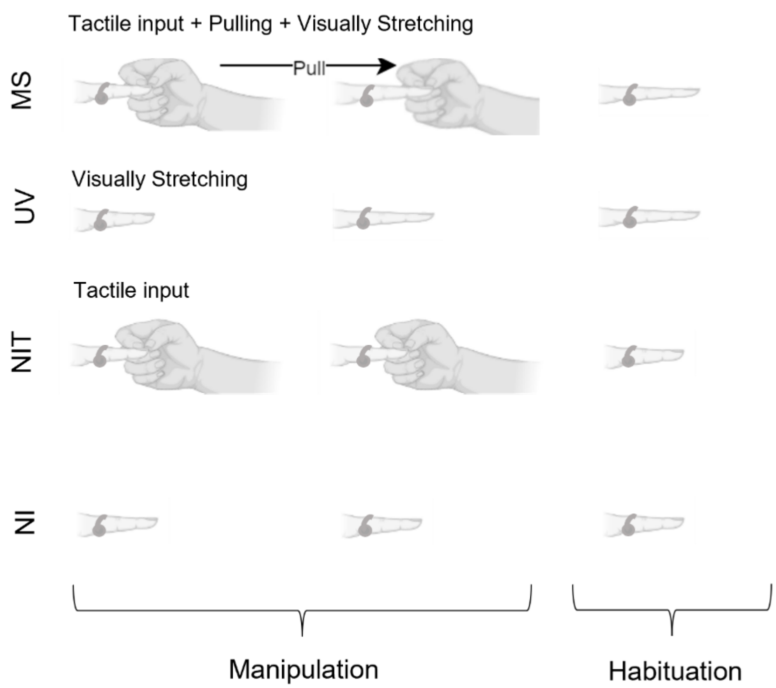

Figure 6.2: Infographic of Experimental Conditions. MS = Multisensory Stretching, UV = Unimodal Visual Stretching, NIT = Non-Illusion Tactile, NI = Non-Illusion. During the manipulation phase (2.4 seconds) the visual image of the finger is stretched in the MS and UV conditions, and/or the experimenter provides tactile input (touch) in the MS and NIT conditions. The tactile input in the MS condition is accompanied by pulling. During the habituation phase (2.4 seconds) participants are free to move their finger. The arrow denotes the direction of the experimenter's action. The vibrotactile stimulator is depicted on the finger in each phase of the experiment as vibrations are presented throughout.

The experimenter was seated opposite the participant, to the other side of the augmented reality machine and touched the digit during MS and NIT conditions by holding onto the distal interphalangeal joint and gently touching (NIT) or pulling (MS) the finger whilst the participant kept their hand in place. Conditions were delivered across 4 blocks, with each block consisting of 24 trials of the same experimental condition, totalling 96 trials over all 4 blocks. The ordering of the blocks was randomised for each participant to prevent ordering effects. The experiment was programmed in, and the conditions randomised using MATLAB R2017a and the Psychtoolbox library (Kleiner et al., 2007; Pelli, 1997: Brainard, 1997). The experimenter was informed of whether to pull the finger or to touch the finger via an indicative box displayed on the screen out of the participant's view. If the box was blue, this indicated a need to pull the finger, if it was white it indicated a need to touch the finger, if there was no box displayed then this indicated no tactile manipulation from the experimenter. The researcher used a button press to indicate the start of the manipulation, and began pulling the finger, when needed, synchronously within the 2.4 second manipulation phase. If the experimenter were to forget to pull the finger on a multisensory condition, or mistakenly pulled the finger in a control trial, then this would noted during the experiment, and that trial would be removed from analysis. Fortunately, no trials needed removal due to experimenter error. Vibrations were delivered to the participant's finger in all conditions using a miniature electromagnetic solenoid stimulator (Dancer Design Tactor; diameter 1.8mm) emitting vibrations produced by sending amplified 26Hz sine wave sound files, with stimulus intensity controlled by an amplifier (Dancer Design TactAmp). The tactor was driven at 50% of the maximum (i.e. a peak input voltage of 3V) using a 26Hz sine-wave, and delivered a peak force of 0.18N. The electromagnetic solenoid stimulator was attached to the participant's finger that was outstretched to receive the manipulations, between the knuckle and the first finger joint, using clear medical tape and gave continuous stimulation for the duration of each trial. Participants were asked before each condition block and then again immediately after each condition block to rate their pain on the 21-point NRS, which was a verbal report that the experimenter entered on a Samsung Galaxy A6 Tablet, resulting in 4 pre and 4 post block pain reports per participant. Participants were encouraged to take a break between each of the blocks to stretch their hand. EEG was recorded throughout as a continuous recording with trial onsets and conditions indicated by numbered 8-bit digital at the start of each trial (USB-TTL Module, Black Box Toolkit Ltd.).

Finally, at the end of each block, the participant was asked to complete a subjective illusory experience questionnaire regarding a condition presented in a given block using a Samsung Galaxy Tab A6 tablet via a questionnaire on Qualtrics (Qualtrics, Provo, UT). The questionnaire consisted of six questions relating to the trials the participant had just experienced. Two statements related to illusory experience: "It felt like my finger was really stretching" / "It felt like the finger I saw was part of my body", two related to disownership: "It felt like the finger I saw no longer belonged to me" / "It felt like the finger I saw was no longer part of my body", and two were control questions: "It felt as if my finger had disappeared" / "It felt as if I might have had an extra finger" (all questions were directed towards the participants manipulated finger). Control questions were included to create an index for the illusion and disownership questions (more detail can be found in section 6.3.4.1 'Preprocessing Steps'), whilst disownership questions were included to assess if the potential experience from the illusions resulted from a disownership of the body part, or from subjective embodiment of the body part (McCabe, 2011). A visual analogue scale from 0 – 100 was used for each statement, with 0 being strongly disagree, 50 being neutral and 100 being strongly agree.

Data collection was terminated after 8 months of recruitment. If a participant needed over 50% of the electrodes removed during preprocessing, or if either electrode F1 or FC1 needed removal, then their data were not included for SSEP analysis, which was the case for one participant. Due to difficulties recruiting participants with hand-based pain affecting the right index and/or middle digits, no additional participants were recruited to replace lost data.

6.3.4 Analysis Pipeline

6.3.4.1 Preprocessing Steps

EEG data were first converted using MATLAB and EEGlab (Delorme & Makeig, 2004) from the ANT EEprobe .cnt format to EEGlab .set format. All subsequent analysis was then conducted using the MNE-Python toolbox (Gramfort et al., 2013). A 50Hz notch filter was first applied to the raw EEG data for all electrodes, followed by calculation of the standard error across time for each electrode for each participant (Luck et al., 2021). Across the standard errors for all participants, the 5% of electrodes which showed the largest standard errors were used to create a standard error threshold. Any electrode with a standard error above this threshold, or with a value of 0, was removed from analysis. Where a participant had over 50% of their electrodes over the standard error threshold or with a value of 0, or if the electrodes requiring removal included both electrodes F1 and FC1 (electrodes of interest), then their data were removed from analysis. Primary analysis of the remaining EEG data then involved averaging the signal across the electrodes of interest (or using just electrode F1 or FC1 in case of electrode removal), and calculating the Fourier transform for each trial per participant. These amplitudes were then averaged across trials to give overall results for each participant. Statistical comparisons were then performed on the Fourier amplitudes at the stimulation frequency (26Hz), across conditions and participants. No additional filtering or denoising steps were applied to the EEG data, in line with Figueira et al. (2022) report that only a Fourier transform is typically needed for this type of EEG data.

Regarding questionnaire data, scores for both illusion experience questions were combined to give median scores, along with both disownership questions and both control questions, resulting in 3 median scores per condition per participant. The median control scores were used to create an index of the illusion and disownership scores by subtracting the median control score from the median illusion and median disownership scores, in line with previous research doing similarly (Hansford et al., 2024c; Kalckert and Ehrsson, 2012; Kilteni and Ehrsson, 2017; Matsumiya, 2021). The normalised (baseline corrected) data were used for analyses, with a new scale from -100 to +100 with 100 indicating strongly agree, 50 indicating a neutral opinion, and scores below 0 indicating strongly disagree with the statements on the questionnaire. 50 is maintained as a neutral opinion so that the normalised data still adhered to the thresholds that the participants were presented with during the experiment.

8 data points were collected per participant for their pain ratings. Median scores were then calculated across pain data for pre and post scores for all experimental conditions.

6.3.5 Power Analysis and Analysis Plan

6.3.5.1 Hypothesis 1 (Positive Control)

(1 – Positive Control) There will be a greater illusory experience, measured via a subjective illusory experience questionnaire, in the (1a) MS condition compared to the NI condition and in the (1b) MS condition compared to the NIT condition.

The subjective illusory experience questionnaire was used as a positive control for the current study. Previous research has shown significantly greater illusion strength for MS conditions compared to non-illusion conditions (Carey et al., 2019; Hansford et al., 2024c, 2023), which we attempted to replicate. Questionnaire data was analysed using R (R Core Team, 2021), in line with preregistered anlaysis plans (https://osf.io/9anjc).

Effect sizes were determined by research from Hansford et al (2023) using the subjective illusory experience questionnaire and comparing MS, UV, and incongruent finger-based resizing illusions to control conditions with no illusory resizing, using the same finger stretching illusions and the same equipment (n = 48), which showed an effect size of $\eta^2 = .33$ (converted to a Cohen's f = .70). Additional effect size information came from a visual capture study (n = 80) using a subjective embodiment questionnaire and visual and tactile manipulations to a mannequin body (Carey et al., 2019), showing an effect size of r = .64 (converted to a Cohen's f = .83) when comparing embodiment scores from the questionnaire against control scores. An effect size of f = .70 was used for hypothesis 1 to adhere to the lower end of previous effect sizes.

A priori power analysis using G*Power for the smallest effect size of interest (f = .70) showed that for a repeated measures, within factors one way ANOVA, with an effect size (f) of 0.70, alpha of 0.05, power at 90% and 1 group with four measurements, 6 participants were needed.

6.3.5.2 Hypothesis 2

(2) There will be a significant difference in SSEP response across the electrodes of interest (F1 & FC1) when comparing (2a) the MS condition to the NI condition, when comparing (2b) the UV condition to the NI condition, but (2c) that there will be no significant difference when comparing the NIT condition to the NI condition.

As mentioned in the EEG pre-processing steps in section 6.3.4.1, EEG data analysis involved taking a Fourier transform for each waveform averaged across the electrodes of interest, to obtain the amplitude for each trial at the vibration frequency (26Hz). These amplitudes were then averaged across trials to give overall results for each participant, before following preregistered analysis plans (https://osf.io/9anjc). Based on the pilot data in Figure G1.2 in Appendix G, we expected to see activation most pronounced over mid-frontal distributions, covering F1 and FC1 electrodes and therefore these electrodes were selected as the electrodes of interest.

Despite our previous work using SSEPs to assess somatosensory response changes during illusory finger stretching, this was the first study to investigate illusory finger stretching using SSEPs in a chronic pain sample, so appropriate effect size estimates were not available. We therefore conducted power calculations based on a smallest effect size of interest, in line with the recommendation of Lakens (2014). Here, we chose an effect size of d = 0.5 (a medium effect, see Cohen, 1988), since this is the smallest effect size we were interested in detecting, which converted to a Cohen's f of 0.25 for power analyses.

A priori power analysis using G*Power showed that for a repeated measures, within factors one way ANOVA, with an effect size (f) of 0.25, alpha of 0.05, power at 90%, and 1 group with four measurements, a total sample size of 30 participants was needed.

6.3.5.3 Hypothesis 3

We expect to find a subjective reduction in pain, measured via a 21-point numeric rating scale, comparing before and after scores for (3a) MS and (3b) UV conditions whilst we expect (3c) no reduction of pain following the NI condition, nor (3d) a reduction of pain following the NIT condition.

Pain data were also analysed using R (R Core Team, 2021) following preregistered analysis plans (https://osf.io/9anjc). Comparisons of the MS and the NIT conditions assessed whether any reduction in pain was due to the illusory manipulations or rather, due to the addition of tactile input.

Effect size was determined using those listed in previous research using the 21-point numeric pain rating scale (Preston et al., 2020) and from previous pilot data using the same MS resizing illusions for analgesic effect, finding post illusion pain scores to be significantly lower than pre illusion scores (t(10)=3.32, p = .008, d = 1.0).

A priori power analysis using G*Power showed that for a Wilcoxon signed-rank test (one-sided, matched pairs), with an effect size (dz) of 1, alpha of 0.05, and power at 90%, for a two tailed test with normal parent distribution, 11 participants were needed in total.

6.3.6 Data and Code Availability Statement

All data for this project can be found at the following OSF page: https://osf.io/dzmf9/. A script which can be used to computationally reproduce the entire manuscript, conduct all analyses, and produce all figures can be found at the following GitHub repository: https://github.com/KJHansford/SSEP_illusory_resizing_cp.

6.4 Results

Positive control analyses of the subjective illusion data can be seen in Figure 6.3. A Friedman test found a significant overall effect of condition with a moderate effect size (χ^2 (3) = 16.44, p = <0.001, Kendall's W = 0.26) and post hoc Wilcoxon tests with Holm corrections found significantly greater combined illusion score in the Multisensory Stretching (MS) condition (Median = 67.5, SD = 30.16) compared to the Non-Illusion (NI; Median = 49, SD = 27.62, z = 13.5, $p.adj$ = 0.003, r = -26.14) and Non Illusion Tactile (NIT; Median = 50, SD = 21.66, z = 29, $p.adj$ = 0.019, r = -26.25) conditions, thereby supporting hypotheses 1, 1a, and 1b and fulfilling the positive control checks. Exploratory analysis also showed a significant difference between the MS and Unimodal Visual (UV) condition (Median = 20.5, SD = 43.02, z = 204, $p.adj$ = 0.001, r = 40.11).

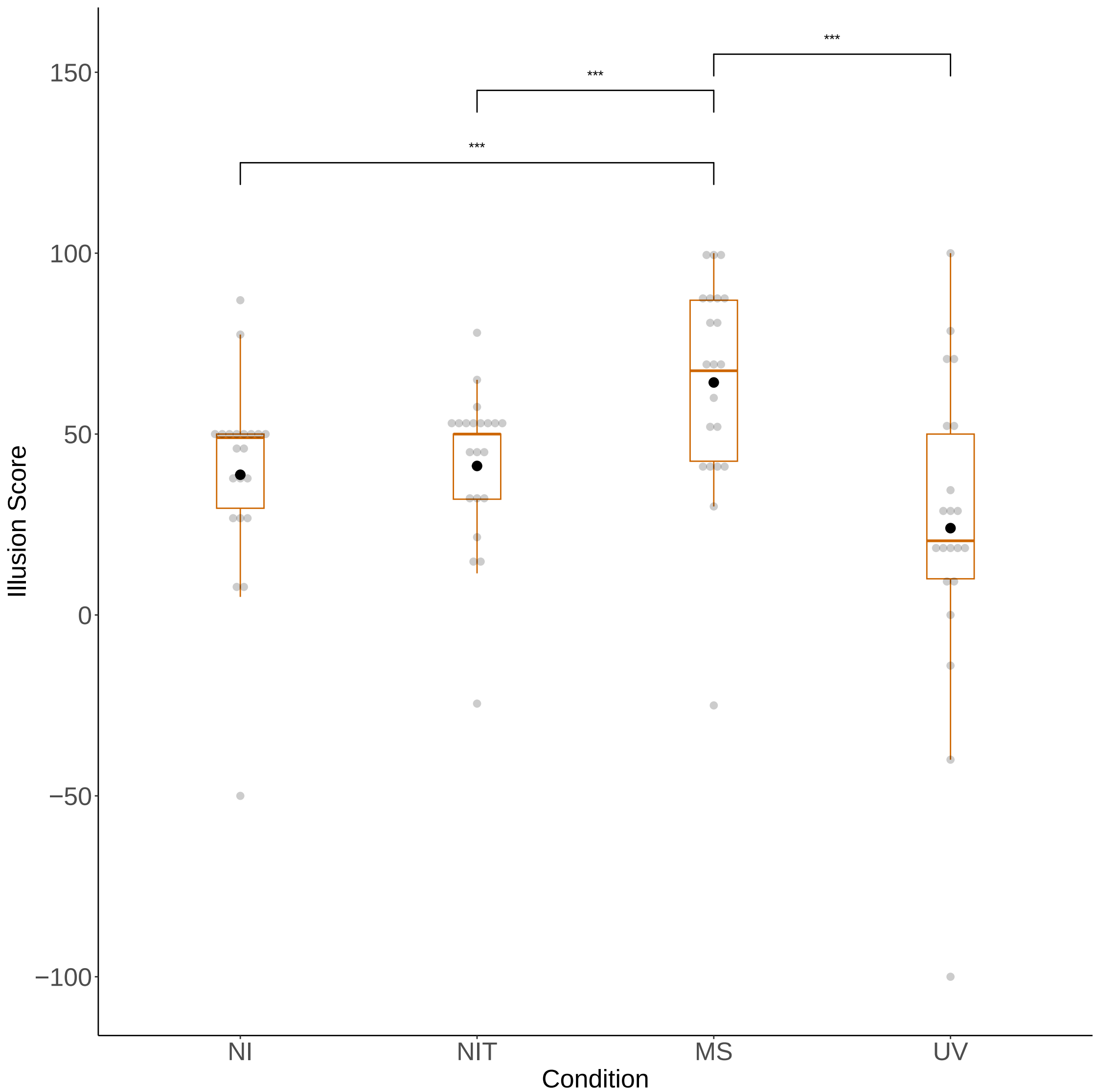

Figure 6.3: Combined Illusion Score Index Across Conditions (NI: Non-Illusion; NIT: Non-Illusion Tactile; MS: Multisensory; UV: Unimodal Visual). Scores below 50 indicate disagreement with experience of illusion statements, whilst scores above 50 indicate agreement. A continuous visual analogue scale was used in data collection, with agreement and disagreement statements located at each end of the scale. Box plots show means, medians and inter-quartile ranges of data. Medians are indicated with a horizontal line whilst means are indicated by a black dot. Data points are shown in grey jitter binned along the y-axis, grouped by condition.

Exploratory analysis of subjective disownership and control data can be seen in Appendix I Figures I1.1 and I1.2. A significant difference in disownership scores was found between the UV condition (Median = 42, SD = 42.32) compared to the NI (Median = 0, SD = 19.63, , z = 16, $p.adj$ = 0.039, r = -39.78), NIT (Median = 0, SD = 15.24, z = 12, $p.adj$ = 0.025, r = -48.25), and MS conditions, (Median = 1.5, SD = 22.34, z = 22, $p.adj$ = 0.042, r = -40). Regarding control data, a significant difference was found between

NI (Median = 0, SD = 21.8) and UV (Median = 6, SD = 24.02) control scores (z = 1, $p.adj$ = 0.031, r = -16).

Analyses of SSEP data can be seen in Figure 6.4. The left panel (a) confirms the presence of a clear steady-state signal at 26Hz, which was strongest over fronto-central electrodes. A Friedman test found no significant overall effect of condition with a small effect size (χ^2 (3) = 2.4, p = 0.494, Kendall's W = 0.04) opposing Hypothesis 2. Despite the MS condition having numerically the lowest median amplitude (Median = 0.16, SD = 0.29), post hoc Wilcoxon tests with Holm corrections found no significant differences between SSEP amplitude when comparing the NI condition (Median = 0.21, SD = 0.38) to the MS condition (z = 100, $p.adj$ = 1.000, r = -0.01), or the UV condition (Median = 0.2, SD = 0.26, z = 95, $p.adj$ = 1.000, r = -0.01), meaning Hypotheses 2, 2a, and 2b were unsupported. There was no significant difference found when comparing the NI condition to the NIT condition (Median = 0.18, SD = 1.71, z = 99, $p.adj$ = 1.000, r = 0), supporting Hypothesis 2c.

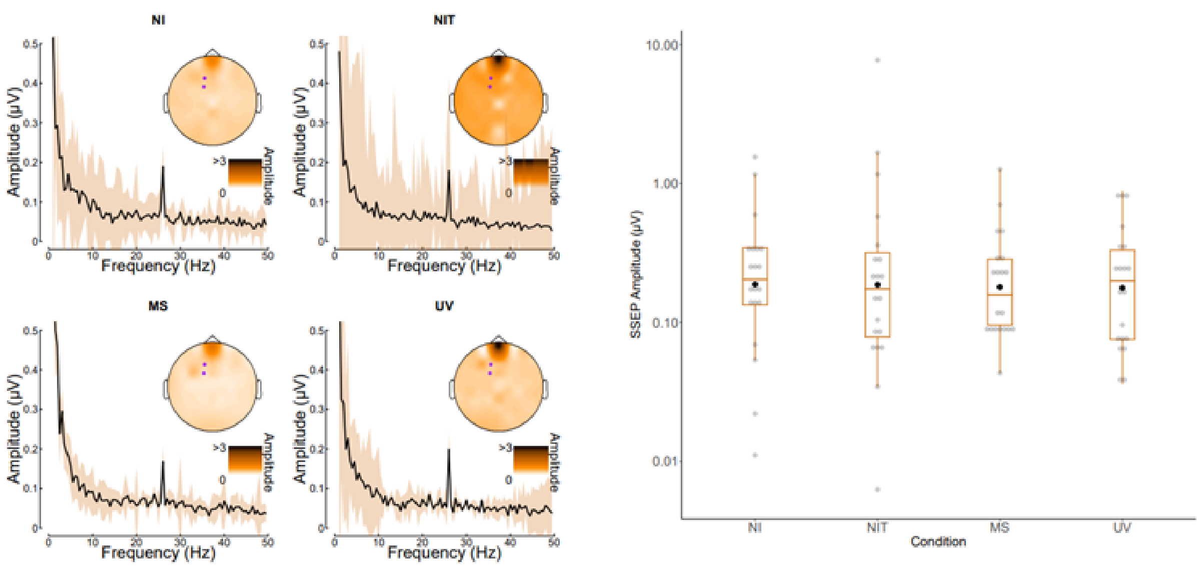

Figure 6.4: (a): SSEP Amplitude Spectra Across Conditions (NI: Non-Illusion; NIT: Non-Illusion Tactile; MS: Multisensory; UV: Unimodal Visual) for electrodes of interest (F1 and FC1). Shading shows ±1 standard error across participants (n=46). (b): SSEP Amplitudes Across Conditions. Box plots show means, medians and inter-quartile ranges of data. Medians are indicated with a horizontal line whilst means are indicated by a black dot. Data points are shown in grey jitter binned along the y-axis, grouped by condition.

Exploratory correlation analyses were conducted to assess the correlation between participant's subjective illusion score and their SSEP amplitude across electrodes of interest (F1 & FC1) for each condition to see if those who experienced a stronger feeling of the illusion had more reduced SSEP amplitudes, results showed no significant correlations. Exploratory correlation analyses and figures can be found in Appendix I.

Analysis of pain data across conditions can be seen in Figure 6.5. Wilcoxon tests found a significant increase in pain when comparing NI pre (Median = 4, SD = 3.27) and post (Median = 6, SD = 4.23) pain levels (z = 113, $p.adj$ = 0.021, r = 2). No significant differences were found when comparing NIT pre (Median = 4, SD = 3.25) and post (Median = 5, SD = 4.02) pain levels (z = 101.5, $p.adj$ = 0.243, r = 0.75), in line with our hypotheses. No differences in pain were found when comparing the MS pre (Median = 4, SD = 3.38) and post (Median = 5, SD = 4.61) levels (z = 85.5, $p.adj$ = 1.000, r = 0) nor the UV pre (Median = 5, SD = 2.56) and post (Median = 5, SD = 3.5) levels (z = 105, $p.adj$ = 0.403, r = 0.5) levels, opposing our hypotheses.

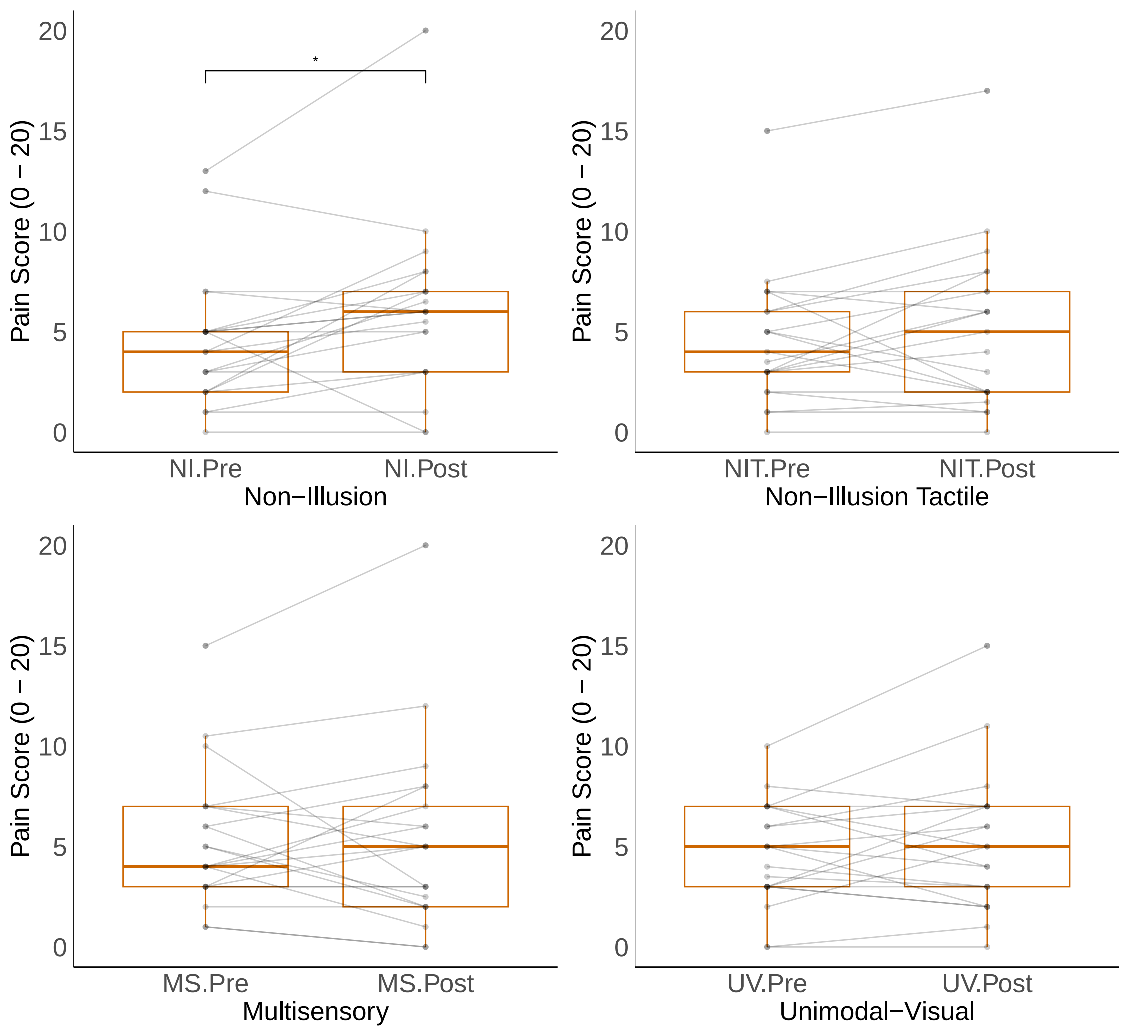

Figure 6.5: Pre and Post Pain Scores Across Conditions. Box plots show medians and interquartile ranges of data. Paired data points are shown in grey.

Despite finding no significant differences in pain levels for illusory conditions when conducting group level analyses, there were cases of pain reduction for each condition for individual participants. The MS condition resulted in 9 participants experiencing a reduction in pain, with 7 participants experiencing a reduction greater than 30%, which is described as a clinically meaningful level of pain reduction (Dworkin et al., 2018) and 6 greater than 50% (described as extremely meaningful). The UV condition resulted in 9 participants experiencing a reduction in pain, 4 of which experienced a reduction greater than 30% and 1 a reduction greater than 50%. These conditions saw more participants experience reductions in pain levels compared to the non-illusion conditions which saw only 3 participants experience a reduction in pain following the NI condition, 1 of which experienced a reduction greater than 30% and 1 a reduction greater than 50%, and 6 participants experience a reduction in pain following the NIT condition, with 5 participants experiencing a reduction greater than 30% and 2 participants experiencing a reduction greater than 50%. Figure 6.6 shows percentage change per participant per condition, showing some participants experiencing a reduction in pain levels along with some experiencing no change in their pain levels (NI: 4, NIT: 3, MS: 3, UV: 2) and others showing increases in pain following each condition (NI: 13, NIT: 11, MS: 9, UV: 9).

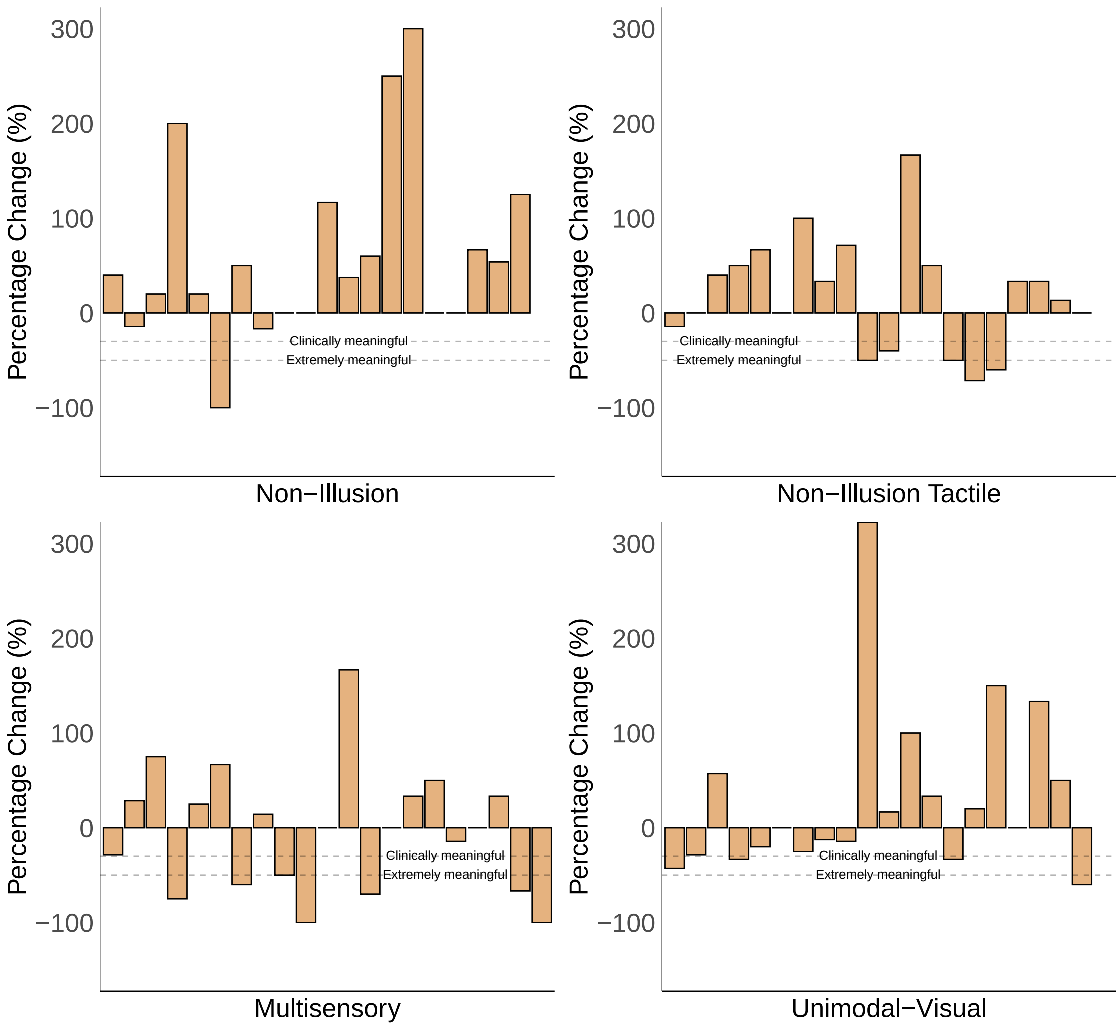

Figure 6.6: Percentage change for pain scores across all conditions per participant. Dashed lines show 30 percent pain reduction (clinically meaningful) and 50 percent pain reduction (extremely meaningful).

To assess if participants experiencing a reduction in pain differed between presentations of chronic primary and secondary pain conditions, data were analysed split by condition type and can be found in Figures I1.6 - I1.8 in Appendix I. No significant differences were found when comparing pre and post pain levels across any condition for either chronic primary or secondary pain.

Exploratory correlations were also run between participants pain percentage change and their SSEP amplitude across conditions, to assess if those experiencing a reduction in pain showed a lower SSEP amplitude, however no significant correlations were found. Further exploratory correlations were run across conditions comparing participant's pain percentage change data and their subjective illusion scores, also finding no significant correlations. All exploratory correlation analyses can be seen in Figures I1.3 - I1.5 in Appendix I.

6.5 Discussion

This study investigated subjective illusory experience and neural response to resizing illusions in participants with chronic hand-based pain to assess whether illusory resizing of the fingers would reduce pain levels and show differences in steady state responses to 26Hz vibrotactile stimulation across illusory conditions. Subjective results replicated previous findings in samples without chronic pain of a significantly greater experience of the illusion in the multisensory condition compared to both non-illusion conditions, with the unimodal visual condition showing a wider range of illusory experience responses. SSEP responses to 26Hz vibrotactile stimulation showed no significant differences in response amplitude across conditions opposing our hypothesis, with pain ratings also showing no significant differences when comparing pre and post levels for both illusory conditions, contrasting previous analgesic findings.

Our work delivering resizing illusions to participants without chronic pain (Hansford et al., 2024c), showed surprising effects of a significantly greater experience of the illusion in the multisensory condition compared to the unimodal visual condition, despite previous findings of visual capture alone being found to elicit embodiment in both virtual (Maselli and Slater, 2013) and physical environments (Carey et al., 2019), and when viewing an illusion of an elongated arm (Schaefer et al., 2007) or from visual-only manipulations of the hand (McKenzie and Newport, 2015). Previously, we found significantly greater levels of disownership during unimodal visual conditions compared to multisensory conditions and therefore posited that the tactile input of touching the hand / finger is needed to ground one's experience of owning their body part within augmented reality. The present study replicated these findings of significantly heightened disownership levels during the unimodal visual condition, further supporting the idea that tactile input grounding one's experience could contribute to greater experiences of illusory stretching, regardless of the presence of a chronic pain condition. Previous commentary regarding experiences of illusory analgesia raises the idea that a reduction in pain following illusory resizing could be due to disownership of the painful body part, which could thereby inhibit its incoming sensory signals including pain (McCabe, 2011). Research using the disappearing hand trick, addresses this concern. The trick consists of participants placing their hands inside an augmented reality system and viewing a live video of their hands on a screen as their hands slowly and without detection move closer together. When the participant is then asked to reach for their hand, it is not where they expect it to be, giving a sense of their hand 'disappearing'. Research using this trick (Preston et al., 2020) attempted to address concerns regarding illusory analgesia being the result of disownership, highlighting that the analgesia experienced following the manipulation could not result from disownership of the hand. The present study provides the first empirical evidence that people with hand-based chronic pain subjectively report experiencing resizing illusions whilst showing comparatively low levels of disownership in the multisensory condition, further supporting the idea that illusory analgesia is not the result of limb disownership.

The somatosensory blurring hypothesis (Haggard et al., 2013) posits that the cortical representation of a painful body part could be blurred and through viewing the body part the representation could become sharpened, which could be the mechanism through which illusory stretching could induce illusory analgesia. Slight reductions in SSEP amplitude have been found before in participants without chronic pain undergoing hand-based resizing illusions (Hansford et al., 2024c), however since these participants did not experience chronic pain in their hands it was thought that their cortical representations might not be as blurred as those with chronic hand-based pain such as in the present study. Since no significant difference in SSEP response across resizing conditions were found, it is possible that illusory analgesia could be driven from an alternate mechanism. However, no significant differences in pain levels were found across illusory conditions, meaning SSEP amplitude reductions might not have been expected due to no observed group level illusory analgesia. Since some participants did experience illusory analgesia, exploratory correlations were run between participant's pain percentage change and their SSEP response, to assess whether those experiencing a pain reduction had reduced SSEP amplitudes, however no significant correlations were found.

It is possible that the lack of illusory analgesia seen across participants in the present study was due to the experimental set up. A significant increase in pain was found when comparing pain ratings before and after the non-illusion condition, with some participants commenting that during participation having their hand inside the augmented reality system was painful for their wrist and shoulder, meaning that they found it difficult to differentiate the pain they were experiencing from the set up itself compared to pain in their manipulated digit. Additionally, participants reported that the need to sit still for 5 minutes per condition block resulted in some additional pain which although reduced through rest breaks between blocks, could have influenced pain ratings taken immediately after a condition.

It is also possible that the vibration elicited during each condition could have reduced participants' pain through a process referred to as vibratory analgesia. Some studies have found vibration to produce up to a 40% reduction in pain intensity (Staud et al., 2011), whereas others report no significant effects of vibration on pain levels (Watanabe et al., 1999). Due to the therapeutic potential of vibratory analgesia, vibrating gloves have been created as a therapeutic option for people with chronic hand-based pain and have been found to effectively reduce pain levels (Jamison et al., 2018). Within the present study, it is therefore possible that the 26Hz vibration could have reduced pain levels through vibratory analgesia, however, since vibration was present across all conditions and more participants reported pain reductions in the illusory conditions compared to the non-illusion conditions, it is clear that there were illusory analgesic effects observed beyond that induced by vibratory analgesia.

Although pain data analyses were conducted at the group level as preregistered, it is important to understand the individual experiences of participants within this sample. Simply because no overall reduction in pain levels were found following either resizing condition (MS or UV), this should not discount the illusory analgesia experiences that several participants reported. Figure 6.6 shows that a substantial proportion of participants experienced either a clinically or extremely meaningful level of pain reduction following these conditions, highlighting the potential of this therapy for day-to-day treatment. Similarly, however, those experiencing an increase in pain level should not be ignored, and It is therefore recommended that should illusory resizing be offered as a treatment for chronic hand-based pain, that it is not provided within a lab setting such as the current study, where significant increases in pain were found due to the experimental set up. Future research should assess the potential of mobile phone based illusory resizing, so that it can be delivered from the comfort of one's home. Illusory resizing delivered through a mobile phone would not be able to deliver visuotactile illusions such as the one delivered in the multisensory condition here but could deliver unimodal visual or visual-auditory manipulations. Visual-auditory resizing illusions using a rising pitch tone as non-naturalistic auditory input have been found to increase illusory experiences compared to visual only manipulations (Hansford et al., 2024a), therefore both unimodal visual and visual-auditory presentations could be used to deliver meaningful analgesia for a substantial proportion of people living with chronic hand-based pain.

6.6 Conclusions

The present study adds to our understanding of the experiences of illusory resizing within a sample with chronic hand-based pain. The subjective data suggest that people living with chronic pain experience the illusion conditions similarly to those without chronic pain, highlighting the potential of these illusions as a therapeutic treatment avenue. SSEP data however, despite showing a reduction in median amplitude in the multisensory condition in line with the somatosensory blurring / sharpening hypothesis, did not show overall significant differences between conditions possibly due to the lack of illusory analgesia experienced for some within the sample. Pain data highlighted the individual nature of chronic pain, with group analyses showing no significant effects, but participant data showing strong experiences of both pain reduction and pain increases. This individuality was not underpinned by type of chronic pain, with both chronic primary and secondary pain condition subgroups showing no significant differences in pain percentage change. These nuances of chronic pain experiences must be considered when designing therapies for pain alleviation, to ensure people understand how varied analgesic effects from resizing illusions can be.

7 Chapter 7: Discussion

7.1 Summary of Findings

The aim of this thesis was to use behavioural and EEG measures to investigate principles of multisensory integration and neural activity associated with bodily resizing illusions, to facilitate understanding of the suitability of hand-based resizing illusions as a form of non-pharmaceutical treatment for chronic hand-based pain.

The experimental work within this thesis starts with an understanding that research into any clinical population is biased by those who can and choose to offer their time to take part in research projects (Karos et al., 2018; Rosenthal, 1965). Typically, those with more debilitating forms of a condition, such as those with chronic pain conditions that make leaving the house difficult, are often not included in lab-based research, meaning their voices can go unheard. To address this bias within lab-based chronic pain research, Chapter 2 details a project asking people living with chronic pain what makes it difficult for them to take part in research, and what could be done to make taking part easier. This research project consisted of a two-phase approach to data collection, the first being online focus groups, and the second consisting of a short questionnaire. This approach was used to encourage people with any level of chronic pain to give their thoughts about what makes it harder (barriers) and what could make it easier (facilitators) when considering taking part in chronic pain research. A mixed methods approach was taken consisting of two phases. Phase 1 collected qualitative data and phase 2 used the themes identified within phase 1 as statements on a questionnaire asking about levels of agreement and disagreement, thereby generating quantitative data. Over both phases key barriers and facilitators were identified and consolidated. The largest barrier arising from this project was "Distrust", relating to a distrust of medical and research professionals, distrust of confidentiality assurances, and distrust that the research would have impact. The greatest facilitator identified was "Improved Accessibility", which related to the accessibility of the research environment, the type of research being conducted, and accessible advertisement of the research within trusted settings. All facilitator themes received high levels of agreement within phase 2, highlighting the need to implement as many of these as possible within research environments to help participants feel welcomed and comfortable when taking part. Barrier themes received a mixture of agreement and disagreement within phase 2, showing the individuality of the needs that people living with chronic pain have. Findings from this project shaped the research environments and practices used for the remainder of the research conducted within this thesis, including implementations such as making sure to create research environments that do not look to medical or lab-like, advertising research participation opportunities through community and trusted routes, communicating research intentions and findings to participants in an accessible manner, being clear about what constitutes “chronic pain” and not requiring a diagnosis for participation, reimbursing participants for their time, and providing space for carers or children to wait during research sessions.

Although Chapter 2 details research about how best to approach projects with participants living with chronic pain, before trying to assess the neural underpinnings of resizing illusions for this population, it was important to first understand the how these illusions impact neural aspects of multisensory integration for people without chronic pain, enabling us to assess how experiencing resizing illusions typically presents within the brain. Chapter 3 describes an EEG study assessing theta and gamma oscillations thought to be associated with cognitive load and multisensory integration processes, respectively. This project also used subjective illusory scales to assess experiences of resizing illusions across seven different presentations; (1) multisensory stretching and (2) multisensory shrinking included congruent tactile input of the finger being pulled or pushed at the same time and pace that the finger visually stretched or shrunk in an augmented image, (3) unimodal visual stretching and (4) unimodal visual shrinking involved no tactile input being given as the participants simply saw their finger stretching / shrinking, (5) an incongruent stretching and (6) an incongruent shrinking condition where the tactile and visual input did not match, so for example the finger was pushed as it was visually stretching, and finally (7) a baseline condition where no visual or tactile stretching inputs were given. EEG and subjective data were collected across all four conditions and showed that participants experienced a significantly stronger illusion in the multisensory conditions compared to the unimodal conditions, and that despite previous findings suggesting the potential of a unimodal visual condition to elicit similar illusory experiences (Carey et al., 2019; Ferri et al., 2014; Maselli and Slater, 2013; McKenzie and Newport, 2015; Schaefer et al., 2007), there were no differences seen between the unimodal visual and incongruent conditions. The chapter discusses that this could be due to the incongruent conditions not acting as expected, as when the finger visually stretched but received tactile input of pushing the finger, participants sometimes reported that this felt like the finger was stretching and pushing through a barrier, and therefore was akin to the multisensory stretching condition. Additionally, the unimodal visual conditions did not elicit experiences of the illusion for the majority of participants, opposing our expectations. This trend of the unimodal visual condition showing a range of illusory experience responses is replicated throughout the thesis, demonstrating that visual presentation alone is not enough for some people to experience illusory resizing, but it is sufficient for others. The EEG findings within this chapter showed increased parietal gamma activity when comparing the multisensory conditions to unimodal visual conditions, and found that this happened at a later stage of the illusion manipulations compared to previous findings from rubber hand illusion studies (Hiramoto et al., 2017; Kanayama et al., 2021, 2007; Kanayama and Ohira, 2009), suggesting a later temporal onset of multisensory integration for resizing illusions. EEG findings also showed increased parietal theta activity when comparing the incongruent condition to the baseline non-illusion conditions, suggestive of the additional cognitive load required when processing incongruent stimuli. Reflecting on the subsample of participants who experienced illusory resizing in the unimodal visual condition, these participants exhibited a different neural signature to those who did not experience the illusion in this condition. Participants who did experience illusory resizing during the unimodal visual condition showed gamma activity focussed around frontal and parietal regions early in the illusory manipulation, compared to the gamma activity found over parietal regions and at a later point in the illusory manipulation for the full sample of participants. This exploratory finding could be suggestive of a different neural response pattern for people who experience unimodal visual illusory resizing, but this would need to be consolidated in replication studies.

Despite previous literature showing the potential of unimodal visual presentations of bodily illusions to elicit subjective embodiment like that of multisensory (typically visual and tactile) manipulations (Carey et al., 2019; Ferri et al., 2014; Maselli and Slater, 2013; McKenzie and Newport, 2015; Schaefer et al., 2007), the work presented in Chapter 3 did not find such a clear effect when using unimodal visual presentations of hand-based resizing illusions. Since the unimodal visual presentation is preferential for clinical use due to its potential to be delivered outside of a lab-based setting and without the presence of a researcher to deliver the tactile manipulations, an idea arose to see of adding auditory input to visual resizing would elicit greater subjective experience of the illusion than visual presentation alone. Chapter 4 details a study using non-naturalistic auditory input in addition to visual input whilst assessing both subjective (questionnaire) and objective (proprioceptive drift and ruler judgement) measures of illusory experience. The non-naturalistic auditory input used was a rising pitch tone due to associations between this tone and changes in height or size (Hubbard, 2018) and because previous research has used a rising pitch tone when investigating finger stretching without the presentation of visual information (Tajadura-Jiménez et al., 2017). Chapter 4 used a between groups design and randomly assigned participants to either a group with auditory input, or a group without. All participants underwent three different conditions using their right hand; no finger stretching, finger stretching without tactile input, and finger stretching with tactile input. After each condition participants were given one of three tasks, either a dot touch task using their right hand, a dot touch task using their left (unmanipulated) hand, or a ruler judgement task. Dot tasks involved participants reaching for the location of a virtual dot, acting as an index of body schema, whereas the ruler task concerned estimates of the participant's own finger length on a ruler whilst the hand was hidden from view, used as an index of body image. After all trials had finished, participants were given one last trial for each condition, and were then asked to complete a subjective illusory experience questionnaire reflecting the previous conditions they had experienced. Subjective results showed that the addition of auditory input significantly increased illusion strength for trials without tactile feedback, but had no effect on trials with tactile feedback, highlighting possible ceiling effects of multisensory integration for trials with tactile input included. There were no facilitatory effects of auditory input for any of the performance-based tasks, meaning that although participants receiving auditory input felt like they were experiencing a stronger illusion compared to participants not receiving auditory input, this subjective effect did not influence body schema or body image measures. However, since subjective experience of the unimodal visual illusion was increased when adding auditory input, this gives the potential for auditory input being added to visual presentations of illusory resizing, creating a multisensory presentation of the illusion which can be delivered outside of a lab-based setting, meaning more people living with chronic pain could use resizing illusions as a non-pharmaceutical treatment option.

It has been suggested that people with chronic pain could have a more diffuse neural representation of their affected body parts, and that viewing the body part, or potentially viewing it stretch during resizing illusions, could sharpen this cortical representation (Haggard et al., 2013). Since illusory analgesia has been found following delivery of resizing illusions (Preston and Newport, 2011), it is possible that this somatosensory sharpening could be the neural component driving these analgesic effects. Steady state evoked potentials (SSEPs) can be used to index the brain's response to a stimulus, and across Chapters 5 and 6 this technique was used with 26Hz vibrotactile stimulation to the fingers to assess any changes in SSEP response during illusory resizing. Chapter 5 details an experiment where participants without chronic hand-based pain underwent four different presentations of resizing conditions whilst wearing an EEG cap to assess differences in subjective illusory experience and steady state responses across the conditions. The four conditions consisted of a multisensory stretching condition, a unimodal visual stretching condition, a non-illusion condition, and a non-illusion condition with tactile input included to provide a comparison for the multisensory condition, and to check if the localisation of cortical representations arise from resizing manipulations to the finger, or from tactile input given to the finger. Subjective results replicated findings in previous chapters of a significantly stronger experience of the illusion in the multisensory condition compared to non-illusion conditions and the unimodal visual condition. SSEP data showed no significant effect of condition from confirmatory parametric tests, however since the data violated assumptions for the preregistered parametric tests, exploratory non-parametric tests were run and did find an overall effect of condition, with the illusory conditions having numerically lower median SSEP amplitudes, although these differences were not found to be significant through post hoc tests. SSEP findings therefore demonstrated no clear effect of resizing illusions on somatosensory SSEP amplitudes, but could hint at a potential sharpening of neural representations as a result of illusory stretching for this sample of participants without chronic pain.

The findings from Chapter 5 provided a basis for the study detailed in Chapter 6 where the same experimental procedure as described in Chapter 5 was used to assess differences in subjective experience and SSEP response to the four resizing conditions within participants with chronic hand-based pain. The only change to procedure was the inclusion of visual analogue scales to assess participants' pain levels in their affected digit before and after each condition. Participants could have any form of chronic hand-based pain, apart from pain resulting from complex regional pain syndrome, as previous research has found that resizing illusions can increase pain for people with this condition (Moseley et al., 2006). Since Chapter 2 found that needing a diagnosis of a chronic pain condition could act as a barrier for people taking part in research, especially for people from ethnic minority backgrounds in the UK, this study did not require a diagnosis to take part. Despite people with chronic pain being thought to have more diffuse neural representations of their affected body parts, which might become sharpened through illusory resizing, the research within this chapter found no significant differences in SSEP amplitudes across all conditions. However, pain data showed no evidence of group level pain reductions following illusory conditions, and changes in SSEP amplitudes are thought to reflect experiences of illusory analgesia. Despite no significant differences being found at the group level, several participants did experience clinically (30% reduction) and extremelly (50% reduction) meaningful levels of pain reduction following illusory resizing in both the multisensory and unimodal visual conditions. A few participants even experienced analgesia following the non-illusion conditions, but fewer than the number experiencing analgesia from illusory conditions. The non-illusion condition did show a significant increase in pain at the group level, which was likely due to the experimental set up increasing people's pain. Sitting in an awkward position for 5 minutes at a time and having your hand formed into a fist apart from one finger for the illusory manipulations were mentioned anecdotally as causing pain for some participants. This finding highlights the need for resizing illusions to be delivered from a home setting rather than a lab setting, to reduce demands on the participants due to experimental set up. Since data were collected regarding the chronic pain conditions that participants had, it was possible to run some exploratory analyses to see if illusory analgesia was underpinned by type of chronic pain, however no significant differences were seen in any analysis when comparing chronic primary and chronic secondary pain conditions. Previous research has found significant decreases in pain for people with osteoarthritis, which is a chronic secondary pain condition (Preston and Newport, 2011). The exploratory analyses within this chapter, however, show that people with chronic primary pain conditions, such as fibromyalgia and Ehlers Danlos Syndrome, do experience illusory analgesia following hand-based resizing illusions, highlighting the suitability of resizing illusions as a non-pharmaceutical treatment option for people with both chronic primary and chronic secondary pain conditions. It has been previously suggested that analgesia following illusory resizing could be due to disownership of the limb, which thereby stops incoming sensory signals from the limb, including pain (McCabe, 2011). The research within Chapter 6 of this thesis however directly assessed disownership levels and found a significantly greater experience of disownership in the unimodal visual condition compared to the multisensory and non-illusion conditions. It is thought that this increase in disownership in the unimodal visual condition could underpin the range of experiences we see throughout this thesis with this condition, as disownership could influence illusory experiences. In the research presented in Chapter 6, we see instances of illusory analgesia in both the multisensory and unimodal visual conditions, therefore it is unlikely that disownership is driving these analgesia experiences, as there were minimal levels of disownership reported for the multisensory condition.

7.2 Limitations

A limitation of the projected completed in Chapter 2 was the small number of participants included from ethnically diverse backgrounds. Some research has suggested that the prevalence of chronic pain is similar between adults from different ethnic groups within the UK (Beasley et al., 2014), whilst research from Versus Arthritis UK reports a higher prevalence of chronic pain in adults from White British and White Irish ethnicities compared to those from all other ethnic backgrounds, but with similar rates between those from White and Black Caribbean ethnicities (Versus Arthritis, 2021). Since the prevalence of chronic pain appears to be either similar or slightly reduced for people from minority ethnic backgrounds in the UK, it is important to understand rates of access to chronic pain services from those groups, to assess if the issue of a lack of representation could be research specific. Unfortunately, research assessing rates of access to chronic pain services in the UK for adults from minority ethnic groups found that data on ethnicity were rarely collected, so conclusions about access rates could not be made (Leach et al., 2023). The lack of representation of people from diverse backgrounds in Chapter 2 was concluded to likely be due to cultural differences in the terminology used for chronic pain. From the few participants included who were from ethnically diverse backgrounds, it was raised that chronic pain can often been seen as a normal part of ageing, rather than being referred to as a clinical condition, which could reduce participation. Despite this concern being addressed through removing the need for a diagnosis and being clear about what constitutes chronic pain for the purposes of the next research project within this thesis that recruited people with chronic pain (Chapter 6), there was still only a small number of people from ethnically diverse backgrounds within this sample. This could be due to the project being an in-person study, and therefore participants were more likely to come from the local area (York, UK) which is predominantly populated by people of a white ethnic group. It is therefore important that data within this thesis are understood to be from predominantly white participants, and therefore generalisability to other ethnic groups could be limited. However, there appears no obvious reason why resizing illusions should work differently for people from different ethnic backgrounds.

In addition to Chapter 6's sample suffering from a reduced number of participants from ethnically diverse backgrounds, the sample size itself was quite small. A priori power analyses showed that we would need a sample size of 30 participants to be able to detect our smallest effect size of interest, which was a medium effect size Cohen (1988), however, only 21 participants were tested. A key reason why recruitment for this project was difficult was the need for participants to be experiencing pain in either their right index or middle fingers, which was not the case for a lot of people who expressed interest in taking part. These digits were chosen for the practicality of attaching the vibrotactile stimulator to elicit the SSEP response, but requiring such a limited range of digits to be experiencing pain did make recruitment difficult. Another reason why recruitment was hard, was because participants needed to be able to come to the University of York to take part, due to the collection of EEG data. Some people with more severe impairments from their chronic pain can find leaving the house and using public transport very difficult, and therefore this in-person participation would have reduced the number of people able to take part even further. Finally, more participants were recruited than the 21 who took part, but since this study required participants to have pain on the day of testing, this often wasn't the case for participants. When this lack of pain occurred, participants were rescheduled to a different participation date, and several were then able to take part on a new date, however, some participants did not start experiencing pain again in the digits required for the study (right index or middle fingers). Whilst this was great for the people who were recruited, as it meant that their hand-based pain was not affecting their daily lives as much, it did reduce the sample size for the research project. Due to time restrictions for data collection, recruitment stopped after 8 months of testing, which resulted in the final sample size of 21 participants. Despite this slightly reduced sample size, the sample did have a wide range of ages (19 – 73 years) and the participants experienced a variety of different chronic pain conditions, which made the sample relatively representative of the population of people living with chronic pain.

There was a lack of patient and public involvement (PPI) within the chapters focussing on chronic pain within this thesis. Chapter 2 sought the experiences and thoughts from the chronic pain population living within the UK, and used mixed methods approaches to try and encourage as many people as possible to have their voices heard. However, patients and the public were not included in the design of this chapter, or Chapter 6, which could have improved the research conducted. For Chapter 2, having people with lived experiences of chronic pain involve as collaborators throughout the project could have increased our sample size, as people could have shared the research participation opportunity more widely than the researchers could, and might have changed parts of the focus group format to decrease the session time and maybe include more scheduled breaks for participants. However, since stakeholders were not worked with throughout the project, these thoughts are only speculative of the benefits this community might have provided. Regarding Chapter 6, if people living with chronic pain had been consulted during the initial design phase of the experiment, then the physical set up could have been adapted in ways to prevent the significant increases in pain that were found. The research detailed in Chapter 6 did undergo pilot testing with participants with chronic pain, and comments were given such as the need for wrist supports, scheduled breaks between conditions, the room being a warmer temperature, and the seat used for participants needing a cushion, which were all addressed before the main experiment took place. Feedback from the findings from Chapter 2 were also included, such as not having the testing environment look too lab-like and having a place for carers / children to wait. However, if people with chronic pain were included in a more collaborative and engaged way throughout this project, more suggestions could have been made and the ones that were given could have been formally credited within the manuscript. Slight engagements in PPI are better than no engagements, but the work within this thesis has clearly demonstrated the need for the voices of people with chronic pain to be heard throughout the research process, and engaging in more formal PPI would have really benefited the projects included within this thesis.

7.3 Future Directions

Chapter 4 discusses an investigation into non-naturalistic auditory input used alongside visual input of hand-based resizing illusions. This chapter used a rising pitch tone and found this increased illusory experience, but it is not known whether this is the only auditory input that could elicit a stronger illusory experience. Naturalistic auditory inputs have been delivered in previous research using the rubber hand illusion (O'Mera, 2014; Radziun & Ehrsson, 2018), and although it is more difficult to replicate the sound of a finger stretching than it is to replicate the sound of a hand being brushed, it would be interesting for future research to attempt this to see if there is a more pronounced effect of naturalistic auditory stimuli over non-naturalistic stimuli. Additionally, Chapter 4 compared non-naturalistic auditory input to a condition without any auditory input, but future research could compare a baseline constant tone to the rising pitch tone, to assess if the congruency of the auditory input and the resizing manipulations is needed for increasing illusory experience. It would also be beneficial to run a study looking at different auditory presentations for people with chronic hand-based pain, to assess which stimulus is best suited to this population rather than the population without chronic pain tested in Chapter 4. It could be that those with chronic pain would need a more realistic auditory input such as bones cracking to feel like there are really changes to the size of their digit, or it could be that including naturalistic auditory stimuli would cause an adverse effect and result in increased pain levels. The work in Chapter 4 of this thesis therefore provides a great starting point for future research looking into visual-auditory presentations of resizing illusions, and the potential of this multisensory implementation to be used as a therapeutic avenue for chronic hand-based pain treatment.

A clear future research project from the work within Chapters 4 and 6 of this thesis would be to run a study using visual-auditory illusory resizing through a phone-based application which delivers resizing illusions. Mobile phone applications are already being used to deliver therapies such as cognitive behavioural therapy (Rathbone et al., 2017) and tinnitus treatments (Mehdi et al., 2020). Mobile phone applications are also being developed for pain management, including for cancer pain management (Jibb et al., 2014) and for pain from conditions such as diabetes, orthodontics, and general chronic pain (Rosser and Eccleston, 2011). Issues have however been raised regarding these apps promising pain relief without any communication about the effectiveness of the apps being used, which when being targeted at a vulnerable chronic pain population, could lead to a risk of individuals who are seeking help being misled and charged for applications which offer no real amelioration of pain (Rosser and Eccleston, 2011). This concern was also voiced by Lalloo et al. (2015) who reviewed 279 pain apps and found that whilst functions of the apps included pain self-care skill support, pain education, self-monitoring, and social support, no app was comprehensive in its pain management functions and only 8.2% of apps included a health care professional in their development. Furthermore, no app was found to provide a theoretical rationale for the advertised functions and only one app underwent scientific evaluation. Given that therapies such as cognitive behavioural therapy and tinnitus treatments are able to be delivered via an app, there is the rationale to attempt to utilise an app for the treatment of chronic hand-based pain which is therefore accessible to patients from their own homes. However, it is important to bear in mind the issues raised by researchers so far regarding pain management apps and to include health care professionals or academics with knowledge of the rationale behind the treatment, to ensure a valid and scientifically tested therapy is what is being delivered to this vulnerable population. This potential future research using a therapeutic application could consist of delivering visual and visuo-auditory hand-based illusions repeatedly across a few weeks within a sample of people living with chronic pain, whereby participants engage in the therapy on a repetitive daily basis, and then the pre- and post-illusion pain ratings can be collected to understand instances of illusory analgesia and to understand the feasibility of delivering resizing illusions via a mobile phone application. Should this be found as a potential therapeutic treatment for chronic hand-based pain, it would allow people to use this therapy from the comfort of their own home, and at times which best suit them, rather than having to come to a lab to receive illusory resizing sessions.

A future research direction drawn from the findings and conclusions within this thesis would be to investigate the impact of neurodiversity on experiences of resizing illusions. There has been reported to be a concurrence between instances of chronic pain and the presence of neurodiverse conditions such as ADHD (Csecs et al., 2022) and Autism (Ryan et al., 2022). Additionally, research has shown that autistic children require a much longer stroking time for them to experience the rubber hand illusion (Cascio et al., 2012), and autistic individuals have been found to display reduced proprioceptive drift towards a rubber hand (Paton et al., 2012). Research assessing autistic experiences of full body illusions has found that autistic participants compared to neurotypical participants were less susceptible to a full body illusion and did not show evidence of illusory self-identification or self-location drift (Mul et al., 2019). These findings suggest that neurodiversity might impact experiences of partial and full bodily illusions, and therefore it is likely that neurodiversity could impact experiences of resizing illusions too. The predictive coding account, specifically the hypo-prior model of autism (Lawson, 2014), posits that autistic individuals might have differences in either the weighting of their prior expectations about sensory stimuli (priors) or in the weighting of their bottom-up experiences of different sensory environments. Both suggestions could lead to differences in experiences and implementation of prediction errors, that being the difference between priors and incoming signals. A bodily focussed predictive coding approach suggests that probabilistic representations of the body and the self emerge from the integration of top-down predictions and bottom-up prediction errors across all modalities, including interoception. Interoception refers to one's ability to sense and perceive internal bodily sensations and signals. This theory suggests that the balance in saliency of interoceptive relative to exteroceptive (sensing of external bodily sensations) prediction errors can determine the malleability of the self, whereby interoceptive prediction errors provide stability and continuity whilst exteroceptive signals provide uncertainty. Within this account individuals with lower interoceptive accuracy are thought to rely less on prediction errors and give more saliency to exteroceptive signals, meaning that representations of self can be updated due to conflicting exteroceptive signals, which would in turn generate stronger body illusions, whereas the opposite would be the case for individuals with high interoceptive accuracy (Palmer and Tsakiris, 2018). This account, however, does not align with the findings from the full body illusion with autistic participants, where there was found to be no relationship between interoceptive awareness and illusion susceptibility (Mul et al., 2019). Additionally, neurodiverse individuals are thought to have less interoceptive sensitivity compared to neurotypical populations (DuBois et al., 2016; Mul et al., 2018; Shah et al., 2016) but appear to be less sensitive to bodily illusions, not more, which would be the case under the bodily focussed predictive coding approach. These research findings highlight that our understanding of how neurodiversity and bodily illusions interact needs further research, but this is especially the case for resizing illusions since the aim of these bodily manipulations is to deliver them to a population of people with chronic pain, where instances of neurodiversity can be higher than the average population. Future research is therefore needed to assess if people who are neurodivergent and who have chronic pain experience illusory analgesia following resizing illusions, or if the difference in how they use prediction errors could impact instances of pain reduction.

7.4 Overall Conclusions

The experiments within this thesis contribute to the literature on different sensory presentations of resizing illusions and their application to populations living with chronic pain, in addition to providing recommendations for approaches to facilitate participation in chronic pain research. Previous subjective illusory findings have been replicated and this thesis provides additional evidence about the nature of experiences for unimodal visual presentations of resizing illusions whilst addressing concerns regarding illusory analgesia arising from experiences of disownership. Non-naturalistic auditory stimuli was found to increase subjective experiences of resizing illusions and is recommended to be used for a home-based presentation of multisensory resizing illusions. EEG findings demonstrated that resizing illusions elicit activity related to multisensory integration processes, and that samples both with and without chronic hand-based pain show limited evidence supporting somatosensory sharpening being the key neural mechanism for illusory analgesia. Previous pain reduction findings were not replicated at the group level for multisensory conditions and were not seen for unimodal visual resizing illusions, indicating the importance of experimental set up and highlighting the individuality of chronic pain. This individuality did not appear to be underpinned by type of chronic pain condition, opening the avenue for resizing illusions to be used as a non-pharmaceutical treatment option for people with varying chronic pain conditions.

As mentioned previously within this thesis, all the work has already been published in either article format (Hansford et al., 2024a, 2023), or is currently under review and available as preprints (Hansford et al., 2024d, 2024c, 2024b). Much of this work has also been presented at national and international conferences. The research within this thesis was supported by a Pain Relief Foundation Professor John Miles Studentship grant. It is hoped that this collection of work will provide a basis for future investigations into using resizing illusions as a non-pharmaceutical treatment option for people living with chronic hand-based pain.

Appendix A: Condition Prevelance and Exploratory Analysis from Chapter 2

Phase 1 Prevelance

Table A1: Prevalence of chronic pain condition within focus group participant sample. Note: Several participants had more than one chronic pain condition, therefore the total of the percentages does not equal the total number of participants.

Chronic Pain Condition	Prevalence
Chronic Back Pain	28%
Rheumatoid Arthritis	24%
Fibromyalgia	17%
Osteoarthritis	14%
Neck Pain	10%
Juvenile Idiopathic Arthritis (JIA)	7%
Chronic Regional Pain	3%
Spinal Stenosis	3%
Ganglion Cysts	3%
IBS	3%
Gynaecological Pains	3%
Crohn's Disease	3%
Facial Pain	3%
Ehlers Danlos Syndrome	3%
Hip Labral Tear	3%
Psoriatic Arthritis	3%
Mixed Connective Tissue Disease	3%
Temporomandibular Joint Disorder (TMJ)	3%

Phase 2 Prevalence

Table A2: Prevalence of chronic pain condition within survey participant sample. Note: Several participants had more than one chronic pain condition, therefore the total of the percentages does not equal the total number of participants. *Unspecified is used for participants who either did not specify a specific condition or said they were awaiting diagnosis.

Chronic Pain Condition	Prevelance
Rheumatoid Arthritis	37%
Fibromyalgia	25%
Chronic Back Pain	19%
Osteoarthritis	12%
Nerve Pain	10%
Arthritis	7%
Ehlers Danlos Syndrome	5%
Chronic Hip Pain	5%
Psoriatic Arthritis	4%
Endometriosis	3%
M.E.	3%
Unspecified*	3%
Hypermobility	3%
Chronic Leg Pain	2%
Migraine	2%
Scoliosis	2%
Chronic Knee Pain	2%
Sjogren's Syndrome	2%
Cervical Spondylosis	2%
PCOS	2%
Chronic Neck Pain	2%
Chronic Fatigue Syndrome	2%
Chronic Shoulder Pain	2%
Chronic Pain Syndrome	2%
Hyperthyroidism	1%

Chronic Pain Condition	Prevelance
Polyarthralgia	1%
Juvenille Idiopathic Arthritis	1%
Scleritis	1%
Idiopathic Musculoskeletal	1%
Polymyalgia	1%
Chronic Bladder Pain	1%
Temporomandibular Joint Disorder	1%
Osteoporosis	1%
Tendonitis	1%
Irritable Bowel Syndrome (IBS)	1%
Gastroiparesis	1%
Pancreatitis	1%
Bursitis	1%
Vulvodynia	1%
Chiari Malformation	1%
Syringomyelia	1%
Muscular Dysfunction	1%
Idiopathic Intracranial Hypertension	1%
Trigeminal Neuralgia	1%

Exploratory Phase 2 Analysis

Within the survey, participants were asked to rank the level of their agreement / disagreement on a Likert scale from -3 to +3, allowing for a more in depth look at the nature of the opinions that participants held regarding the barrier and facilitator themes gained within phase 1. Exploratory data presentation can be seen in Figure A1.

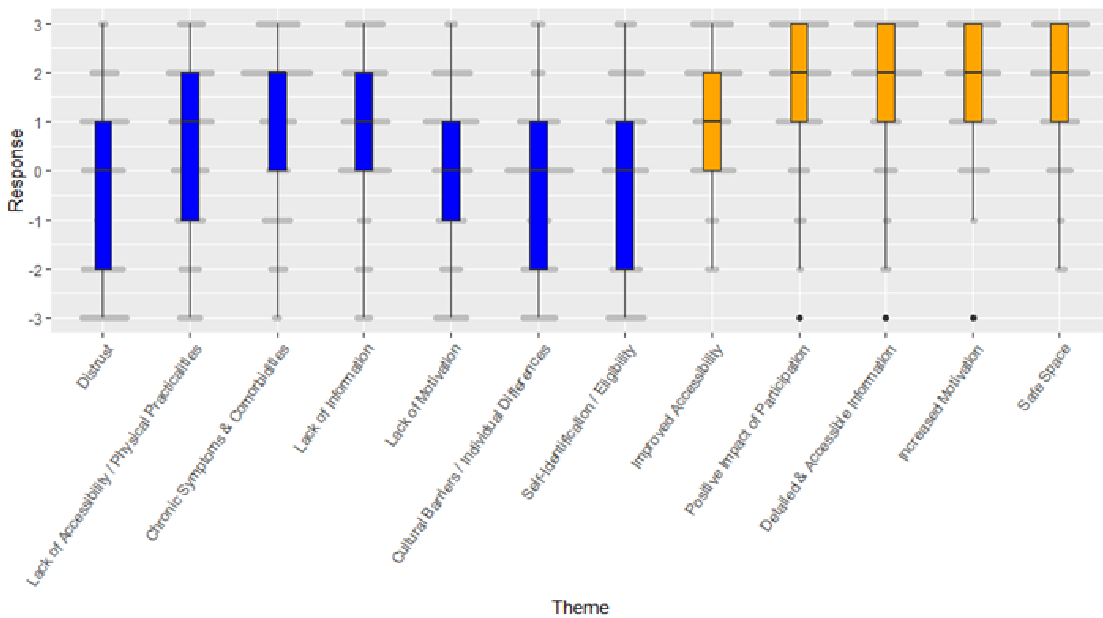

Figure A1.1: Boxplot with jitter showing distribution of Likert scale responses regarding the strength of agreement, disagreement, or neutral opinion of themes. +3 indicates strong agreement, 0 indicates a neutral opinion and -3 indicates strong disagreement with the theme. Blue bars represent Barriers, Orange bars represent Facilitators. Jitter can be seen in grey, with outliers shown in black.

Appendix B: Control and Disownership scores from Chapter 3

Table B1: Mean Scores for Averaged Control and Disownership Statements.

Conditions	Control	Disownership
Baseline	-2.63	-2.35
MS	-2.23	-1.36
IC	-2.02	-0.94
UV	-1.89	-0.66

Appendix C: Additional analysis on the UVP sample from Chapter 3

We assessed MS Stretch compared to NI in the UVP sample. Two significant clusters were found when comparing these conditions in the gamma band (30-60Hz) between 0 and 2000ms (p = .01; P <.001). The effect was strongest at electrode CPZ.

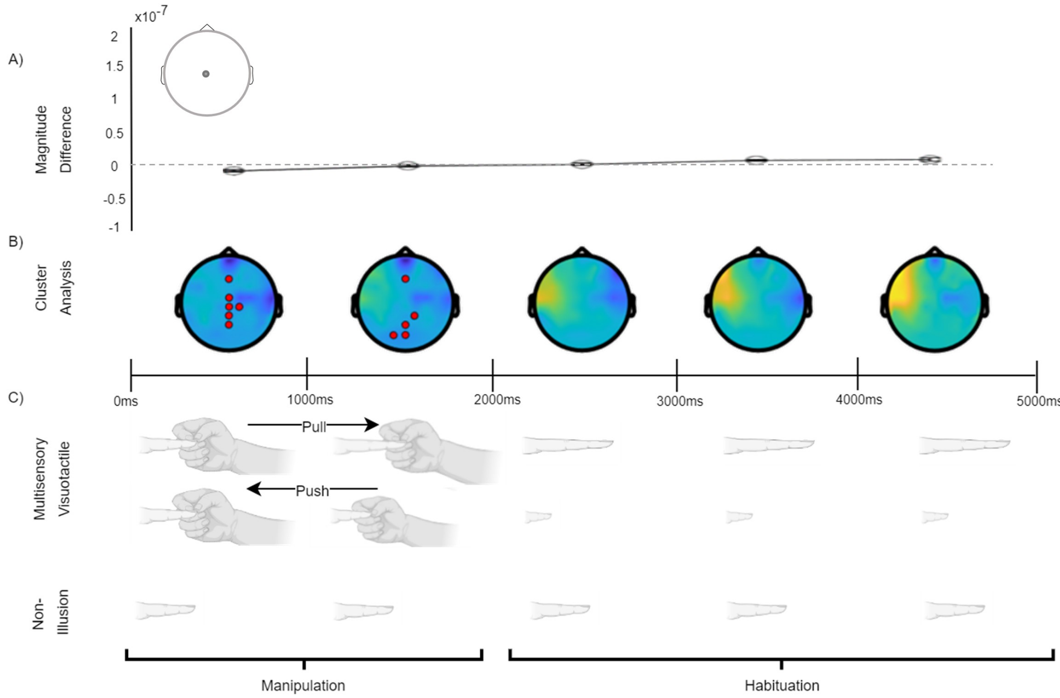

Figure C1.1: Comparison of gamma band activity between MS Stretch and NI conditions in the UVP Sample. The Magnitude Difference plot (a) shows time course of CPZ electrode, which was the significant electrode showing the largest effect size (d = 1.25). In panel (b), colour indicates the magnitude difference (blue: negative, yellow: positive), and significant clusters are highlighted by red dots. In panel (c), arrows denote the manipulation that the researcher's hand is applying to the finger.

We assessed UV Stretch compared to NI in the UVP sample. A significant cluster was found when comparing these conditions in the gamma band (30-60Hz) between 0 and 2000ms (p = .012). The effect was strongest at electrode M1.

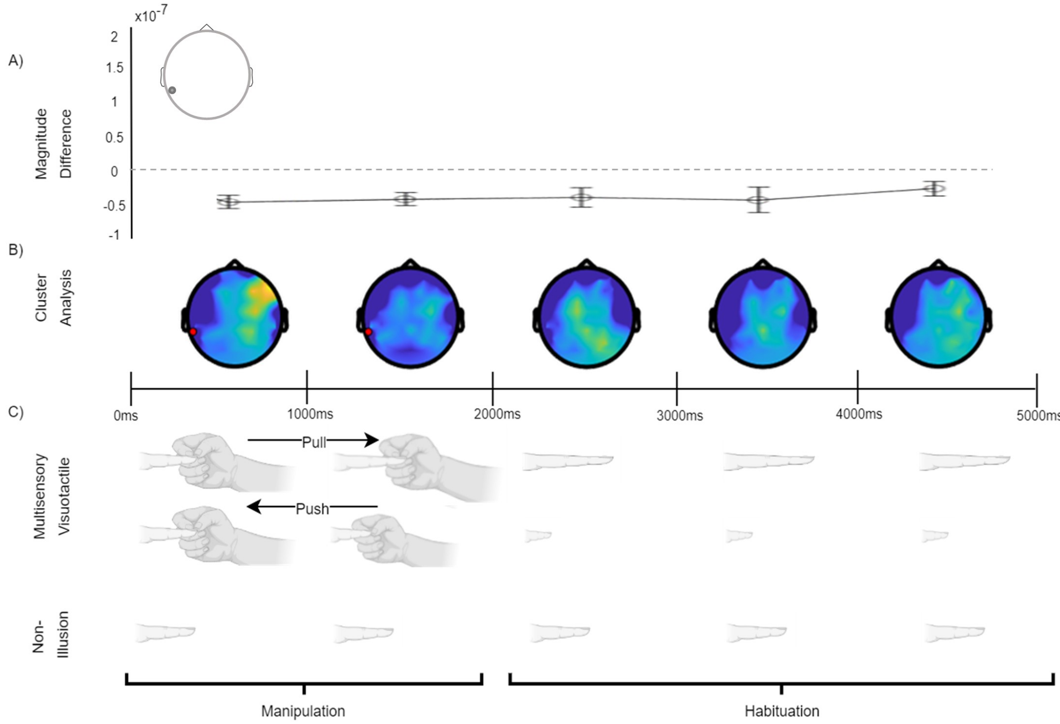

Figure C1.2: Comparison of gamma band activity between UV Stretch and NI conditions in the UVP Sample. The Magnitude Difference plot (a) shows time course of M1 electrode, which was the significant electrode showing the largest effect size (d = .98). In panel (b), colour indicates the magnitude difference (blue: negative, yellow: positive), and significant clusters are highlighted by red dots. In panel (c), arrows denote the manipulation that the researcher's hand is applying to the finger.

We assessed MS Shrink compared to NI in the UVP sample. Two significant clusters were found when comparing these conditions in the gamma band (30-60Hz) between 0 and 1000ms ($p = .002$; $p < .001$). The effect was strongest at electrode F7.

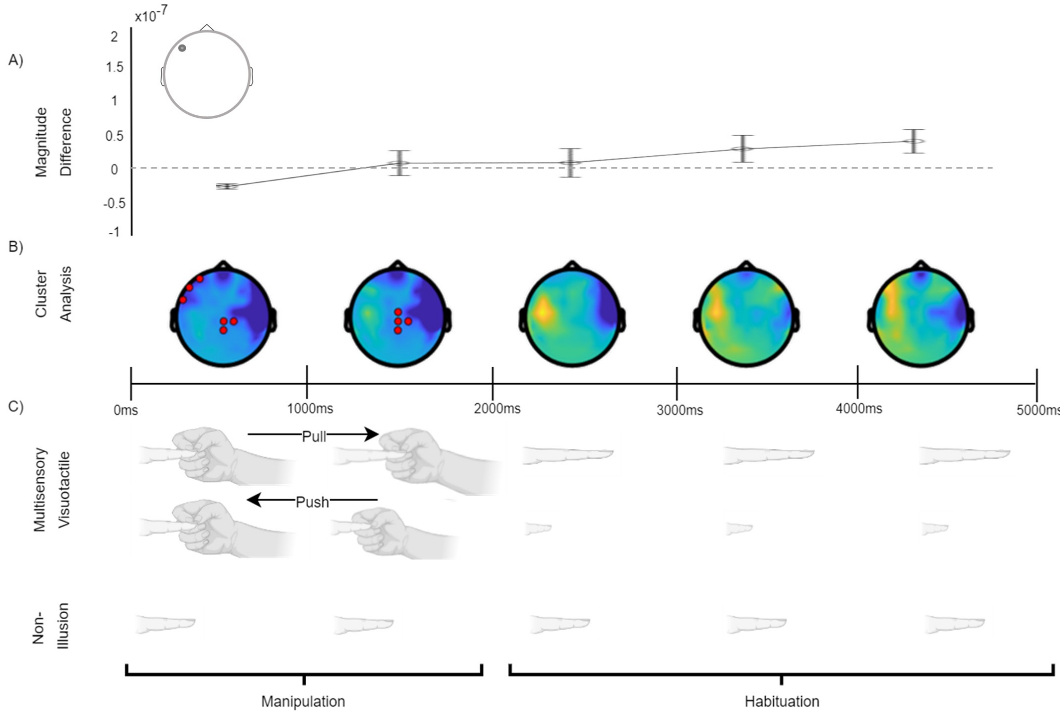

Figure C1.3: Comparison of gamma band activity between MS Shrink and NI conditions in the UVP Sample. The Magnitude Difference plot (a) shows time course of F7 electrode, which was the significant electrode showing the largest effect size ($d = 1.15$). In panel (b), colour indicates the magnitude difference (blue: negative, yellow: positive), and significant clusters are highlighted by red dots. In panel (c), arrows denote the manipulation that the researcher's hand is applying to the finger.

We assessed UV Shrink compared to NI in the UVP sample and found no significant clusters.

Appendix D: Full Sample Analyses from Chapter 4

Full Sample Subjective Data

A factorial ANOVA with a within-subjects factor of condition and a between-subjects factor of group was used to assess if there was an effect of group (Audio vs Non-Audio) on subjective illusory experience score in the V/VA and VT/VTA conditions. Analysis showed no statistically significant interaction between condition and group (F (2, 100) = 0.78, p = 0.460. Main effects analysis showed that condition (p = <0.001) but not group (p = 0.129) had a significant effect on subjective illusory experience score.

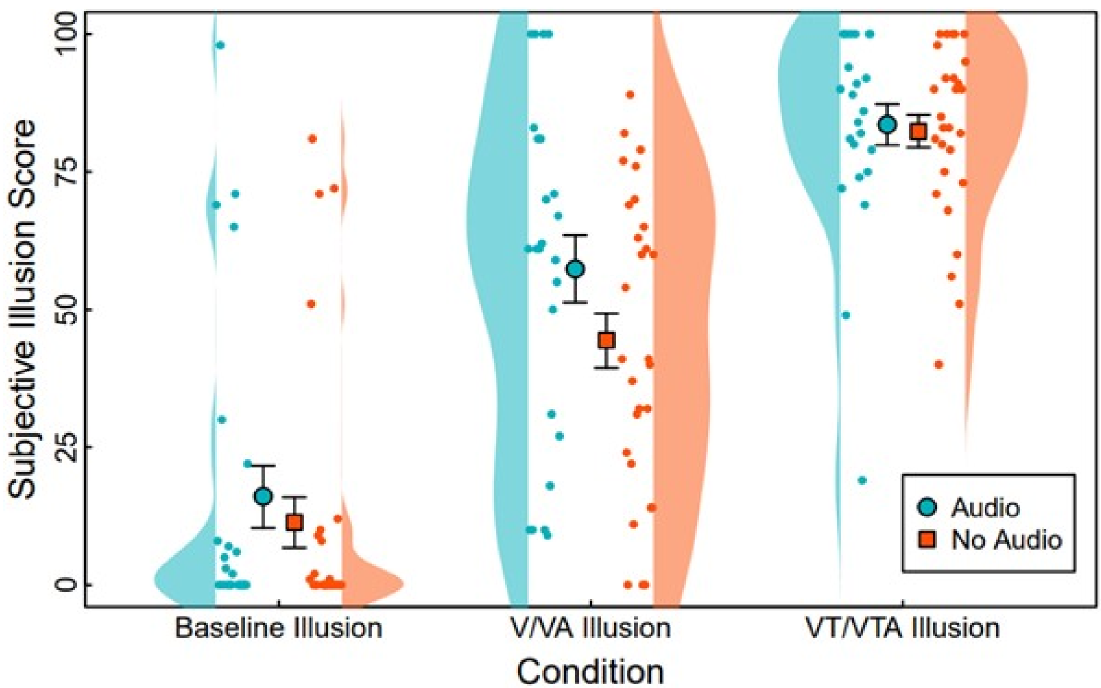

Figure D1.1: Subjective Illusory Experience Score for full sample Baseline, V/VA and VT/VTA conditions. Group is indicated by colour, with red showing the no audio group and blue showing the audio group.

Full Sample Dot Touch Data

A factorial ANOVA with a within-subjects factor of condition and a between-subjects factor of group was used to assess if there was an effect of group (Audio Vs Non-Audio) on dot touch data in the V/VA and VT/VTA conditions. Analysis on right dot touch data showed no significant interaction between condition and group $F(1, 50) = 0.24$, $p = 0.628$ and main effects showed no effect of condition ($p = 0.524$) or group ($p = 0.707$). Analysis on left dot touch data showed no significant interaction between condition and group $F(1, 50) = 0$, $p = 0.992$ whilst main effects showed no effect of group ($p = 0.581$) but did show an effect of condition ($p = <0.001$), with participants placing their finger significantly lower in the V/VA condition (M =-0.6, SD =0.7) compared to the VT/VTA condition (M =-0.24, SD =0.6).

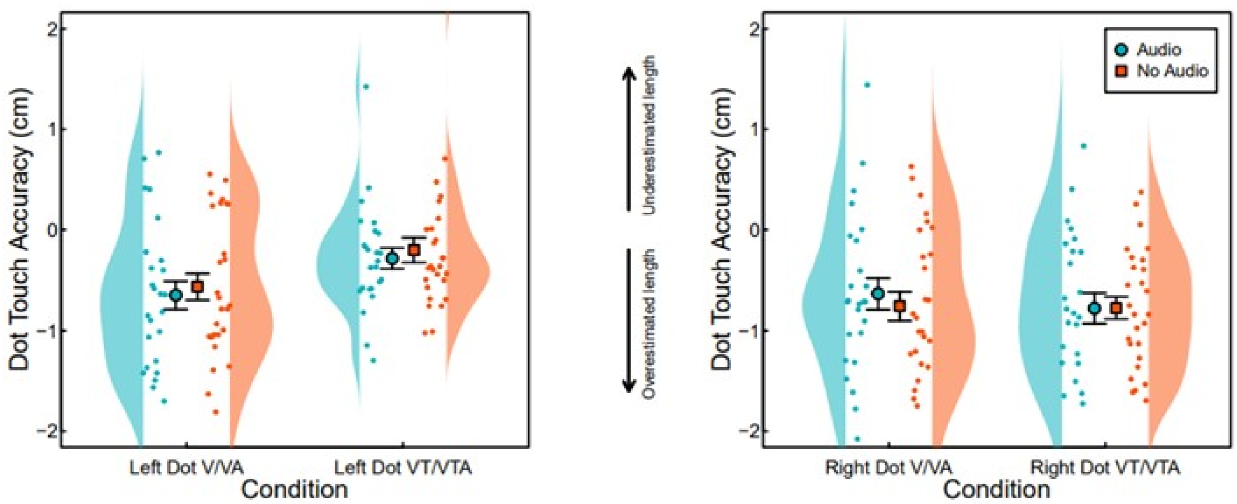

Figure D1.2: Dot Touch Data in relative centimetres for full sample V/VA and VT/VTA conditions for both left and right hand data. Group is indicated by colour, with red showing the no audio group and blue showing the audio group. Arrows denote the direction of finger length estimation.

Full Sample Ruler Judgement Data

A factorial ANOVA with a within-subjects factor of condition and a between-subjects factor of group was used to assess if there was an effect of group (Audio Vs Non-Audio) on ruler judgement data with no outliers removed in the V/VA and VT/VTA conditions. Analysis showed no significant interaction between condition and group $F(1, 50) = 0.283$, $p = 0.597$ and main effects showed no effect of condition ($p = 0.152$) or group ($p = 0.904$).

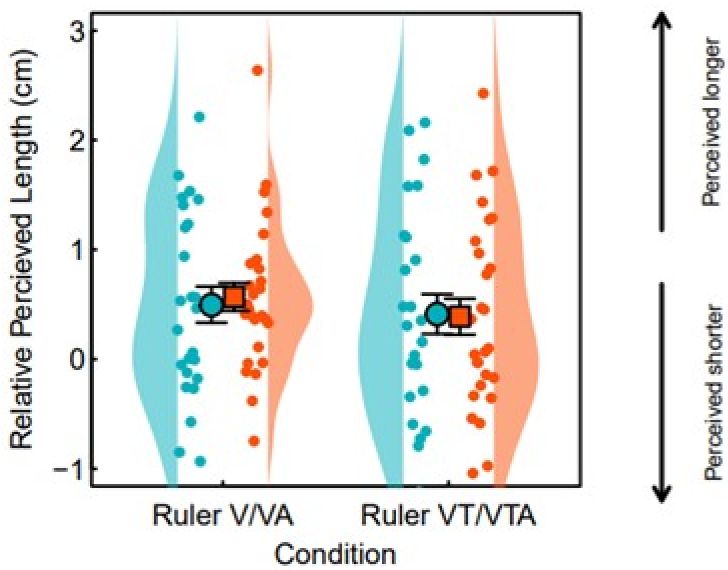

Figure D1.3: Ruler Judgement data for full sample in relative centimetres for V/VA and VT/VTA conditions. Group is indicated by colour, with red showing the no audio group and blue showing the audio group. Arrows denote direction of perceived finger length.

Appendix E: Ownership, Disownership, and Control Data from Chapter 4

Ownership Data

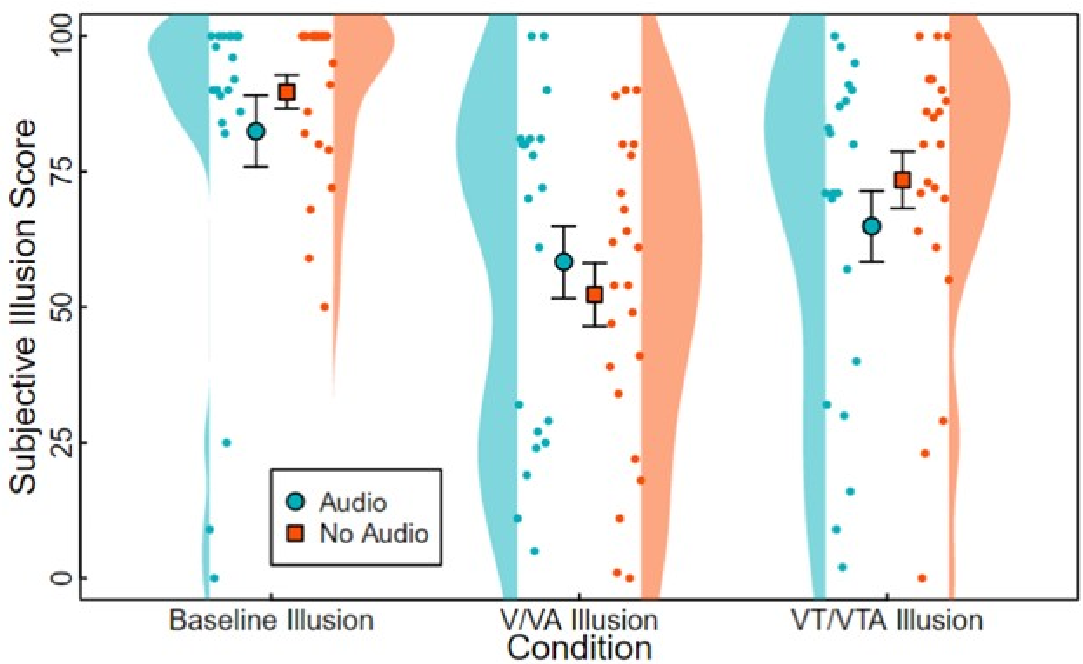

Figure E1.1: Ownership data for participants across all conditions. Each mean rating is above 50 indicating experience of ownership of the hand during the illusion (Baseline Audio: M = 82.4, SD = 30.6, Baseline Non-audio: M = 89.7, SD = 15.1, V/VA Audio: M = 58.4, SD = 31.3, V/VA Non-Audio: M = 52.3, SD = 27.9, VT/VTA Audio: M = 64.9, SD = 30.8, VT/VTA Non-Audio: M = 73.4, SD = 25.8).

Disownership Data

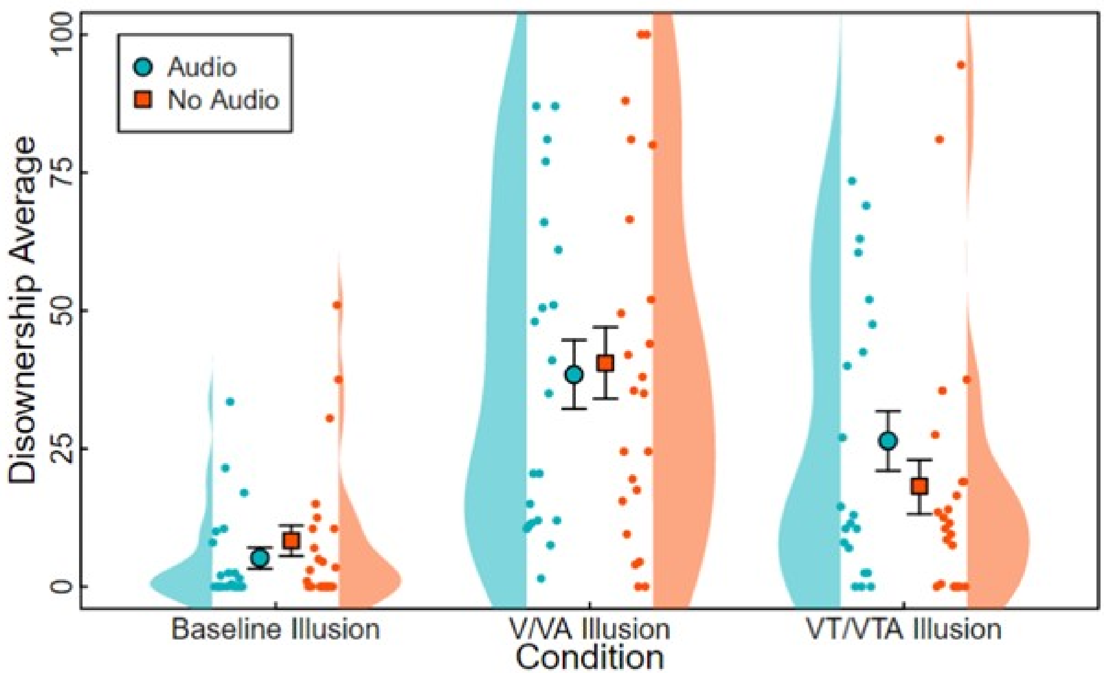

Figure E1.2: Disownership average data for participants across all conditions. Each mean rating is below 50 indicating experience of no experiences of disownership of the hand during the illusion (Baseline Audio: M = 5.21, SD = 8.93, Baseline Non-audio: M = 8.33, SD = 13.6, V/VA Audio: M = 38.4, 29.0, V/VA Non-Audio: M = 40.5, 32.0, VT/VTA Audio: M = 26.4, SD = 25.6, VT/VTA Non-Audio: M = 18.2, 24.6).

Control Data

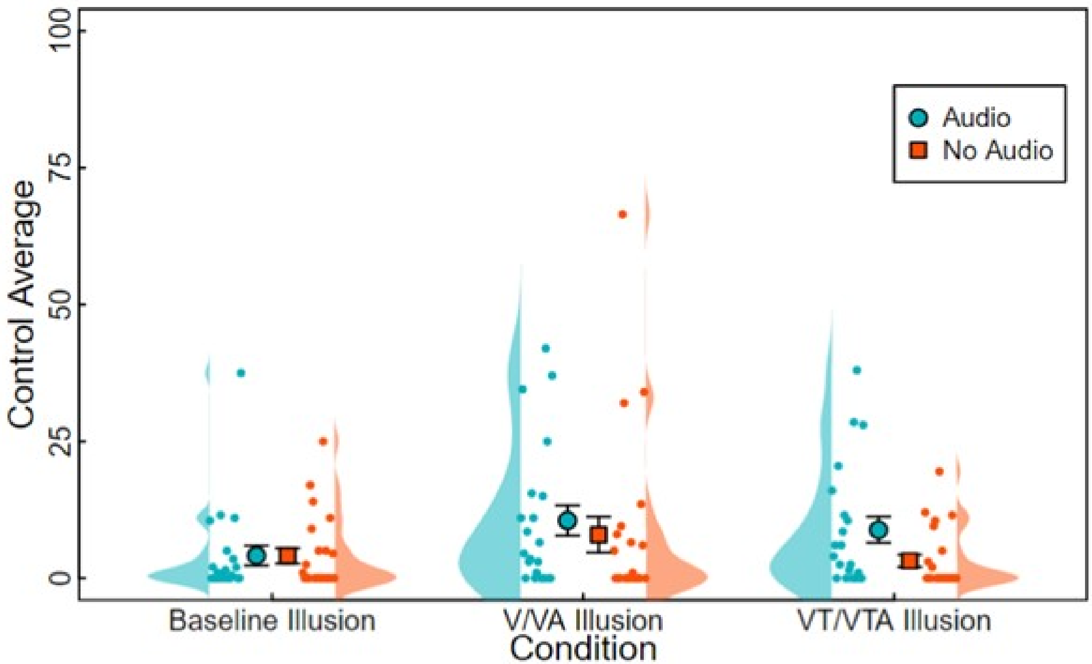

Figure E1.3: Control average data for participants across all conditions. Each mean rating is below 50 indicating no violation of control statements during the illusion (Baseline Audio: M= 4.12, SD = 8.55, Baseline Non-audio: M = 4.09, SD = 6.76, V/VA Audio: M = 10.5, SD = 13.2, V/VA Non-Audio: M = 7.91, SD = 16.0, VT/VTA Audio: M = 8.81, SD = 11.2, VT/VTA Non-Audio: M = 3.17, SD = 5.49).

Appendix F: Positive Control and Exploratory Analyses from Chapter 4

Positive Control Subjective Data

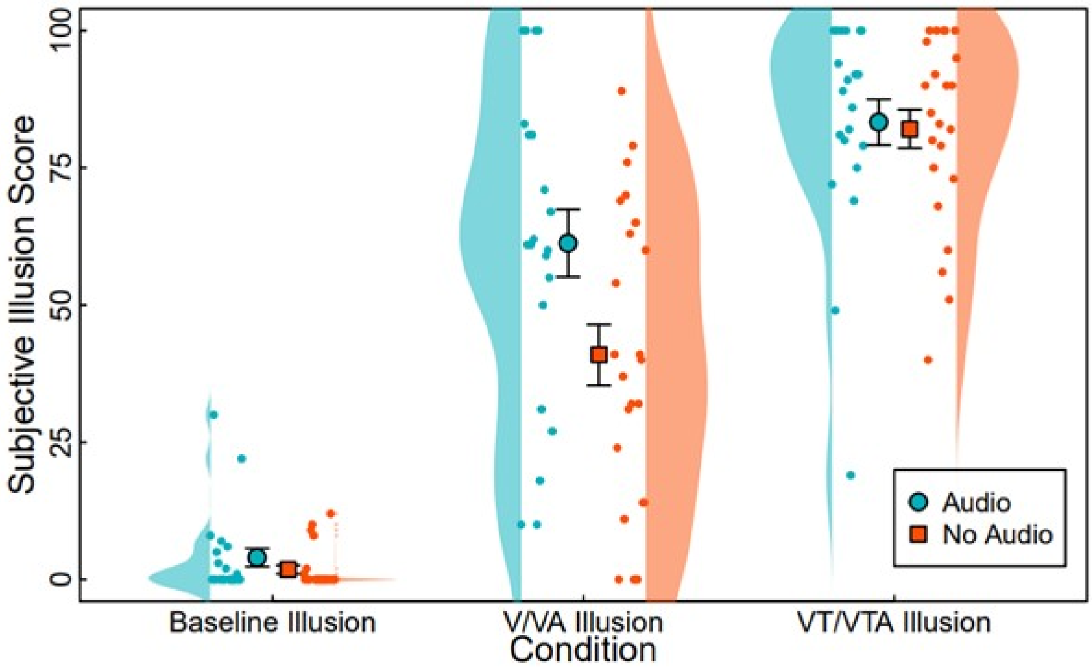

Figure F1.1: Subjective Illusion Data for Baseline, V/VA, and VT/VTA conditions. Group is indicated by colour, with red showing the no audio group and blue showing the audio group.

Positive Control Right Dot Touch

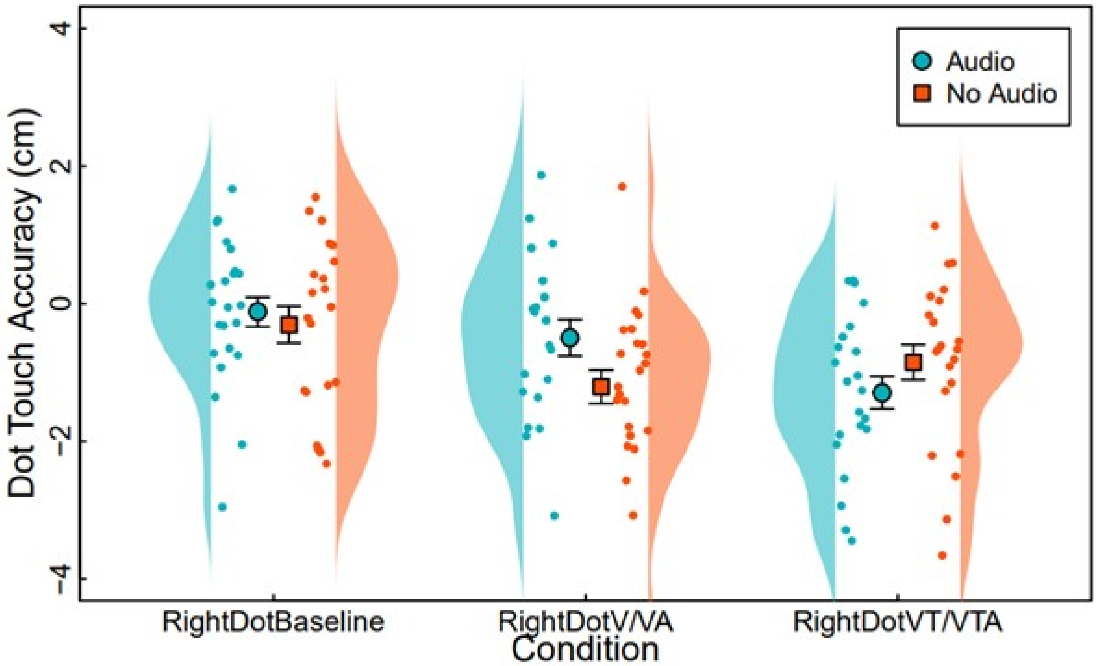

Figure F1.2: Dot Touch Data in centimetres for Baseline, V/VA, and VT/VTA conditions for right hand data. Group is indicated by colour, with red showing the no audio group and blue showing the audio group.

Positive Control Left Dot Touch

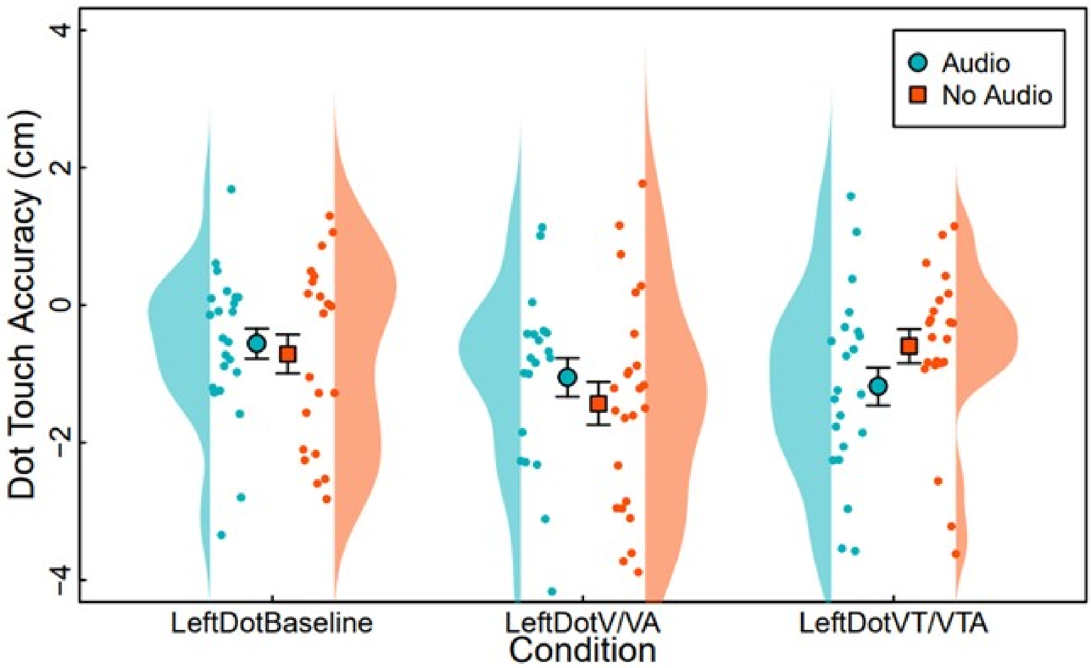

Figure F1.3: Dot Touch Data in centimetres for Baseline, V/VA, and VT/VTA conditions for left hand data. Group is indicated by colour, with red showing the no audio group and blue showing the audio group.

Positive Control Ruler Judgement

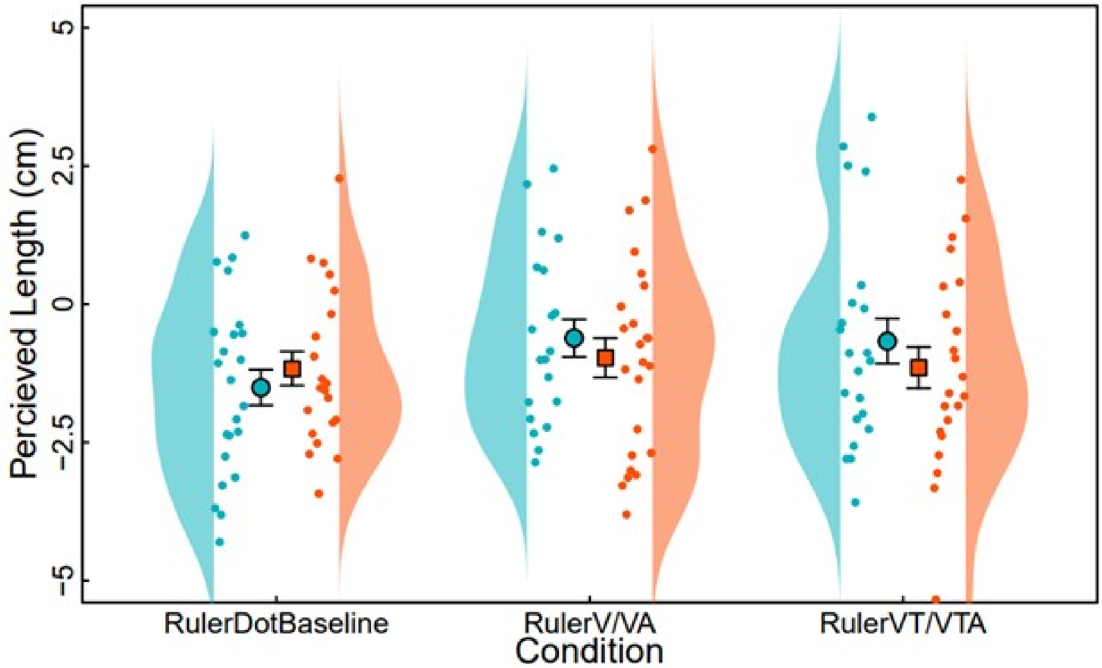

Figure F1.4: Ruler Judgement data in centimetres for baseline, V/VA, and VT/VTA conditions. Group is indicated by colour, with red showing the no audio group and blue showing the audio group.

Exploratory Correlation Analysis

Exploratory correlation analyses were run to assess relationships between subjective illusion score and performance-based measures of resizing illusions and can be seen in Figure 4. These were not included in our preregistration, but were suggested by a reviewer. Significance was assessed against Bonferroni correction for 4 comparisons within each correlation, at an initial alpha of .05, resulting in significance now being assessed at a revised alpha of .0125. Spearman rank correlation analyses found no significant relationships between subjective illusion score and performance on the right dot task (VA: r(42) = -0.52, p= 0.015; V: r(42) = 0.16, p=0.456; VTA: r(42) = -0.18, p= 0.437; VT: r(42) = -0.28, p= 0.203), or when comparing subjective illusion data to left dot touch data (VA: r(42) = 0.2,p= 0.381; V: r(42) = -0.071, p= 0.747; VTA: r(42) = 0.027, p= 0.908; VT: r(42) = 0.0094, p= 0.966), or comparing subjective data ruler judgement data (VA: r(42) = 0.23, p= 0.314; V: r(42) = -0.27, p= 0.214; VTA: r(42) =0.21, p= 0.353; VT: r(42) = 0.35, p= 0.098).

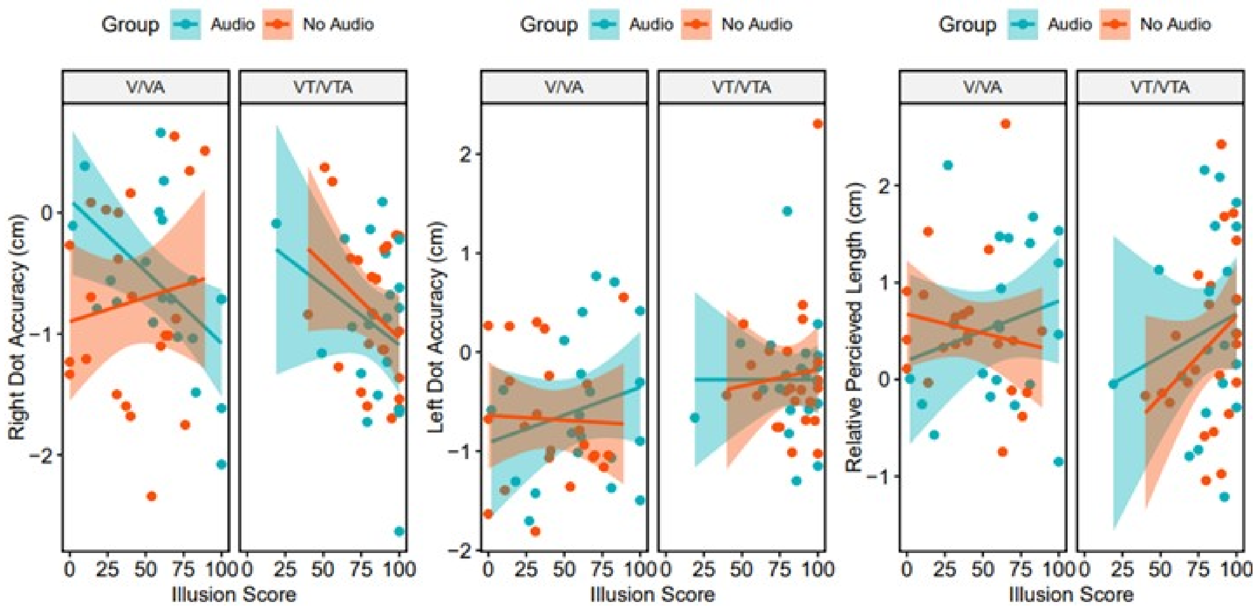

Figure F1.5: Correlations between Illusion Score and Right Dot, Left Dot, and Ruler Judgement data respectively. Shading shows confidence intervals and group is indicated by colour, with red showing the no audio group and blue showing the audio group.

Appendix G: Pilot Data from Chapter 5

Illusory Resizing Pilot Data

Pilot data regarding the experience of the illusion for healthy participants undergoing synchronous and asynchronous illusory resizing of the index finger can be seen in Figure 7. 9 participants had either synchronous or asynchronous multimodal manipulations delivered first in a random order, and were then given the other condition, after which all participants were given an illusion scale. Findings showed that across all participants, no significant difference in illusion experience between the synchronous and asynchronous conditions, $t(8) = 1.877$, $p = 0.097$, however as can be seen in figure F1, despite the small sample size, illusion strength was seen to be greater in the synchronous condition compared to the asynchronous condition.

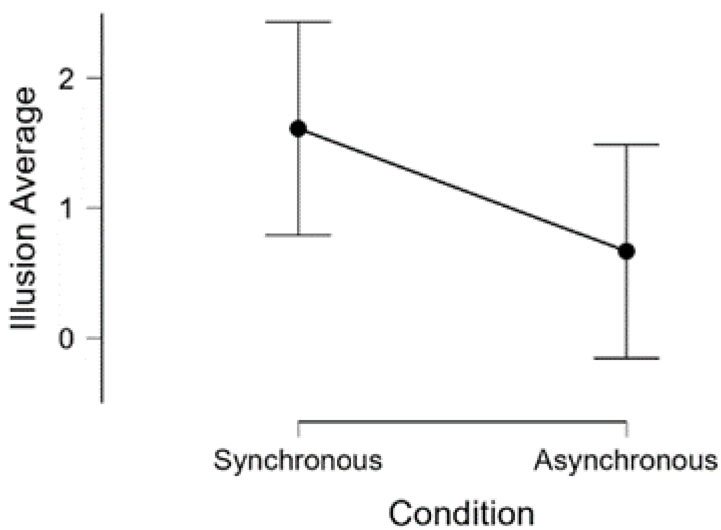

Figure G1.1: Pilot data from Healthy Participants Undergoing Synchronous and Asynchronous Illusory Finger Resizing.

Vibrotactile EEG Data

Previous literature stated that the ideal vibration frequency to use to elicit somatosensory SSEPs is approximately 26Hz (Muller et al., 2001; Breitweiser et al., 2016; Pokorny et al., 2016; Snyder, 1992). Due to resizing illusions often manipulating the index finger, and previous studies using the index finger supporting around 26Hz as an optimal frequency (Muller et al., 2001; Breitweiser et al., 2016; Pokorny et al., 2016), it was hypothesised that 26Hz would elicit a dependable somatosensory SSEP response. Therefore, we ran a pilot study to check that our setup and equipment can reliably elicit and record a somatosensory SSEP at 26Hz, using the resizing illusion and EEG.

Pilot data were collected for 3 healthy participants. Participants underwent the same experimental protocol as mentioned in the "Experimental Procedure" section, minus the subjective illusory experience questionnaire. A Fourier transform was calculated for each waveform at each electrode for all conditions, and then averaged across repetition to obtain individual results. These were then averaged across all 3 participants to give the result seen in Figure 8.

As can be seen in Figure 8, there was a clear somatosensory SSEP response at 26Hz, which was strongest around electrodes F1 and FC1. Previous research using vibrotactile stimulation at 21Hz have also found the scalp topography of the activation to be most pronounced over mid-frontal distributions (Porcu et al., 2014; Timora & Budd, 2018), in line with the scalp topography seen here. Given these finding of a distinct 26Hz signal and mid-frontal scalp location, it appeared appropriate for 26Hz to be used as the vibration frequency in the current study.

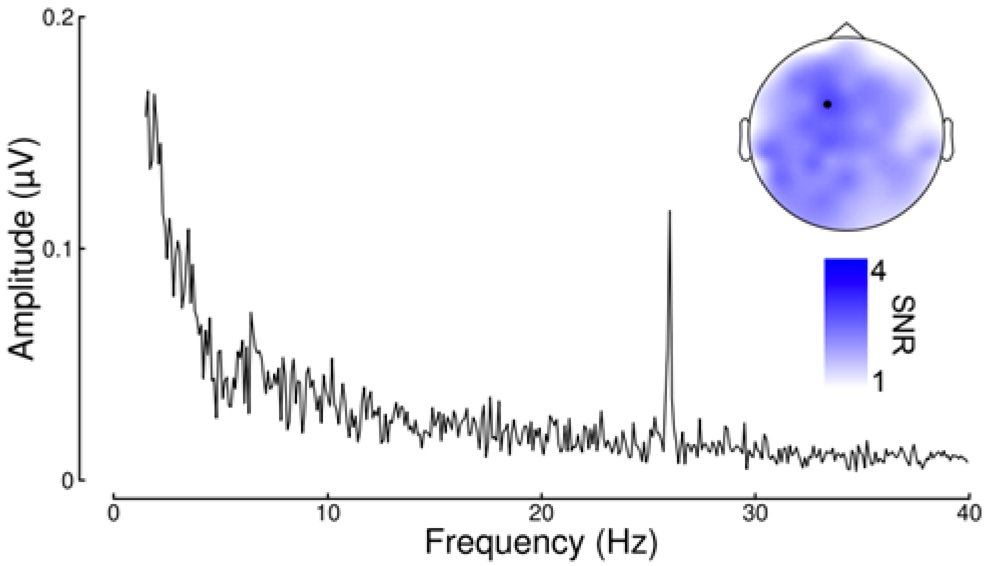

Figure G1.2: Averaged Pilot Data showing peak frequency at 26Hz, centred between electrodes F1 and FC1. The spectrum is derived from electrode FC1. Saturation bar represents signal to noise ratio (SNR). SNR is a measure of signal quality and describes the ratio of signal power (at 26Hz) to noise power (averaged across 10 adjacent frequency bins). SNR was used for the pilot figure because with a small sample (3 participants) we did not want a noisy electrode to influence the electrodes chosen as electrodes of interest.

Illusion Data with Vibrotactile Stimulator

Pilot data were also collected using the vibrotactile stimulator at 26Hz to make sure that the illusory experience is not affected by the addition of vibrotactile input. Pilot data were collected from 4 additional healthy participants, who underwent the same experimental protocol as mentioned in the "Experimental Procedure" section, but without EEG caps fitted. Illusory experience was calculated using the median of both illusion scores for each participant minus their median control scores, as per the preprocessing steps regarding the control index, and then the data were averaged over participants to give the results seen in Figure 9. As can be seen, there is a greater subjective experience of the resizing illusion, indexed by participant's illusion score, in both experimental conditions (UV average = 64.25; MS average = 67.88) compared to both control conditions (NI average = 32.38; NIT average = 24.13). Scores below 50 are indicative of disagreement of experience of the illusion, whilst a score of 50 is a neutral option regarding the illusion experience, and scores above 50 are indicative of agreement of experiencing the illusion. This therefore shows that the experience of illusory resizing was maintained when vibrotactile stimulation was added to the procedure and can therefore be used in the current study to elicit somatosensory SSEPs without affecting the subjective illusory experience of the resizing illusion.

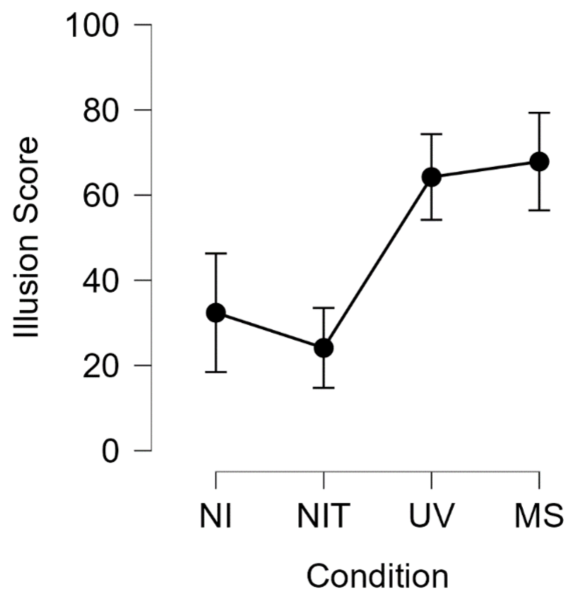

Figure G1.3: Averaged Illusion score for each condition. Error bars represent standard errors. NI represents the non-Illusion condition, NIT refers to the non-illusion tactile condition, UV refers to the unimodal-visual condition, and MS refers to the multisensory condition.

Appendix H: Disownership, Control & Correlational Analyses from Chapter 5

Exploratory Disownership Analysis

Exploratory analyses of the subjective disownership data using a Friedman test found a significant overall effect of condition with a small effect size ($\chi^2(3) = 19.33$, $p < .001$, Kendall's W = 0.14) and post hoc Wilcoxon tests with Holm corrections found significantly greater combined disownership score in the UV condition (Median = 23.25, SD = 27.6) compared to the NI (Median = 1.75, SD = 22.4, $z = 211.5$, $p.adj = .014$, $r = -15.5$), NIT (Median = 0, SD = 19.8, $z = 132$, $p.adj < .001$, $r = -18.25$), and MS conditions, (Median = 7, SD = 25.11, $z = 254$, $p.adj = .033$, $r = -10.25$).

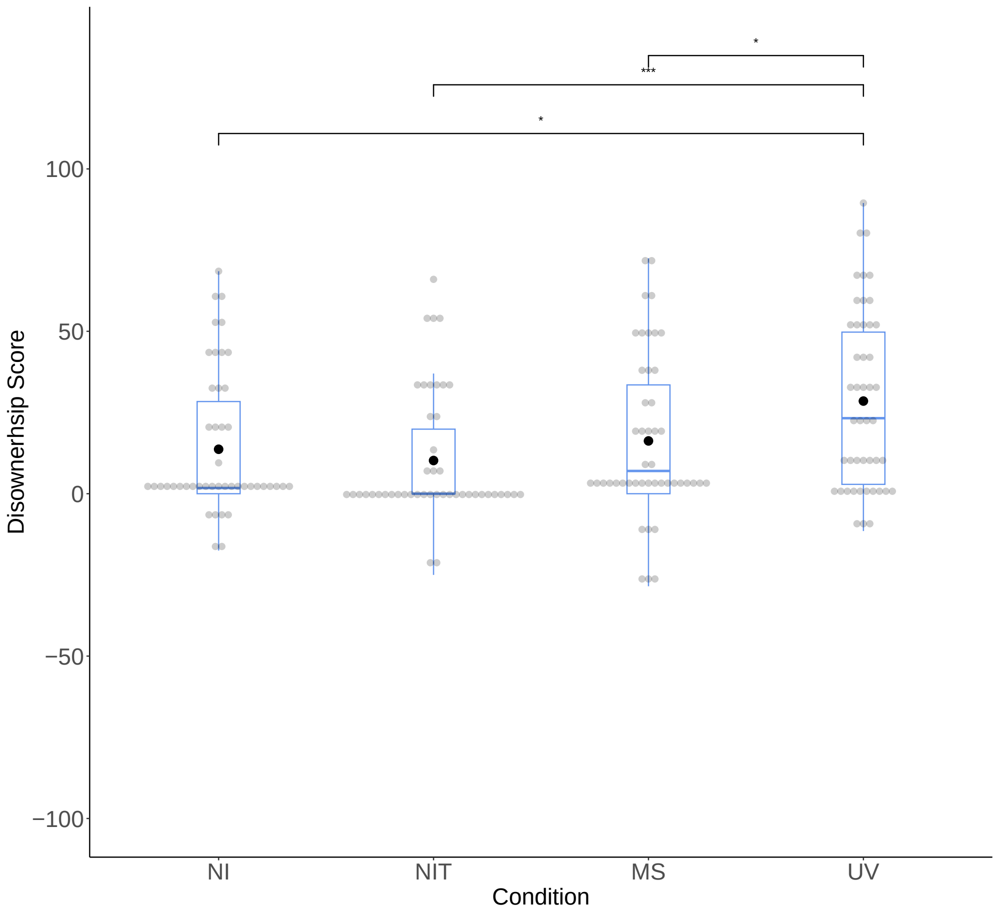

Figure H1.1: Combined Disownership Score Indexs Across Conditions (NI: Non-Illusion; NIT: Non-Illusion Tactile; MS: Multisensory; UV: Unimodal Visual). Scores below 50 indicate disagreement with experience of disownership statements, whilst scores above 50 indicate agreement. A continuous visual analogue scale was used in data collection, with agreement and disagreement statements located at each end of the scale. Box plots show means, medians and inter-quartile ranges of data. Medians are indicated with a horizontal line whilst means are indicated by a black dot. Box and wiskers show inter-quartile ranges.Data points are shown in grey jitter binned along the y-axis, grouped by condition.

Exploratory Control Analysis

Exploratory analyses of the subjective control data using a Kruskall-Wallis test (due to multiple ties) found no significant overall effect of condition ($\chi^2(3) = 4.53$, $p = .210$) and post hoc Dunn's tests with Bonferroni corrections found no significant differences between combined control scores when comparing the NI condition (Median = 0, SD = 15.58), to the NIT (Median = 0, SD = 13.24, $z = 1$, $p.adj = 1.000$), MS (Median = 0, SD = 18.15, $z = 0.02$, $p.adj = 1.000$), or UV condition (Median = 1.5, SD = 16.34, $z = -1.13$, $p.adj = 1.000$).

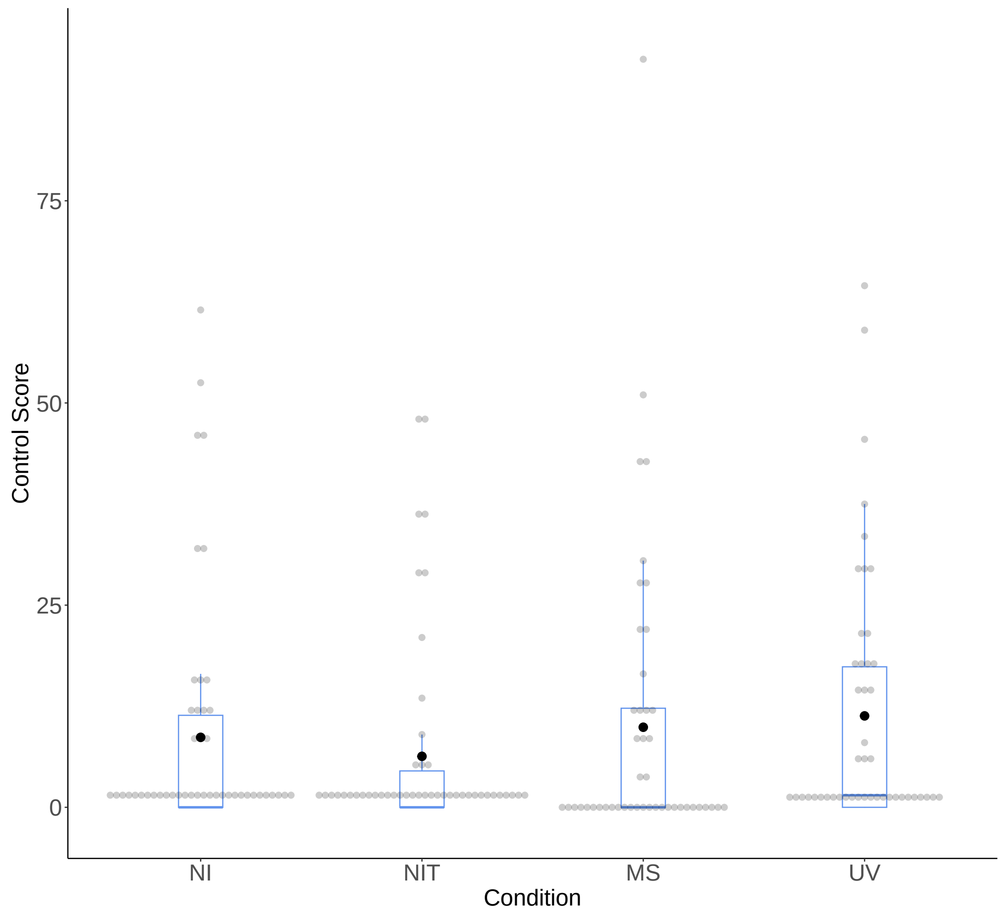

Figure H1.2: Combined Control Scores Across Conditions (NI: Non-Illusion; NIT: Non-Illusion Tactile; MS: Multisensory; UV: Unimodal Visual). Scores below 50 indicate disagreement with experience of control statements, whilst scores above 50 indicate agreement. A continuous visual analogue scale was used in data collection, with agreement and disagreement statements located at each end of the scale. Box plots show means, medians and inter-quartile ranges of data. Medians are indicated with a horizontal line whilst means are indicated by a black dot. Box and wiskers show inter-quartile ranges. Data points are shown in grey jitter binned along the y-axis, grouped by condition.

Exploratory Correlation Analysis

Spearman's correlations were run to identify any correlations between participant's illusion score and their SSEP amplitude across electrodes of interest (F1 & FC1) for each condition found no significant correlations across conditions.

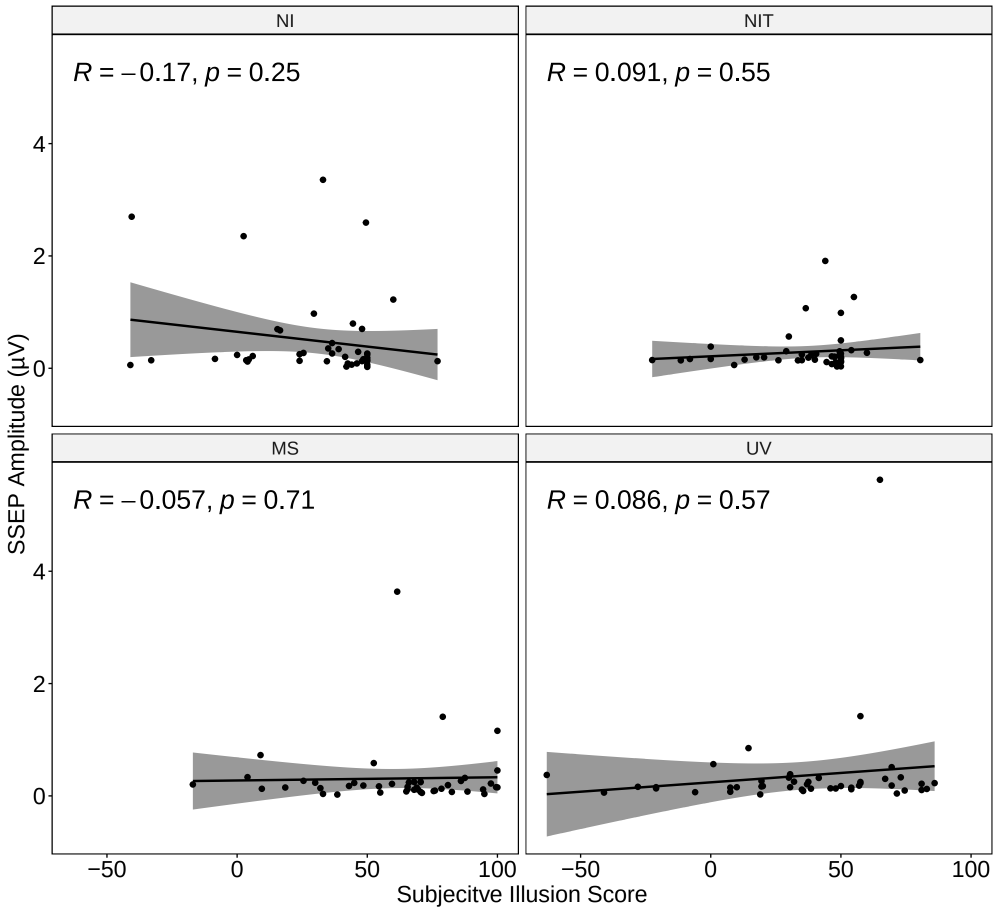

Figure H1.3: Correlation Between Amplitude and Subjective Illusory Score for Each Condition (NI: Non-Illusion; NIT: Non-Illusion Tactile; MS: Multisensory; UV: Unimodal Visual).

Appendix I: Disownership, Control, Correlational & Subgroup Analyses from Chapter 6

Exploratory Disownership Analysis

Exploratory analyses of the subjective disownership data using a Friedman test found a significant overall effect of condition with a small to moderate effect size ($\chi^2(3) = 13.12$, $p = 0.004$, Kendall's W = 0.21) and post hoc Wilcoxon tests with Holm corrections found significantly greater combined disownership score in the UV condition (Median = 42, SD = 42.32) compared to the NI (Median = 0, SD = 19.63, $z = 16$, $p.adj = 0.039$, $r = -39.78$), NIT (Median = 0, SD = 15.24, $z = 12$, $p.adj = 0.025$, $r = -48.25$), and MS conditions, (Median = 1.5, SD = 22.34, $z = 22$, $p.adj = 0.042$, $r = -40$).

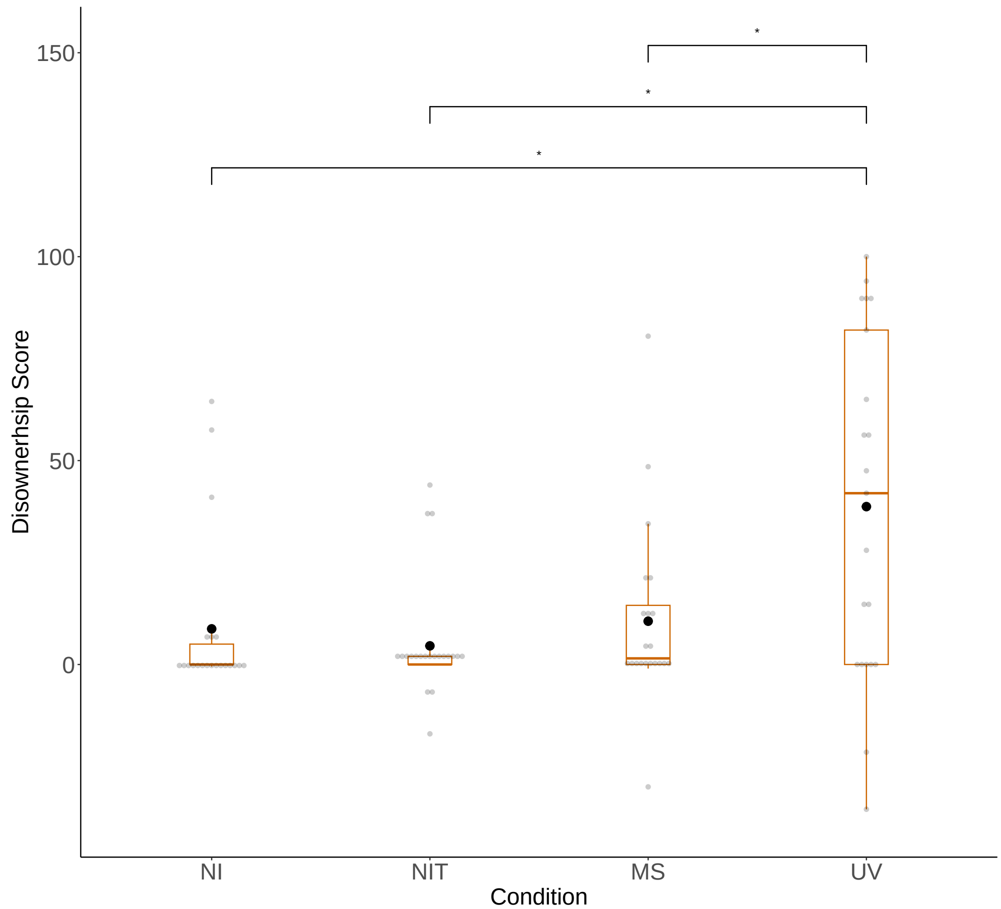

Figure I1.1: Combined Disownership Score Index Across Conditions (NI: Non-Illusion; NIT: Non-Illusion Tactile; MS: Multisensory; UV: Unimodal Visual). Scores below 50 indicate disagreement with experience of disownership statements, whilst scores above 50 indicate agreement. A continuous visual analogue scale was used in data collection, with agreement and disagreement statements located at each end of the scale. Box plots show means, medians and inter-quartile ranges of data. Medians are indicated with a horizontal line whilst means are indicated by a black dot. Data points are shown in grey jitter binned along the y-axis, grouped by condition.

Exploratory Control Analysis

Exploratory analyses of the subjective control data using a Friedman test found a significant overall effect of condition with a small effect size (χ^2 (3) = 11.61, p = 0.009, Kendall's W = 0.18). Post hoc Wilcoxon tests with Holm corrections for multiple comparisons found a significant difference between NI and UV control scores (z = 1, $p.adj$ = 0.031, r = -16) however found no significant differences between control scores across any other condition: NI (Median = 0, SD = 21.8), NIT (Median = 0, SD = 9.2), MS (Median = 0, SD = 17.28), UV (Median = 6, SD = 24.02).

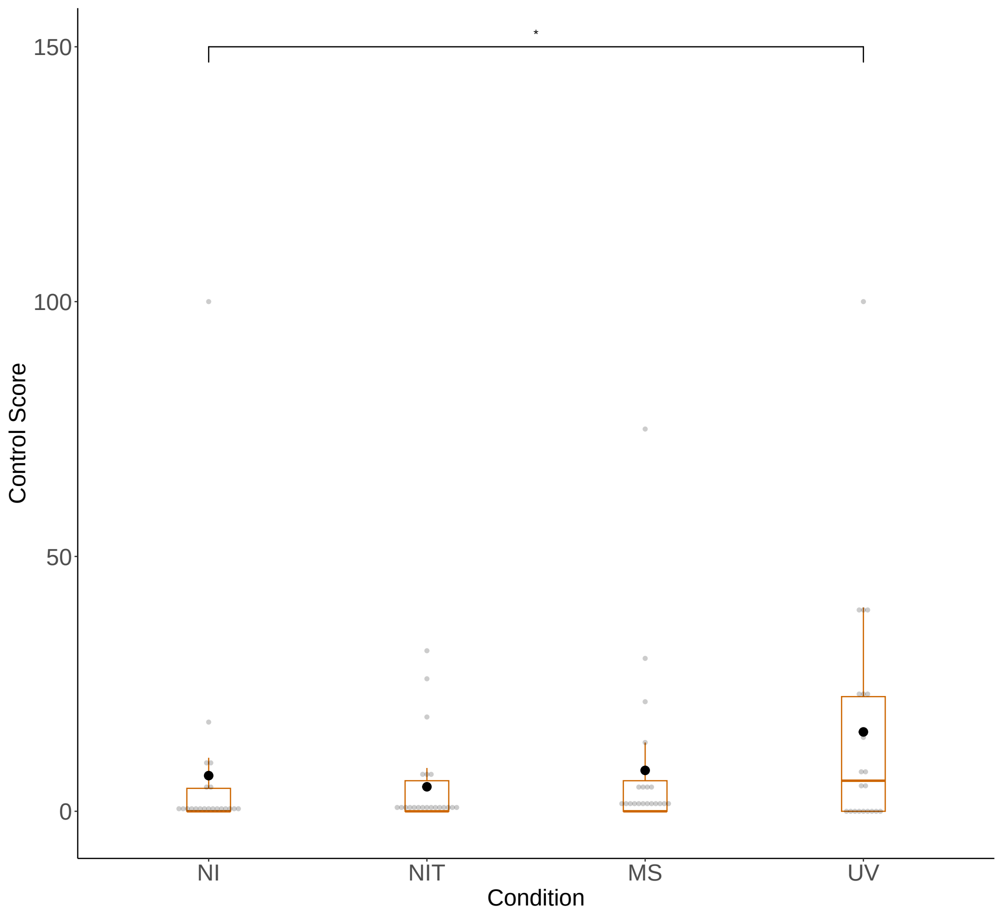

Figure I1.2: Combined Control Scores Across Conditions (NI: Non-Illusion; NIT: Non-Illusion Tactile; MS: Multisensory; UV: Unimodal Visual). Scores below 50 indicate disagreement with experience of control statements, whilst scores above 50 indicate agreement. A continuous visual analogue scale was used in data collection, with agreement and disagreement statements located at each end of the scale. Box plots show means, medians and inter-quartile ranges of data. Medians are indicated with a horizontal line whilst means are indicated by a black dot. Data points are shown in grey jitter binned along the y-axis, grouped by condition

Exploratory Correlation Analysis

Spearman's correlations were run to identify any correlations between (1) participant's illusion score and their SSEP amplitude, (2) participant's pain percentage change and their SSEP amplitude, and (3) participant's subjective illusion scores and their pain percentage change, finding no significant correlations across any analyses.

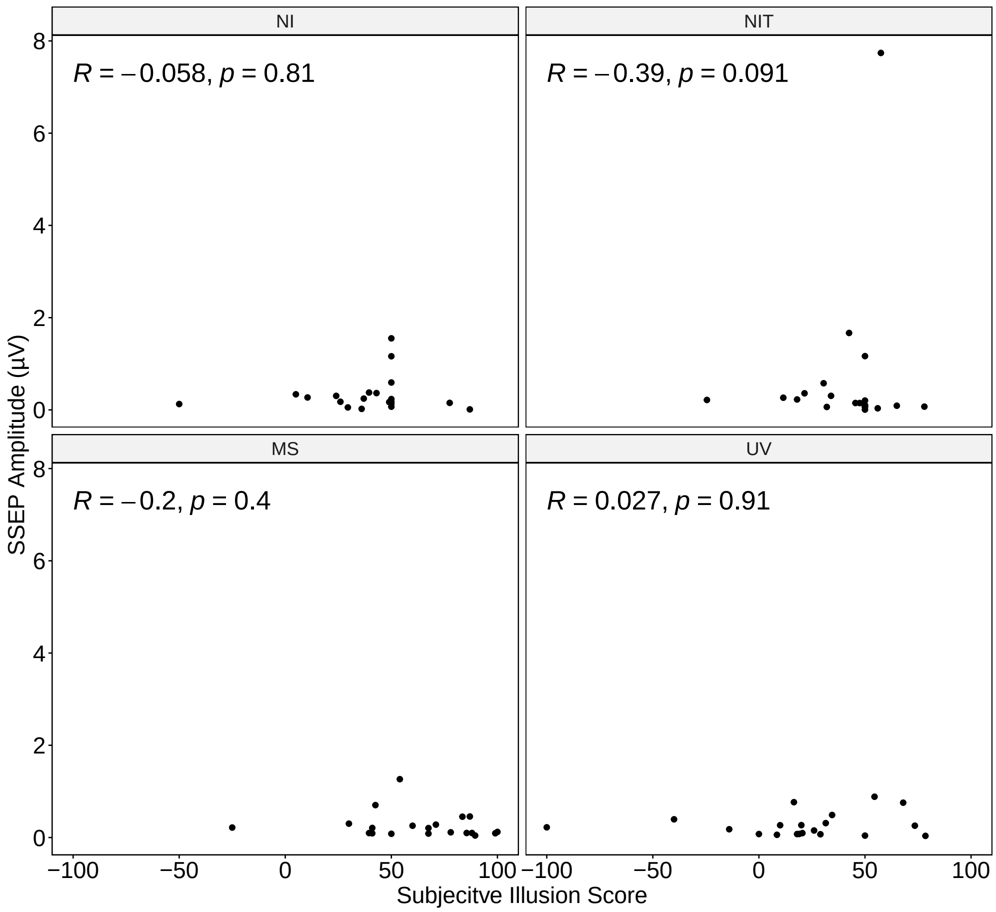

Figure I1.3: Correlation Between Amplitude and Subjective Illusory Score for Each Condition.

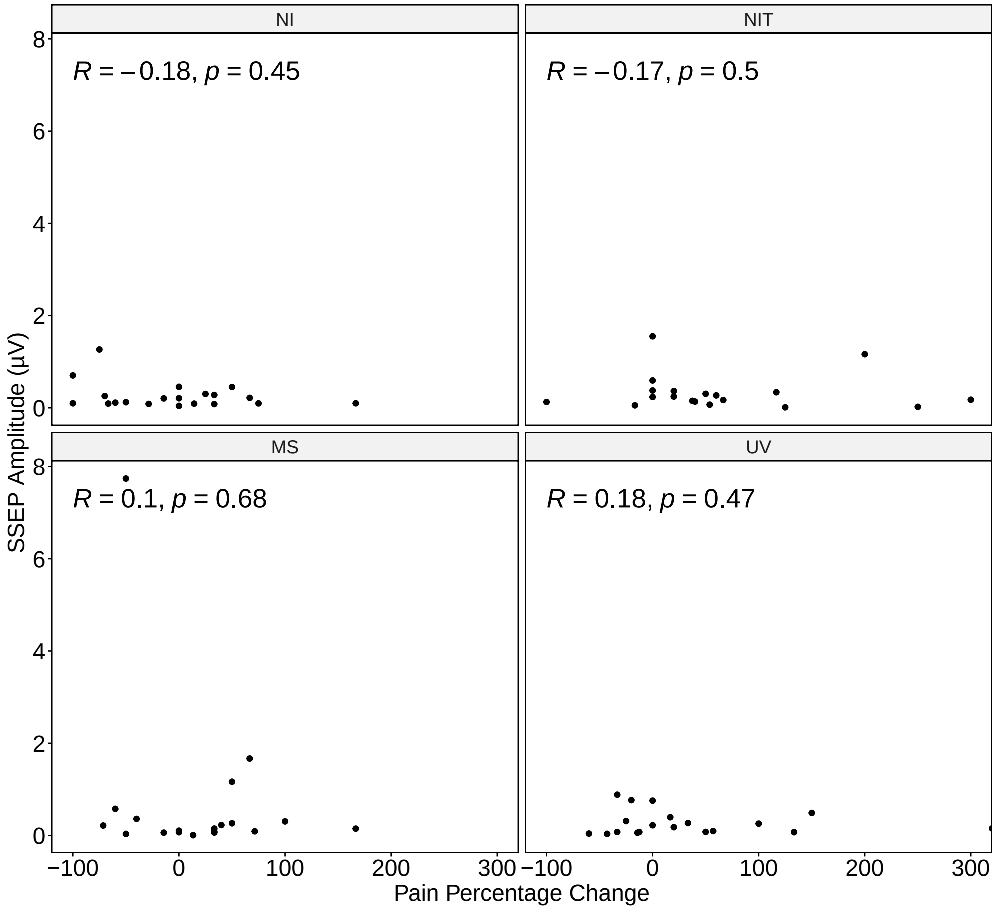

Figure I1.4: Correlation Between Amplitude and Pain Percentage Change for Each Condition.

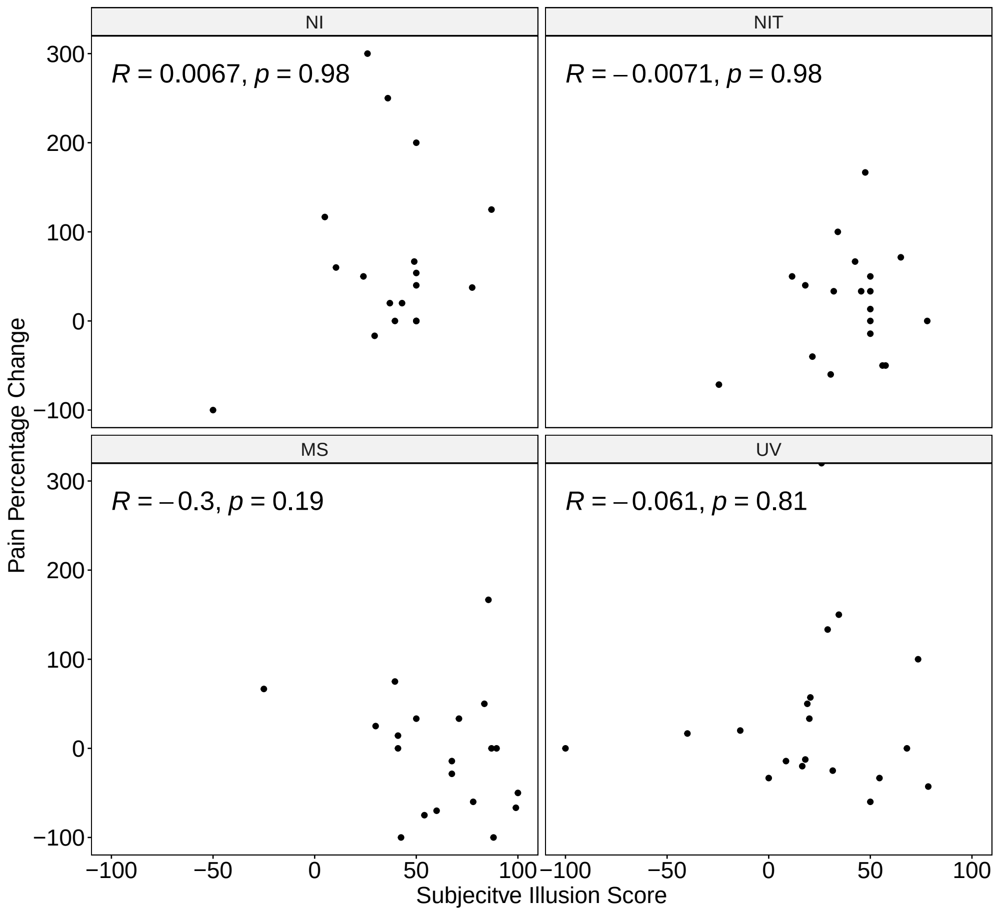

Figure I1.5: Correlation Between Pain Percentage Change and Subjective Illusory Score for Each Condition.

Pain Condition Subgroup Analyses

Chronic Primary Pain

Since this sample consisted of participants with both primary and secondary chronic pain conditions, data were analysed split by either primary or secondary pain condition and can be seen in the figures below. Chronic primary pain is plotted in magenta, chronic secondary pain is plotted in green, and participants with either no diagnosis or a mix of primary and secondary pain conditions are plotted in grey.

Regarding chronic primary pain conditions, Wilcoxon tests found no significant differences when comparing NI pre (Median = 5, SD = 1.41) and post (Median = 6, SD = 0.87) pain levels ($z = 13$, $p.adj = 0.170$, $r = 1.25$), nor when comparing NIT pre (Median = 5, SD = 1.48) and post (Median = 7, SD = 2.28) pain levels ($z = 8$, $p.adj = 0.345$, $r = 2$), MS pre (Median = 4, SD = 2.88) and post (Median = 5, SD = 2.61) levels ($z = 6$, $p.adj = 0.855$, $r = 1.14$) nor UV pre (Median = 6, SD = 0.84) and post (Median = 7, SD = 2.74) levels ($z = 10$, $p.adj = 0.586$, $r = 1$).

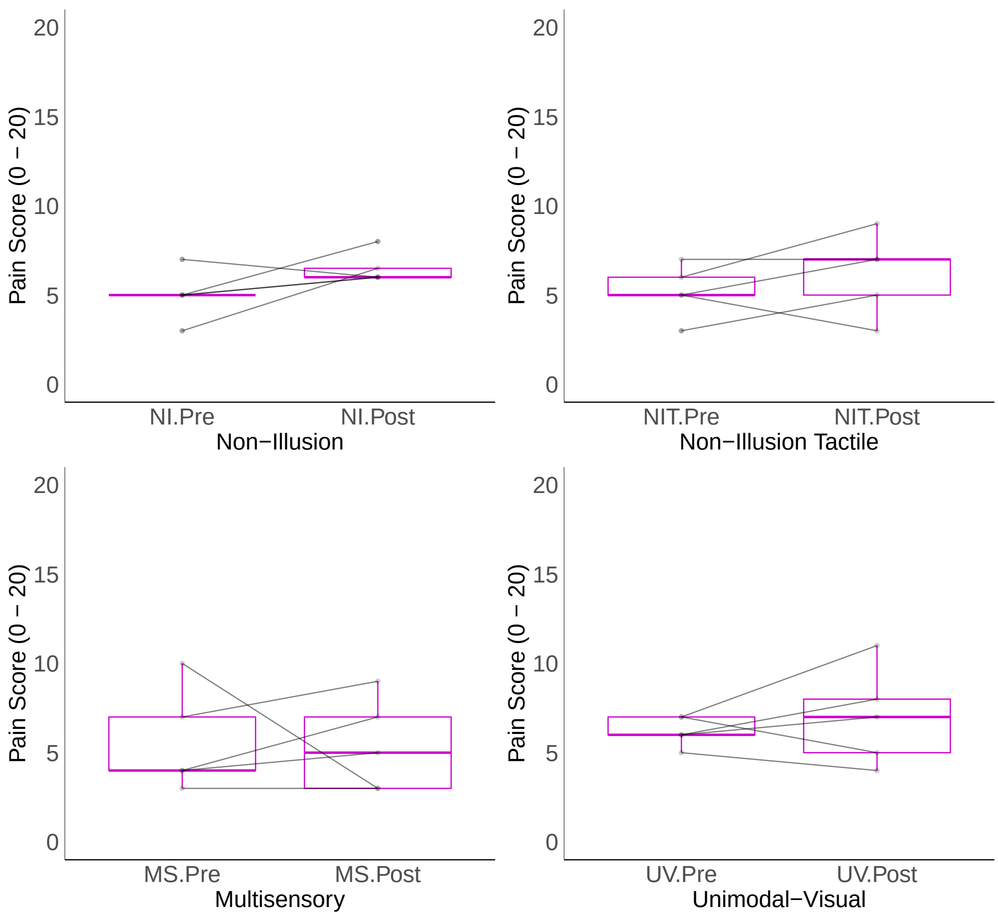

Figure I1.6: Pre and Post Pain Scores Across Conditions for Participants with Chronic Primary Pain. Box plots show medians and inter-quartile ranges of data. Paired data points are shown in grey.

Chronic Secondary Pain

No differences in pain levels were found for chronic secondary pain conditions when comparing NI pre (Median = 4.5, SD = 3.47) and post (Median = 6, SD = 3.7) pain levels ($z = 13.5$, $p.adj = 0.595$, $r = 13.5$), nor when comparing NIT pre (Median = 3.5, SD = 2.57) and post (Median = 2, SD = 3.43) pain levels ($z = 15$, $p.adj = 0.932$, $r = 15$), MS pre (Median = 4.5, SD = 3.06) and post (Median = 3.5, SD = 3.62) levels ($z = 16$, $p.adj = 0.474$, $r = 16$) nor UV pre (Median = 3.5, SD = 2.85) and post (Median = 3, SD = 2.37) levels ($z = 8.5$, $p.adj = 0.386$, $r = 8.5$).

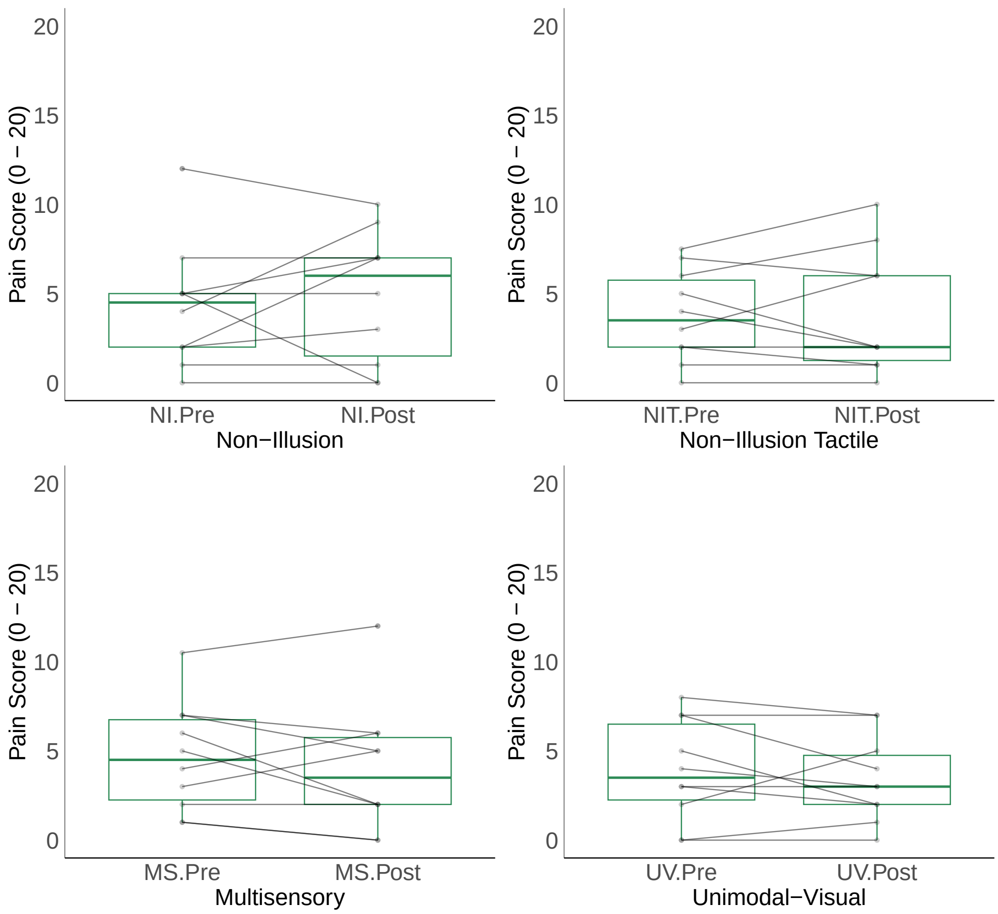

Figure I1.7: Pre and Post Pain Scores Across Conditions for Participants with Chronic Secondary Pain. Box plots show medians and inter-quartile ranges of data. Paired data points are shown in grey.

Chronic Primary and Secondary Pain Percentage Change

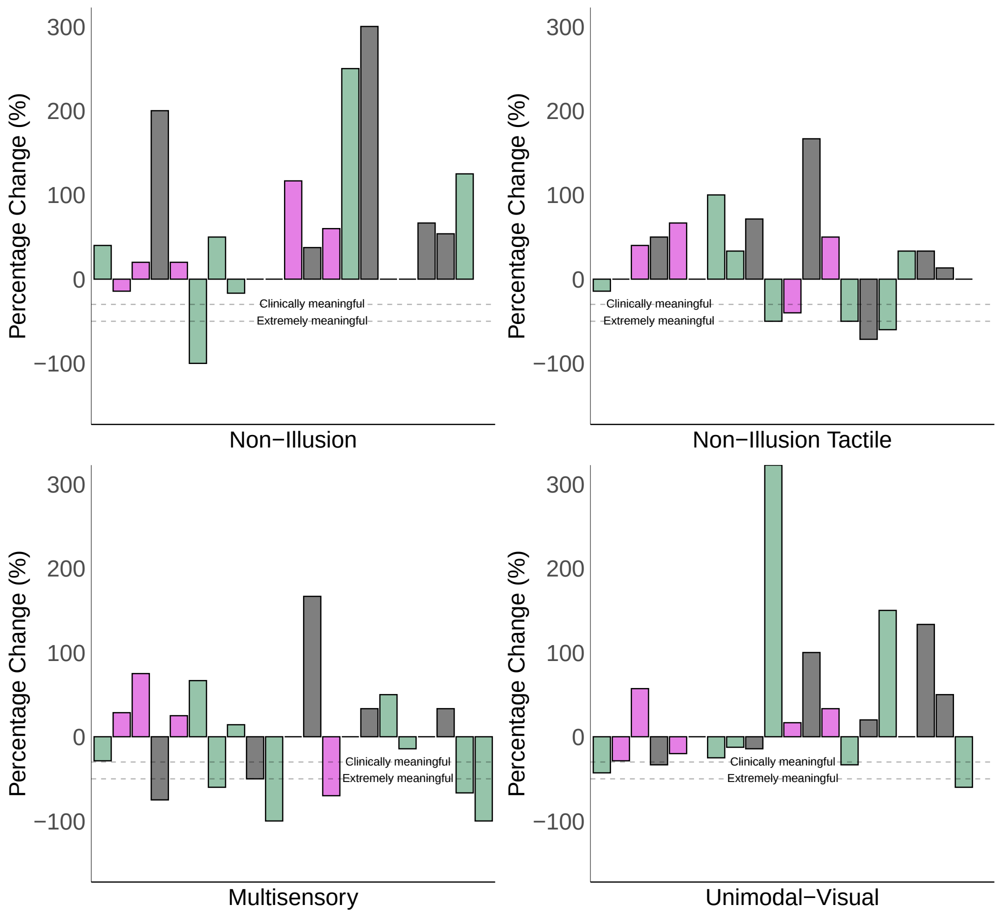

Figure I1.8: Percentage change for pain scores across all conditions per participant. Dashed lines show 30 percent pain reduction (clinically meaningful) and 50 percent pain reduction (extremely meaningful). Bars showing in magenta show participants with chronic primary pain, green for those with chronic secondary pain, and grey for participants with either no diagnosis or a mix of primary and secondary pain conditions.

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