Investigating the effects of multisensory illusions on pain and body perception

Kristy Themelis, BSc., MSc

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Abstract

The amount of pain we feel is not always directly related to the amount of damage our body suffers. In fact, research over the last decade has shown that the experience of pain is strongly linked with how we feel about our body, including its shape and how much we like it. Chronic pain is associated with a distorted mental representation of the body, which can have a significant impact on everyday live. Evidence suggests that multisensory illusions can modulate pain and can lead to changes in body perception. However, the factors that may contribute to previously observed analgesic effects remain unclear. This thesis aimed to systematically asses the effects of these illusions on pain and body representation in both healthy individuals and individuals with chronic pain. First, this thesis aimed to investigate the effects of multisensory illusions on body representation, sense of body ownership, and pain in healthy individuals. Chapter 2 found that multisensory illusions can alter perceived body shape, body satisfaction, without losing ownership. Chapter 3 examined whether distorting the size and shape of the virtual hand could modulate pain in healthy participants. No evidence was found for this, which could indicate that pain is not necessarily affected by virtual body ownership over a distorted hand. Having established that multisensory illusions can alter body perception and the affective experience of the body, the second aim of this thesis was to investigate the effect of multisensory illusions on body representation, body ownership, and pain in individuals with hand osteoarthritis (HOA). Chapter 4 investigated whether people with HOA performed differently on a hand laterality motor task to investigate whether

people with HOA present with a disruption of the working body schema. Though no evidence was found for a general impairment on this task, the findings suggested that performance on the task was mediated by the presence of pain. Chapter 5 investigated effects of multisensory illusions on pain and pain sensitivity in individuals with HOA. The results demonstrated that viewing the body could modulate pain; and affected body representation, body ownership, and agency. Chapter 6 examined the effects of multisensory illusions on subjective and objective aspects of body perception in people with HOA of the hands, compared to healthy controls. Though no evidence was found for an analgesic effect of the illusion, results showed that participants with HOA have a disturbed experience of the size of their hand compared to healthy controls. Furthermore, the results suggest that individuals with HOA may have an abnormally high body dissatisfaction that cannot readily be altered by multisensory illusions. This thesis found mixed support for the analgesic effects of multisensory illusions on pain in HOA and concludes that the specific context in which pain occurs is important. It also highlights the many perceptual and cognitive factors that may contribute to the modulation of pain. The findings imply that future work should focus on interventions that are more portable and accessible for home use, and focus on developing research around the effects of repeated and prolonged exposure to multisensory illusions on pain, body image disturbances and body dissatisfaction.

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Chapter 1 General introduction

In his book, A Leg to Stand On (1984), the late Oliver Sacks described a patient who had suffered from a brain lesion and whose internal body representation no longer included his left leg. As a consequence, his leg no longer felt as his own, perceiving it instead as an alien, foreign object; as 'someone else's leg'. This strange dissociation between oneself and one's body part meant that many patients experiencing similar perceptions were often diagnosed as having a dissociative disorder such as hysteria or schizophrenia (Sacks, 2011). The delusion of dis-ownership described here, termed somatoparaphrenia, provides some valuable insight into the complex relationship that exists between the body and the mind.

The representation of the body in the brain is at the core of understanding the self and others. We need an intact representation of our body to know that our body belongs to us, which can in turn be of great importance for our sense of identity and self-esteem (Longo, 2015a). Our body representation is not merely a registration of peripheral inputs, but relies on a large neural network that is constantly updated based on the multimodal input that it receives (Graziano & Botvinick, 2002). Disturbances in body representation can significantly impact upon the way the body is perceived, as can be seen in some chronic pain conditions.

Chronic pain is generally known as pain that persists beyond normal healing time, if associated with structural damage. Furthermore, chronic pain has no clear end-point and serves no biological purpose (Grichnik & Ferrante, 1991). According to the Gate Control Theory (Melzack & Wall, 1965), pain is a

multidimensional experience influenced by several physiological and top-down cognitive factors, including prior experiences, beliefs, social factors, attention, expectations, and emotion. Indeed, pain is by definition a subjective experience that can only be known to the person who suffers from its effects. Despite the widespread prevalence of chronic pain, treatment options aimed at alleviating pain and improving body representation remain relativity inadequate (Breivik, Collett, Ventafridda, Cohen, & Gallacher, 2006). A key issue here is that pain is generally regarded as a conscious, subjective experience that is influenced by many physiological and psychological factors.

A growing body of evidence suggests that disturbances in body representation might contribute to some chronic pain states (Moseley & Flor, 2012). Interventions targeting cortical representation of the body, including the use of multisensory illusions, show promising results for the modulation of pain (Moseley & Flor, 2012). A greater understanding of how these illusions might operate in order to modulate chronic pain is needed.

This thesis has two main objectives. First, it will use a range of behavioural methods to investigate the effects of multisensory illusions on body representation, sense of body ownership, and pain in healthy individuals. This will help to develop a greater understanding of the relationship between pain and the body, serve as a reference point to assess the nature of distorted body representation, and help elucidate the possible implications of multisensory illusions for chronic pain. The second aim of the thesis is to investigate how distorted body representation might relate to pain and examine the effects of multisensory illusions on body representation, sense of body ownership and pain in individuals with osteoarthritis of the hands (HOA).

This chapter will begin by exploring the concept of body representation and how it influences our perception of the world and our sense of self. First, it will discuss the notion of multiple body representations and how we achieve a coherent representation of the body at a cortical level. Then, it will examine body representation and examine the notion that healthy participants may present with a disruption in body representation. This is followed by a discussion of multisensory integration and how this underlies the feeling of body ownership. Subsequently, the literature on pain will be reviewed before discussing the research on body representation and chronic pain. Furthermore, current strategies aimed at reducing pain and improving body representation will be discussed. The chapter will close with an outline of the research questions and how this thesis attempts to answer them through a succession of empirical research studies.

1.1 Body representation

1.1.1 The concept of body representation

Body representation refers to the way the body is represented in the brain, which relies on the information derived from interacting and moving within the external world and the integration of a range of sensory inputs. Specifically, the way our body is represented relies on a complex neural network and involves the integration of a range of multisensory (visual, auditory, proprioceptive, somatosensory and visceral) as well as motor signals (Dijkerman & De Haan, 2007; Gallagher, 2005; Ionta, Gassert, & Blanke, 2011). An intact body representation is also important for the bodily self, for example, to know that our body belongs to us and does not belong to someone

else or is part of the furniture. Thus, it is crucial for body awareness and distinguishing the self from others (Gallagher, 2000).

The concept of body representation remains a heavily theorised and debated topic (de Vignemont, 2006; Gallagher, 2005). The relationship between body and cognition has been investigated across multiple different disciplines in several ways, drawing influence from psychology, neuropsychology, neurophysiology, neuroscience, developmental psychology, social psychology, philosophy and phenomenology (Assaiante, Barlaam, Cignetti, & Vaugoyeau, 2014; Brownell, Zerwas, & Ramani, 2007; Gallagher, 2005; Vanderhaeghen et al., 2000). This thesis will focus on the key elements of the neuroscientific and psychological understanding of body representation in general, followed by what is known about this topic in relation to chronic pain.

1.1.2 The neural basis of body representation

To achieve a coherent representation of the body at a cortical level, the somatosensory cortex needs to integrate tactile and proprioceptive inputs with visual and vestibular inputs (Dijkerman & De Haan, 2007). A somatotopic representation of the body was first described by Penfield & Boldrey (1937), who introduced the “homunculus” serving as pictorial (albeit distorted) representation of the primary (s1) and secondary (s2) somatosensory cortex. In addition to the somatosensory cortex, there are several other areas thought to be related to the representation of the body, including: the parietal cortex for body-related multisensory integration, the insula for interoception and bodily signals, and the extrastriate and fusiform body areas for the visual processing

of human body parts (Berlucchi & Aglioti, 2010; Dijkerman & De Haan, 2007; Tsakiris, 2010).

It is perhaps not surprising that several components of what we know regarding the neural representation of the body stem from clinical observations, such as the case mentioned in the introduction of this thesis, describing a patient with loss of ownership over a body part. Indeed, changes in body representation can be observed in patients with lesions to the peripheral and central nervous system (Dijkerman & De Haan, 2007). Patients with Phantom Limb pain, for example, display signs of reorganization of cortical representations of the hand with some reporting changes in the size or shape of the Phantom Limb, also referred to as telescoping (Giummarraa et al., 2010). Similarly, a large number of stroke patients suffer from body representation impairments and represent with impaired knowledge on the shape or size of the body or impaired performance on tasks that require an accurate estimate of body posture (Schwoebel & Coslett, 2005). These and other forms of double dissociation have been used to support the notion of the existence of multiple body representations (Berlucchi & Aglioti, 2010; Dijkerman & De Haan, 2007).

On this account, one might assume that healthy individuals generally possess a fairly accurate representation of their body and that misperceptions or distortions only occur in clinical groups. Yet, an emergent area of research is indicating that healthy controls present with a distortion of the representation of the body (Longo, 2016), including distortions in visual perception, proprioception, and tactile perception (Azañón et al., 2016). The Weber Illusion, first described by E.H. Weber in 1834 (Goudge, 1918), is one such

example of a general ‘distortion’ in tactile perception. Specifically, individuals experience two points touched on the skin using a compass, for example, to feel further apart when applied on a sensitive skin surface (e.g. palm-side of the hand) as opposed to a less sensitive skin surface (e.g. forearm), this was originally thought to reflect cortical magnification, a disproportionate cortical representation of sensory surfaces in the somatosensory cortex (Longo, Ghosh, & Yahya, 2015). This was supported by the finding that the illusion was dependent on stimulus orientation, thought to reflect characteristics of the somatosensory homunculus (L. E. Miller, Longo, & Saygin, 2016).

Further studies indicate that healthy participants may present with a disruption of body representation, and demonstrate perceptual distortions in implicit measures of body image (Fuentes, Longo, & Haggard, 2013; Longo, 2015b, 2017). For example, in a series of studies by Longo (2015b), participants rested their hand palm-up on a table, whilst a webcam placed above the table recorded the exact location of the participant’s hand. In the first experiment participants were asked to estimate the location of their knuckles by placing the tip of a baton on their palm. In the second experiment participants were asked to close their eyes and thus, localisation of the knuckles relied on touch and proprioception alone. In the third experiment participants were asked to judge both the position of their hands as well as the experimenters hand. The findings show a distal bias in the estimation of hand position, which occurred independently of whether participants had their eyes open or closed when making the judgement.

Furthermore, Longo (2015b) argued that this finding represented a distortion of the conceptual knowledge of hand anatomy since the distal bias

also occurred when judging the position of the experimenter's hand. Similarly, when participants were asked to judge both the location of the fingertip and knuckle, they represented an overestimation of hand width but an underestimation of finger length (Longo & Haggard, 2010), which could explain the distal bias of the location of the knuckle found in Longo's (2015b) study. Together, these findings from experimental studies in healthy cognition support the idea that distortions of body representation may not only occur in clinical states and that instead, our different body representations may represent a continuum rather than different entities (Longo, 2017). However, less is known about how perceptual distortions induced by multisensory illusions can alter the usual (distorted) experience of our body, so an additional aim of this thesis is to examine this possibility further.

1.1.3 Cognitive aspects of body representation

Research into a range of body disorders has demonstrated that parts of bodily awareness can be lost independent of each other. Therefore, it has been suggested that more than one representation of the body must exist to account for these clinical findings (Kammers, Kootker, Hogendoorn, & Dijkerman, 2010). The notion of multiple body representations was first introduced by Head and Holmes (1911), and later led to the general consensus of the existence of at least two distinct types of body representation; the body image and the body schema (Frederique de Vignemont, 2010; Dijkerman & De Haan, 2007; Gallagher, 2005). There is an on-going debate as to the number of body representations, which may be reflected by the lack of consensus in the literature concerning the several taxonomies of body representations (de

Vignemont, 2010; Lotze & Moseley, 2007), as well as the fact that these terms are applied across a great variety of fields with different meanings.

However, the most common distinction is arguably that between the body image and the body schema (also referred to as somatoperception and somatorepresentation, respectively). The body image is generally accepted as a conscious process and reflects the subjective feeling of the size and shape of our body (Carruthers, 2008; Longo, 2015c; Lotze & Moseley, 2007; Medina & Coslett, 2010), although there is currently limited consensus in the literature about a clear definition. Some authors use the term body image to refer to all the representations of the body that are not associated with an action (de Vignemont, 2010), whilst others use the term to refer to how the body feels or is perceived to be like (Fuentes, Longo, & Haggard, 2013; Lotze & Moseley, 2007).

Gallagher (2005), attempts to provide a clear conceptual distinction between the body image and body schema, referring to body image as a system consisting of "perceptions, attitudes, and beliefs pertaining to one's own body" (p.197). In his interpretation of body image, he makes the distinction between three types of contents: *body percept* ("subject's perceptual experience"), *body concept* ("subject's conceptual understanding") and *body affect* ("subject's emotional attitude toward his/her own body"), thereby grouping together all the representations that are not considered to be part of the body schema. de Vignemont (2007) notes that these components of body image may vary over time and argues for the existence of multiple body images referring to short-term body images and long-term body properties.

Longo (2015) has since elaborated upon this notion by describing the body image to “reflect our conscious, subjective feeling of the size and shape of our body” (p.1117) and presents support for the idea of the conscious body image representing the body as a three-dimensional object. The conscious body image is therefore distinct from more implicit body representation in terms of their spatial scale and reference frame (Longo, 2015a, 2015c; Longo, Ghosh, et al., 2015). Although, somatotopic areas in the somatosensory cortex represent body surfaces as distinct two-dimensional skin surfaces (i.e. different forearm and upper arm representations) which we are not implicitly aware of, it has been found that we may consciously experience our body as a three-dimensional object with volume and surface which is consistent with the visual experience of our body (Longo, Ghosh, et al., 2015; Sur, Merzenich, & Kaas, 1980).

On the other hand, the body schema (Head & Holmes, 1911), or postural schema (Longo & Haggard, 2010), is generally considered to be a dynamic and internal representation of the body (Tsay, Allen, Proske, & Giummarraa, 2015), derived primarily from sensory and motor inputs necessary for posture and action (Longo, Schüür, Kammers, Tsakiris, & Haggard, 2009; Newport, Pearce, & Preston, 2010; Schwoebel & Coslett, 2005). In addition, Gallagher (2005) refers to the body schema as “a system of sensory-motor capacities that function without awareness or the necessity of perceptual monitoring” (p37-8).

This notion was elaborated upon by de Vignemont (2006), who draws a distinction between a first-order body schema (pertaining perceptual features of the body important for movement) and a second order-body schema

(representing a functional map of the body), thus emphasizing the existence of multiple body schemas. Indeed, a topological map of the body is by several authors considered to be separate from the body schema and has been termed the 'body structural description' (Medina & Coslett, 2010; Schwoebel & Coslett, 2005; Sirigu, Grafman, Bressler, & Sunderland, 1991).

Despite varying interpretations, de Vignemont (2006) acknowledges that using a dual distinction when referring to the representation of the body serves as a good starting point for the experimental exploration of the relationship between the body and the brain. Furthermore, whether a dual distinction is made or not, there is empirical support for a dynamic interaction between the conscious body image and the body schema on a behavioural level (Gallagher, 2005; Schwoebel & Coslett, 2005). Indeed, following complete anaesthesia of a body part, such as the thumb, individuals demonstrate perceptual distortions in body image by significantly overestimating the perceived size of that body part (Gandevia & Phegan, 1999). Conversely, top-down visual information, such as the visual distortion of a limb, can modulate pain and swelling in healthy participants (Moseley, Parsons, & Spence, 2008) or alter postural or motor performance (Gallagher, 2005).

For clarity, this thesis will refer to two types of body representation and whilst aware of other descriptions, will use definitions commonly used in pain research whilst acknowledging the issues that may arise from adopting a conceptual distinction. Here, 'body image' will be used to refer to the conscious perception of our body in terms of size, shape and distinctive features (Longo, Schüür, et al., 2009) as well as beliefs, attitudes and conceptual understanding

of our body (Newport et al., 2010; Tsay et al., 2015). The term 'body schema' will be used to refer to the unconscious dynamic, internal representation of the body derived from bottom-up multisensory inputs (e.g. visual, tactile, vestibular) which are necessary for action and posture (Newport et al., 2010; Schwoebel & Coslett, 2005).

1.2 Multisensory integration and the feeling of body ownership

Multisensory integration is critical for the representation of our body in the external world. Furthermore, it has been argued that the integration of multisensory information underlies our sense of body ownership (Botvinick & Cohen, 1998; Ehrsson, 2011; Ehrsson, Spence, & Passingham, 2004). Body ownership has been referred to as the perceptual status of our body and the feeling that our body belongs to us (Gallagher, 2000; Tsakiris, 2010; Walsh, Moseley, Taylor, & Gandevia, 2011). We typically perceive the body to be a unified, coherent entity resulting from the brain's access to a set of sensory information (Kilteni, Maselli, Kording, & Slater, 2015). In other words, we know that our body belongs to us because we use proprioception (the sense of where our body is in space), exteroception (sensations originating from outside of the body) and interoception (sense of the physiological status of our body) (Tsay et al., 2015) which is not available for the perception of external objects or bodies that are not our own (Kilteni et al., 2015).

Whilst psychophysiological methods such as Transcranial Magnetic Stimulation (TMS) are used to investigate the neural basis of one's own body through the study of unimodal modalities such as vision, touch and proprioception (Azañón & Haggard, 2009), it has proven difficult to investigate

topics such as body ownership using these methods. The use of body ownership paradigms such as the rubber hand Illusion (RHI) have made it possible to investigate the neural and behavioural aspects of the sense of body ownership (Ehrsson, Wiech, Weiskopf, Dolan, & Passingham, 2007; See Makin et al., 2008 for a review). In this well-known illusion, participants view a rubber hand being touched with a brush simultaneously and in the same location as their hidden hand is being touched (see Figure 1.1). In most cases, this results in a feeling of ownership over the rubber hand, with people reporting that the rubber hand has become part of their body (Botvinick & Cohen, 1998).

According to the authors (Botvinick & Cohen, 1998), the embodiment of the artificial limb is the result of the integration of synchronous visual, tactile and proprioceptive input. However, studies have demonstrated the influence of top-down cognitive processes on the strength of the illusion, showing that factors like posture and shape of the rubber hand can directly influence illusion strength (Costantini & Haggard, 2007; Tsakiris & Haggard, 2005). Tsakiris & Haggard (2005) demonstrated that ownership over the artificial hand only occurs when the object is a realistic-looking rubber limb, not when it is a neutral object such as a wooden stick. In contrast, asynchronous correlations between vision and touch have been shown to lessen or even diminish the RHI (Botvinick & Cohen, 1998; Kalckert & Ehrsson, 2014; Kokkinara & Slater, 2014; Longo, Schüür, Kammers, Tsakiris, & Haggard, 2008). This suggests that the RHI relies on bottom-up-processes of synchronous visuotactile stimuli, which can be modulated by prior (top-down) knowledge about our own body (Tsakiris & Haggard, 2005).

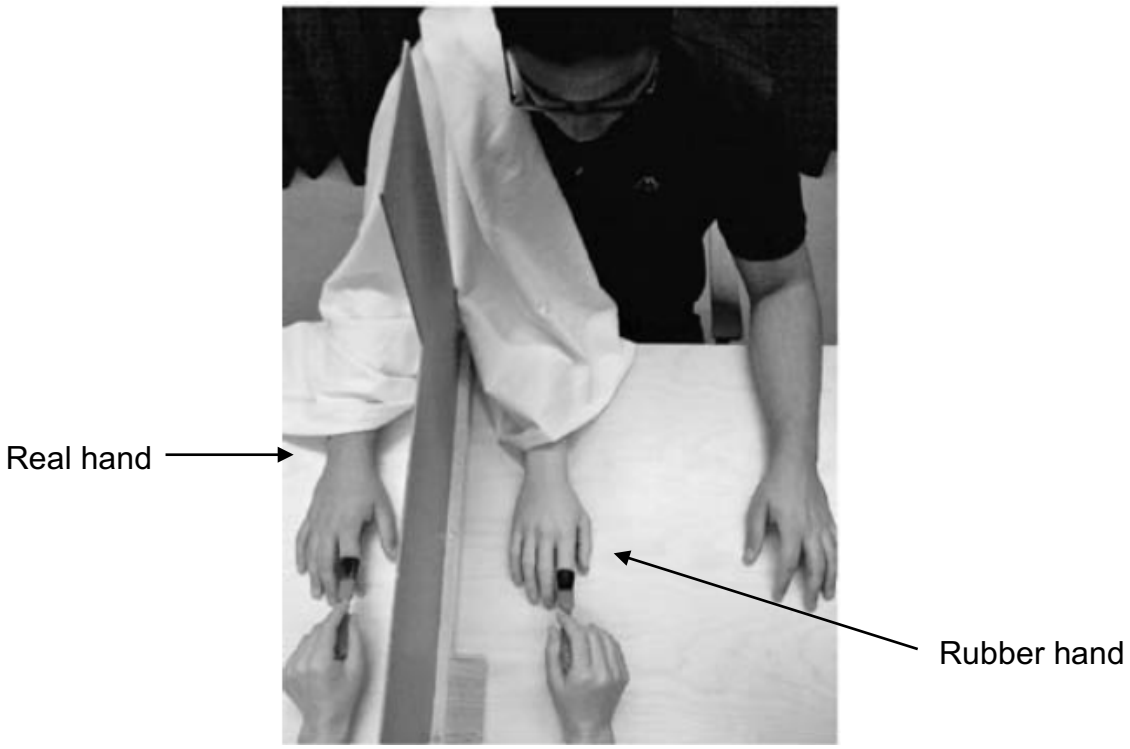


Figure 1.1 Example of the classical set-up used in the rubber hand illusion. Participants view a rubber hand being touched, at exactly the same time and in the same location as their unseen hand is being touched often leading to a feeling of ownership over the fake hand when the seen and felt touches are synchronous. Illustration of a study by Ehrsson (2011).

1.3 Body representation and chronic pain

1.3.1 Pain

In 1872, soon after the American Civil War, renowned physician S.W. Mitchell reported several cases of wounded soldiers who immediately after waking up from surgery felt the presence of their recently amputated limbs (Mitchell, 1872). Not only were these subjects perpetually aware of the existence of the limb, but they often tried to use their limb as they normally would: attempting to get up and walk with a lost leg, touching a limb that was no longer there, or even trying to pick objects up with the lost limb. Patients would be reminded by the existence of a 'phantom' limb and report pain or other sensations in a body part that was no longer there. These reports illustrate the complexity of

the different factors that might contribute to people's pain experience and the complex interactions between them.

Aside from people who are congenitally unable to experience pain (Thrush, 1973), most of us will have experienced pain in one form or another. The International Association for the Study of Pain (IASP) currently defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (Merskey & Bogduk, 1994). Though not stated explicitly, the IASP committee of taxonomy notes that pain is always subjective (Merskey & Bogduk, 1994). The current thesis is concerned with understanding the many factors that can modulate the subjective experience of pain. Thus, pain in this specific context refers to a subjective experience that can be influenced by many variables and is not defined by an association with tissue damage. As such, the interpretation of pain in this thesis is broadly in line with that of Katz & Melzack (1999) who note, *"*Pain is a personal, subjective experience influenced by cultural learning, the meaning of the situation, attention, and other psychological variables*"* (p.231).

Under normal circumstances, pain serves an evolutionary purpose as a warning signal often occurring in response to threat or damage to the body (Vrancken, 1989). For example, pain urges us to stop walking on a broken leg, attend to the area that has been stung by an insect, or remove our hand from a hot stove to prevent it from getting severely burned, thereby promoting the healing process. In these cases, pain is often acute, with a known origin, and often transient in nature (Loeser & Melzack, 1999). In contrast, chronic pain

has no clear end-point and does not serve a useful purpose for survival (Grichnik & Ferrante, 1991).

Whilst acute and chronic pain are often distinguished by their artificial timeline (i.e. pain is considered as chronic after 3 to 6 months), it has been argued that they are both part of a shared continuum, with chronic pain being recognized as pain that persists beyond the normal or expected healing time (Bonica 1953; as cited in Merskey & Bogduk, 1994; Conn, 2005). However, what is commonly referred to as 'expected healing time' is often ambiguous and others have therefore proposed that the conceptualisation of acute and chronic pain should be based on both the dimensions of time and physical pathology (Fishman, Ballantyne, & Rathmell, 2010). As such, the interpretation of chronic pain offered in the current thesis is broadly in line with that of Loeser & Melzack (1999), who note, "It is not the duration of pain that distinguishes acute from chronic pain but, more importantly, the inability of the body to restore its physiological functions to normal homoeostatic levels'' (p.1609).

Chronic pain is a major social and economic burden that affects many people worldwide. It can have a serious impact on people's quality of life and significantly affect daily activities (Breivik et al., 2006). It is estimated that around 7.8 million people in the UK alone suffer from moderate-to-severe chronic pain that has lasted for over six months, with the prevalence of chronic pain increasing with age (Bridges, 2011). The estimated societal costs of just one chronic pain condition alone, back pain, are placed at around £12.3 billion a year (Bridges, 2011). Unlike acute pains that are often evoked by noxious stimuli and generally well understood, in chronic pain there is often no clear link between injury and pathology and the amount of pain people experience.

As a result, chronic pain syndromes are often poorly understood (Melzack, 2005). For example, knee pain is a poor predictor of radiographic knee osteoarthritis, and similarly the amount of radiographic damage provides little information on the amount of pain or symptoms an individual may experience (Bedson & Croft, 2008).

With millions of people suffering from chronic pain worldwide, it is perhaps unsurprising that it has prompted considerable attention from researchers. Yet for many people, there remains little relief from the pain and suffering experienced as a consequence of the condition. Whereas pain was initially considered as being merely an injury-produced sensation or symptom perceived in the brain, in recent years it has become increasingly acknowledged as a disease in its own right (European Federation of IASP Chapters, 2001). As noted by Melzack (2008), “Pain experience must not be confused with physical injury”. That is, the brain can generate perceptual qualities of pain with or without sensory inputs and sometimes even spontaneously (Melzack & Wall, 1996).

Additionally, whilst still often used interchangeably in the literature, pain must not be confused with nociception. Nociception has been defined by the International Association for the Study of Pain (IASP) as, “the neural process of encoding and processing noxious stimuli”, with noxious stimuli defined as “a stimulus that is damaging or threatens damage to normal tissues” (International Association for the Study of Pain, 2012). These noxious stimuli are detected and transduced by the peripheral terminal of nociceptors, where action potentials along the axon to the central nervous system are generated and can eventually lead to the conscious awareness of pain (see Woolf & Ma

(2007) and Smith & Lewin (2009) for extensive reviews). Crucially, pain is always subjective, multidimensional and includes a strong emotional component. Additionally, pain can occur without nociception and similarly, nociception can occur without pain sensation (Loeser & Melzack, 1999).

1.4 Osteoarthritis

Osteoarthritis (OA) is a joint disorder often accompanied by functional limitations and reduced quality of life (NICE, 2014). Affecting around 8.75 million people in the UK alone, it is one of the leading causes of pain and disability worldwide, typically affecting more women than men (Arthritis Research UK, 2013). The total costs in Westernized countries related to osteoarthritis alone are estimated to be between 1% and 2.5% of the gross domestic product (Hiligsmann et al., 2013). The criteria developed by the American College of Rheumatology are often used to guide diagnosis and include factors such as patient history, physical examination, and radiographic findings (Altman et al., 1990).

The causes of OA remain unclear although several risk factors have been identified, including obesity, age, bone density, and genetics (Jordan et al., 2000). Due to the general complexity of OA, what may subsequently cause pain is currently unknown (Hunter et al., 2009). Nevertheless, several explanations for pain or contributors to pain have been suggested, including biological differences, psychological and social factors (Jordan et al., 2000; McDougall & Keefe, 2009; Somers, Keefe, Godiwala, & Hoyler, 2009).

There is substantial discordance between radiographic OA severity and the amount of pain people experience (Bedson & Croft, 2008; Hannan, Felson, & Pincus, 2000). That is, pain can occur with minimal symptoms or visible changes on an X-ray, and conversely people with structural changes to the joints may experience a minimal number of symptoms (Haugen, Slatkowsky-Christensen, Bøyesen, van der Heijde, & Kvien, 2013; Wajed et al., 2012), suggesting that there are additional underlying mechanisms responsible for the pain people experience (Wajed et al., 2012).

For this reason it has been proposed that pain in OA is associated with changes in both peripheral and central processes (Wajed et al., 2012); pressure pain thresholds are reduced in OA compared to controls, irrespective of whether tested at affected, distal or remote sites (Suokas et al., 2012). However, the vast majority of treatments target the periphery and there is a need for treatments that address central pain mechanisms.

Body perception disturbances have recently been described in osteoarthritis, with changes in perceived size of the painful body part (Gilpin, Moseley, Stanton, & Newport, 2014). Interventions that target body representation have been shown to have beneficial effects for several chronic pain conditions (Boesch, Bellan, Moseley, & Stanton, 2015; Moseley & Flor, 2012; Wittkopf & Johnson, 2016), including OA (Preston & Newport, 2011). Recent findings from this group showed that illusory stretching or shrinking of the hand using a mediated reality device, can modulate pain and perceived hand size in people with HOA (Preston & Newport, 2011). The research presented in this thesis intends to assess whether such treatments might also affect alterations and reorganization in the nociceptive system by delivering

static quantitative sensory testing (QST) of pressure pain thresholds before and after multisensory illusions previously demonstrated to modulate hand pain in hand OA. Additionally, it aimed to investigate their effects of multisensory illusions on hand function, based on researcher observations in previous studies indicating improved hand mobility and range of motion after illusory stretching of the affected hand (Preston & Newport, 2011).

This thesis will focus on the way in which higher-order cognitive factors such attention, appraisal and multisensory integration can modulate pain in a top-down fashion. In particular, it will examine how multisensory illusions using vision, proprioception and touch (see Section 1.6) can alter the sense of one's body and the experience of pain in both healthy controls and people with HOA.

1.4.1 Theories of pain

Theories about pain perception have developed our understanding and shaped the way we now interpret pain. As described in Moayedi and Davis's (2012) comprehensive review on the history of pain, there are four main theoretical frameworks.

The Specificity Theory, which was heavily influenced by Descartes, Von Frey, and Charles Bell, supports the existence of pain receptors that project to specific areas in the brain via the so-called 'pain pathway', a sensory pathway between specific pain receptors in the skin to a pain centre in the brain (Melzack, 2005; Melzack & Wall, 1965). However, as the theory supports the existence of a separate sensory system for pain, such as for touch and hearing, and does not account for the psychological contributions to pain, it

has subsequently failed to inform treatments for people suffering from chronic pain (Melzack & Katz, 2006).

Nevertheless, the Specificity Theory has led to the development of several new theories of pain, including the Intensity Theory, a theory first postulated by Plato (as cited in Moayedi & Davis, 2012) suggesting a direct link between the intensity of pain and the amount of tissue injury, and the similar Pattern Theory (Nafe, 1929). Though these theories support the notion of the existence of sensory receptors specific to nociceptive stimuli, the Specificity Theory and The Pattern Theory did not account for the complexity of pain and, in particular, its persistence. Various clinical observations have since disproved the theories and the specificity of “pain pathways”, appreciating the role of central mechanisms for the experience of pain (Besson, 1999; Wall, 1991).

Arguably the most influential theoretical framework of pain was presented by Melzack & Wall (1965). The Gate Control Theory of Pain does not support the existence of a single ‘pain pathway’ and instead suggests that pain is modulated by a range of ‘bottom up’ nerve impulses in the spinal cord in addition to being influenced as by ‘top-down’ descending information from the brain. Unlike Specificity and Pattern Theory, the emphasis placed by the Gate Control Theory of Pain on the modulation of inputs at the level of the brain and the spinal cord offers an explanation for the observed variability of pain and the discrepancy between peripheral pathology and pain. Indeed, it was one of the first theories to consider the role of psychological factors as an intrinsic part of pain processing and all the other cognitive factors that could

influence pain, such as the meaning of a situation and prior experiences (Melzack & Wall, 1996)

However, some aspects of the Gate Control Theory of Pain have been shown to be incorrect considering new advances. For example, interactions within the dorsal horn serving inhibition and facilitation have shown to be much more complex (Cervero & Jensen, 2006; Sufka & Price, 2002). Furthermore, the debate between the Specificity Theory and the Pattern Theory has re-surfaced, with scientists again reassessing the value of the latter (Moayedi & Davis, 2012). Nevertheless, the core theoretical components of the theory still stand. The focus on modulatory factors that may influence pain still occupy a role in pain research and management up to this day. The following section now examines the concept of pain as a multidimensional experience and why this is relevant for the research questions in the current thesis.

1.4.2 Pain as a multidimensional experience

Following Melzack and Wall's (1965) seminal work on the Gate Control Theory of Pain and its emphasis on central processing, it has become increasingly clear as to why there is not always a clear link between the level or extent of pain experienced and the extent of structural damage. The causes of many chronic pain conditions still remain poorly understood, and various cognitive, physical, affective and behavioural factors can influence pain and are likely to contribute to the pain duration and intensity (Bushnell, Čeko, & Low, 2013; Loeser & Melzack, 1999). In recent decades, our understanding of pain has shifted from the Cartesian view of pain as merely a sensation produced by injury to pain as a subjective and complex experience. Pain as a

multidimensional experience is not a novel concept in itself, but it is a relatively recent development that theories supporting a multidimensional framework of pain have been applied to both research and clinical practice (McGuire, 1992).

According to Melzack and Casey (1968), the pain experience consists of and varies on three different dimensions: sensory-discriminative (magnitude and intensity), affective-motivational (affect, arousal and defence behaviour) and evaluative-cognitive (evaluation of seriousness of the situation). The conceptualisation of pain in this way is not only important in terms of taking into consideration the multidimensional influences on pain perception, but it also allows for a more detailed assessment and diagnosis of pain and perhaps most importantly, a better understanding of the person in pain (McGrath, 1994; McGuire, 1992). Although presented as three separate dimensions, they cannot be seen as totally independent but instead interact, with the person experiencing pain in an integrated way (McGuire, 1992; Moayedi & Davis, 2012). In addition, the link between some of the dimensions has been explained by overlap in brain networks likely to be involved in pain experience (Price, 2000), although as discussed below, this remains a controversial topic.

At the core of understanding pain as a multidimensional experience is the notion of a ‘Neuromatrix”, as proposed by Ronald Melzack (1990). The Neuromatrix, notably not specific for pain, is thought to represent a genetically determined neural network (or neurosignature) produced by genetic and sensory influences that can be modulated by both nociceptive and non-nociceptive input. For example, the neurosignature can be modulated or triggered by sensory information such as cutaneous or visceral inputs, as well as cognitive and emotional events (Melzack, 2005). Evidence in support of this

theory comes from clinical observations in conditions such as Phantom Limb pain, in which the pain cannot be explained by the influence of peripheral mechanisms alone. In some cases, pain, can be experienced years after amputation and can persist even after removal of parts of the somatosensory cortex or spinal cord (Melzack, 1990).

Other factors that are thought to modulate the Neuromatrix are visual and sensory inputs influencing top-down processing, intrinsic neural inhibitory modulation and the body's stress modulatory system (Melzack, 1999; Melzack & Katz, 2006). Furthermore, pain is conceived as an output of the central nervous system that perceives tissues to be under threat. Subsequently, pain depends on the perceived severity of this threat (Moseley, 2007). Indeed, when the perceived threat is conceived to be greater or when pain is highly salient, pain is perceived to be more unpleasant (Price, Harkins, & Baker, 1987). This is an example of the importance of the physiological context in which pain occurs and the many factors that can modulate the experience of pain.

Melzack (2005) argued that a large proportion of the brain is involved in the pain experience and that there is no such thing as a specific "pain centre" in the brain. Indeed, the existence of a "pain matrix" and the neural mechanisms underlying pain has been a subject of sustained debate in recent years. The rapid development of brain scanning measurements, such as functional magnetic resonance imaging (fMRI), has resulted in a new stream of research focusing on the 'location' of nociception in the brain. The aim of such research is to understand the neural mechanisms that are thought to be involved or underlie the experience of pain (Makin, 2016). Advocates of this

perspective argue that it could help to characterise, locate and ultimately alleviate pain and improve well-being (Leknes & Tracey, 2008; Wager et al., 2013), whereas critics argue that the notion of a specific pain centre poses a dangerous risk (Davis, Bushnell, Iannetti, St Lawrence, & Coghill, 2015). For instance, several US-based medical companies are already offering brain scans to serve as evidence for the existence of chronic pain in the case of an accident, with at least one workers' compensation case where this has been used as evidence in court (Miller, 2009).

Recent findings indicate that areas associated with the 'pain matrix' are not specific for pain and that the same areas could be activated by salient stimuli such as loud sounds or bright lights (Iannetti, Salomons, Moayedi, Mouraux, & Davis, 2013). Furthermore, studies have demonstrated that the very same pain matrix has been activated by painful stimuli in people that are congenitally unable to experience pain (Salomons, Iannetti, Liang, & Wood, 2016). Together these findings indicate that the use of brain imaging techniques as an objective measure of pain might not be straightforward.

In summary, pain is a subjective experience that can be influenced by numerous factors. Though pain has been initially explained in terms of its relationship to injury, it has become apparent that it can occur in the absence of peripheral damage and is conceptually distinct from nociception. Indeed, chronic pain is often unrelated to tissue damage and despite its prevalence, treatment options are limited. As discussed previously, there is increasing evidence demonstrating that disturbances in body representation are apparent in chronic pain and might contribute to some chronic pain states (Moseley & Flor, 2012). The following sections will focus specifically on key elements of

the relationship between pain and the body, before linking body representations to chronic pain.

1.4.3 Altered body representation in chronic pain

Sensitization or inhibition of the neural system has been suggested to play a role in several chronic pain conditions including fibromyalgia, headaches, complex regional pain syndrome and osteoarthritis (Staud, 2002; Woolf, 2011). Clinically, this may manifest itself as a reduction in pain thresholds and reduced nociceptive thresholds so that normally non-painful stimuli are now experienced by individuals as painful, also referred to as allodynia. Furthermore, individuals may experience hyperalgesia: an increased response to stimuli that provoke pain. Sometimes, the expectation of pain is sufficient to elicit changes. For example, viewing a painful body part being touched may increase pain or swelling without actual contact of the painful limb (Moseley & Flor, 2012). Cortical changes associated with chronic pain can have cascading effects on psychological and cognitive functioning (Wand et al., 2011). For example, Apkarian et al., (2004) demonstrated a relationship between chronic pain and poor performance on an emotional decision-making task, whereby pain intensity correlated negatively with performance on the task.

Additionally, sensitisation and disinhibition can lead to systemic changes in the cortical functioning of areas that represent the body; a process known as cortical reorganization (Moseley & Flor, 2012). For example, patients with chronic low back pain exhibit a shift of the S1 representation of the lower back towards the area of leg (Wand et al., 2011). Furthermore, amputees with

Phantom Limb pain present with changes in the somatosensory and motor cortices, with some exhibiting a shift of the S1 representation of the mouth towards the hand in the somatosensory cortex. However, this reorganization was not observed in amputees not experiencing pain (Flor, Nikolajsen, & Jensen, 2006).

The extent of these changes has been found to relate to pain levels and tactile acuity, measured by two-point discrimination. Furthermore, the extent of reorganization increases the longer that pain persists (Flor et al., 2006; Maihofner, Handwerker, Neundorfer, & Birklein, 2003; Moseley & Flor, 2012). In contrast, it has been argued that the causal relationship between cortical reorganization and pain might not be as clear, with other factors contributing to the observed cortical reorganization (Makin, Scholz, Henderson Slater, Johansen-Berg, & Tracey, 2015). In addition, experimental studies have shown that some of these brain changes can occur rapidly, further supporting the idea that the reorganization might also give rise to chronic pain (Moseley & Flor, 2012). Nonetheless, these processes highlight the variable link between lingering damage and on-going pain, and the many ways that the central nervous system can modulate, worsen or distort pain (Woolf, 2011).

Reorganization of the primary cortex is known to occur in several chronic pain conditions (Flor et al., 2006; Maihofner et al., 2003; Moseley & Flor, 2012), and has been associated with disturbances in body representations as well as altered body perceptions (Haggard, Iannetti, & Longo, 2013). Clinically, altered body perceptions are seen in various forms and people suffering from chronic pain may misperceive the size and shape of their affected body part. For example, individuals with complex regional pain

syndrome (CRPS) often report abnormal attitudes towards their affected limb, with patients reporting the affected limb as feeling foreign, strange or distorted in shape and size (Lewis, Kersten, McCabe, McPherson, & Blake, 2007). Furthermore, some people with chronic back pain report their back to be "missing" (Moseley, 2008). For some individuals this can lead to hostile feelings towards the affected limb, including the desperate desire to amputate that part of the body (Lewis et al., 2007).

As mentioned in Section 1.2, TMS and neuroimaging methods are useful for investigating unimodal modalities in relation to the body. However, complex topics such as body ownership, body schema and body image cannot be elucidated using these methods (Bray & Moseley, 2011; Moseley & Flor, 2012). Behavioural tasks are often used instead and have led to an increased understanding of the relationship between body representation and pain. As will be discussed in Chapter 4, one commonly used task is the hand laterality task, which is a motor task used to examine working schema. In this task, participants view images of a hand often presented at different angles and in a variety of postures. Reaction times on the task reflect the degree of mental rotation: that is, if a hand is displayed at 180 degrees from upright, it takes longer to recognize the laterality compared to when a hand is displayed at 0 degrees (Parsons, 1987b). Making laterality judgments is thought to rely on several processes, including an intact body schema, CNS processing speed and information processing (Moseley & Flor, 2012).

Motor imagery in chronic pain has been investigated by several studies of individuals with chronic pain. In Schwoebel et al.'s (2001) study, individuals with complex regional pain syndrome (CRPS) viewed photographs of a hand

in a variety of postures on a monitor. Participants were then asked to decide whether the picture they were viewing was of a right or left hand by pressing buttons, whilst reaction times and accuracy were measured. Compared to controls, the results showed that patients with CRPS took longer to recognize hands that were of the same laterality as their affected side. Similar findings were found in Moseley's (2004) study using the same task in patients with unilateral CRPS, showing an effect of reaction times but not accuracy.

In contrast, Stanton et al., (2012) demonstrated that individuals with osteoarthritis were less accurate but not slower in making left/right judgements compared to healthy controls. In these tasks, participants make judgements of images depicting other people's hands. Consequently, performance on this task may reflect difficulties in processing information related to someone else's body, especially when there are obvious differences in the physical appearance of that limb compared to someone's own (painful) limb, as is often the case in people suffering from painful hand osteoarthritis (Hodkinson, Maheu, Michon, Carrat, & Berenbaum, 2012). In support of this, Ferri, Frassinetti, Ardizzi, Costantini, & Gallese (2012) demonstrated that participants respond quicker to images depicting one's own hand, as opposed to someone else's hand. Yet, very few studies have investigated whether this 'self-advantage' is apparent in individuals suffering from chronic pain, or whether previous findings in chronic pain reflect a bias in information processing of healthy hands compared to painful hands (Moseley, Gallace, & Spence, 2011).

As noted by Moseley & Flor (2012a), cortical reorganization is not limited to disruptions in higher-order sensory and motor representations.

Indeed, perceptual and autonomic disturbances are common in a range of chronic pain syndromes including CRPS, fibromyalgia and chronic low back pain (Moseley & Flor, 2012). For instance, patients with chronic low back pain exhibit poorer two-point discrimination, which is related to differences in perceived body image (Moseley, 2008; Nishigami et al., 2014). Furthermore, patients with CPRS demonstrate a bias in tactile processing of the unaffected side of the body away from the affected limb, which can be reversed when the arms are crossed (Moseley, Gallace, & Spence, 2009). Together, these findings appear to demonstrate that chronic pain is associated with changes in the brain.

However, as pointed out by Moseley & Flor (2012a), some of these functional shifts may to some extent be reversible. In support of this, Pleger et al., (2005) demonstrated a reverse of cortical reorganization in the primary and secondary somatosensory cortex in people with CRPS undergoing sensorimotor training, finding that this was correlated with a reduction in pain. Moseley & Wiech (2009) demonstrated similar findings when CRPS patients underwent tactile discrimination training over a consecutive period of 10 days. However, the sustained improvement in pain and functional ability was dependent on the stimuli during training. That is, the residual effect was only apparent when participants viewed a reflected mirror image of their hand during training, not when viewing the affected limb. Thus, stimulation alone had no effect, which according to Moseley & Flor (2012a) could be explained by the salience of certain stimuli. The following sections will focus on a range of strategies that are aimed at reducing pain and target body representation, before going on to outline the methods used in the current thesis.

1.4.4 The body as pain relief

As noted by Haggard et al., (2013), pain itself is about the body. That is, pain is perceived in reference to the body and disembodied pain does not exist. It is perhaps not surprising therefore, that we can use our own body as means for pain relief (Martini, 2016). Indeed, in experimental settings vision of the body is found to reduce acute pain (Longo, Betti, Aglioti, & Haggard, 2009; Longo, Iannetti, Mancini, Driver, & Haggard, 2012; Sadibolova & Longo, 2014). This effect, known as visual analgesia, is often specific to the participants' own body and does not seem to occur, or at least does so to a lesser degree, when viewing a neutral object or the experimenters hand (Haggard, Iannetti, & Longo, 2013)

Through their seminal work on mirror box therapy for the relief of Phantom Limb pain, Ramachandran, Rogers-Ramachandran, & Cobb (1995) were amongst the first to experimentally investigate the complex interaction between pain and sensory modalities, in this case particularly, vision. The original mirror box consisted of a wooden or cardboard box whose top and front surfaces were removed with a mirror placed in the centre. Patients suffering from Phantom Limb pain, much like the patients described by Mitchell (1872), were asked to place their non-affected limb on one side of the mirror and the phantom limb on the other, whilst looking at the mirror image of the intact limb so that the amputated limb appeared to be 'normal'. The participant was then asked to generate symmetrical movements such a making a fist, with or without vision. Most patients reported being able to move their phantom limb, several patients were relieved from painful spasms, and in one patient it even led to a total disappearance of the phantom. Ramachandran and

colleagues hypothesised that significant plasticity of the brain allowed reorganisation of topography in the primary somatosensory cortex (Ramachandran & Altschuler, 2009; Ramachandran & Rogers-Ramachandran, 1996), suggesting that visual information of our body can influence the way in which the body is perceived.

Although Ramachandran's theory has since been challenged (Michielsen et al., 2011), mirrors have been extensively used in the treatment of numerous conditions including complex regional pain syndrome (McCabe et al., 2003), Phantom Limb pain (Brodie, Whyte, & Niven, 2007) and in patients with subacute strokes (Yavuzer et al., 2008). However, conflicting data exist regarding the benefit of mirrors for pain relief (Boesch et al., 2015; Bultitude & Rafal, 2010; Chan et al., 2007; For reviews see: Moseley, Gallace, & Spence, 2008; Ramachandran & Altschuler, 2009). Nevertheless, it has paved the way for a whole new avenue of research including mirror boxes (Brodie et al., 2007), mirror therapy (Cacchio, De Blasis, Necozione, di Orio, & Santilli, 2009; Cacchio, De Blasis, De Blasis, Santilli, & Spacca, 2009; Chan et al., 2007), minifying and magnifying binoculars (Moseley, Parsons, et al., 2008). These methods have all been used to investigate the relationship between pain and the representation of the body and as a possible treatment targeting functional brain changes (Boesch et al., 2015).

1.4.5 Body ownership illusions & chronic pain

As discussed in Section 1.2, the feeling of body ownership is thought to rely on the interaction between multisensory input and top-down cognitive factors. In light of this, compelling body-ownership illusions tend to involve the

integration of different sensory modalities such as vision, touch and proprioception, or vision and proprioception (Botvinick & Cohen, 1998; Daenen, Roussel, Cras, & Nijs, 2010; McCabe, Cohen, & Blake, 2007). However, methods such as the rubber hand illusion show temporal, spatial and anatomical constraints (Ehrsson, 2011). Indeed, the experience of the feeling that the rubber hand belongs to oneself is significantly lower when a temporal delay between vision and touch is introduced (Botvinick & Cohen, 1998). Additionally, the illusion depends on the posture of the rubber hand and the distance between the spatial location of the real hand and the rubber hand, with the strength of the illusions decreasing when there is a postural miss-match or when the distance between the rubber hand and the real hand is greater (Ehrsson, 2011).

To illustrate, Lloyd (2007) demonstrated that the strength of the illusion significantly decreased when the distance between the participant's hand and the rubber hand was greater than 27.5 cm. Furthermore, Shimada, Fukuda, & Hiraki (2009) found that a temporal delay between visual and tactile stimulation of more than 500 ms significantly reduces the strength of the rubber hand illusion. Introducing six delay conditions ranging from 0-500 ms, the authors demonstrate that the RHI was most effective when the visual feedback delay was less than 300ms. The importance of temporal and spatial proximity in the RHI share common similarities with the temporal and spatial principles for optimal multisensory integration (Ehrsson, 2011). Consequently, these constraints might also explain individual differences in the susceptibility to the rubber hand illusion (Costantini et al., 2016; David, Fiori, & Aglioti, 2013; Ehrsson, 2011; Haans, Kaiser, Bouwhuis, & IJsselsteijn, 2012).

Kilteni (2015) argued that unlike the study of multisensory perception where the focus is generally on the relationship between the manipulated stimuli, it is difficult to experimentally investigate topics like body ownership without the use of cameras and mirrors to introduce delays between the seen and felt position of our body. Subsequently, methods have been developed that make it possible to create far more complex multimodal illusions to investigate the complicated interaction between pain and one's body, and to interrogate processes like body ownership. The following section will now provide an overview of the main methods used in this thesis.

1.5 Methods

The current thesis is concerned with the implications of multisensory illusions on chronic pain. Multisensory illusions are illusions that use the combination of sensory input (touch, vision and proprioception) to alter the way people perceive their body. Boesch et al., (2015) present a working definition whereby they define a bodily illusion as, *"a phenomenon in which an external stimulus is interpreted by the neural system in such a way that the resultant perception of the body is significantly different from reality"* (p.517). Specifically, this thesis examines how these illusions may alter body representation and sense of body ownership in both healthy and clinical groups, in an attempt to understand how they might be used as means for pain relief. Here, body representation refers to the presentation of the body in the brain, and body ownership refers to knowing that one's body belongs to oneself.

1.5.1 MIRAGE system

The experiments in this thesis were conducted using a MIRAGE mediated reality device, developed at the University of Nottingham (Newport & Preston, 2010). Mediated reality has been defined by Mann (2005) as: “a general framework for artificial modification of human perception by way of devices for augmenting, deliberately diminishing, and more generally, for otherwise altering sensory input” (p.626). The concept is well differentiated from virtual reality, in which the real world is blocked and replaced, in that it adds to, takes away from, alters and engages with an already existing world (Mann, 1994). In this thesis, mediated reality refers to an immersive device that can alter human perception through the alteration of sensory input (Mann, 2002).

The MIRAGE system consists of a set-up of cameras and mirrors so that participants can view a real-time live video image of their own hands in the same spatial location as their actual hands and captured at 100Hz (see Figure 1.2). A rectangular mirror placed above the work surface reflects the image of the hands and objects on a computer screen positioned further above the mirror (Karok & Newport, 2010). This set of mirrors and cameras allows for the display of actual visual feedback and movement as if participants are viewing their hand directly. The image can be displayed raw, or manipulated by a custom LabVIEW (National Instrument, Austin, TX) script. Digital manipulations can present altered images of the hands with a ~10ms temporal delay between image capture and display, which has been referred to as the ‘visual-proprioceptive integration threshold’, making it unlikely for people to detect the delay between movement and feedback (Leube et al., 2003; but see Greenfield, Ropar, Smith, Carey, & Newport, 2015).

The MIRAGE system reconfigures reality by visually mediating the representation of one's own hands, whilst presenting them in the same spatial reference frame as the actual hands, and in the same real world environment. As pointed out by Martini (2016), immersive methods such as novel virtual reality and augmented reality have a greater potential for effective pain relief compared to non-immersive environments. The sense of presence, referring to the feeling that the events that are happening in virtual set-up appear to actually be happening to the participant (Slater, Perez-Marcos, Ehrsson, & Sanchez-Vives, 2009), has been suggested as a possible explanation for why immersive environments appear more effective for pain-relief than non-immersive environments (Malloy & Milling, 2010; Sanchez-Vives & Slater, 2005).

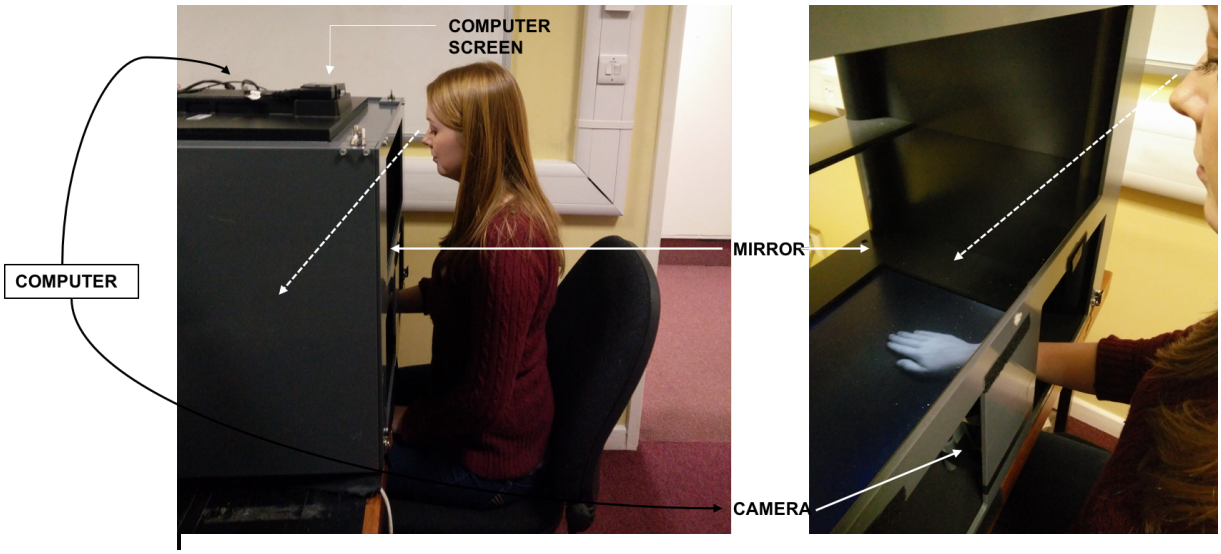


Figure 1.2 General set-up of the MIRAGE system. The participant places their dominant (or most affected) hand inside MIRAGE whilst viewing their hand in the same spatial location and from the same visual perceptive as his/her actual hand. Note: for some experiments conducted in this thesis, participants were asked to make a fist and extend their index finger.

Using MIRAGE, Preston & Newport (2011b) demonstrated that illusory manipulation of the painful hand in HOA can modulate the experience of pain. In their study, a total of 20 HOA sufferers were asked to place their most painful hand inside the MIRAGE system whilst viewing their hand in the same spatial location and from the same perspective as their real hand. The device allowed for digital manipulations of the hand which was coupled with tactile input. Two control conditions were included which consisted of stretching or shrinking the non-painful part of the hand and visually enlarging or reducing the entire hand (instead of just the painful part of the hand), albeit only tested in a subset of participants (Preston & Newport, 2011). Illusory stretching or shrinking of the finger (visually elongating the finger whilst gently pulling or pushing the finger) resulted in a reduction of the pain experience in more than 85% of the participants suffering from osteoarthritis of the hands (HOA).

These results raise the potential for a strong analgesic effect of multisensory illusions in chronic pain. Possible explanations for the observed pain relief include the role of expectation, reduction of apparent swelling, attention, restorations of the disrupted body schema by bringing back the appearance of a ‘normal’ limb, placebo, and even simply distraction (Giummarraa, Georgiou-Karistianis, Verdejo-Garcia, & Gibson, 2015; McCabe, 2011; Moseley, 2011). However, how these factors interact or contribute to the observed effects appear to have received limited attention in the literature to date. Furthermore, without conditions in Preston and Newport’s (2011a) study controlling for the effect of vision or tactile input alone and in a systematic manner, it is hard to interpreted these findings.

1.6 Ethical considerations

There are several important ethical considerations in the conduct of pain research. For the current thesis, participants ranged from healthy students to elderly people suffering from chronic pain. When testing individuals with chronic pain, and when participants are particularly vulnerable, one should be especially vigilant about using methods that may cause further discomfort or pain. This often requires striking a balance between the aims of the study and the interests of the participant. For the current thesis, compromises were made that were always in the best interests of the participants. For all of the experiments reported in the empirical chapters to follow, participants were provided with a clear explanation of the aims and implications of the research, and were made aware of the possibility to withdraw from the study at any given time.

In the studies that involved participants suffering from chronic pain (see Chapter 4, 5 and 6), the main objective was to ensure that no unnecessary discomfort or pain was elicited, and this was a crucial factor in deciding on the specific methods to be used in this thesis. Indeed, the health, safety and dignity of the participant should always hold the highest priority and research should therefore focus on the direct or indirect benefits of the patient (Charlton, 1995). All of the experiments in this thesis that investigated pain were developed with strict adherence to the Ethical Guidelines for Pain Research in Humans as developed by the Committee on Ethical issues of the International Association for the Study of Pain (Charlton, 1995).

1.7 Conclusions and thesis aims

The representation of our body is fundamental for how we experience ourselves and others. An intact body representation is important for knowing that our body belongs to us and does not belong to other people or objects. The representation of our body in the brain relies on inputs from a range of sensory modalities as well as information derived from interacting and moving within the external world.

However, research suggests that body representation may be disrupted in some clinical conditions, including chronic pain. This notion is supported by evidence from brain imaging studies demonstrating systematic changes in cortical areas that represent the body in patients with chronic pain, known as cortical reorganization. Furthermore, behavioural studies demonstrate perceptual and autonomic disturbances in a range of chronic pain conditions, which are thought to indicate disruptions to the body image and body schema.

Despite the high incidence and prevalence, current treatments targeting chronic pain are often unsatisfactory. Consequently, strategies that target body representation and cortical reorganization show promising results for individuals with chronic pain. Specifically, research indicates that multisensory illusions may improve pain and functional disability. However, the effects of these illusions on pain and body representation in both healthy individuals and individuals with chronic pain have not been systematically assessed.

Seeking to understand which factors might contribute to previously observed analgesic effects of multisensory illusions, and what the main implications might be for chronic pain are the core objectives of this thesis. First, this thesis will investigate the effects of multisensory illusions in healthy

individuals with the hope to advance our knowledge of how these methods may alter our body representation, sense of body ownership, and pain. Second, this thesis aims to examine the effects and clinical implications of multisensory illusions in individuals with HOA. Specifically, it will test the effects of multisensory illusions on body image, body schema, and body ownership and investigate the role of vision and contextual factors underlying the effect of these illusions.

1.8 Summary of experimental chapters

Chapter 2

The study in Chapter 2 investigated the link between body image and the sense of body ownership in healthy individuals. The results showed that visually distorting the shape of the hand can alter perceived body shape and body satisfaction, without losing ownership. Moreover, the findings support the notion that the representation of the body is a dynamic process that can easily be altered.

Chapter 3

The study in Chapter 3 tested whether the methods used in Chapter 2 can alter the experience of pain in healthy individuals. Although the study replicated the findings of chapter 2 in terms of body image and the affective experience of the body, the study did not find support for a modulatory effect of the multisensory illusions on pain. This could indicate that pain sensitivity or pain ratings measured on a NRS scale are not necessarily modulated by changes of the virtual body in healthy participants.

Chapter 4

The study in Chapter 4 investigated whether individuals with HOA may present with a disruption of the working body schema. The findings partially supported this hypothesis, indicating that performance on a hand laterality judgement task is mediated by the presence of, or strength/severity of pain.

Chapter 5

The study in Chapter 5 investigated the effects of multisensory illusions on pain and body representation in people with HOA. The results demonstrated an analgesic effect of the stretch-illusion as well as changes in body representation, body ownership and agency. However, similar effects were also elicited when directly viewing the hand being stretched, suggesting that vision of the body and contextual factors may contribute to the analgesic effect observed in this and other studies.

Chapter 6

The final study used an adaptation of the methods used in Chapter 5 to investigate whether the effects of the stretch-illusion were similar in people with HOA compared to healthy individuals. The study did not find evidence for an effect of pain on the susceptibility to body illusions, demonstrating an effect of multisensory illusions on subjective and objective measures of body perception. Though no differences in pain ratings were found between study conditions and groups, individuals with HOA presented with high levels of body dissatisfaction, which unlike in healthy controls could not be altered by

multisensory illusions. Again, the findings highlighted the importance of contextual factors for the analgesic effects to occur.

Chapter 2 The effects of multisensory illusions on body representation and sense of body ownership in healthy individuals

2.1 Introduction

Multisensory illusions can provide invaluable insights into the complex relationship between the brain's representation of the body and the sense of self. Body ownership illusions have been suggested as a method to alter perceived body shape and relieve pathological pain (Mohan et al., 2012). However, how these methods might alter body shape and modulate pain is not well understood.

As reported in section 1.5.1, Preston and Newport (2011) report analgesic effects of multisensory illusions in people with painful HOA. They propose that the analgesic effects of illusory shrinking or stretching of the hand may in part be due to correction of a faulty representation of the body (body schema). However, others suggest that the that the analgesic effects produced by these and other illusions may result from a loss of ownership or awareness over the "real" affected limb as well as an increased ownership over the artificial limb (McCabe, 2011; Petrini & Arendt-Nielsen, 2016). Indeed, whilst it has been shown that vision of a limb alone can be analgesic, it has been suggested that for the analgesic effect occur there needs to be a feeling of ownership over the viewed body part (Martini, Perez-Marcos, & Sanchez-Vives, 2015).

Conversely, it has been suggested that the effects of this and other bodily illusions on pain perception may simply be the result of distraction or a shift in attention from pain (Gilpin, Bellan, Gallace, & Moseley, 2014). The aim

of this first empirical chapter is to test the claims that illusory stretching or shrinking of the hand changes perceived body shape, whilst maintaining a sense of body ownership over the virtual limb in healthy participants, before moving on to examine the effect of the illusion on pain in Chapters 3, 4, 5 and 6.

For an individual to perceive their body as theirs, the brain needs to integrate visual and somatosensory signals resulting in a multisensory representation of the body (Graziano & Botvinick, 2002; Makin, Holmes, & Ehrsson, 2008, see also Chapter 1). The perception of the body in terms of size, shape and distinctive features is an intrinsic part of the body image and plays a fundamental role in our everyday live (Ehrsson, Kito, Sadato, Passingham, & Naito, 2005). Studies indicate that it is relatively easy to manipulate the perceived body in terms of size and shape, and this has been shown by various authors (Botvinick & Cohen, 1998; Kammers, de Vignemont, Verhagen, & Dijkerman, 2009; Newport et al., 2015; Preston & Newport, 2012).

As discussed previously, the rubber hand illusion (RHI) is a classical paradigm used to investigate the neural and behavioural aspects of the feeling that our body belongs to us (Ehrsson, Wiech, Weiskopf, Dolan, & Passingham, 2007; See Makin et al., 2008, for a review). In the RHI, an artificial hand becomes part of someone's body when it is stroked simultaneously and in the same location as the real unseen hand, as measured by embodiment questionnaires and behaviourally by a proprioceptive drift towards the fake hand (Botvinick & Cohen, 1998[1]). The feeling of ownership over the rubber

[1] See Rohde, Di Luca, & Ernst (2011) for evidence that ownership and proprioceptive drift are dissociated.

hand is generally considered to be the result of synchronous multisensory correlations (Jeannerod, 2003). In contrast, asynchronous stimulation has been found to lessen, or even entirely diminish the feeling of ownership over the rubber hand (Botvinick & Cohen, 1998; Kalckert & Ehrsson, 2014; Kokkinara & Slater, 2014; Longo, Schüür, et al., 2008). This notion is evidenced by studies showing activity in brain areas that receive visual, tactile and proprioceptive input and are important for multisensory integration, which correlates with the strength and is affected by the onset of the illusion (Ehrsson, 2005; Ehrsson et al., 2004).

However, emerging evidence suggests that there are other factors contributing to the feeling of body ownership (Ehrsson, 2011; Tsakiris, 2010). For example, there are limitations to which objects can be used to induce the RHI (Tsakiris, 2010; Tsakiris & Haggard, 2005). Furthermore, the RHI is not induced or is induced to a lesser degree when the limb is presented incongruently with the participants hand (Tsakiris & Haggard, 2005), or when the rubber hand does not match the posture of the participant's hand (Costantini & Haggard, 2007). This suggests that ownership over an artificial body or object is not the mere result of synchronous multisensory information and is also influenced by top-down cognitive factors.

Recent studies have shown that the feeling of ownership over an artificial limb can extend to virtual limbs and even entire bodies (e.g. Martini, Perez-Marcos, & Sanchez-Vives, 2013; Romano, Llobera, & Blanke, 2016; Slater, Perez-Marcos, Ehrsson, & Sanchez-Vives, 2008, 2009). Newport, Pearce and Preston (2010) used the same device (MIRAGE) to that of the current study to investigate whether a virtual hand could be incorporated into

both the body image and body schema of healthy controls. Participants viewed a live dynamic video image of their hand in the same spatial location as their real hand, which could be manipulated so that participants viewed two “fake” hands, either with one in the location of their real hand and one displaced, or with both hands displaced. They found that participants experienced a sense of ownership over the video image of the hand, with the highest ownership ratings when touch on the seen hand occurred simultaneously with that of the real hand. Additionally, they showed that a fake limb could be incorporated into both the body schema and even multiple fake hands into the body image as measured by ownership questionnaires and a pointing task. This indicates that body representation is malleable and easily altered, lending support to the idea that these methods could be of promising use in a range of conditions where body image disturbances may be apparent.

Using a full-body illusion, a recent study by Preston and Ehrsson (2014) demonstrated that illusory ownership over a thinner body led to participants perceiving their actual body to be thinner. In this case, not only did the researchers show that ownership over an artificial body can change the perceived shape of one’s body, participants also reported an increase in their body satisfaction, suggesting a link between perceptual and affective body representations. A further study by Serino et al., (2016) showed that alterations in body image and body dissatisfaction could potentially be addressed using virtual reality paradigms, indicating that illusory ownership over a thinner body improved bodily experience and motivation for undertaking healthy behaviour in a morbidly obese patient.

Slater et al. (2008) argued that ownership over a virtual limb may not be rigorously constrained by how realistic the limb looks or the environment it is presented in. Instead, it can be induced by congruent visual feedback and active movements. More recently, Newport et al. (2015) showed that visual manipulations coupled with real tactile input can result in the feeling that the participant's limb has actually changed in shape and size, and that this can lead to analgesic effects in people with HOA (Preston & Newport, 2011). Although these findings suggest that people take ownership over the virtual hand even when the appearance of the virtual hand is incongruent with the actual hand or is in fact anatomically implausible, this has not been systematically explored. I therefore aim to establish that people can take ownership over a virtual hand even when it is in an anatomical implausible configuration, whether stretched or shrunken.

Another theme emerging from studies of limb ownership is the possible link between body ownership and the experience of somatic sensations. Specifically, McKenzie and Newport (2015) used a mediated reality system to demonstrate how the application of visual manipulations to the hand can in some participants lead to experiencing increased somatic sensations in the experimental hand. The sensations are thought to be the results of a disparity or conflict between bottom-up sensory factors and top-down cognitive processes. Furthermore, in the study by McKenzie and Newport (2015), people who reported the lowest ratings of ownership over the video-manipulated hand tended to report more physical sensations in response to these illusions.

Conversely, Moseley, Olthof and colleagues (2008) showed that the feeling of ownership over an artificial hand can lead to a reduction in skin temperature in the real hand, resulting from a selective reduction of blood flow to that hand. This result and the effects of the RHI on the innate immune system, have been further investigated by Barnsley and colleagues (2011), who found that ownership over a rubber hand increases the reactivity to histamine in the real arm. Furthermore, in patients with chronic hand pain, visually changing the size of the affected limb can lead to reduction in pain and swelling, which again is thought to relate to the reported loss of ownership over the affected hand (Moseley, Parsons, et al., 2008). These results support the idea of a bi-directional relationship between pain, physical symptoms and body representation (Barnsley et al., 2011; Moseley, Parsons, & Spence, 2008; Preston & Newport, 2011.) It has thus been proposed that bodily responses to these and other sensory illusions may serve as a marker of susceptibility to everyday experiences of distortions in body schema (Burrack & Bruger, 2005). The present study will further investigate the link between virtual body ownership and bodily sensations using a series of statements asking about physical sensations in the hand after the different conditions.

2.1.1 Summary

The current study has three overall aims. First, it will investigate the effects of the stretch and shrink-illusion on perceived body shape. The current study will use the MIRAGE as described in the introduction of this thesis to alter perceived body size in healthy participants. Participants are asked to view their hand inside MIRAGE, whilst undergoing eight experimental conditions with

four conditions relating to stretching of the hand and four conditions relating to shrinking of the hand. The illusion that the index finger of the participant has changed in shape and size is assessed by two outcome measurements. The first is an eight-item questionnaire aiming to investigate the subjective experience of the stretch/shrink-illusion. The study will also use a motor task in which participants are asked to draw an image of the perceived size of their hand. If the illusion leads to an alteration in body image, I would expect the drawn image of the hand to be clearly disrupted (Moseley, 2008). Furthermore, I would expect participants to report a change in perceived body shape consistent with the hand drawings.

The second aim is to test the effects of the stretch/shrink-illusion on the feeling of body ownership. In light of previous findings, it is hypothesised that participants will still perceive ownership over the illusory hand, despite the fact that the virtual hand no longer matches a plausible representation of the actual hand. This should be reflected by people still rating the seen hand as belonging to them. Furthermore, based on previous findings in both rubber- and virtual hand paradigms, it is expected that ownership might be reduced for the asynchronous condition where there is a delay between the seen and perceptual stretch or shrink (e.g. Botvinick & Cohen, 1998; Newport et al., 2010). Thus, the purpose of the asynchronous condition is to control for the perceptual effects of the illusion conditions, that is, the synchrony between visuo-tactile stimulation.

The third aim is to provide further insight into the findings of somatosensory changes following a visual distortion of the body, by using a combination of multisensory illusions. Based on previous findings (McKenzie

& Newport, 2015), I expect to find a relationship between the sense of body ownership and the amount of reported physical sensations in response to the stretch and shrink-illusion, in that the lower the amount of body ownership, the higher the number and intensity of reported physical sensations.

2.2 Materials and methods

2.2.1 Participants

The overall sample consisted of 16 participants (7 males and 9 females). The mean age was 22 years, and ranged from 18 to 30 years (*SD* = 3.74). All participants were right-handed. Participants provided informed consent and were pain-free on the day of testing with normal or corrected-to-normal vision. All participants were students at the University of Nottingham and received course credits for their participation. The study was approved by the Ethics Committee of the University of Nottingham and informed consent was taken prior to assessment.

2.2.2 Design

This study utilised a 2x4 repeated measures design with two levels of manipulation (Stretch or Shrink) and four levels of condition (illusion, vision-only, asynchronous and tactile-only (control)). The conditions were counterbalanced in order to reduce the likelihood of any order effects (see Figure 2.1).

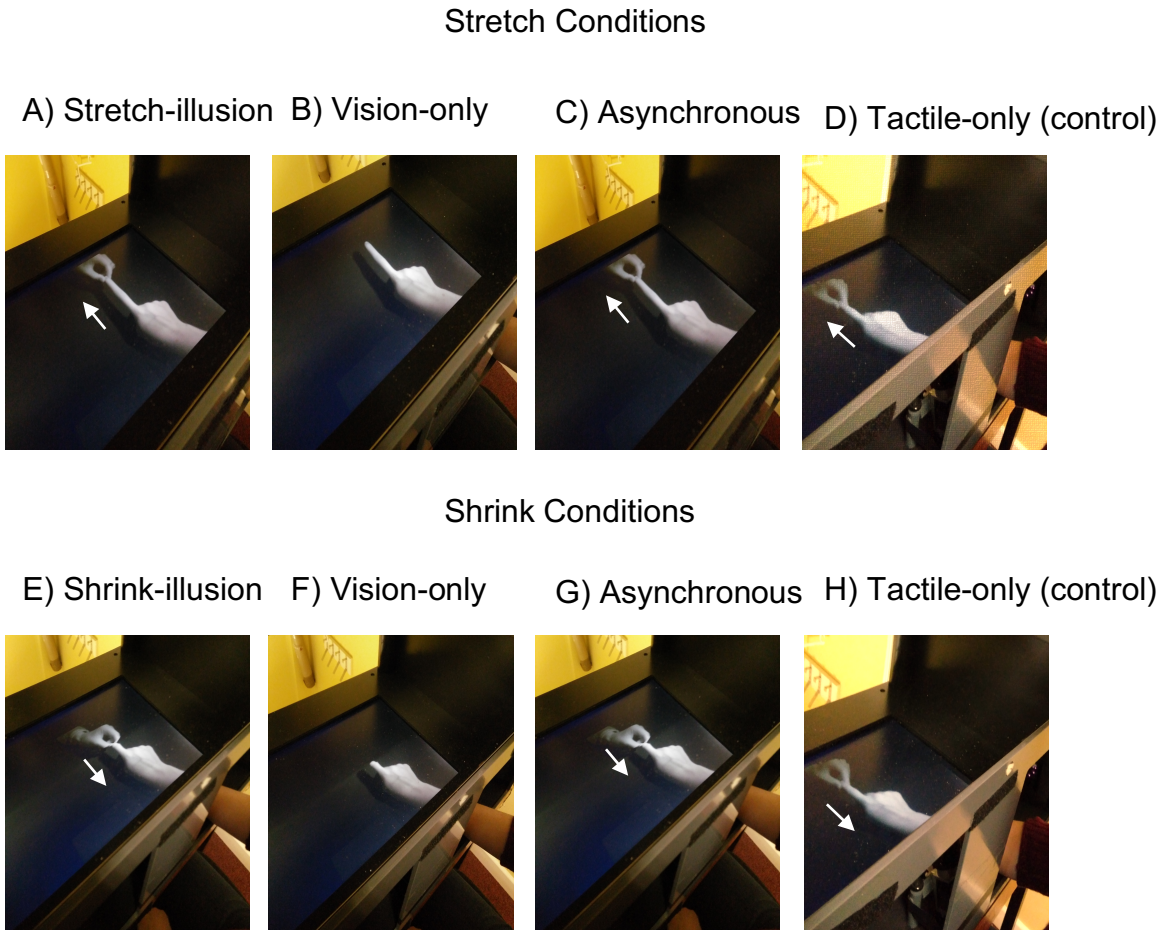


Figure 2.1 Pictures showing each of the eight conditions. Illusion: the experimenter took hold of the distal part of the index finger and gently pulled (A) or pushed (E) the finger whilst simultaneously increasing or decreasing the visual image of the finger respectively; Vision-only: participants viewed the visual image of the finger getting longer (B) or shorter (F); Asynchronous: same as illusion condition except the pull (C) or push (G) and the computerized stretch or shrink occurred asynchronously (with a ~1 sec. delay); Tactile-only; the experimenter gently pulled (D) or pushed (H) the finger without any visual manipulation (control condition). Note: white arrows included for illustration purposes only and indicate direction of push or pull.

2.2.3 MIRAGE System and experimental conditions

For the multisensory illusions, the MIRAGE system was used so that participants could view their dominant hand in real-time and in the same spatial location as their actual hand (See section 1.5.1 for details). The video representation was manipulated using a custom written LabVIEW 2010 program (National Instruments, Austin, TX).

The experiment consisted of eight conditions: Two illusion conditions (stretch and shrink), two vision-only conditions (stretch and shrink), two

asynchronous conditions (stretch and shrink) and two tactile-only control conditions (stretch and shrink). For the stretch and shrink-illusion conditions the experimenter took hold of the distal part (phalanx) of the index finger and gently pulled (for the stretch-illusion) or pushed (for the shrink-illusion) the finger. This was done whilst simultaneously operating the computer software, so that the visual image gradually appeared longer or shorter. The stretch-illusion is thought to be convincing as it involves congruent visual, tactile, and proprioceptive manipulation of the participant's own hand (Newport et al., 2015).

For the vision-only conditions, participants viewed an image of their finger being stretched or shrunk so that it appeared longer or shorter, without providing any tactile input (the experimenter holding the finger). The vision-only condition is a multisensory condition as there are at least two senses being integrated (vision and proprioception) to update body representations-not including touch (on the table) and kinaesthesia. This creates the illusion that one can see their own hand whereas it is, in fact, a pictorial representation. This is different from just viewing a photograph of one's hand as in that instance there is no illusion that it is their own real hand.

For the asynchronous conditions, the experimenter first pulled or pushed the finger before expanding or compressing the live video feed so that the tactile information (pulling or pushing) and visual information (computerized stretch or shrink) occurred asynchronously (with a ~1 sec. delay). For the tactile-only control conditions, the experimenter either pulled (for stretch-illusion control) or pushed (for shrink-illusion control) in an identical setup as in the other conditions, but without manipulating the visual feedback.

2.2.4 Subjective experience of the illusion

After each condition, participants were asked to respond to a series of statements, asking about somatosensation, including changes in pain, itch and temperature (see Table 2.1), as well as perceived ownership, affective experience, and perceived change in body shape (see Table 2.2). Statements were based on recent studies by Foell and colleagues (2013) and McKenzie & Newport (2015) investigating body perception and somatic sensations. The aim was to investigate the subjective experience of the illusions and any physical sensations that may result from it. Immediately after each condition, the investigator started with the questionnaire, during which participants were asked to hold their finger in the same position as during experimental conditions, with the finger still in manipulated or un-manipulated form, depending on the condition. Participants responded to the statements using an 11-point scale ranging from 0 (No, definitely not) to 10 (Yes, lots and lots).

Table 2.1 Statements used for calculating a somatosensation score

Pain	Do you perceive any slight pain in the finger apart from gripping the finger?
Itch	Do you perceive tickling or pins and needles in the finger?
Warmth	Do you feel your finger is getting warmer?
Coldness	Do you feel your finger getting colder?
Lightness	Do you feel your finger getting lighter?
Heaviness	Do you feel your finger getting heavier?
Peculiarity	Do you perceive strange, not clearly identifiable sensations in the finger?
Pressure	Do you feel a change in pressure in the finger apart from gripping the finger?
Numbness	Do you perceive numbness in the finger?
Nausea	Do you perceive nausea or dizziness?
Other part	Do you perceive sensations in any other part of your body?

Table 2.2 Statements used to capture the Illusion experience

Ownership	Did you feel like your finger was part of your body?
Affective experience	Did you like the way your hand looks during the experiment?
Shape	Did you perceive a change in length, width, or shape of the finger during the experiment?

2.2.5 Hand Drawings

Participants were instructed to sit in a chair at a table away from the MIRAGE system where they were asked to draw a sketch of the dorsal side of their hand using their dominant hand. This was done at baseline and after every condition. Similar to the methods described by Moseley (2008), participants were instructed to *'draw a sketch of how your hand feels like and not how you think it looks'*. Participants could take all the time they needed to complete the drawings. Both the length of the drawn index finger and the drawn middle finger were measured manually, as shown in Figure 2.2. The length of the middle finger was measured to investigate whether any perceived change in size would be specific to the manipulated finger or not.

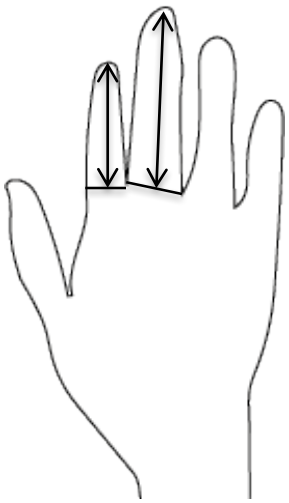


Figure 2.2. Example of a participant hand drawing. Double arrows indicate the measurements that were included for statistical analysis. The length of the index and middle finger was measured from midway base to fingertip.

2.2.6 Procedure

At the start of the experiment, participants were asked to draw a sketch of their dominant hand on an A4 piece of paper with the following instruction: *'' I am going to ask you to draw your hand, as you perceive it at this particular moment. Your drawing should relate to your own sense of your hand. Do not draw what you think your hands looks like - draw what it feels like. You can take all the time you need''.* Additionally, they were asked to rate any current pain on a 0-10 verbal rating scale, with 0 (no pain at all) to 10 (worst pain imaginable). Participants were then asked to place their dominant hand inside the MIRAGE system, which was referred to as a "mediated reality device" and participants were told that they would view their hand inside the system with the possibility that the appearance of the hand could change.

All participants completed the eight conditions, with four conditions relating to illusory stretching and four conditions relating to illusory shrinking of the finger (See Figure 2.1). Before each condition, participants were asked to make a fist and point out their index finger and look at their hand for 30 seconds after which the condition started. After each condition, participants were asked to verbally respond to the questions and subsequently take their hand out of MIRAGE to draw an image of their hand.

2.2.7 Data analysis

To examine the effects of the illusions on body image, hand drawings were analysed using a three-way repeated measures ANOVA to determine the effects of manipulation (2 levels: stretch or shrink), condition (5 levels:

baseline, illusion, vision-only, asynchronous, control), and perceived body image (2 levels: drawn Index finger or middle finger) (see Figure 2.2).

Outliers were assessed by examination of studentized residuals for values greater than ±3. Hand drawing measurements were normally distributed, as assessed by Shapiro-Wilk's test of normality. All reported results are significant after Bonferroni adjustment.

To investigate the subjective experience of the illusion, a two-way repeated measures analysis of variance (ANOVA) was used with manipulation (2 levels: stretch or shrink) and condition (4 levels: illusion, vision-only, asynchronous, control) for each of the statements relating to ownership, perceived body shape and affective experience.

As with the preceding analysis, several assumptions were checked prior to running the repeated measures ANOVA. Data were negatively skewed for a number of ownership, affective experience and shape variables, as assessed by Shapiro-Wilk's test of normality on the studentized residuals. Although these could not be rectified by transformation, analysis of variance are generally considered to be robust against moderate violations of the assumption of normality (Tabachnick & Fidell, 2007). All reported results are significant after Bonferroni adjustment for multiple comparisons.

Somatosensation scores were calculated using the maximum ratings on each of the statements (see Table 2.1), for each participant during the different conditions. A two-way repeated measures ANOVA with manipulation (stretch x shrink) and condition (illusion, vision-only, asynchronous, control) was used. The Shapiro-Wilk test suggested a highly positively skewed distribution and

data were therefore transformed to meet the assumptions of linear regression using a Square-Root transformation.

2.3 Results

2.3.1 Hand drawings

The three-way repeated measures ANOVA showed a main effect of manipulation, $F(1,15) = 9.790$, $p = .007$, $\eta^2 = .395$, indicating that participants drew a longer index finger after the stretch conditions compared to shrink conditions, with no difference in the mean length in drawings for the middle finger. This was driven by an effect of condition on the drawn length of the index finger for the stretch conditions. However, this effect did not survive adjustment for multiple comparisons.

There was also a main effect of length, $F(1,15) = 53.075$, $p < .001$, $\eta^2 = .780$, indicating that participants drew a longer middle finger compared to the index finger in all conditions. There was no main effect of condition, $F(1.780, 26.697) = .271$, $p = .895$, $\eta^2 = .018$, and no significant interaction between condition and length $F(4, 60) = 1.548$, $p = .200$, $\eta^2 = .094$. All other main effects and interactions were non-significant, all Fs ≤ 1.492, all ps ≥.13, η^2 's ≤ .062. The findings are illustrated in Figure 2.3.

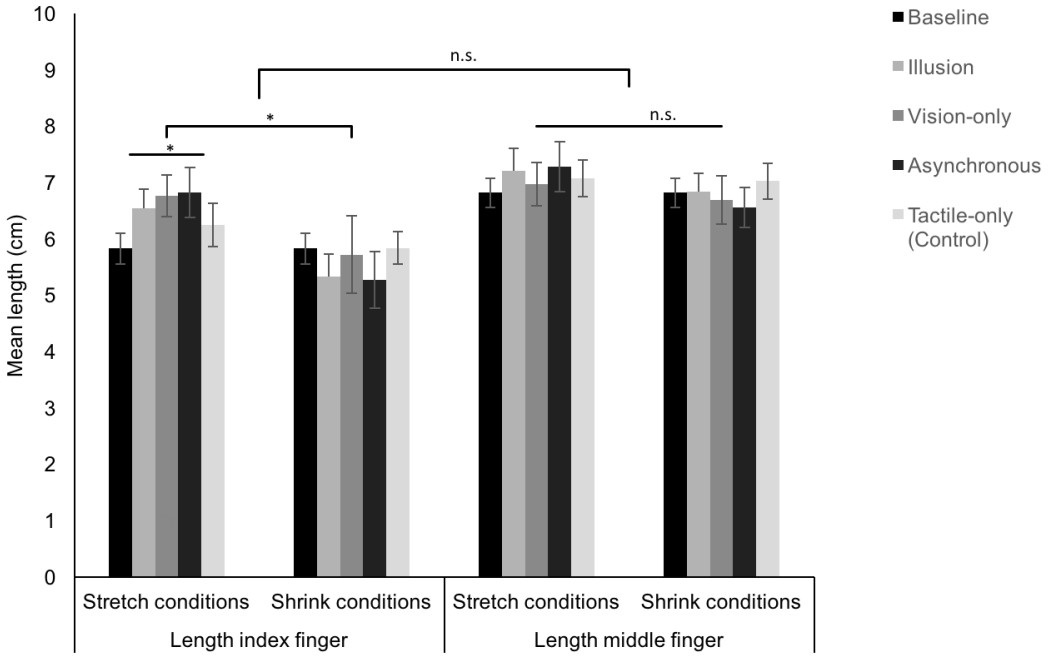


Figure 2.3 Changes in perceived length of the index finger and middle finger measured by hand drawings. Error bars represent standard error of the mean. * Represents statistically significant difference between conditions after Bonferroni corrections. n.s.= not significant.

2.3.2 Illusion experience

Ownership

Mean ownership ratings are presented in Figure 2.4A. The two-way repeated measures ANOVA indicated that there was a main effect of condition, $F(3, 42) = 10.673$, $p < .001$, $\eta^2 = .433$. There was no main effect of type, $F(1, 14) = .121$, $p = .733$ $\eta^2 = .009$, and no two-way interaction between type and condition, $F(4, 42) = .216$, $p = .885$, $\eta^2 = .015$, indicating that there were no differences in the responses for the stretch or shrink trials. Post-hoc analysis of the main effect of condition revealed that reported ownership was lowest after the asynchronous conditions, which was statistically significantly different to the control, with a difference in NRS score of 1.63 (95% CI 5.80 to 2.69), $p = .002$. Furthermore, there was a statistically significant mean difference between the illusion conditions and control of 1.33 (95% CI 0.402 to 2.264),

p = .004. There was no statistically significantly difference between the other conditions (all *p*s > .05).

Shape

Mean perceived change in shape ratings are presented in Figure 2.4B. The two-way repeated measures ANOVA indicated that there was a main effect of condition, $F(3, 45) = 22.051$, $p <. 001$, $\eta^2 = .595$. There no main effect of type, $F(1, 15) = .122$, $p = .732$, $\eta^2 = .008$, and no interaction between type and condition, $F(3, 45) = 1.897$, $p = .144$, $\eta^2 = .112$, indicating that there were no differences in the responses for the stretch or shrink trials. Post-hoc analysis of the main effect of condition revealed that change in shape was highest after the illusion conditions, which was statistically significantly different compared to control, with a difference of 5.07 (95% CI, 2.48 to 7.66), $p < .001$. Furthermore, there was a statistically significant mean difference between the vision-only conditions and control of 4.65 (95% CI, 1.72 to 7.58), $p < .001$ and the tactile-only conditions and control of 4.50 (95% CI, 1.67 to 7.32), $p < .001$. There was no statistically significant difference between the other conditions (all *ps* > .05).

Affective experience

Mean affective experience ratings are presented in Figure 2.4C. The two-way repeated measures ANOVA indicated that there was a main effect of condition, $F(3, 45) = 44.878$, $p = .0005$, $\eta^2 = .749$. There was no main effect of type, $F(1, 15) = .122$, $p = .732$, partial $\eta^2 = .008$, and no interaction between type and condition, $F(3, 45) = 1.897$, $p = .144$, $\eta^2 = .112$, indicating no differences in the

responses for the stretch or shrink trials. Post-hoc analysis of the main effect of condition revealed that the reported liking of the hand was lowest after the illusion conditions, which represented a statistically significant difference compared to the control, with a difference in NRS score of 5.18 (95% CI, 3.60 to 7.6.77), $p < .001$. Furthermore, there was a statistically significant mean difference between the vision-only conditions and control conditions of 5.0 (95% CI, 3.05 to 6.94), $p < .001$, and the tactile-only conditions and control of 4.75 (95% CI, 3.44 to 6.06), $p < .001$. There was no statistically significant difference between the other conditions (all *p*s > .05).

Somatosensation score

Mean somatosensation scores are presented in Figure 2.4D. There was a main effect of condition, with a significant difference in somatosensation scores between conditions, $F(3,45) = 3.566$, $p = .021$, $\eta^2 = .654$. There was no two-way interaction between illusion and condition, $F(1.606, 24.086) = .287$, $p = .705$, $\eta^2 = .019$, indicating that there was no difference in somatosensation scores between shrink/stretch across conditions and no main effect of manipulation, $F(1,15) = .017$, $p = .897$, $\eta^2 = .001$. Further analysis of the main effect of condition (for stretch and shrink trials combined), using post-hoc pair-wise comparisons revealed that there was a significantly higher somatosensation score in the illusion conditions compared to the control conditions, with a difference in NRS scores of .110 (95% CI, .001 to .219). There was no statistically significant difference between the other conditions (all *ps > .05).*

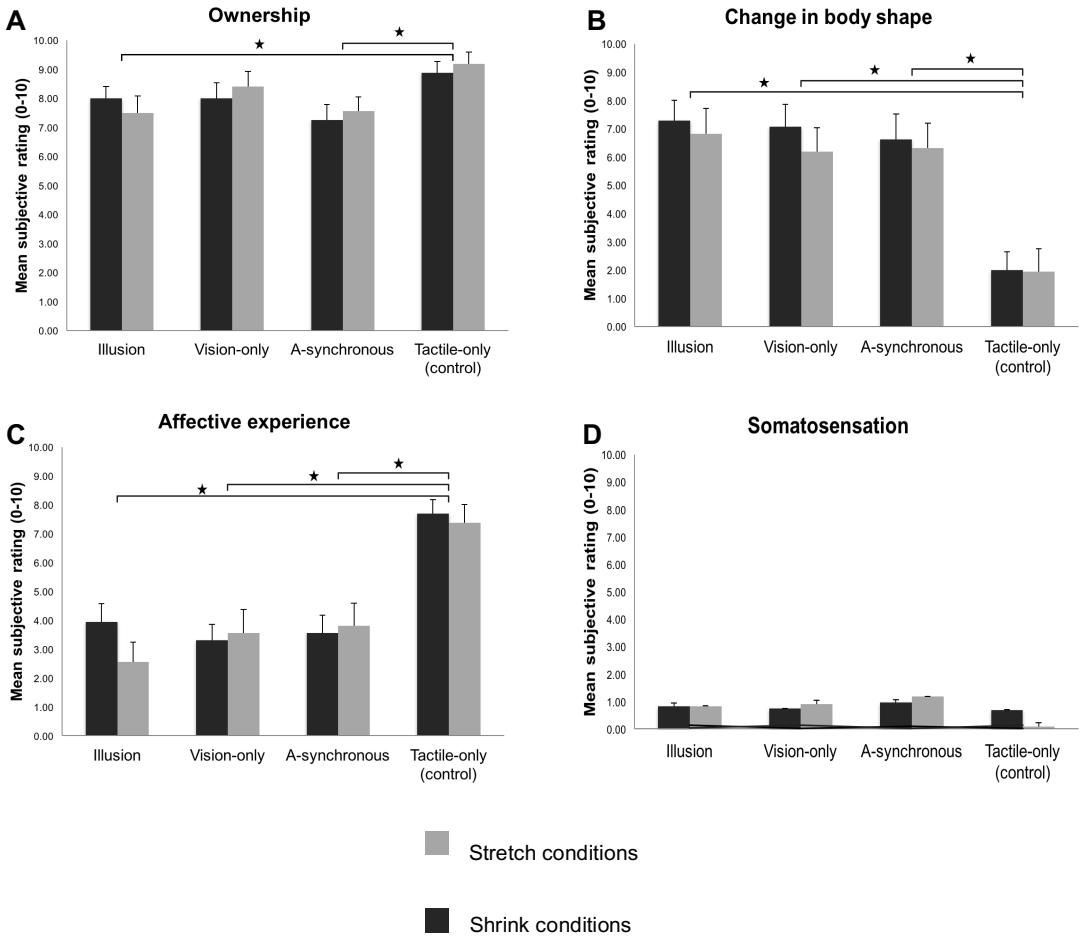


Figure 2.4 Mean objective ratings of the responses for each of the statements relating to: A) body ownership, B) change in perceived body shape, C) affective experience taken after every condition (higher score denotes greater body satisfaction) and D) somatosensation score using the maximum ratings for each participant during the different conditions. Error bars represent one standard error of the mean.

2.3.3 Relationship between ownership and perceptual changes

Correlation analyses were conducted to investigate the relationship between the sense of body ownership and reported physical sensations, including somatosensation (see Table 2.3A), change in perceived body shape (see Table 2.3B) and, change in affective experience of the body (see Table 2.3C). As there was no statistically significant difference between the stretch or shrink conditions, correlations were performed on the stretch and shrink conditions combined. Table 2.3 shows the Pearson correlation coefficients and the corresponding significance levels for all conditions and perceptual changes.

Table 2.3 Pearson's Correlations between ownership and perceptual effects (significant correlation is highlighted in bold).

a) Relationship between ownership and somatosensation	***r***	***p***
Stretch & Shrink Conditions		
Illusion	**-0.59**	**.008**
Vision-only	**-0.60**	**.007**
Asynchronous	**-0.59**	**.008**
Tactile-only (control)	**-0.66**	**.002**
b) Relationship between ownership and change in body shape		
Stretch & Shrink Conditions		
Illusion	0.23	.20
Vision-only	0.18	.25
Asynchronous	0.37	.08
Tactile-only (control)	**-0.70**	**.001**
c) Relationship between ownership and affective experience		
Stretch & Shrink Conditions		
Illusion	**0.55**	**.013**
Vision-only	**0.50**	**.024**
Asynchronous	**0.57**	**.01**
Tactile-only (control)	0.32	.113

r= Pearson correlation coefficient, *p* = *p* value

2.4 Discussion

The current study had three aims. The first aim was to investigate the effects of the stretch/shrink-illusion on perceived body shape. Furthermore, it aimed to examine the relationship between perceived body size and body ownership, and examine the occurrence of somatosensory changes following a visual distortion of the body. The results demonstrate that illusory stretching or shrinking of the finger changes perceived body shape, whilst retaining ownership. Body ownership over the virtual hand was accompanied by a reduction in liking of that hand, but only in the visuo-tactile conditions. The data

further show that, whilst the general reporting of changes in somatosensations in the finger was low, the stretch/shrink-illusion did increase reports of somatosensation compared to the control. Finally, people with higher somatosensation scores reported lower ownership ratings across all conditions.

These findings are important because they demonstrate that the stretch/shrink-illusion can produce changes in body representation and body satisfaction in healthy participants. Furthermore, the results support previous findings of the ability to take ownership over a virtual limb that is not limited by anatomical constraints and physical appearance. The finding that the illusions change perceived body shape as reflected by perceptual ratings and hand drawings is in line with the first hypothesis and consistent with other studies showing a change in perceived body shape after undergoing bodily illusions (Normand, Giannopoulos, Spanlang, & Slater, 2011; Preston & Ehrsson, 2014; Preston, Kuper-Smith, & Henrik Ehrsson, 2015; Preston & Newport, 2011).

A core aim of the current study was to examine sense of body ownership over the virtual hand, particularly in the context of a longer or shorter finger. The high ownership ratings (min 7.25/10) over the displayed hands demonstrate that the stretch/shrink-illusion changed perceived body shape whilst maintaining ownership. These findings provide further support for the idea that a close resemblance between participant's actual body and the presented external object is not a prerequisite for ownership to occur (Ma & Hommel, 2015). Indeed, in the rubber hand paradigm, the illusion can be induced even though the hand does not entirely match the representation of the actual hand (Longo, Schüür, et al., 2009). Furthermore, in virtual limb

paradigms ownership over a virtual hand can be induced even if it does not meet the anatomical constraints of the actual body (Maselli & Slater, 2013), or even when the hand is completely missing (Schmalzl & Ehrsson, 2011). The current findings thus contrast with the idea of a sole top-down account of body ownership in which the feeling of ownership is constrained by prior knowledge of the body and instead support the idea of an interplay between top-down and bottom-up factors (Longo, Cardozo, & Haggard, 2008).

The findings further demonstrate that participants' sense of body ownership reduced, albeit remaining relatively high, in both multisensory conditions in which both visual and tactile input was provided. The finding of a reduction in ownership after the asynchronous condition is in line with previous findings in both rubber hand (Botvinick & Cohen, 1998) and virtual paradigms (Newport et al., 2010), showing that a conflict between the seen and felt stimulation often results in a loss or reduction of ownership over the fake hand.

However, that the reduction in ownership was apparent in both the synchronous and asynchronous condition suggests that the decrease in ownership is not the mere result of asynchronous multisensory input. Indeed, studies have shown that when the experimental virtual body is realistic and in the same spatial reference frame, as in the current paradigm, incongruent cues do not necessarily diminish the illusion of body ownership. In fact, they are not necessarily perceived as incorrect (Maselli & Slater, 2013). The discrepancy between the visuo-tactile and proprioceptive inputs in relation to the participants' hand in both conditions would constitute an alternative explanation for the difference in sense of ownership between the visuo-tactile conditions and the other conditions.

Nevertheless, despite the reduction in ownership, there was no complete loss of ownership in any of the conditions. That is, participants still reported the virtual hand as belonging to them across all manipulations. Although not directly tested, that the majority of the virtual body was in the same spatial location as the real hand and was coherent with the actual hand in terms of body shape and physical appearance could explain why ownership was still high despite parts of the hands violating anatomical constraints of the body. The current paradigm allows the 'fake' hand to be placed in the same peripersonal space as the real hand, meaning that there are no spatial constraints. This begs the question as to whether some of the previously found constraints in body ownership over artificial limbs and objects are in fact due to anatomical and postural constraints, or whether they may also reflect boundaries of peripersonal space.

Indeed, placing the rubber hand further away from the space surrounding the body reduces the strength of the illusion (Lloyd, 2007). Furthermore, in a recent study Schmalzl & Ehrsson (2011) showed that individuals can take illusory ownership over a full body when there is spatial congruence between visual, somatosensory and proprioceptive information for the majority of body parts, even when part of the virtual body (in this case, resembling an amputated limb) is incongruent with the real body. In contrast, detaching the finger of an embodied limb can not only disembody the detached finger but also the whole remaining limb (Newport & Preston, 2010), suggesting that the role of contextual factors and physiological arousal associated with threat may also play an important role in maintaining or losing the feeling of ownership.

Contrary to the predictions, there were no differences in the responses to the statements between the illusion and vision-only conditions. This contrasts with studies emphasizing the contribution of synchronous visual and tactile information on the feeling of ownership (e.g. Tsakiris & Haggard, 2005). The finding that ownership and a change in perceived body shape was elicited in both the vision-only condition and the visuo-tactile conditions, suggest that there are multiple accounts for the perceived ownership in this and other illusions: mere visual exposure within the spatial boundaries of the real hand and multisensory integration (Longo, Schüür, et al., 2008). This is in line with a small number of studies showing that the rubber hand illusion can be induced with visual exposure alone (Farnè, Pavani, Meneghello, & Ladavas, 2000; Ingvar, 1999; Martinaud, Besharati, Jenkinson, & Fotopoulou, 2016; Pavani, Spence, & Driver, 2000).

Furthermore, in a study of the effects of visual capture of arm position on reaching performance, Holmes, Crozier, & Spence (2004) found that reaching accuracy was significantly lower when participants viewed a mirror image of their left hand (appearing to be their right) compared to a non-mirror condition. When participants moved their mirror-reflected left hand in synchrony with their unseen right hand, participants reported that they felt as if they were viewing their right hand directly. Together, these findings demonstrate the dominance of visual input (visual capture) when conflicting visual-proprioceptive information is given.

The findings of the current study further show that the general reporting of somatosensations in the finger was low, which is perhaps not surprising in light of the high ownership ratings. Indeed, Longo et al., (2009) reported that

following the rubber hand illusion, some participants experienced “pins and needles” in the hand, but only in the asynchronous condition in which the experience of ownership was low (Longo, Schüür, et al., 2009). This is in line with recent findings by McKenzie and Newport (2015), who showed that the reporting of physical sensations is associated with a reduction in ownership over the digitally presented hand.

However, despite the low reports of changes in somatosensation in the finger, the current findings give support for the proposed link between the experience of bodily sensations and the amount of body ownership. That this link was also apparent in the tactile-only condition in which the image was presented without any modifications supports the notion that individuals who report higher amounts of somatosensory sensations might be less aware of sensory signals deriving from one’s own body and more susceptible to anomalous bodily sensations resulting from viewing the body (McKenzie and Newport (2015).

Finally, a significant reduction in liking of the hand was found, but only in the conditions in which the illusion was experienced. Few studies have looked at the relationship between the emotional disposition towards the body and the feeling of body ownership, though Preston and Ehrsson (2014) suggest a link between perceptual and affective body representations, illustrating that they can directly affect each other. Although Preston & Ehrsson (2014) found an increase in body satisfaction following a change in body size, our findings demonstrate that ownership over a hand with a stretched or shrunken finger can significantly reduce body satisfaction. That the reduction in body satisfaction only occurred in the conditions which changed perceived

body shape suggests that the changes in the affective experience of the hand were not merely due to viewing a virtual image of the hand. In fact, I found a positive correlation between ownership and affective experience across all conditions, such that the higher the amount of ownership, the more people liked the hand they were viewing.

Given the apparent link between perceptual and affective body representations, and the fact that emotion can directly influence or exacerbate pain (Melzack & Wall, 1965), the use of the stretch/shrink-illusion opens promising avenues for a range of chronic conditions where pain, body image disturbances and body dissatisfaction may be apparent.

2.5 Conclusions

The present chapter provides evidence for a change in perceived body shape, body satisfaction and somatosensation after ownership over a digitally altered image of the hand is induced. This argues against a pure top-down account for the feeling of body ownership, and demonstrates that ownership over a virtual body can occur even when the body does not satisfy the anatomical constraints of the real body. Having established the ability of these methods to alter body perception and body satisfaction, these methods will serve as a basis for examining the relationship between body representation, body ownership, and pain in the remaining experiments of this thesis.

Chapter 3 Investigating the effects of virtual body ownership on pain and body perception in healthy individuals

3.1 Introduction

The findings in Chapter 2 demonstrated that viewing a virtual hand that appears to be in the same spatial location as the real hand can induce feeling of ownership over that hand, even when it does not necessarily align with the anatomical constraints of the real hand. They further demonstrate that multisensory illusions may be used as a promising tool to alter body perception and investigate the link between body ownership and body image. However, it remains unknown whether ownership over a virtual hand that may be distorted in shape or size can influence pain perception using these methods. The first aim of this study is to investigate the effects of virtual body ownership over a resized hand on pain sensitivity in healthy participants.

As mentioned in the introduction of this thesis, vision of the body, but not necessarily viewing someone else's body, has been found to modulate the experience of pain (Haggard et al., 2013; Martini, Kilteni, Maselli, & Sanchez-Vives, 2015). Research into this area stems from previous findings reporting a strong cross-modal interaction between vision of the body and somatosensation (Longo, Betti, et al., 2009; Martini, 2016). One prominent example is the work from Tipper and colleagues (1998), who showed that viewing the body can lead to faster reaction times for detecting tactile stimuli. Furthermore, it has been shown that mere vision of the hand can enhance processing of sensory information in the somatosensory cortex (Torta, Legrain, & Mouraux, 2015), as measured by the amplitudes of somatosensory event-related potentials (Taylor-Clarke, Kennett, & Haggard, 2002), or improve tactile

acuity measured by two-point discrimination. These studies illustrate that simply viewing the hand can alter the perception of different modalities (Longo, Betti, et al., 2009).

Studies have also focused on the cross-modal effects of vision on the perception of pain. It has been shown that vision of the body can modulate pain, an effect known as visual analgesia. In their study, Longo and colleagues (2009) showed that viewing the hand either directly or indirectly via a mirror can reduce the intensity and unpleasantness of pain following laser stimulation, and can also reduce the amplitude of N2/P2 potentials associated with multimodal neural processing. Again, this effect was only apparent when viewing one's own hand, not when viewing that of the experimenter. In a further study, Mancini and colleagues (2011) asked participants to view their hand through a mirror, using concave or convex mirrors to manipulate the viewed size of the hand in one of three conditions: reduced, actual size or enlarged. They confirmed previous findings of an analgesic effect of viewing the hand compared to viewing an object. They further showed that viewing an enlarged hand increases analgesia, whereas viewing a smaller sized hand reduced the analgesic effect relative to viewing a normal sized hand.

While these experiments clearly show an analgesic effect of viewing the real hand and that a change in perceived body size can affect pain perception, less is known about the effects of viewing a virtual body on pain sensitivity. More specifically, it is not known whether the analgesic effect of embodying a virtual body part can be modulated by distorting the size of the viewed body. A previous study suggests that ownership over a stretched or shrunken hand can be analgesic for people with HOA (Preston & Newport, 2011), however an

understanding of what multisensory components might contribute to this effect is still required.

It has been questioned whether illusory ownership over a body part is crucial for any analgesic effects to occur (Wittkopf & Johnson, 2016). Several studies have shown an effect of viewing the virtual body when passive movements of the virtual finger are synchronous with the real finger and ownership is high, but no analgesic effect when the movement of the virtual body occurs asynchronously with the actual hand and ownership is low. Furthermore, simply viewing a virtual hand appears to be insufficient for the analgesic effects to occur (Martini, Perez-Marcos, et al., 2015; Martini, Perez-Marcos, & Sanchez-Vives, 2014). That the analgesic effect found in these studies was greatest in the synchronous condition, in which the illusions of ownership was higher, indicates that pain intensity is modulated by the degree of ownership over the virtual hand. However, others have argued that the analgesic effects could be explained by simply being immersed in a virtual environment (Gilpin, Bellan, et al., 2014). Indeed, it has been shown that virtual reality on its own can be analgesic due to its interactive properties (Hoffman et al., 2011 as cited in Martini et al., 2014). The present study will include five different conditions, one of which will simply involve viewing the virtual hand without any visual distortions to control for merely being immersed in the mediated reality environment.

Another important and relevant theme emerging from studies investigating the relationship between vision of the body and pain is the apparent link between perceptual and affective body representations and how this might influence pain. As mentioned in Chapter 2, research supports this

finding though the notion that emotion can directly influence or exacerbate pain (Melzack & Wall, 1965).

As highlighted by Martini et al., (2014), to date studies have paid little attention to the role of affective experience during virtual body ownership on pain. As demonstrated in Chapter 2, visually distorting the hand can have a major impact on the affective experience of the embodied virtual hand in healthy controls. It has been suggested that pain may increase following dislike of a body part (Osumi, Imai, Ueta, Nakano, et al., 2014), providing an alternative explanation for the modulatory effect that distorting the visual appearance of the body may have on pain. Therefore, the second aim of the present study is to investigate the affective experience during virtual body ownership and the effect on pain sensitivity in healthy controls using questionnaires and measures of pain sensitivity. To do that, the present study includes additional statements on affective experience, ownership, body representation, and control to more specifically investigate the role of perceptual and affective experience and how it might affect pain sensitivity using the same task. If participants feel negatively towards the virtual body, I might expect this to increase pain (Martini et al., 2015).

Another important distinction between previous research in this area and the current study is in the form of the methods used and specifically, the difference between using a mediated reality paradigm opposed to a virtual reality paradigm (Figure 3.1). Although I will not be comparing the two methods directly, it is expected that in the present study, ownership over the virtual body will remain high (as it did in Chapter 2), as participants will be viewing a live (delay 10ms) video feed of their own hand, as opposed to having to embody a

completely new ‘virtual’ hand. Having established in Chapter 2 that high ownership ratings are associated with the stretch/shrink-illusion, the current study will seek further evidence for the analgesic effects of virtual body ownership after a multisensory induced distortion of body size.

The current study will use an almost identical set-up to that used in Chapter 2, but as there were no significant differences between the stretch and shrink conditions in relation to affective experience, body representation and the perceived body ownership, the present study will use a reduced number of shrink conditions. The guiding rationale for still including one shrink condition is that reducing the size of the hand might still modulate pain sensitivity, as it has in previous studies (Mancini et al., 2011; Newport & Preston, 2011).

Pain sensitivity will be measured using Pressure Pain Thresholds (PPT). Pain sensitivity in experimental settings has been measured using quantitative sensory testing (QST), which investigates the relationship between sensory input and pain perception. PPT are considered as a “static” QST measure as it provides an assessment of the state of the peripheral nervous system and is helpful for detecting altered pain sensitivity (Arendt-Nielsen & Yarnitsky, 2009; Kong, Johnson, Balise, & Mackey, 2013). The current study will also include pain-intensity ratings, as this will provide more insight into the perceptual and affective components of pain (Melzack & Casey, 1968).

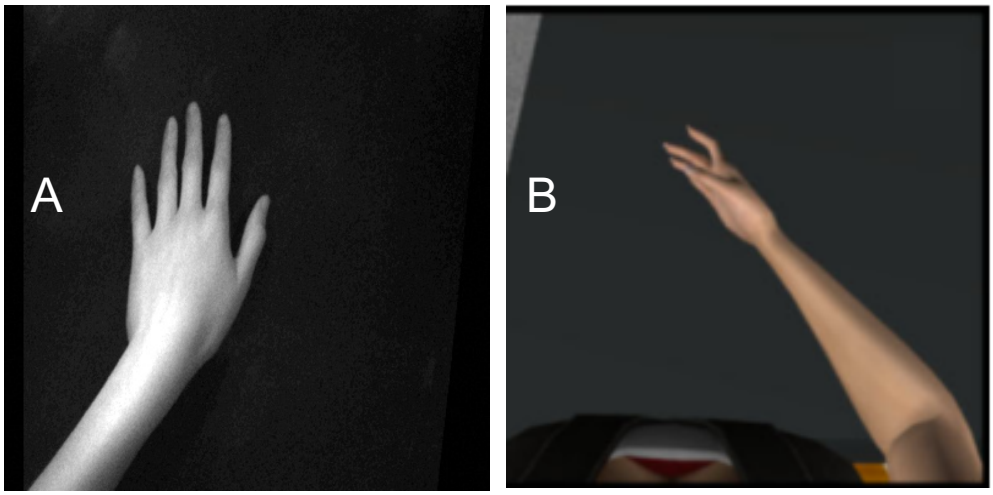


Figure 3.1 Example of the experimental setup up in **A)** the present study using mediated reality (MIRAGE) and **B)** An example of the experimental setup used in Martini et al., (2014) study investigating modulation of pain using a virtual reality set-up where the participant views the body through a head-mounted display.

3.1.1 Summary

To summarise, the current study has two overall aims. First, it will investigate whether visually distorting the size of the virtual hand modulates pain sensitivity, as defined by Pressure Pain Thresholds (PPT) in healthy participants. Although there was no effect of synchronicity on illusion strength as described in Chapter 2, it remains unclear whether both the synchronous and asynchronous conditions would both influence pain sensitivity. Thus, the same asynchronous condition described in Chapter 2 will be included in the current study.

Based on previous findings, the study is expected to find an effect of visual distortion on pain sensitivity (Mancini et al., 2011). It is also expected that a difference will be found in body perception and the experience of pain between the conditions in which participants are simply viewing the hand and in the conditions with visual changes. That is, I would expect enhanced analgesia, as reflected by higher PPT, in the conditions in which the hand was

visually stretched compared to vision of the hand alone. Furthermore, based on findings from previous studies (Mancini et al., 2011), I might expect this effect to be reversed after the shrink-illusion.

The second and final aim of this study is to replicate the findings of a link between perceptual and affective body representation, and further investigate how this might contribute to pain sensitivity or intensity.

3.2 Materials and methods

3.2.1 Participants

The overall sample consisted of 20 healthy participants (17 females, mean age: 19 years, SD = 2.47, 19 right-handed). Originally 21 participants were recruited, but one had to be excluded due to a history of chronic pain. All participants gave informed consent and reported being pain-free on the day of testing, with vision that was either normal or corrected-to-normal. The overall sampling strategy was opportunistic and participants were sampled primarily from the University of Nottingham and mainly recruited via the School of Psychology's Research Participation Scheme (95%) and face-to-face recruitment (5%).

3.2.2 Design

The study used a within subjects repeated measures design with condition (Illusion, vision-only, asynchronous, tactile-only) as the independent variable. The conditions were counterbalanced to control for any order effects. The dependent variables of interest were subjective pain ratings, pressure pain thresholds and the subjective experience of the illusion.

3.2.3 MIRAGE system and experimental conditions

The current study utilised the same apparatus (MIRAGE) as described in Chapter 2. The experimental hand was the dominant hand. The conditions were identical to those used in the experiment in Chapter 2 except for that there were fewer shrink conditions (see Figure 3.2). Thus, there were five conditions in total: two illusion conditions (stretch-illusion and shrink-illusion), one vision-only condition, one asynchronous condition, and one tactile-only (control) condition. During the conditions, half of the screen was made blank so that participants were unable to see their non-dominant hand and that they could focus entirely on the experimental hand. Baseline PPT measurements were taken for both the dominant and non-dominant hand before the start of the experimental conditions, whilst participants viewed their hand inside MIRAGE in the same posture and without any distortion.

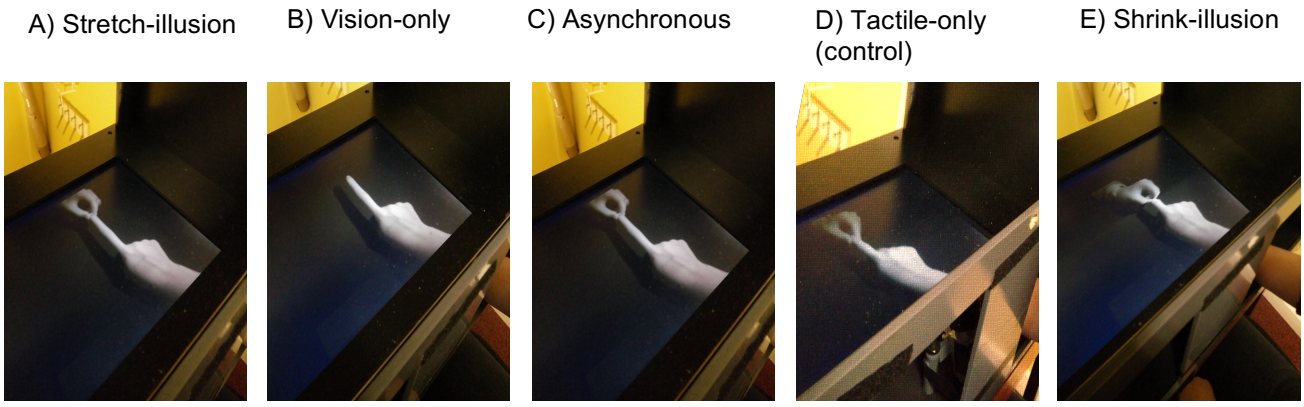


Figure 3.2 Experimental set-up showing the five conditions used in this study. Illusion: the experimenter took hold of the distal part of the index finger and gently pulled (A) or pushed (E) the finger whilst simultaneously increasing or decreasing the visual image of the finger respectively; (B) Vision-only: participants viewed the visual image of the finger getting longer (C); Asynchronous: same as illusion condition except the pull and the computerized stretch or shrink occurred asynchronously (with a ~1 sec. delay); (D) Tactile-only; the experimenter gently pulled the finger without any visual manipulation (control condition).

3.2.4 Outcome measures

Subjective ratings of pain

To capture the objective nature of pain, participants were asked to rate any pain at baseline and on completion of the questionnaire after every condition. An 11-point Numerical Rating Scale (NRS) was used, consisting of integers from 0, representing 'No pain at all', to 10, representing 'Worst pain imaginable'. Participants were asked to select the single number that best described their pain intensity. The NRS has previously been shown to be a valid and reliable tool to measure perceived pain intensity (Ferreira-Valente, Pais-Ribeiro, & Jensen, 2011).

Pressure Pain Thresholds

PPT was measured using a hand-held pressure algometer (Mark-10, Series 3, Compiague, NY, USA) with a $1cm^2$ rubber tip. The study used a testing protocol proposed by Chesterton, Sim, Wright, & Foster (2007), as it demonstrated high reliability (ICC 0.91). PPT measurements were taken on the dorsal interosseous muscle of both the dominant and non-dominant hands. The measurement points were localized and marked with a felt-tipped pen. Prior to formal testing, the procedure was explained and the participant was asked to verbally indicate as soon as the pressure became painful or unpleasant upon which the experimenter immediately ceased pressure. This was repeated at least twice to enable the participant to become familiar with the procedure and learn how to differentiate between tactile and painful stimuli (Chesterton et al., 2007). After each condition, three PPT readings were taken from both points, 10 seconds apart. Steady pressure was applied in an approximate rate of

0.1kg/second. The mean of these three readings was used for statistical analyses as recommended by clinical practice (Chesterton et al., 2007). The participants were unable to see the digital display of the algometer during PPT testing.

Subjective experience of the illusion

A 7-item questionnaire was used to investigate subjective changes in body perception (see Table 3.1)**.** The construction of the items used in this study were partially influenced by Longo and colleagues' (2008) psychometric questionnaire and were further adapted based on the study in Chapter 2. Each item was measured using a 7-point Likert scale, ranging from -3 for *'Totally disagree'* to +3 *'Totally agree'* with the remaining prefixes of 'Neither *agree nor disagree'* on point 0.

3.2.5 Procedure

Prior to the start of the experiment, the method of Pressure Pain Testing was explained and demonstrated and measurement points were marked using a felt-tipped pen. Participants were asked to place their hands inside MIRAGE before taking the baseline PPT measurements. These baseline measurements were always taken before the start of the first condition. Each condition lasted between 3 to 4 seconds. The questionnaire was administered immediately after the first condition, with participants still able to view the experimental hand. This lasted approximately 30 seconds. PPT was performed on the dominant hand immediately following completion of the questionnaire, whilst the other half of the screen remained blank. Consequently, both sides of the

screen were made visible so that participants could see both hands whilst PPT measurements of the non-dominant hand were taken. This meant that in some conditions of the PPT testing, participants were able to view one 'manipulated' and one 'non-manipulated hand'.

Table 3.1 Statements used to measure the subjective experience during the conditions

Category	
Susceptibility	a) It felt as though my hand was being stretched[a]
Ownership	b) I feel like the hand I am looking at is my hand
Agency	c) It feels as though my hand is in my control
Physiological changes	d) My finger feels longer than normal[b]
Affective experience	e) I do not like the way my hand looks now
Control	f) I feel as though I have two right hands

[a] In the shrink-illusion condition 'stretched' was replaced with 'shrunk'.
[b] in the shrink-illusion condition 'longer' was replaced with 'shorter'.

3.2.6 Sample size

Sample size was determined a priori to enable the detection of small effect sizes at a 2-tailed 5% alpha level and with 80% power. Sample size calculation was performed in G*Power (Faul, Erdfelder, Buchner, & Lang, 2009). A minimum sample size of n = 14 was required to detect small effects with an estimated power of 0.80. The effect size for the difference of PPT between conditions was set at 0.20. This effect size is based on effects reported in previous studies employing a similar experimental design (Wand et al., 2014). A power calculation for repeated measures, within factors design was performed for the main outcome measure of PPT over the palm of the dominant hand. Prior research reports that the correlation between three

repeated measures of pressure pain thresholds collected at baseline ranges from 0.91 to 0.95 in healthy controls (Chesterton et al., 2007; Wand et al., 2014). Taking a conservative approach and considering a correlation pattern with a possible decay across time, I set the correlation level among repeated measures to be 0.80 (Guo, Logan, Glueck, & Muller, 2013).

3.2.7 Data analysis

For the outcome measure of Pressure Pain Thresholds, the mean of the three PPT measurements was calculated per condition and used as the data for the main analysis. An additional analysis was performed on the first PPT measurements for every condition, as the first measurement is likely to be most responsive to change (Wand et al., 2014). To determine the intra-rater reliability of PPT testing, the intra-class correlation coefficient (ICC) was calculated over the three baseline measurements. The ICC was computed to test the degree of agreement among the repeated measures, with a two-way random effect model used to determine the ICC value. The Shapiro-Wilks test suggested a highly positively skewed distribution for the Pressure pain thresholds, so data were transformed to meet the assumptions of linear regression using a base-10 logarithmic transformation. An anti-log of the mean of the log10-transformed values was used to present the results as mean (see Table 3.2). For the main analysis, mean Pressure pain thresholds were analysed using a two-way repeated measures ANOVA with condition (baseline, stretch-illusion, asynchronous, vision-only, shrink-illusion, tactile-only (control)) and body site (dominant hand, non-dominant hand).

After exploring the data, the Shapiro-Wilks test and visual inspection of the data suggested a highly-skewed distribution for the questionnaire data which could not be transformed. The intensities of the responses were therefore compared across conditions for each item using the non-parametric Friedman's two-way analysis of variance, followed by the Wilcoxon signed rank test for pairwise comparisons. A Bonferroni correction was applied for the number of possible comparisons resulting in a significance level set at $p < .008$. A similar analysis of the questionnaire data was performed on the subjective ratings of pain, in order to identify any differences between intensities across conditions.

3.3 Results

3.3.1 Pressure Pain Thresholds

The two-way repeated measures ANOVA showed no main effect of condition, $F(5, 85) = 1.185$, $p = .322$, $\eta^2 = .065$, suggesting that the mean PPT was not significantly affected under the experimental conditions. There was no main effect of body site, $F(1, 17) = .266$, $p = .613$, $\eta^2 = .015$, and no statistically significant two-way interaction between condition and body site, $F(5, 85) = .949$, $p = .454$, $\eta^2 = .053$. Analysis of the first PPT scores between conditions for both the dominant and the non-dominant hand showed significant differences between conditions ($p = .034$). Planned contrasts (using Bonferroni) were used to follow up this finding, but did not reveal a significant difference between groups after controlling for pairwise comparisons (all ps $> .008$), thus demonstrating that there was no difference in first PPT scores between the different conditions.

Finally, the intra-rater reliability for the measurement point of the dominant hand determined for the three repeated measures collected at baseline was 0.90 (95% C.I.: 0.80 - 0.96). Though the use of qualitative cut-offs is debated, ICC values above 0.81 are generally considered as having excellent reliability (Landis & Koch, 1977).

Table 3.2 Mean Pressure pain thresholds per condition for dominant hand (DH) and non-dominant hand (NDH) (mean ± standard deviation). An anti-log of the mean of the log10-transformed values was conducted to present the results as mean (SD).

Condition	Mean PPT (kgf)		1st PPT (kgf)	
	DH	NDH	DH	NDH
Baseline	1.56 ± .75	1.72 ± 1.09	1.62 ± .69	1.70 ±1.15
Stretch-Illusion	1.58 ± 1.00	1.64 ± .98	1.46 ± .70	1.45 ±.70
Asynchronous	1.66 ± 1.15	1.59 ± .95	1.53 ± .97	1.60 ± .96
Vision-only	1.62 ± .84	1.62 ± .95	1.60 ± .87	1.52 ± .80
Shrink-illusion	1.54 ± .91	1.53 ± .96	1.52 ± .92	1.53 ± 1.13
Tactile-only (control)	1.66 ± 1.16	1.21 ± 1.44	1.53 ± .89	1.58 ±1.14

3.3.2 Illusion experience

Susceptibility

Statement 1: Friedman's test showed a significant difference in the susceptibility to the illusion across conditions, $\chi^2(4) = 26.50$, $p < .001$. Pairwise comparisons (with a Bonferroni correction for multiple comparisons) revealed a significant difference in the susceptibility to the illusion between the *stretch-illusion, asynchronous*, and *shrink-illusion* conditions compared to the control (all *ps < .008)*, but not between the *vision-only* condition compared to the control (all *ps > .05).* In addition, susceptibility in the *stretch-illusion* condition was significantly greater compared to vision-only ($p = .001$), with no differences

between stretch-illusion and asynchronous (p < .458). Thus, only the conditions with both a tactile and visual manipulation increased susceptibility to the illusion compared to the control (see Figure 3.3A).

Body ownership

Statement 2: To investigate whether the feeling of body ownership changed depending on the condition, ownership ratings were compared across conditions and compared to the control. Friedman's test showed a significant difference in ownership ratings across conditions, X^2 (4) =35.342, p < .001. Pairwise comparisons showed significant differences in ownership compared to control (tactile-only) in the *stretch-illusion, asynchronous, vision-only* and *shrink-illusion* conditions (all *ps* < 0.008). Ownership ratings did not significantly differ between the other conditions of *stretch-illusion vs. asynchronous* (p = .119), and *stretch-illusion vs. vision-only* (p = .49) (see Figure 3.3B).

Agency

Statement 3: Agency ratings significantly changed between conditions, X^2 (4) = 25.567 p < .001. Agency significantly increased in the *stretch-illusion, asynchronous, vision-only* and *shrink-illusion* conditions compared to control (all *ps* < .008). No differences were found between the other conditions. Agency ratings did not significantly differ between the other conditions of *stretch-illusion vs. asynchronous* (p = .88), and *stretch-illusion vs. vision-only* (p = .06) (see Figure 3.3C).

Physiological changes

Statement 4: Participants reported a significant difference in physiological experience between conditions, X^2 (4) = 22.493 *p* <.001. Participants reported their finger to feel longer (or shorter in the shrink condition) in the *stretch-illusion, asynchronous, vision-only* and *shrink-illusion* compared to the control (all *ps* < 0.008). There was no significant difference between the other conditions of *stretch-illusion vs. Asynchronous*, *p = .174,* and *stretch-illusion vs. vision-only (p* = .399) (see Figure 3.3D).

Affective experience

Statement 5: The Friedman test rendered that the extent to which participants 'liked' the way their hand looked differed significantly across conditions, X^2 (4) = 54.476, *p* < 001. It appeared that affective experience significantly decreased in the *stretch-illusion, vision-only, asynchronous* conditions and the *shrink-illusion conditions* compared to the control condition *(*all *ps* < 0.008). There was no significant difference between the other conditions of *stretch-illusion vs. asynchronous* (*p* = .180*),* and *stretch-illusion vs. vision-only (p* = .011) (see Figure 3.3E).

Control

Statement 6: The Friedman test revealed no differences in the responses to the control question between conditions, X^2 (4) = 4.460, *p* = .347. This finding is illustrated in Figure 3.3.

3.3.3 Subjective pain ratings:

A Friedman test was run to determine if there were differences in subjective pain ratings across conditions and this was found to be nonsignificant, X^2 (4) =1.500, p = .827. This finding is illustrated in Figure 3.3F.

3.3.4 Correlation between pressure pain threshold and body ownership

Correlation analysis showed a significant negative relationship between the amount of perceptual change and the amount of body ownership, Pearson's r (17) = .74, p < .01), but only for the shrink-illusion condition. In other words, the higher the amount of shrink reported by the participants, the lower the amount of body ownership. There was no significant correlation between the perceived sense of body ownership, affective experience or perceived body size of the virtual hand and PPT (all *ps* > .05).

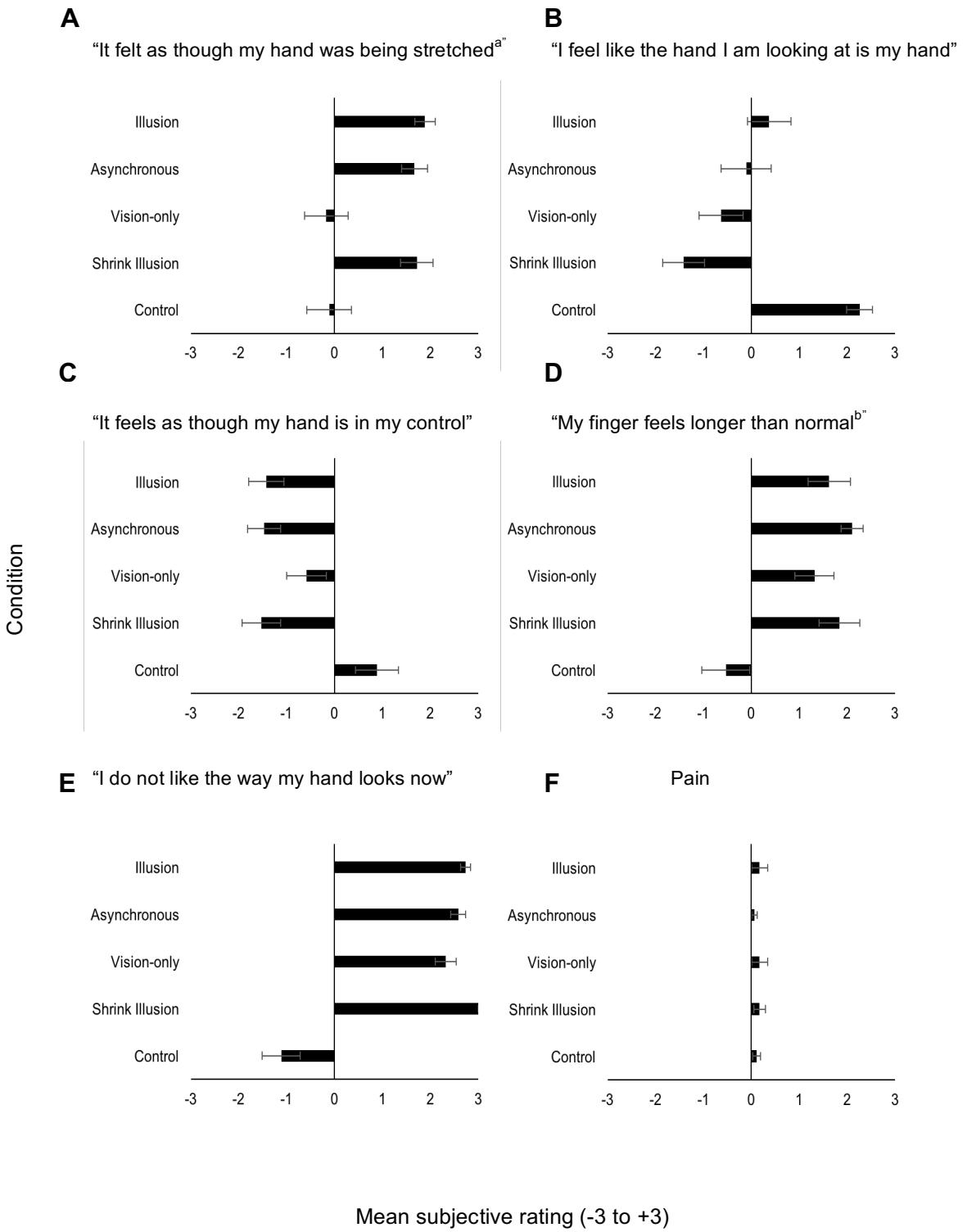


Figure 3.3 Mean subjective ratings of the responses to the statements investigating the experience of the illusion taken after every condition. [a] In the shrink illusion condition 'stretched' was replaced with 'shrunk'.[b] in the shrink illusion condition 'longer' was replaced with 'shorter' Error bars represent one standard error of the mean. -3= no, not at all, +3= yes, lots and lots.

3.4 Discussion

The current study examined whether distorting the size of the virtual hand would modulate pain sensitivity. It also aimed to replicate the findings in Chapter 2 of a relationship between perceptual and affective body representation, and further investigate how this might link to pain. Visually distorting the perceived body size did not affect PPT or pain ratings compared to simply viewing the virtual hand. The data further show that visually distorting the virtual body changes perceptions of body shape and affective experience of the body. Finally, perceptual and affective body representations were not associated with a change in PPT. Despite using a reliable and valid measure of pain sensitivity, support was not found for modulatory effects of multisensory illusions on pain in healthy participants.

Based on previous studies (Mancini et al., 2011; Preston & Newport, 2011), the prediction was that visually distorting body size in the form of stretching or shrinking the finger would modulate pain sensitivity measured by PPT. Contrary to this hypothesis, however, the findings did not yield the predicted results. Indeed, main pressure pain thresholds and pain ratings were almost identical across conditions for both the dominant and the non-dominant hand. This contrasts with the findings reported by Mancini et al., (2011), who showed that distorting the visual size of the hand through the use of convex and concave mirrors modulated pain thresholds for stimuli applied to that body part. Subsequently, the authors suggested a causal effect of alterations in body perception on sensory pain processing.

There are several differences between the findings of Mancini et al., (2011) and the current study, including the methods and experimental design

used. First, Mancini et al., (2011) manipulated the size of the whole hand, whereas in the current study only the finger was distorted in size, whilst the appearance of the rest of the hand was still that of the participant. It is possible that stretching or shrinking the whole hand in the current study would have yielded different results. Indeed, there are well-known limits to the illusion of body ownership over a virtual limb, resulting from top-down knowledge (Slater, Spanlang, Sanchez-Vives, & Blanke, 2010). The current findings show a significant loss of ownership in the conditions in which the distortion took place. As discussed previously, some studies have found a modulation of pain thresholds, but only when people reported ownership over the virtual body (Martini et al., 2014). This could explain why in the current study there were no changes in pain sensitivity or pain ratings after distorting the hand compared to control, in which ownership remained high.

However, a sensitivity analysis of only the first PPT, taken immediately following completion of the questionnaire, showed a trending effect towards a reduction in pain thresholds after the stretch-illusion compared to the control. Although this effect is not significant after the correction of multiple comparisons, it hints that there might be an effect of visual distortion on PPT, but that this effect may be very transient. However, as this effect is only trending towards significance, no strong claims can be made.

Additionally, the finding of loss of ownership after the illusory conditions is in contrast with the results of Chapter 2 in which, despite a significant reduction of ownership, there was no complete loss of ownership in any of the conditions. This could be due to differences in the type of scale used and

indeed, the effect of distortion on ownership will be further investigated in Chapters 5 and 6.

With respect to the second aim, the study replicated the findings of Chapter 2, which showed that visually distorting the virtual body changes perceived body shape and the affective experience of the body. Resizing the hand or distorting parts of the painful body seems to reduce pain in some chronic conditions (Diers et al., 2013; Moseley, Parsons, et al., 2008; Newport & Preston, 2011; see Boesch et al., 2015 for a review). The feeling of ownership, restoration of a normal body representation, reduction of apparent swelling and reduction of anxiety and fear associated with the appearance of the affected limb (Giummarraa, Georgiou-Karistianis, Verdejo-Garcia, & Gibson, 2015; McCabe, 2011b; Moseley, 2011), have all been suggested as possible mechanisms underlying the analgesic effects.

More recently, it has been proposed that the affective experience towards the painful body part might play a role in the experience of pain of that body part (Osumi, Imai, Ueta, Nakano, et al., 2014; Osumi, Imai, Ueta, Nobusako, & Morioka, 2014). For instance, Osumi, Imai, Ueta, Nobusako, et al., (2014) found that PPT decreased when participants viewed a magnified mirror image of their body, which was associated with a negative emotional experience. Despite the observation that pain sensitivity was not modulated by the affective experience of the virtual body, the current findings show a clear link between body perception and the affective experience of the virtual body. That is, the findings demonstrate an increase in dislike of the hand following a perceptual distortion of the hand compared to control (tactile-only). How this might relate to chronic pain will be further investigated in Chapter 5 and 6.

Since the purpose of the study was to investigate the effect of distorting the visual size of the virtual hand on pain sensitivity, I compared the conditions in which the resizing occurred to a control condition where people were viewing the virtual hand without any visual distortions. It is possible that the reasons for not finding any differences in pain sensitivity may be due to the fact that I did not compare viewing the virtual hand with viewing the real hand outside of the virtual setup (Martini et al., 2014), or investigate the differences in pain sensitivity in reference to viewing an non-corporeal object (Mancini et al., 2011). Indeed, it is possible that viewing the virtual hand, independent of a distortion in size, is sufficient to reduce pain compared to viewing a neutral object. A recent study lending support for this theory showed that the analgesic effect of viewing an artificial limb is similar to that of viewing one's own body (Hegedüs et al., 2014). The effects of the stretch/shrink-illusion compared to viewing an object or real hand outside of the virtual set-up will therefore be further investigated in Chapter 5 and Chapter 6. However, I did not find evidence for an effect of visual distortion of the virtual hand on pain compared to simple viewing the virtual hand.

Finally, it may be possible that despite following a standardised protocol, the reason for not finding any changes in pain sensitivity could be due to the location of the PPT measurement. Fernández-De-Las-Peñas et al., (2010) reported topographical pressure pain sensitivity maps of the hands in both clinical and healthy populations, showing that pressure hyperalgesia – that is, increased pain from a stimulus that usually provokes pain - is not uniformly distributed over the palm of the hand. In other words, PPT levels differ depending on the anatomical location and even vary depending on which

hand is measured or the size of the probe used (Fernández-De-Las-Peñas et al., 2010). It has been suggested that spatial specificity is important in pain-body interactions (Haggard et al., 2013) and I can therefore not rule out the possibility that changing the location of PPT measurements may have yielded different results.

3.5 Conclusions

The current study did not find support for a modulation in PPT or subjective pain scores after visually distorting the virtual hand compared to simply viewing the virtual hand in healthy controls. However, it replicated the findings of Chapter 2, showing that visual changes in body appearance are sufficient to elicit changes in body representation, body ownership and affective experience of the hand. The latter findings are particularly important as they demonstrate that these methods invoke changes in body perception and body satisfaction, which may be of clinical importance in chronic conditions where pain, body images disturbances and body dissatisfaction may be apparent, such as osteoarthritis. Thus, Chapters 5 and 6 of this thesis will investigate the effects of these illusions on pain, body perception, and body satisfaction in participants with painful HOA.

Chapter 4 Motor Imagery performance in people with hand osteoarthritis

4.1 Introduction

The findings of Chapter 2 and 3 demonstrated that our body representation is malleable and that the perception of our body, including the conscious body image, can be altered using bodily illusions. The aim of this chapter is to further investigate mental representations of the hand in people with and without osteoarthritis of the hands (HOA), before moving on to investigate the analgesic effects of multisensory illusions in people with HOA in Chapter 5. Specifically, this chapter will focus on performance in a motor task involving left/right laterality judgements and the effect of seeing the self and others in different perspectives (i.e. first person vs third person). This task will be used as a means of investigating whether those with OA present with a distorted representation of the affected body part when a more objective measure of body schema is used.

An intact body schema is important for the actual accomplishment of a movement and for maintaining posture, which involves certain motor capacities and abilities (Newport et al., 2010; Schwoebel & Coslett, 2005). In order to move around in a room or reach to grasp an object in front of us, one has to have a frame of reference and a representation of the body in relation to other objects or people around us (Holmes & Spence, 2004). Furthermore, from a developmental perspective the development of the body schema is critical for social interactions and distinguishing the self from others, as it not only relies on action but also on perception of the world around us (Assaiante et al., 2014).

As mentioned in the introduction of this thesis, several cortical and subcortical areas are thought to underlie the representation of the body, including the somatosensory cortex, parietal cortex, insula and the extrastriate and fusiform body areas (Berlucchi & Aglioti, 2010; Dijkerman & De Haan, 2007; Tsakiris, 2010). As the body schema is not represented in a single area in the brain, it is difficult to use brain imaging techniques to tell us more about the state of the working body schema (Bray & Moseley, 2011; Moseley & Flor, 2012). An alternative and commonly used approach is the use of behavioural measures, for example, evaluating motor imagery performance using a left/right hand judgment task. Both imagining a movement using motor imagery and actually performing the action are thought to share common cortical circuits, as evidenced by behavioural studies and data from fMRI and transcranial magnetic stimulation studies (Coslett, Medina, Kliot, & Burkey, 2010; Decety, 1996). Moreover, motor imagery is limited by the body's constraints in movement, in that it takes longer to imagine a movement when it is in an implausible anatomical position (Parsons, 1994).

In the hand laterality task, individuals view images of hands and are asked to decide whether the image they are viewing is of a left or right limb. The ability to distinguish between left or right is essential for spatial cognition and future planning, and the task has been used to test for an intact body schema as it is thought to rely on the mental rotation of that body part (e.g. Parsons, 1987a; Schwoebel & Coslett, 2005; Schwoebel, Friedman, Duda, & Coslett, 2001).

The left and right judgement task often has two main outcome measurements: accuracy and reaction time. Accuracy, measured in terms of

percentage correct, is used to provide information about acuity of the working schema or the representation of the space surrounding the body. Reaction times reflect the time it takes to decide on sidedness (Moseley & Flor, 2012; Stanton et al., 2012). According to the Confirmation Method (Parsons, 1987b), when individuals are faced with an image of a left or right hand they mentally manoeuvre their own hand in order to come to a decision. This is evidenced by individuals often spontaneously rotating their own hands to match the presented image, as well as reaction times reflecting the degree of rotation such that larger response times occur when images are displayed at a 180° third-person perspective rather than a 0° first-person perspective. Moreover, in healthy controls accuracy is generally lower when an image of a hand is displayed in third-person rather than first-person perspective (Schwoebel et al., 2001).

Motor imagery in chronic pain has been investigated by several studies with sometimes conflicting results. Schwoebel et al., (2001) examined the effects of pain on the working schema in patients with unilateral Complex Regional Pain Syndrome (CRPS), using a hand laterality judgement task. In this study, participants were presented with pictures of a left or right hand presented either at 0°, 90° medial, 90° lateral or 180° (see Figure 4.1). In line with previous findings, participants' reaction times reflected the degree of mental rotation, with an effect of orientation on accuracy scores which was similar for patients and controls. Furthermore, they found that participants with CRPS displayed significantly slower reaction times for images in the same orientation as their affected hand compared to their non-affected hand. This was taken as evidence that the mental representation of the body may be influenced by pain.

These results of the painful limb on motor performance have since been replicated by several studies in a range of chronic pain conditions (Moseley, 2005b; Moseley, Nicholas, & Hodges, 2004).



0° (1pp) 90°M 90°L 180°(3pp)

Figure 4.1 Example of left/right stimuli presented at different orientations. Adapted from "Pain and the body schema Evidence for peripheral effects on mental representations of movement", by Schwoebel et al., 2001, *Brain, 124,* 2098-2104.Copyright 2001 by the Oxford University Press. 1pp = first person perspective, M = medial, L=lateral, 3pp = third person perspective.

Hudson, McCormick, Zalucki and Moseley (2006) examined whether the difference in reaction times on the hand laterality task represents a bias in information processing. Here, a group of asymptomatic participants performed the laterality task under three different conditions: with hypertonic saline induced hand pain, during the anticipation of hand pain, and a control. They found that both the experience of pain and the expectation of pain resulted in an increase in reaction times, which they interpreted as a bias in information processing towards pain or the expectation of pain. However, as the authors pointed out, here the experience of pain or expectation of pain led to a delay to recognise the other hand, contrary to the results observed in CRPS patients where there is often a delay to recognize the painful hand (Moseley, 2004a;

Schwoebel et al., 2001). The discrepancies in these findings are perhaps not entirely surprising given the fundamental differences between clinical and experimentally induced pain and between CRPS and other chronic pain states (Hudson et al., 2006).

Recent research carried out by Stanton and colleagues (2012) focused specifically on motor imagery performance in individuals with knee osteoarthritis. In this study, participants were shown images of hands and feet and were asked to discriminate between left or right. They found reduced accuracy for the OA group and a spatially defined effect of pain compared to healthy controls. That is, if left-sided pain was present, accuracy on images of the left limb was worse but not for the other way around. It has been argued that this could be the result of spatially defined disruptions in sensory processing, as seen in patients suffering from CRPS (Moseley et al., 2009). Namely, when individuals with CRPS undergo a temporal-order judgement task they tend to prioritize stimuli to the unaffected arm, however, crossing the limbs over the body midline leads to a reversal of that effect. A spatially defined effect of pain has since been implicated in patients with lower back pain (Moseley, Gallagher, & Gallace, 2012) and crossing the hands has been found to impair the temporal order judgement of not only tactile but also nociceptive stimuli (Sambo et al., 2012); an effect since termed, ‘crossed-hands analgesia’ (Torta et al., 2013).

Several studies have provided evidence for the laterality task as a measure of the integration between the working body schema, information processing and premotor processes (Bray & Moseley, 2011; Hudson et al., 2006; Reinersmann et al., 2012). As discussed in Section 1.4.3, stimuli are

processed more quickly when they depict information of our own body as opposed to someone else's (Ferri, Frassinetti, Costantini, & Gallese, 2011). Individuals with chronic pain tend to perform worse on a hand laterality motor task, with some studies showing difficulties in recognising images that correspond to the laterality of the affected limb (Bowering et al., 2012; Moseley, 2004b; Schwoebel et al., 2001; Stanton et al., 2012). Despite the widespread use of the hand laterality task, very few studies appear to have looked at the effects of viewing images of one's own body versus someone else's in chronic pain. This is important to investigate as it might reveal that those with hand OA present with a bias in the processing of information related to someone else's healthy limbs, in line with a distorted representation of the affected body part.

The current study used a novel approach to investigate motor imagery performance in people with HOA and the effects of personal body-relevant information (own affected limb) versus general body-relevant information (pictures of someone else's limbs). Participants placed both hands into the MIRAGE whilst vision of the hands was occluded, and viewed images of both their left or right hand, or someone else's hand, displayed at different angles. The experiment consisted of a 10-minute computer task that involved left/right judgements to investigate how chronic pain status may influence the ability to recognise body parts. The performance on the hand laterality test was tested and compared with a group of healthy controls.

Based on previous research it was hypothesised that left/right performance for the OA group would be worse compared to the HC group. Moreover, it was hypothesised that people with painful HOA would be slower and less accurate in recognising their affected hand and when images are displayed in third-

person versus first-person perspective. Combining this left/right judgement task with images of “own hands” versus “other hands” will provide important information about how our brain processes personal body-relevant information (our own hands) versus body-relevant information of others (pictures of someone else’s hands).

Moreover, recent research into the perceived size or shape of the painful area of the hand has found that people with HOA perceive their affected hand to be smaller compared to healthy controls, suggesting a distortion of the mental representation of the affected body part (Gilpin, Moseley, et al., 2014). As the laterality task requires the participant to first recognize the image of the hand, it can be speculated that presenting the image of the hand in coherence with the perceived hand size might aid the recognition of that body part. To test this hypothesis, the image of the hand was presented in three different sizes (small, normal, large).

4.2 Materials and methods

4.2.1 Participants

Two groups of participants took part in this study. The first group consisted of 32 volunteers with confirmed HOA (mean age 70.34 years, SD = 6.03. 24 females, 22 right handed). The second group consisted of 16 healthy controls (mean age = 63.5, SD = 3.705, 4 females, 13 right handed) without a history of other chronic pain or rheumatic conditions. Participants gave informed consent and completed a questionnaire providing demographic information (see Table 4.1).

Table 4.1 Participant demographics

#	Group	Age	Gender	Handedness	Pain location	Most affected hand	Occurrence hand pain 12m	Chronicity	Pain intensity			Function		Medication
									Current pain 0-10	Pain all joints >48h	Pain most painful hand > 48 h	Satisfaction with function 48 h [b]	FIHOA (0-30) [c]	
1	HOA	74	Male	Right	Both hands	No difference	>3 months	5-10 years	5	5	6	7	6	Missing
2	HOA	65	Female	Right	Both hands	No difference	>3 months	>10 years	3	9	9	9	20	Co-codamol, morphine, aspirin, omeprazole, levothyroxine, rosuvastatin
3	HOA	74	Female	Right	Both hands	Right	>3 months	>10 years	3	5	5	2	8	Paracetamol, tramadol
4	HOA	80	Male	Right	Both hands	Right	>3 months	>10 years	0	1	1	3	10	Missing
5	HOA	65	Female	Both	Both hands	Right	>3 months	5-10 years	9	8	9	4	18	Paracetamol, co-codamol
6	HOA	86	Female	Right	Left hand	No difference	>3 months	5-10 years	5	5	5	3	17	Ibuprofen
7	HOA	70	Female	Right	Both hands	Right	>3 months	5-10 years	6	7	8	6	13	Paracetamol, amlodipine, gabapentin, naproxen, omeprazole, tramadol
8	HOA	72	Female	Left	Both hands	Left	>3 months	>10 years	0	4	6	2	10	None
9	HOA	68	Female	Right	Both hands	No difference	>3 months	5-10 years	5	6	7	4	12	Paracetamol and codeine
10	HOA	61	Female	Right	Both hands	Right	<7 days	>10 years	0	4	6	6	2	Paracetamol, ibuprofen, codeine
11	HOA	75	Female	Right	Both hands	No difference	>3 months	>10 years	2	2	2	2	10	None
12	HOA	68	Female	Right	Both hands	Left	>3 months	>10 years	5	5	5	4	8	Codeine phosphate
13	HOA	67	Female	Right	Both hands	Right	1-4 weeks	1-5 years	5	5	7	4	11	None
14	HOA	77	Male	Left	Both hands	Right	>3 months	1-5 years	1	7	8	7	12	Paracetamol, meloxicam
15	HOA	67	Female	Left	Right hand	Right	>3 months	5-10 years	5	7	7	5	12	None
16	HOA	62	Male	Left	Left hand	Left	>3 months	>10 years	9	9	9	9	15	Antidepressants
17	HOA	60	Female	Right	Both hands	No difference	>3 months	>10 years	4	6	7	5	10	None
18	HOA	77	Female	Right	Right hand	Right	>3 months	<12 months	7	7	7	7	15	Paracetamol, ibuprofen, Morphine patch
19	HOA	74	Male	Both	Both hands	Right	>3 months	5-10 years	1	8	8	6	8	Morphine patch

20	HOA	77	Female	Right	Both hands	Right	>3 months	>10 years	3	8	7	6	15	Ibuprofen
21	HOA	77	Female	Right	Both hands	No difference	>3 months	>10 years	6	9	9	8	19	None
22	HOA	69	Female	Right	Both hands	left	>3 months	5-10 years	5	6	7	5	8	Co-codamol, antidepressants
23	HOA	71	Female	Right	Both hands	Right	>3 months	5-10 years	5	5	8	6	10	Ibuprofen
24	HOA	62	Female	Right	Both hands	Right	>3 months	>10 years	1	1	2	1	3	Missing
25	HOA	78	Male	Right	Right hand	Right	>3 months	5-10 years	1	4	4	5	11	Missing
26	HOA	64	Female	Right	Both hands	Left	>3 months	<12 months	0	4	5	4	6	Missing
27	HOA	85	Male	Right	Both hands	Right	1-4 weeks	>10 years	0	0	0	5	9	Missing
28	HOA	70	Male	Right	Both hands	Right	Missing	Missing	0	Missing	Missing	Missing	Missing	Missing
29	HOA	62	Female	Right	Both hands	Right	>3 months	5-10 years	5	4	4	5	5	Missing
30	HOA	71	Female	Right	Both hands	Right	>3 months	5-10 years	0	2	3	6	8	Missing
31	HOA	69	Female	Right	Right hand	Right	1-3 months	<12 months	1	1	1	1	0	Missing
18	Control	64	Female	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a	n/a
19	Control	64	Male	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a	n/a
20	Control	65	Female	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a	n/a
21	Control	60	Female	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a	n/a
22	Control	66	Female	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a	n/a
23	Control	58	Male	Left	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a	n/a
24	Control	61	Male	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a	n/a
25	Control	65	Male	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a	n/a
26	Control	66	Male	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a	n/a
27	Control	69	Male	Left	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a	n/a
28	Control	61	Male	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a	n/a
29	Control	65	Male	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a	n/a
30	Control	58	Male	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a	n/a
31	Control	60	Male	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a	n/a
32	Control	68	Male	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a	n/a
33	Control	70	Male	Left	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a	n/a
34	Control	68	Male	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a	n/a
35	Control	66	Female	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a	n/a
36	Control	65	Female	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a	n/a

= participant number [a] Pain intensity measured on a 0-10 numerical rating scale (NRS) rated from 0=no pain at all to 10=worst pain imaginable. [b] 0=very satisfied, 10= not at all satisfied. [C] higher scores denote decreased hand function.

4.2.2 Laterality judgment task

Stimuli for laterality judgements were presented using the MIRAGE system and the task was created using a LabVIEW (National Instruments, Austin, TX) script. In this task, participants were asked to place both hands inside MIRAGE whilst they viewed images of both their left and right hand and previously recorded images of someone else's hands on the MIRAGE screen, either presented in 0° first-person (1pp) or 180° third-person (3pp) perspective (see Figure 4.2). The 'other' hand was always of another person of the same sex as the participant. Images were displayed centrally on the screen, and always at an angle of 30° to the left or the right of the sagittal plane so as to control for confirmation bias.

Participants were asked to indicate whether the image was of a left or right hand by pressing one of the foot pedals under their feet, with the left foot pedal assigned to left hand images and vice versa. As soon as the participant pressed the foot pedal, the next image appeared. In case of a 'no press' eventuality, the image was automatically advanced after 8000ms and no press (NP) was recorded for that stimulus. The task consisted of two blocks of 1.5 minutes each with a maximum of 50 images per block (100 in total). The task duration was fixed to limit discomfort caused by participants needing to keep their hands in the same position. The order of orientation, side of hand, and display of self/other hand were randomised within and between participants and reaction times and accuracy of trials were automatically recorded.

In order to control for participants using any distinctive characteristics of the hands to help identify the hand from left or right or self and other, the image of the hand could be mirrored so that the participant's right hand was

displayed as a left hand and vice versa. To investigate whether the size of the hand would influence laterality judgements, images were either displayed as small (80% of actual size), normal (100% of actual size) or large (125% of actual size). Images could be displayed in four views (Left hand as left, left hand as right, right hand as left, and right hand as right), four perspectives (self in 1pp (SS), self in 3pp (SO), other in 1pp (OS), and other in 3pp (OO) and three sizes (small, normal, large).

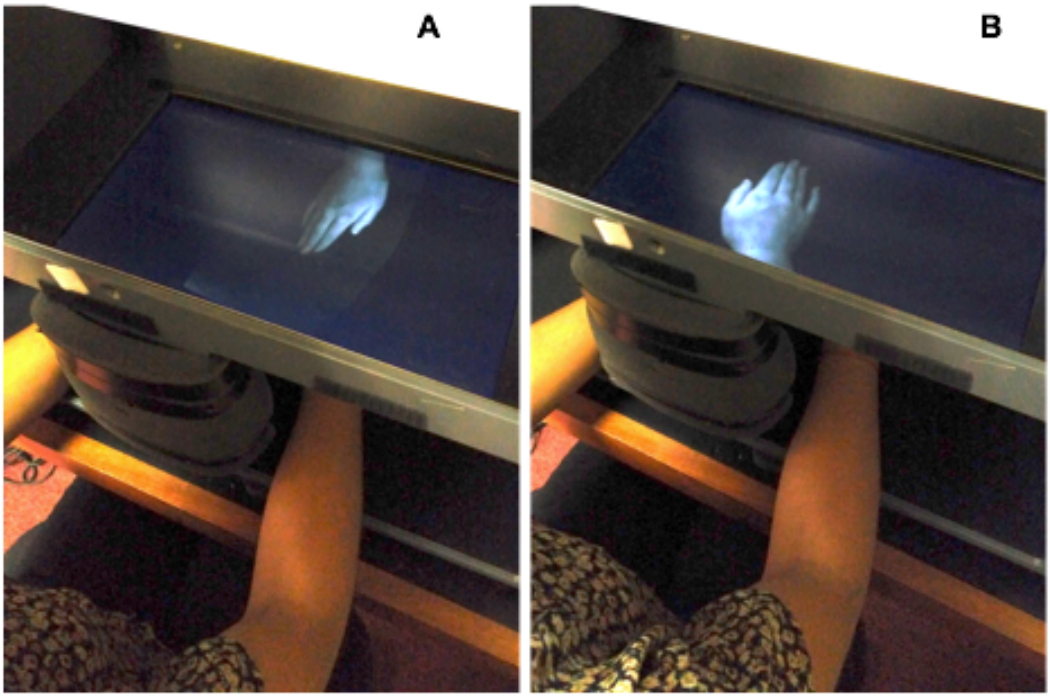


Figure 4.2 Experimental set-up. Example of a stimuli presented in 3pp (A) and 1pp (B).

4.2.3 Procedure

Participants were asked to remove any jewellery or watches from their hands to prevent them from using these as cues for identifying the hand. Care was taken to explain that images of the participant's hand could be mirrored, and that they could be viewing images of their hands or someone else's hands. Participants sat in front of the MIRAGE system and were asked to place both

hands inside. Participants were instructed not to move their head or hands during the conditions. The first trial was given as a test trial to familiarize the participants with the laterality task and the experimental set-up. After completion of the test trial and having understood the task, participants completed the two parts. A short break in between the blocks was introduced in which participant could take their hands out of MIRAGE. Participants were asked to respond as quickly and accurately as possible, and no feedback was provided during or between the trials.

4.2.4 Data analysis

Prior to running the analysis, a number of assumptions were evaluated. Accuracy data were normally distributed as assessed by Shapiro-Wilk's test of normality. Outliers were assessed through examination of studentized residuals for values greater than ±3, and checked for data or measurement errors. After it was established that data points were referring to genuinely unusual data points, whether the outliers had an appreciable effect on the analysis was evaluated by running the analysis with and without the outlier(s) included in the analysis and the patterns of results remained the same. The reaction time data were not normally distributed and analysis were run on transformed and non-transformed data to see if there were any meaningful differences in statistical conclusions. The pattern of results remained the same, thus the results reported below refer to the non-transformed data. In cases where Mauchly’s test of sphericity was significant, the Greenhouse-Geisser correction was used for the data set.

The main outcome measures were accuracy (percentage of correct trials) and reaction times (RTs). Trials for which “no press” was recorded (> 8000ms) and trials with a reaction time <500ms were discarded, which equated to being more than 2.5 deviations from the mean. Furthermore, only RTs of correct trials were included in the analysis (Parsons, 1987a).

A one-way ANOVA was conducted to determine if general performance on a laterality judgement task differed between HOA and HC for both accuracy and reaction times. Data met both homogeneity of variances (p > .05), as assessed by Levene’s test of homogeneity of variances. All HOA participants were included, regardless of their baseline pain scores measured using a 0-10 NRS.

The effect of most painful hand on perspective and viewing the self or others was investigated using a three-way mixed ANOVA with limb (Most painful and Least painful) and perspective (self in 1pp (SS), self in 3pp (SO), other in 1pp (OS), and other in 3pp (OO)), with group (HOA and HC) as the between-subjects factor for both accuracy and RTs (for HC, limb refers to the non-dominant and dominant hand respectively). For the HOA group, only individuals with current and predominantly unilateral pain of > 3 (NRS) were included in the analysis.

The effect of body size on laterality performance was investigated using a three-way mixed ANOVA with limb (Most painful and Least painful) and size (small, normal, large) as the repeated-measures factors, with group (HOA and HC) as the between subjects’ factor for both accuracy and RTs (for HC, limb refers to the non-dominant and dominant hand respectively). For the HOA

group, only individuals with current and predominantly unilateral pain of > 3 (NRS) were included in the analysis.

To ensure that participants were not using distinctive characteristics of the hands to help identify the hand in the laterality task, a two-way mixed ANOVA was run with image display (left hand as left, left hand as right, right hand as left, right hand as right) as the within-subjects factor and group (HOA and HC) as the between-subjects factor for both accuracy and RTs.

4.3 Results

On average, the HOA group responded to 68 images (*SD* = 15) and the healthy control group responded to 60 images (*SD* = 16). As the mean age of the HOA group was slightly higher than the HC group, a sensitivity analysis was performed using a one-way ANOVA with age entered as a covariate, for both accuracy and RTs. Age was not related to reaction times ($p = .421$) or accuracy ($p = .902$) of left/right judgments, and entering age as a covariate did not change the results of the analysis.

4.3.1 General performance of left/right judgements

Mean accuracy scores did not significantly differ between HOA participants (*M* = 47.99%, *SD* = 5.90) and HC (*M* = 50.69%, *SD* = 6.40), $F(1, 46) = 2.120$, $p = .152$, $\eta^2 = .044$. Consistent with the accuracy data, mean reaction times did not significantly differ between HOA participants (*M* = 1786 ms, *SD* = 571 ms) and healthy controls (*M* = 1634.35 ms, *SD* = 436.88), $F(1, 46) = 868$, $p = .356$, $\eta^2 = .019$.

To investigate whether current pain influenced general motor imagery performance, the analysis was re-run only including HOA participants with a baseline NRS score > 3. The pattern of results remained the same for both accuracy and reaction times.

4.3.2 Effect of most painful hand on perspective and viewing the self or others

Effect of most painful hand on accuracy

A three-way mixed ANOVA found a statistically significant three-way interaction between limb, perspective, and group, $F(3,102) = 3.330$, $p = .023$, partial $\eta^2 = .089$. There was a trend toward an simple two-way interaction between limb and perspective for the HOA group, $F(3,57) = 2.599$, $p = .064$, partial $\eta^2 = .119$, and a statistically significant simple two-way interaction between limb and perspective for the HC group, $F(3,45) = 3.018$ $p = .040$, partial $\eta^2 = .167$. For the HOA group, there was a significant simple main effect of perspective when the image was of the participant's most painful hand, $F(3,60) = 4.462$, $p = .007$, partial $\eta^2 = .182$, but not when the image was of the participant's least painful hand, $F(3,575) = .349$, $p = .790$, partial $\eta^2 = .018$. There was a trend towards a statistically significant simple main effect of perspective for the HC group when the image was of the participant's dominant hand, $F(3,45) = 2.513$, $p = .070$, partial $\eta^2 = .143$, but not when the image was of the participant's non-dominant hand, $F(3,45) = 1.529$, $p = .220$, partial $\eta^2 = .092$.

Data are mean ± standard deviation unless otherwise stated. Bonferroni corrections were made with comparisons within each simple main effect considered a family of comparisons. Adjusted *p*-values are reported. For the

HOA group, accuracy was highest when the image was of the participant's dominant hand displayed in 1pp (SS), (53.81%, *SD* =19.72), and lowest when the image was of someone else's hand displayed in 3pp (OO), (38.89%, *SD* = 11.22). There was a significant mean difference between the SS and OO trials of 14.91% (95% CI, 3.23 to 26.61), $p = .008$, but not between the other trials (all *Ms* < 10.96 all *ps* >.05). For the HC group, accuracy was also highest when the image was of the participant's dominant hand displayed in 1pp (SS), (57.97%, *SD* =16.61), and lowest when the image was of someone else's hand displayed in 1pp (OS), (43.429%, *SD* = 18.58). There was a trend towards a statistically significant mean difference between the SS and SO trials of 13.20% (95% CI, 1.19 to 27.60), $p = .083$, but not between the other trials (all *Ms* < 14.56, all *ps* >.05).

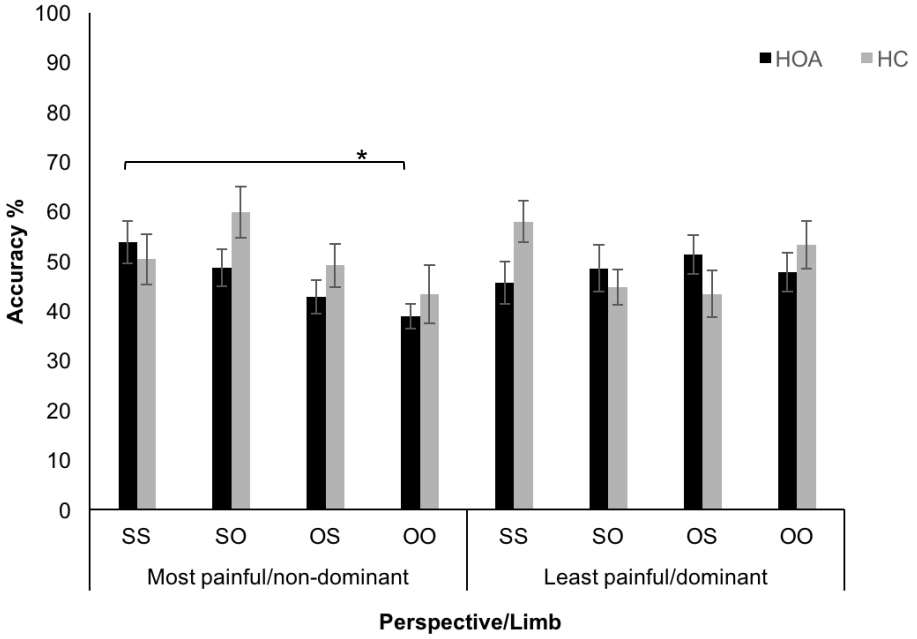


Figure 4.3 Mean accuracy for laterality judgments involving the most painful and least painful limbs of HOA participants in the four different perspectives (for HC, limb refers to the non-dominant and dominant hand). For the HOA group, accuracy scores were significantly higher for the most painful hand when displayed in the SS perspective compared to the OO perspective. For the HC group, there was a trend towards a significant difference in accuracy between the SS perspective compared to the SO perspective. SS= self in 1pp, SO= self in 3pp, OS= other in 1pp, OO= other in 3pp Error bars represent standard error of the mean. * represents statistically significant at the p < .05 level.

Effect of most painful hand on reaction times

A three-way mixed ANOVA found no significant effect of group upon reaction times of the limb displayed in different perspectives, $F(3,93) = 1.123$, $p = .344$, $\eta^2 = .035$. No other main effects or interactions were significant at $p > .05$ (see Figure 4.4).

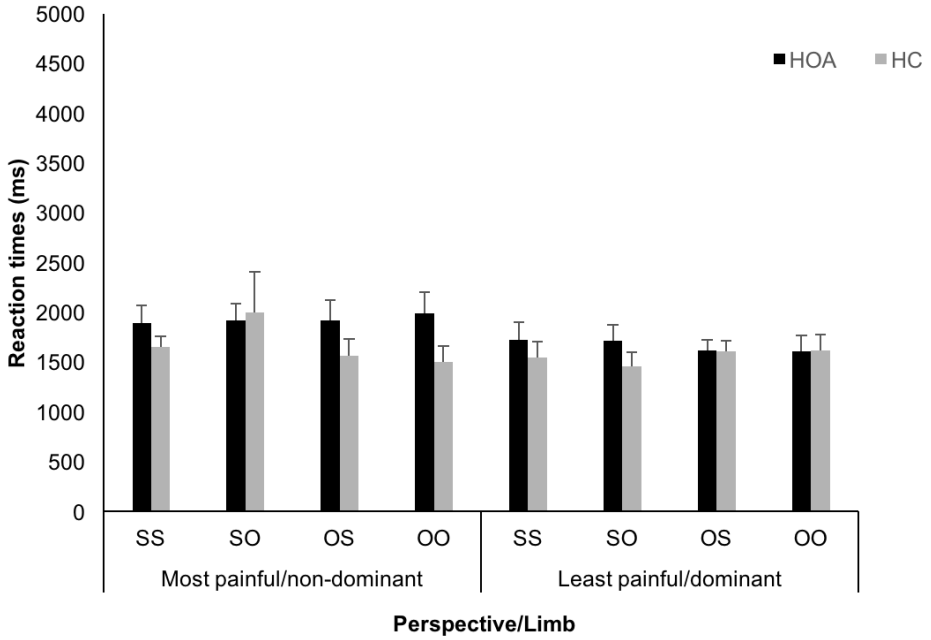


Figure 4.4 Mean reaction times for laterality judgments involving the most painful and least painful limbs of HOA participants in the four different perspectives (for HC, limb refers to the non-dominant and dominant hand). SS= self in 1pp, SO= self in 3pp, OS= other in 1pp, OO= other in 3pp. Error bars represent standard error of the mean.

4.3.3 The effect of body size on mental rotation

The effect of body size on Accuracy

The three-way mixed ANOVA on accuracy scores indicated that there was a main effect of image size on accuracy, $F(1.705,61.377) = 8.071$, $p = .001$, $\eta^2 = .183$, and a significant two-way interaction between size and group, $F(2, 72) = 4.130$, $p = .020$, $\eta^2 = .103$. The significant interaction was followed up with two-way ANOVA's (limb x size) for the HOA group and the HC group separately.

There was a significant main effect of size on accuracy for the HOA group, $F(2,42) = 4.215$, $p = .021$, partial $\eta^2 = .167$, with HOA participants exhibiting highest accuracy for the limb when displayed smaller than normal (M=51.80%, SE = 1.71), and lowest accuracy for the limb when displayed at normal size (M=43.71%, SE = 2.5). On average, mental rotations of the limb were 8.09% less accurate (95% CI, .815 to 15.36) when displayed normally than those displayed smaller than normal, $p = .027$ and 6.33% less accurate (95% CI, .477 to 13.14) when displayed larger than those smaller than normal, $p = .074$ (Bonferroni corrected). There was no main effect of limb and no interaction between limb and hand size, with both $p > .05$.

Consistent with the HOA group, there was a main effect of size on accuracy for the HC group, $F(2,30) = 7.318$, $p = .003$, $\eta^2 = .328$, with HC participants exhibiting highest accuracy for the limb when displayed smaller than normal (M=54.34%, SE=1.89) and lowest accuracy for the limb when displayed larger than normal (M=42.32%, SE = 2.77). On average, mental rotations of the limb were 12.01% less accurate (95% CI, 5.42 to 18.60) when displayed larger than those displayed smaller than normal, $p = .002$, and 11.32% (95% CI, .284 to 22.93) less accurate when displayed larger than those displayed at normal hand size, $p = .057$ (Bonferroni corrected). There was no main effect of limb and no interaction between limb and size, with both $p > .05$. No other main effects or interactions were significant, with all at $p > .05$ (see Figure 4.5.)

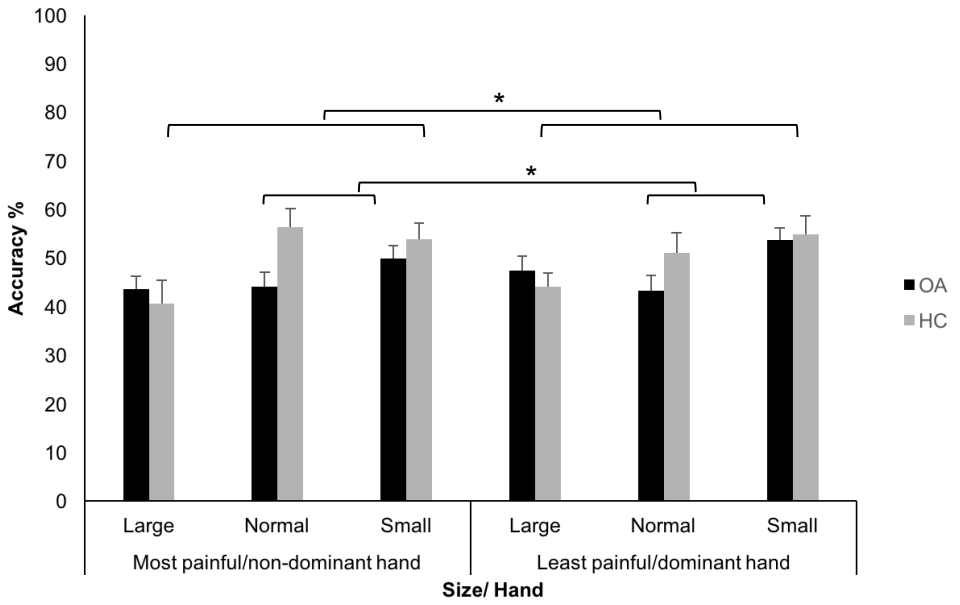


Figure 4.5 The effect of group, size and limb on accuracy (percentage correct). For the HOA group, accuracy scores were significantly lower for images of the limb when displayed normal than those displayed smaller than normal, whereas for the HC group accuracy was significantly lower when images were displayed larger than those displayed smaller than normal. There was no main effect of limb in neither the HOA nor the HC group. Error bars represent standard error of the mean. * represents statistically significant at the $p < .05$ level.

The effect of body size on reaction times

A three-way mixed ANOVA found no main effect of hand size, $F(1,34) = .383$, $p = .540$, $\eta^2 = .011$. However, there was a significant interaction between size and group, $F(1.891,64.288) = 5.867$, $p = .005$, $\eta^2 = .147$) which was followed up with separate two-way ANOVA's for the HOA and the HC group. There was no significant main effect of hand size on reaction times for the HOA group, $F(2,38) = 2.753$, $p = .076$, $\eta^2 = .127$) and no other significant main effects or interactions, with all at $p > .05$.

In contrast, there was a main effect of size on reaction times for the HC group, $F(2,30) = 3.758$, $p = .035$, $\eta^2 = .20$, with HC participants exhibiting slower reaction times for the limb when displayed normal. On average, mental rotations of the limb were 231ms slower (95% CI, 19.08 to 482.14) when displayed normally than those displayed larger than normal, although pairwise

comparisons were not significant after Bonferroni correction (p = .075). No other main effects or interactions were significant, with all at p > .05 (see Figure 4.6).

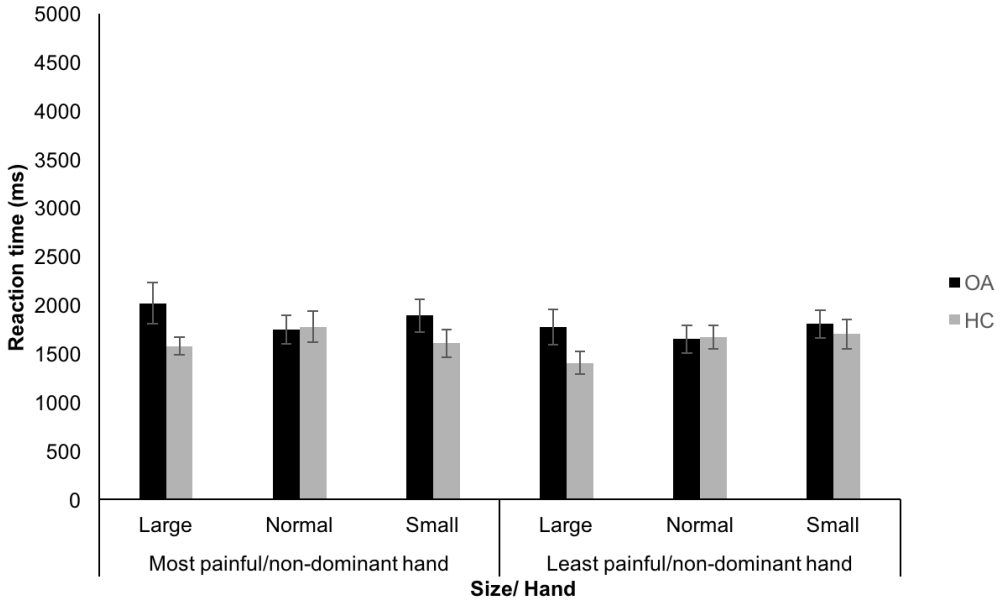


Figure 4.6 The effect of group, size and limb on reaction times (correct trials only). Error bars represent standard error of the mean.

4.3.4 Effect of image display

There was no main effect of image display on accuracy scores for both the OA group, $F(3, 93) = 1.789$, $p = .153$, $\eta^2 = .055$, or the HC group, $F(3, 45) = 1.404$, $p = .254$, $\eta^2 = .086$. There was also no effect of image display on RT for both the OA group, $F(3, 93) = 1.898$, $p = .135$, $\eta^2 = .058$, and the HC group, $F(1.812,27.186) = 1.250$, $p = .299$, $\eta^2 = .077$, suggesting that participants were not using hand characteristics for deciding whether the image they were viewing was of a left or a right hand.

4.4 Discussion

The aim of the current study was to investigate whether individuals with HOA present with a disruption of working body schema. Here, motor imagery performance was examined in individuals with and without HOA using a hand laterality task. The current study combined the left/right judgement task with images of “own hands” versus “other hands” and is the first study to investigate the effect of displayed hand size on left/right judgements in chronic pain.

Consistent with previous findings (Coslett et al., 2010), accuracy was influenced by hand orientation for both the HOA and the HC group. The hypothesis that people with HOA would be worse in recognizing their most painful hand was also partially supported. The accuracy of responses to images varied when the picture depicted the most painful limb presented in different perspectives.

The most painful limb influenced the accuracy of images presented in different perspectives. However, the hypothesis that general performance on the left/right judgement task would be worse for the OA group was not supported. There were no group differences in general laterality performance on either accuracy or reaction times. Lastly, body size influenced accuracy performance but not reaction times, with the highest accuracy for the OA group when images were displayed smaller than actual hand size. The results will now be discussed in relation to previous findings.

Motor imagery performance

Consistent with previous studies, accuracy scores were reflective of the amplitude of rotation, with significantly lower accuracy scores for images that

required a larger mental rotation reflecting the disparity between participants' actual hand posture and that of the presented limb (Parsons, 1987a; Schwoebel & Coslett, 2005). This further supports the notion that performance on this task relies on a working body schema (Flor & Moseley 2012). Furthermore, there was an effect of mental rotation on accuracy when the displayed limb was of the most painful hand. Coslett and colleagues (2010) interpreted this to be the result of the expectation of the imagined movement to produce pain, based on the idea that imagined movement and motor intent share common neuronal mechanisms.

This finding is in line with recent research by Meulders, Harvie, Moseley, & Vlaeyen (2015), who combined the left-right judgement task with a conditioning task to investigate the effect of pain-related fear. In this task, some hand postures were followed by a painful electrical stimulus whereas others were not. Conditioned pain-related fear was assessed using eye blink startle modulation and self-report. The results indicated that the images associated with the painful stimuli triggered more fear and expectation of pain compared to non-painful postures (Meulders et al., 2015). This would explain why in the current study, when images were of the most painful hand, there was an effect of perspective on laterality performance (Moseley, Zalucki, et al., 2008).

Moreover, there was an effect of viewing the self and others on accuracy. The findings not only demonstrate a general effect of mental rotation, but also an effect of personal body-information vs. general body-information. That is, it took significantly longer to recognise someone else's hand and when they were displayed in third-person perspective compared to viewing the own hand in first-person perspective. There is a known advantage in the processing of

self-related body information versus other body information, termed the ‘body self-advantage’ (Frassinetti et al., 2009; Frassinetti, Maini, Romualdi, Galante, & Avanzi, 2008).

The current results are consistent with those of Ferri et al., (2012), who found that participants respond quicker to images of their own hands compared to someone else’s hand on a hand laterality task. Although care was taken to instruct the participants to keep their hands still during the task, the fact that a real-time video image of their hands was used could have helped participants to identify their own hands compared to other hands. However, whilst I cannot exclude the possibility that this was the case, the finding of a non-effect of image display and an effect of hand and perspective on laterality performance suggests that if this was the case, the effect must have been very small. The current findings provide further evidence for the presence of a self-advantage in the processing of one’s own body. That this was the same for both HOA participants and normal participants suggests that people with HOA use similar processes for body recognition.

Another intriguing finding is the effect of body size on performance accuracy. Body-size (size of displayed hand) affected accuracy performance for both the HOA group and the HC group. That accuracy was highest for HOA when most painful images were displayed smaller than normal hand size could be explained by the recent finding that individuals with osteoarthritis tend to perceive their painful hand to be smaller than normal (Gilpin et al.,2014). That healthy participants were also most accurate when images were displayed smaller than the normal hand size could be explained by the recent finding that healthy participants tend to underestimate hand size (Longo, 2015a). Together

these findings suggest the importance of body size for visual perception and the presenting stimuli to be coherent with the body-self reference frame.

Several studies have demonstrated an impairment in motor imagery performance in some pathological states including chronic pain (Coslett et al., 2010; Hudson et al., 2006; Schwoebel et al., 2001; Stanton et al., 2012). In the current study, people with HOA were not more or less accurate, nor slower or quicker at the general motor rotation task compared to healthy controls. The lack of general group differences on laterality performance contrasts with previous findings from Stanton et al., (2012), who found that people with knee osteoarthritis are less accurate in performing the judgement task but have similar reaction times compared to controls. There are several methodological differences between the studies, both in the specific symptoms of the population – namely, knee osteoarthritis versus hand osteoarthritis - as well as in the task used, which could explain some of the discrepancies in findings.

Stanton and colleagues' study used images of both hands and feet with a range of rotations as well as postures. In contrast, the current study used images of hands (own hands vs. other hands) in a variety of different angles and sizes, but in one set posture. This may have made it easier for people in the current study to recognize laterality of the limb. Furthermore, in the present study images were presented in the same horizontal plane as the actual position of the real hands. The absence of group differences could also be explained by better recognition of objects, such as body parts, when they are presented in a certain picture plane (Kitada, Dijkerman, Soo, & Lederman, 2010). Indeed, it is well established that mental rotation is influenced by the

position of the actual limbs (Hoyek, Di Rienzo, Collet, Creveaux, & Guillot, 2014).

Another possible explanation for the difference between studies could be the recent finding that mental imagery performance decreases with age (De Simone, Tomasino, Marusic, Eleopra, & Rumiati, 2013; Wallwork et al., 2013). Thus, the finding that laterality performance was the same for both groups could be because the current study used an age-similar control group, whereas some previous investigations have not always controlled for this systematic difference. However, findings from Stanton et al., (2012) could counter this, since in their study group differences in motor imagery performance were still present when people with knee osteoarthritis were compared to age-matched controls.

Instead, it is possible that motor imagery performance is predominantly influenced by pain and is not necessarily influenced by the condition itself. In support of this hypothesis, Stanton et al., (2012) demonstrated that left/right laterality performance was not influenced by pain location and was similar between patients with upper limb pain compared to people with lower limb pain. This could explain the lack of group differences in laterality performance of individuals with HOA (regardless of pain status) compared to healthy controls, but group differences when individuals with HOA were also experiencing pain in their affected limbs. Furthermore, the finding that general performance on the laterality task was not affected in the current study is important as it suggests that people with HOA have no problems in executing the task (Coslett et al., 2010).

Several studies have demonstrated a delay in response times in chronic pain for images corresponding to the affected limb (Coslett et al., 2010; Moseley et al., 2004; Reinersmann et al., 2010). Coslett and colleagues (2010) found that individuals with arm/shoulder pain are generally slower but not less accurate on the motor imagery task. In the present study, I did not find support for the finding that patients might take longer to recognize their affected hand. These results contrast with general findings of a delay in response times in chronic pain for images corresponding to the affected limb (Coslett et al., 2010; Moseley et al., 2004; Reinersmann et al., 2010). In fact, participants were more accurate at recognising their own hand compared to someone else's hands, suggesting a lack of speed-accuracy trade off. It could be that HOA participants were using physical characteristics of their hands to aid laterality judgments. However, I did not find an effect of image display, suggesting that participants were not using hand characteristics to help.

One limitation of the current study is that to determine the effect of painful limbs on pain, participants with HOA were included based on their current pain ratings. Thus, I did not control for daily fluctuations in pain in other limbs which could have influenced general laterality performance. A future study could control for this by only including individuals with unilateral HOA and no previous history of pain in the other hand.

4.5 Conclusions

The aim of this study was to examine performance on a laterality task in individuals with HOA, as a more objective measure of body representation. Individuals with HOA performed similarly on a left/right judgement task

compared to healthy controls. However, when pain was present in one of the limbs, accuracy of images corresponding to the most painful hand was influenced by the degree of rotation. Furthermore, individuals with painful HOA respond differently to the size of the depicted hand compared to healthy controls. The finding that displayed hand size affects body-recognition raises the possibility that performance of this task relates to the coherence of the presented stimuli within the body-self reference frame.

Support was not found for impaired performance of stimuli corresponding to the painful hand. Rather, performance was better when images were of the participant's own hand compared to others' hands, providing further evidence for the presence of a self-advantage in the recognition of body parts. Although support was not found for a general impairment on this task in patients with HOA, the findings suggest that the performance on this task is mediated by the presence of pain and is dependent on size and perspective of the body part in view. This provides some evidence for a distorted representation of the affected body part in HOA. Thus, Chapter 5 used a similar procedure to the one employed in Chapter 3 to investigate whether the perceived size and shape of the body can modulate pain perception.

Chapter 5 Investigating analgesic effects of multisensory illusions in people with hand osteoarthritis

5.1 Introduction

In Chapter 2 it was argued that given the apparent link between perceptual and affective body representations, multisensory illusions might be used as a promising tool to change perceived hand shape and potentially reduce clinical pain. Although the findings of Chapter 3 do not support an effect of visually distorting the virtual hand on pain sensitivity in healthy individuals, the utility of the stretch-illusion on clinical pain in terms of pain ratings and pain sensitivity remains unclear. Indeed, as shown in Chapter 4 individuals with HOA present with a worse performance on a motor imagery task, which may suggest a disruption of the working body schema. Explanations as to the analgesic effects of multisensory illusions include restoring the disrupted body schema (Plumbe et al., 2013). In this chapter, I will further investigate the previously observed analgesic effects of the stretch-illusion in people with HOA using Quantitative Sensory Testing (QST).

As discussed in Chapter 1, Section 1.1.1, chronic pain conditions are associated with cortical reorganisation of the somatosensory areas (Moseley & Gandevia, 2005 [2]), and these alterations have been shown to relate to the severity of pain (Maihofner, Handwerker, Neundorfer, & Birklein, 2004). Clinically, this may present itself in the form of body perception disturbances, in which the size or shape of the affected body part can be misperceived

[2] See Moseley & Flor (2012b) for an insightful review on cortical changes that are associated with chronic pain.

(Bultitude & Rafal, 2010; Haggard et al., 2013; Moseley, 2005a). For some individuals, altered body perceptions can even lead to hostile feelings towards that limb, such as the desperate desire to amputate the affected part of the body (Lewis et al., 2007), thus highlighting the need for the development of interventions that target these body disturbances in chronic pain conditions. In people with Complex Regional Pain Syndrome (CRPS), a positive correlation was found with body disturbances (measured using the Bath CRPS body perception disturbance scale) and pain, such that people who had greater pain had more extensive body disturbances (Lewis & Schweinhardt, 2012). Body perception disturbances have recently been described in osteoarthritis, with a decrease in the perceived size of the painful body part (Gilpin, Moseley, et al., 2014). Additionally, illusory resizing of the painful body part has been shown to have analgesic effects and anecdotally improve function (Preston & Newport, 2011b), as well as leading to perceptions of increased hand size in people with OA (Gilpin et al., 2014).

Although the causal relationship between chronic pain and the representation of the body remains unclear, links between body representation and pain and the implications for multisensory approaches have been made (Haggard et al., 2013). Due to the personal and subjective nature of body representations it can be challenging to understand how they may affect the person who experiences the distortion (Newport et al., 2015). However, multisensory approaches such as bodily illusions allow for a novel investigation in both healthy volunteers and clinical populations into the robust relationship between the body representation, the sense of body ownership and pain (Moseley et al., 2011).

There are multiple theories that attempt to explain the analgesic effects of multisensory illusions. One explanation for the observed analgesic and perceptual changes using these methods is based upon the idea that these techniques might work through restoring disrupted body schema (Giummarraa & Moseley, 2011; Moseley et al., 2011; Tsay et al., 2015). Evidence for this notion comes from studies showing that therapies targeting cortical representation of the body show promising results for the treatment of chronic pain (Moseley & Flor, 2012; Senkowski & Heinz, 2016; Wittkopf & Johnson, 2016).

Nevertheless, despite the increasing popularity of virtual multisensory interventions (Boesch et al., 2015; Moseley & Flor, 2012; Wittkopf & Johnson, 2016), other factors that may contribute to the observed analgesic effects of these illusions are frequently overlooked. Indeed, as mentioned previously, in experimental settings vision of the body is found to reduce pain (Longo, Betti, et al., 2009; Longo et al., 2012; Sadibolova & Longo, 2014) and several other non-specific factors, including patient expectations and physician factors, are known to modulate pain perception (Abhishek & Doherty, 2013; Haggard et al., 2013). Attention, for example, is thought to play a powerful role in experimental investigations, especially so in virtual- or mediated-reality settings (Martini et al., 2014). Indeed, attention and distraction have been considered as one possible explanation for the analgesic effects observed in some experimental virtual reality paradigms (Gilpin, Bellan, et al., 2014).

Preston & Newport (2011b) showed that illusory stretching or shrinking of the hand using a mediated reality device could reduce pain and perceived hand size (measured through questionnaire items) in people with HOA (see

Section 1.6 for more details). The results demonstrate a reduction of clinical pain following the stretch/shrink-illusion, however, it remains unclear as to what other factors may have contributed to the observed effects. As Haggard et al., (2013) point out, the analgesic and functional effects of illusory resizing were only apparent when distorting the painful part of the hand and not when distorting the whole hand. These findings suggest that the specific visual context of the manipulation is important for the experience of pain (Haggard et al., 2013), as well as body perception. Indeed, as discussed previously, vision of the body has been found to be analgesic in healthy controls.

In contrast, evidence for visual analgesia in chronic pain is mixed. For some individuals with chronic hand pain, an enlarged view of their painful limb can increase movement-induced pain, whereas a magnified view of their hand decreases pain (Moseley, Parsons, et al., 2008). Similarly, in patients with Phantom Limb pain, visual shrinkage of the phantom limb corresponding with its perceived size dramatically reduced pain, whereas visually increasing the phantom limb did not (Ramachandran & Altschuler, 2009). Thus, the first aim of the present study is to directly compare the effects of multisensory illusions on pain and body perception with other combinations of multisensory information as well as investigate factors that may contribute to the previously observed analgesic effects (Preston & Newport, 2011).

In addition, from previous studies it remains unclear whether the stretch-illusion might also affect central pain mechanisms. Thus, the second aim of the current study is to replicate the previously observed effects on the experience of pain (Preston & Newport, 2011) and investigate the effects of the illusion on pain sensitivity using similar methods as described in Chapter 3

(PPT). Furthermore, the study investigates the effects of multisensory illusions on hand function, based on researcher observations in previous studies indicating improved hand mobility and range of motion after illusory stretching of the affected hand (Preston & Newport, 2011).

Finally, an alternative recent explanation for the observed analgesic and perceptual changes observed in these studies is based upon changes in the affective evaluation of the painful body part. Indeed, previous studies have demonstrated a link between perceptual and affective body representations, illustrating that they can directly affect each other (Preston & Ehrsson, 2014). Specifically, Preston and Ehrsson (2014) showed that illusory ownership over a thinner body led to participants perceiving their actual body to be thinner and increasing their body satisfaction. Thus, the final aim of the present study is to investigate the link between perceptual and affective body representations.

To summarize, this chapter has three aims. The first aim of this study is to replicate the previously observed analgesic effects of multisensory body illusions and further investigate their effects on pain sensitivity in people with HOA. Analgesic effects of viewing the hand are expected to be stronger when viewing the hand in the stretch-illusion condition compared to the other conditions, accompanied by an increase in PPT compared to baseline.

The second aim is to investigate whether the previously observed analgesic effects of the illusion are specific to the stretch-illusion, or whether they can be explained by other contextual or attentional effects. If the previously observed analgesic effects of the stretch-illusion are specific to the multisensory illusion, I would expect to find a reduction in pain (both ratings and sensitivity) in the stretch-illusion condition compared to the hand-only

condition or contextual control. If instead, the stretch-illusion leads to a reduction in pain, but is due to the contextual (attentional) effects of being immersed in a mediated reality setting, I would expect to find a difference in pain reduction between the stretch-illusion and the hand-only condition, with no differences between the stretch-illusion and the contextual control. Furthermore, if any analgesic effects are due to viewing a tactile manipulation to the most painful hand, I would expect to find a difference in pain reduction after the stretch-illusion condition compared to the contextual control, with no differences between the stretch-illusion and hand-only condition.

The third and final aim is to investigate the link between perceptual and affective body representations. The affective response might be stronger in the stretch-illusion condition in which the painful hand is visually distorted. Together, these investigations will provide valuable insight into the effects of multisensory illusions on chronic pain.

5.2 Materials and methods

5.2.1 Participants

Thirty adults with a diagnosis of HOA were recruited through the medical record system of the Arthritis Research UK Pain Centre database and via a printed advertisement in a local newspaper. One participant was excluded due to technical issues and one participant dropped out due to an unexpected yet clinically significant change in medication. Thus, a total of 28 participants took part in the study (21 women, 7 men). The mean age of the group was 70.50 years (SD = 7.85). Participants were eligible if they (1) met the American College of Rheumatology criteria for OA of the hand (Altman et al., 1990), (2)

had normal or corrected-to-normal vision and (3) did not receive any new hand treatment in the two months preceding the experiment. The study was approved by the Ethics Committee of the University of Nottingham. Written informed consent was obtained prior to assessment. See Table 5.1 for participant demographics.

5.2.2 Design

The study used a two-period, randomized cross-over design consisting of two visits (stretch-illusion visit and hand-only visit), with a one-week washout period before switching interventions. The stretch-illusion visit consisted of a stretch-illusion condition and a contextual control, while the hand-only visit consisted of a hand-only condition and the same contextual control (see Figure 5.1). The main reason for including two separate study visits was to limit the assessment burden placed on the participants. Cross-over designs are often used in clinical trials in which two treatments or interventions are compared and where the treatment or intervention it thought to alleviate but not cure a condition (Hills & Armitage, 1979). The visits were separated by a minimum washout period of five days and under the condition that any changes in pain levels after the study visit were returned to baseline. The washout period was included to ensure that the effects of the first visit were diminished before continuing with the second visit to prevent any carryover effects (Wellek & Blettner, 2012). The order of visits was counterbalanced, with half of the participants starting with the stretch-illusion visit and half starting with the hand-only visit, with conditions randomised within the two visits (see Figure 5.1).

Table 5.1 Participant demographics

								Pain intensity 1st visit [a]			Function 1st visit		Pain intensity 2nd visit [a]				Function 2nd visit	
#	Age	Gender	Handedness	Pain location	Most affected hand	Occurrence hand pain 12m	Chronicity	Current pain 0-10	Pain all joints >48h	Pain most painful hand > 48 h	Satisfaction with function 48 h [b]	FIHOA (0-30) [c]	Current pain 0-10	Pain in all joints >48 h	Pain most painful hand >48 h	Satisfaction with function 48 h [b]	FIHOA (0-30)[c]	Medication
1	58	Female	Right	Both hands	No difference	>3 months	5-10 years	6	8	8	7	16	6	6	7	6	15	Missing
2	70	Male	Left	Both hands	No difference	>3 months	>10 years	3	3	4	3	4	2	2	3	2	3	Missing
3	87	Male	Right	Both hands	Left	>3 months	1-5 years	5	5	5	7	6	0	5	5	2	10	Missing
4	68	Female	Right	Both hands	No difference	1-3 months	>10 years	3	3	3	10	6	2	5	5	10	9	Missing
5	53	Female	Right	Both hands	Left	>3 months	5-10 years	9	9	10	9	18	8	9	9	10	17	Paracetamol, Naproxen
6	74	Male	Right	Both hands	No difference	>3 months	5-10 years	5	5	6	7	6	3	5	5	4	7	Missing
7	65	Female	Right	Both hands	No difference	>3 months	>10 years	3	9	9	9	20	5	8	8	5	19	Co-codamol, morphine, aspirin, omeprazole, levothyroxine, rosuvastatin
8	74	Female	Right	Both hands	Right	>3 months	>10 years	3	5	5	2	8	2	2	2	2	10	Paracetamol, tramadol
9	80	Male	Right	Both hands	Right	>3 months	>10 years	0	1	1	3	10	0	2	2	5	13	Missing
10	69	Female	Right	Both hands	Right	>3 months	5-10 years	8	5	8	5	17	0	5	5	4	16	Missing
11	65	Female	Both	Both hands	Right	>3 months	5-10 years	9	8	9	4	18	9	8	9	4	17	Paracetamol, co-codamol
12	86	Female	Right	Left hand	No difference	>3 months	5-10 years	5	5	5	3	17	6	8	8	1	26	Ibuprofen
13	70	Female	Right	Both hands	Right	>3 months	5-10 years	6	7	8	6	13	7	7	7	3	13	Paracetamol, amlodipine, gabapentin, naproxen, omeprazole, tramadol
14	72	Female	Left	Both hands	Left	>3 months	>10 years	0	4	6	2	10	6	7	7	7	11	None

15	68	Female	Right	Both hands	No difference	>3 months	5-10 years	5	6	7	4	12	5	5	5	6	9	Paracetamol and codeine
16	61	Female	Right	Both hands	Right	<7 days	>10 years	0	4	6	6	2	7	8	8	5	2	Paracetamol, ibuprofen, codeine
17	75	Female	Right	Both hands	No difference	>3 months	>10 years	2	2	2	2	10	6	3	5	7	13	None
18	68	Female	Right	Both hands	Left	>3 months	>10 years	5	5	5	4	8	3	5	5	7	9	Codeine phosphate
19	67	Female	Right	Both hands	Right	1-4 weeks	1-5 years	5	5	7	4	11	4	4	5	5	5	None
20	77	Male	Left	Both hands	Right	>3 months	1-5 years	1	7	8	7	12	4	4	5	3	13	Paracetamol, meloxicam
21	62	Male	Left	Left hand	Left	>3 months	>10 years	9	9	9	9	15	7	8	8	8	17	Anti-epressents
22	60	Female	Right	Both hands	No difference	>3 months	>10 years	4	6	7	5	10	5	5	6	5	10	None
23	77	Female	Right	Right hand	Right	>3 months	<12 months	7	7	7	7	15	6	8	8	5	11	Paracetamol, ibuprofen, Morphine patch
24	74	Male	Both	Both hands	Right	>3 months	5-10 years	1	8	8	6	8	5	7	7	5	12	Morphine patch
25	77	Female	Right	Both hands	Right	>3 months	>10 years	3	8	7	6	15	7	8	8	5	2	Ibuprofen
26	77	Female	Right	Both hands	No difference	>3 months	>10 years	6	9	9	8	19	6	8	8	7	20	None
27	69	Female	Right	Both hands	left	>3 months	5-10 years	5	6	7	5	8	7	7	7	6	8	Co-codamol, anti-depressants
28	71	Female	Right	Both hands	Right	>3 months	5-10 years	5	5	8	6	10	5	5	5	5	12	Ibuprofen

= participant number. [a] Pain intensity measured on a 0-10 numerical rating scale (NRS) rated from 0=no pain at all to 10=worst pain imaginable. [b] 0=very satisfied, 10= not at all satisfied. [C] higher scores denote decreased hand.

5.2.3 MIRAGE system and experimental conditions

The current study utilised the same MIRAGE apparatus as described in the previous chapters. Participants attended two visits, both consisting of two conditions (see Figure 5.1). For the stretch-illusion condition, participants viewed their most painful hand through MIRAGE, as assessed by subjective pain ratings. Unlike the previous studies, here participants were asked to keep their hand flat in order to retain a comfortable position during the illusion. The part of the hand that was identified as most painful prior to the start of the experiment was the part that was visually stretched.

In the hand-only condition, the participant placed their most-painful hand on a table in front of them with their elbow comfortably resting on a table. Identical to the stretch-illusion condition, the experimenter took hold of the most painful part of the hand and pulled gently in three increments. Both contextual control conditions involved the participant looking at their most-painful hand inside MIRAGE without any tactile or visual manipulation. The hand position, duration of condition, interaction and timings were kept identical to the stretch-illusion condition and was therefore considered a contextual control for the purposes of this study. For all conditions, participants were asked to look at their experimental hand.

5.2.4 Outcome measures

Primary and secondary outcome measures used in the present study are outlined in Table 5.2.

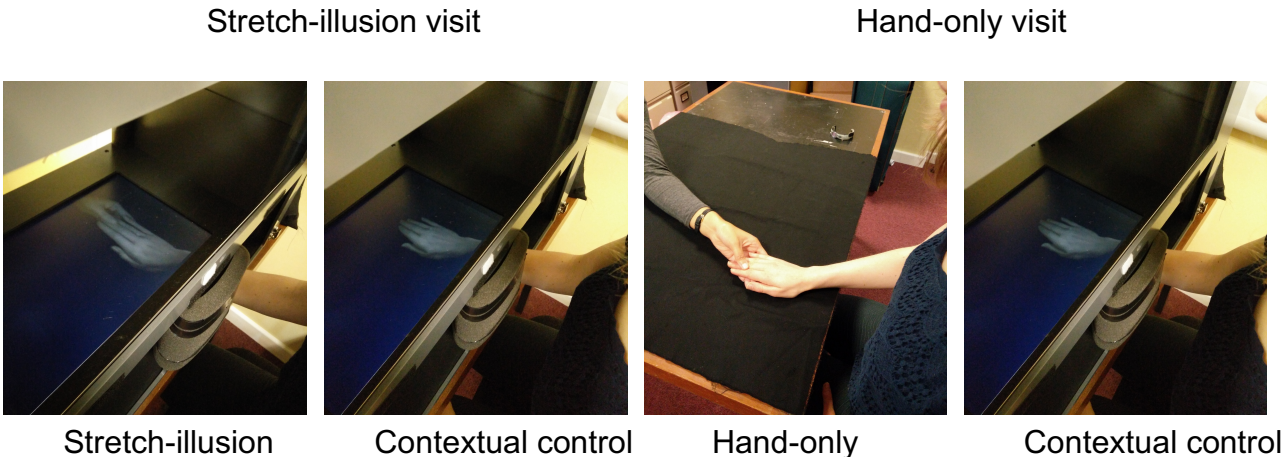


Figure 5.1 Experimental set-up showing: the two visits that were counterbalanced between participants (illusion-visit and hand-only visit), and the conditions that were randomized in each visit. The contextual control was the same for both visits. Baseline measures were included in both visits (always first).

Subjective Ratings of pain

An 11-point Numerical Rating Scale (NRS) was used as a measurement of pain intensity after every condition. The NRS scale has robust psychometric properties and is considered as an appropriate tool in the therapeutic evaluation of osteoarthritis (Ferreira-Valente et al., 2011; Ornetti, Dougados, Paternotte, Logeart, & Gossec, 2011). The NRS scale was administered using the phrase: “On a scale of 0 to 10, with 0 being no pain at all and 10 being the worst pain you could imagine, how would you rate the pain you are experiencing right now?’’.

Subjective experience of the illusion

The subjective experience of the illusion was measured using the same 7-item questionnaire as in Chapter 3 (see Table 3.1), with questions relating to the affective experience, physiological changes, susceptibility, ownership and agency of the most painful hand.

Table 5.2 Primary and secondary outcome measures

	Baseline[1]	Post-intervention	48 hours
Primary outcome measures			
Pain level most painful joint (0-10 NRS)	✓	✓	✓
Pressure Pain Thresholds (PPT)	✓	✓	
Secondary outcome measures			
Grip strength	✓	✓	
Illusion strength	✓		
FIHOA	✓		✓
11-point NRS and VAS scales for:			
Average overall hand severity/ pain in most painful joint of the past 2 weeks/48 hours	✓		✓
Global disease activity/ average thumb pain/ average pain other joints	✓		✓
Satisfaction with function past 48 hours	✓		✓
Hand pain/aching or stiffness over the last month	✓		
Onset of hand pain	✓		
Demographics and medical history	✓		
Medication on the day	✓		✓

NRS, numerical rating scale, PPT: Pressure Pain Threshold, FIHOA, functional index for HOA, VAS, visual analogue scale.[1] Baseline measures were taken at both study visits.

Pressure pain thresholds

As in Chapter 4, pain sensitivity was measured using Pressure pain thresholds (PPT). The only difference in PPT procedure between this and the previous study was that only two measurements were included to limit participant assessment burden (Chesterton et al., 2007). The mean of the two measurements was used for statistical analysis. Furthermore, in keeping with previous studies of osteoarthritis, PPT measurements were taken on the most affected hand, the other hand and on the breastbone. This was to investigate whether any alterations in PPT would be specific to the affected joint or instead

also affect remote site, which could be indicative of central sensitisation (Suokas et al., 2012; Wajed et al., 2012; Wylde, Palmer, Learmonth, & Dieppe, 2013). The measure points were first localised on the most affected hand, corresponding to the most painful part of the hand on the day of testing and marked with a felt-tipped pen. PPT measure points were then mirrored on the other hand. If there was no difference between the hands in terms of pain severity, the dominant hand was chosen. For the localisation of the breastbone measure point, ordinary latex-free dressing tape was used. After each condition, two measurements were taken from all measurement points, 10 seconds apart and in an alternating manner.

Measurement of grip strength

In the current study, a six second measurement of grip strength was used, measured in kilograms (kgf) at baseline and after every condition. During testing, participants were seated with the elbow at about 90° and their forearm rested on the table in front of them. Participants were asked to press the algometer as hard as they could when instructed to begin pressing, and to stop when instructed to relax without causing themselves more pain. Although various studies calculate the mean of three trials of grip strength for statistical analysis (Ceceli, Gül, Borman, Uysal, & Okumuş, 2012; Massy-Westropp, Gill, Taylor, Bohannon, & Hill, 2011), collecting one or two grip-strength trials has been found to be as reliable, and more importantly, less painful and tiring in both symptomatic and asymptomatic participants (Coldham, Lewis, & Lee, 2006; Kennedy et al., 2010). Therefore, two measurements of grip strength were collected after the baseline and after every condition.

Force-time curves were assessed using a customised LabVIEW (National Instruments, Austin, TX) program. The rising force phase (isometric phase) and the declining phase of the force-time curves were removed to control for participants generating force before or after the recording period, which was done manually under blinded conditions (see Figure 5.2). The first and last quartiles were then automatically removed to further control for force generation and relaxation segments (Dias, Singh, Taub, & Thompson, 2013). Peak force was the maximum grip strength in the remaining force-time curve. Average force was calculated over the remaining half of the force-time curve after excluding the first and last 25%. The peak time was calculated as the time to reach maximum strength, again excluding the first and last quartile.

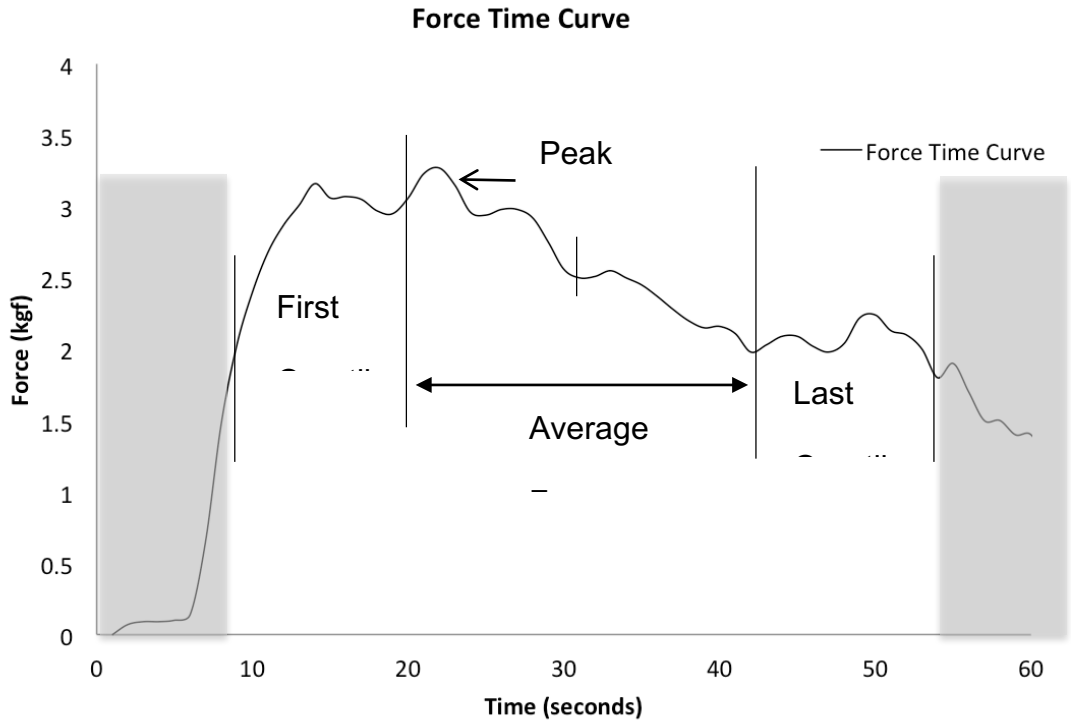


Figure 5.2 Force-time curve showing the different attributes that were calculated. The grey areas showing the rising force phase and the declining phase were removed from analysis. The peak force, average force and peak time were calculated from the middle half of the force-time curve after removing the first and last quartile.

Measurement of hand function

The Functional Index for Hand Osteoarthritis (FIHOA) was used as a subjective measurement of hand function (Dreiser, Maheu, Guillou, Caspard, & Grouin, 1995). The FIHOA is a self-report measurement of hand function in people affected by hand osteoarthritis, consisting of 10 items rated on a 4-point scale. Statements included; “Are you able to turn a key in a lock?’’ and “Are you able to clench your fists?’’. The FIHOA takes less than 3 minutes to complete and is a reliable and valid method, making it suitable choice for the current study. Scores range from 0 - 30, with higher scores denoting worse hand function. The FIHOA has high internal consistency (Cronbach’s alpha= 0.85-0.90). The test-retest reliability of the FIHOA administered twice in one week (close to the frequency in this study) established an intraclass correlation coefficient (ICC) of 0.74. In addition, scores on the FIHOA correlate with additional self-reports, including hand strength.

5.2.5 Procedure

After the procedure was explained and consent was given, baseline demographic and clinical characteristics were collected including pain ratings, chronicity, hand function, medication, and handedness. At the start of each visit and before the start of the first condition, participants were asked to complete a number of self-report measures asking about hand pain and hand function (over periods ranging from 48 hours to one year) and to fill in the Functional index for hand osteoarthritis (FIHOA) (Dreiser et al., 1995). Participants were asked about their most affected hand and to rate their pain,

if any on an 11-point Numerical Rating Scale (NRS) with 0 denoting no pain and 10 denoting the worst pain imaginable.

Following completion of the questionnaire, participants were instructed to position their arm with their most affected hand on the table for baseline PPT testing using a hand-held pressure algometer (Mark-10, Series 3, Compiague, NY, USA) with a $1cm^2$ rubber tip. In addition, a measurement of grip strength of the most affected hand was taken using an isometric hand dynamometer (Neolog hand dynamometer logger sensor, Model NUL-237). Each condition lasted between three to four seconds after which participants were asked to continue looking at their hand for one minute. Immediately after completion of the condition, the questionnaire was administered with participants still looking at their hand. After completion of the questionnaire, participants were instructed to position their arm with their most affected hand on the table for PPT testing and a measurement of grip strength. After each visit, participants were given a follow-up questionnaire to fill in 48 hours after the visit asking about any changes in pain (see Table 5.2).

5.2.6 Data analysis

For the analysis of subjective pain ratings, all participants were included, regardless of their baseline pain scores. Prior to analysis, the normality of the data was tested by Kolmogorov-Smirnov tests and outliers were identified by examination of studentized residuals for values greater than ±3. Where the assumption of sphericity was violated as indicated by the Mauchly's test, Greenhouse-Geisser corrected values are reported.

Subjective pain ratings were analysed using a repeated measures ANOVA with condition (baseline, intervention, contextual control) and visit (illusion-visit, hand-only visit) as the within-subjects factors. Significant interactions were followed up with separate repeated measures ANOVAs per visit. To ensure that baseline pain ratings did not differ between visits, a paired samples t-test between baseline pain ratings was used. The potential for visit order to contribute to the variability in outcome responses on pain scores was investigated using a three-way mixed ANOVA with condition (intervention, contextual control) and time (pre-, post) as the within-subjects factors and visit order (start with illusion-visit, start with hand-only visit) as the between-subjects factor.

The Shapiro-Wilks test suggested a highly positively skewed distribution for the Pressure pain threshold data and were therefore transformed to meet the assumptions of linear regression using the base-10 logarithmic transformation. An anti-log of the mean of the log10-transformed values was conducted to present the results as mean. PPT were analysed using a three-way mixed ANOVA with the factor body site (Most affected hand, other hand, sternum), condition (baseline, intervention, contextual control) and visit (stretch-illusion visit, hand-only visit) as the within-subjects factors. Any significant two-way interactions were investigated using one-way repeated measures ANOVAs for the illusion-visit and the hand-only visit separately.

Differences in the subjective experience of the illusion (measured on the questionnaire) were investigated using multivariate analysis of variance (MANOVA) for repeated measures with condition (stretch-illusion, hand-only, and both contextual controls) as the within-subject factor on the dependent

variables (affective experience, physiological effects, susceptibility, ownership, agency, control). Univariate ANOVAs were used to follow up a significant interaction. FIHOA scores were analysed using a repeated measures ANOVA with visit (Stretch-illusion visit, hand-only visit) and time (pre-visit, 48hrs) as the within-subjects factor.

After exploring the data, the Shapiro-Wilks test suggested a highly-skewed distribution for the grip-strength data. Neither Log transformation nor square-root transformation helped to normalize the data. The data was therefore analysed using the non-parametric Friedman test on the non-transformed data. The test was conducted with condition as the repeated factor on the dependent variables of peak force, average force and time to peak force. Effect of condition (baseline, intervention, contextual control) within each visit (illusion-visit or hand-only visit) was assessed using Wilcoxon signed-rank tests with Bonferroni corrections for planned pairwise comparisons.

Finally, as has been reported in previous studies, there appears to be a large inter-individual variability in the susceptibility to various bodily illusions (Haans, Kaiser, Bouwhuis, & Ijsselsteijn, 2012; Preston & Newport, 2011). For that reason, Pearson correlations were used to examine the relationships between current pain and illusion strength on the ownership and susceptibility subscales. Additionally, correlation analyses were used to examine the relationships between current pain and recall of pain 48 hours and two weeks before the visit and between both visits.

5.2.7 Sample size

Sample size was determined a priori to enable the detection of a medium effect size at a 5% significance level and with a desired power of 80% to test for main effects of condition on NRS pain scores per visit. The sample size calculation was performed in G*Power (Faul et al., 2009). The calculation was based on the main outcome measure of pain, measured on an 11-point NRS scale. A sample size of 20 was required to provide 80% power to detect a medium effect size f of 0.30, based on the findings in Chapter 4 and the threshold sufficient to detect a clinically important difference of a reduction in pain of 2-points on a NRS scale (Farrar, Young, LaMoreaux, Werth, & Poole, 2001; Preston & Newport, 2011). A minimum of 30 participants were included in order to allow for a 30% dropout rate.

5.3 Results

5.3.1 Demographic data

All participants experienced hand pain due to primary OA of the distal interphalangeal joints or the proximal interphalangeal joints, with involvement of other joints including the hip, knee and ankle. Of the 28 participants, 22 were taking regular analgesic medication with the most common types being oral Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) (29%), paracetamol (39%) and opioids (39%). After asking about study expectations, no participants expressed any expectations of pain relief with the current study.

5.3.2 Subjective ratings of pain

Mean pain ratings are displayed in Figure 5.3. There was no statistically significant two-way interaction between condition and visit, *F(*1.596, 43.081) = .319, *p* = .728, η2 = .012. However, there was a main effect of condition, *F(*1.510, 54) = 4.364, *p* = .028, η2 = .139, therefore simple main effects were run. NRS pain scores were significantly lower in the intervention trial compared to the baseline trial, *F*(2,26) =5.500, *p* = .013, η2 = .297, with a mean difference of .82 (95% CI, .151 to 1.492). NRS scores were not significantly different in the contextual control (M = 3.964 (95% CI 3.013-4.915) compared to the baseline (M = 4.554 (95% CI 3.751-5.356), *F*(2,26) = 5.500, *p* = .332, η2 = .302, or between the intervention trial (M = 3.732 (95% CI 2.807-4.657) compared to contextual control. There was no main effect of visit, *F*(1,27) = .130, *p* = .722, η2 = .005, as illustrated in Figure 5.3. A sensitivity analysis only including people with a baseline NRS score > 3 on both visits yielded the same results.

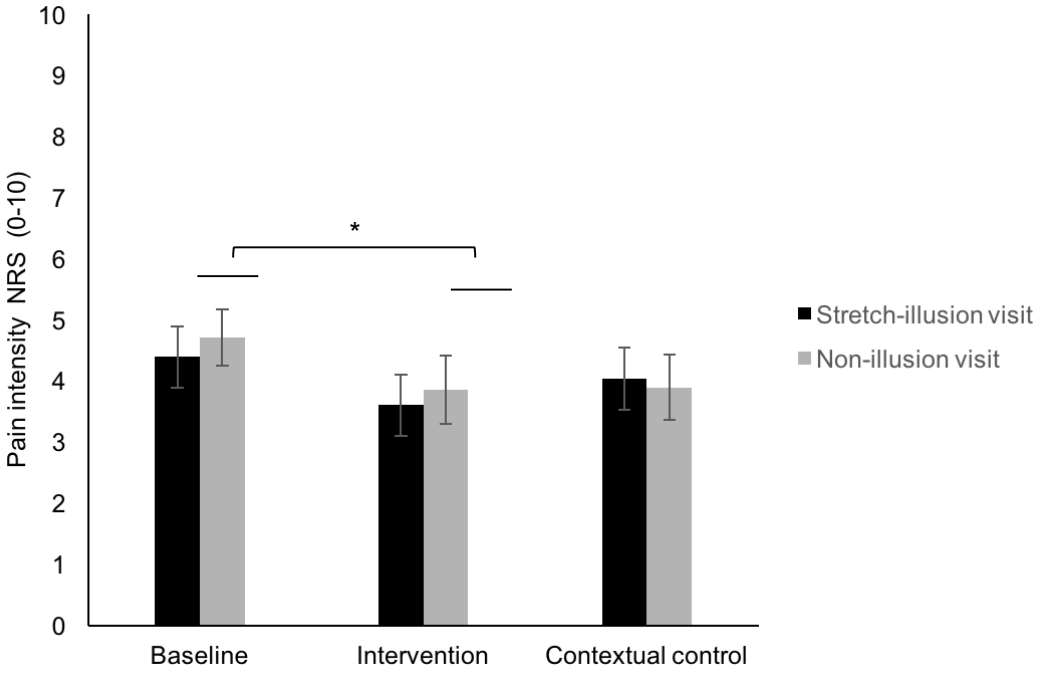


Figure 5.3 The mean effect of condition on pain intensity (NRS ratings). NRS scores were significantly lower after the intervention condition compared to baseline for both visits. The intervention refers to the stretch-illusion and hand-only condition in the stretch-illusion visit and hand-only visit respectively. Error bars represent standard error. * Represents statistically significant difference between conditions after Bonferroni corrections.

5.3.3 Pressure pain thresholds

Mean PPTs in each condition are displayed in Figure 5.4. There was a main effect of body site, $F(2,50) = 3.416$, $p = .041$, $\eta^2 = 120$. There was also a significant interaction between body site and condition, $F(4,100) = 2.73$, $p = .033$, partial $\eta^2 = .099$, and a marginal interaction between body site, condition and visit, $F(4,100) = 2.357$, $p = .059$, $\eta^2 = .086$. There was no significant effect of condition, $F(1.378,34.451) = 1.720$, $p = .199$, $\eta^2 = .064$, or visit, $F(1,25) = .233$, $p = .634$, $\eta^2 = ·009$, and no significant interaction between body site and visit, $F(2,50) = 1.245$, $p = .297$, $\eta^2 = 047$, or condition and visit, $F(2,50) = .948$, $p = .395$, $\eta^2 = .037$.

For the stretch-illusion visit there was a two-way interaction between body site and condition, $F(3.142, 87.99) = 3.679$, $p = .014$, $\eta^2 = .116$, with a statistically significant difference in PPT scores between the most affected hand (M = 1.017, SD = .127), the other hand (M = 1.157, SD = .190) and sternum (M = 1.240, SD = .170) after the stretch-illusion condition, $F(2,58) = 3.152$, $p = .050$, $\eta^2 = .098$. However, there were no significant pairwise comparisons (all *ps* > .05). There was no significant difference in PPT scores between body sites at baseline, $F(2,58) = .046$, $p = .956$, $\eta^2 = .003$, or after contextual control, $F(2,56) = 3.040$, $p = .056$, $\eta^2 = .098$. Furthermore, there was no statistically significant difference in PPT ratings between the different conditions for the most affected hand ($p = .073$), other hand ($p = .304$) or sternum ($p = .627$).

For the hand-only visit there was no significant effect of condition, $F(1.454,36.347) = .099$ $p = .845$, $\eta^2 = .004$. However, there was a significant effect of body site, $F(2,50) = 5.764$, $p = .006$, $\eta^2 = .187$, with highest PPT scores measured at the other hand (M = 1.010, SD = .117) and the lowest PPT scores measured at the sternum (M = .735, SD = .082) and no interaction between body site and condition, $F(4,100) = 1.358$, $p = .254$, $\eta^2 = .052$.

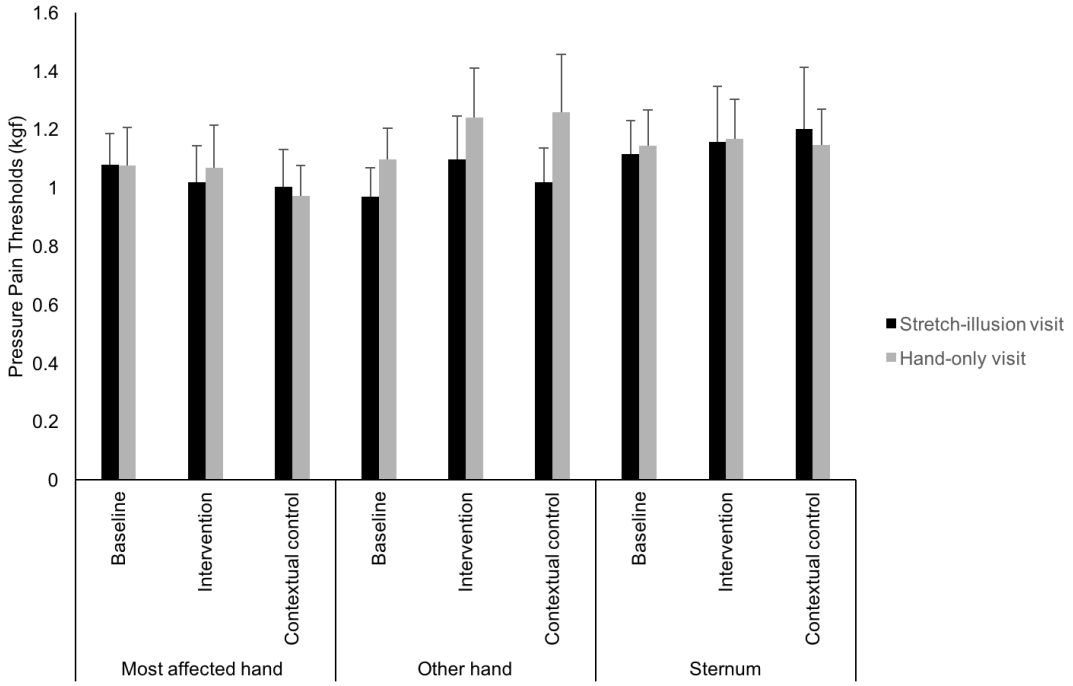


Figure 5.4. Mean Pressure Pain Thresholds (kgF) after each condition. The intervention refers to the stretch-illusion and hand-only condition in the stretch-illusion visit and hand-only visit respectively. Error bars represent standard error of the mean.

5.3.4 Subjective experience of the illusion

The MANOVA showed a statistically significant difference between the conditions on the combined dependent variables, $F(18, 147.563) = 3.325$, $p < .001$; Wilks' $\Lambda = .390$; $\eta^2 = .269$, suggesting that the illusion strength was not the same for the stretch-illusion, hand-only, and both contextual controls (see Figure 5.5). Follow-up univariate ANOVAs showed that there were statistically significant differences in physiological effects ($p < .001$) susceptibility ($p < .001$), ownership ($p = .010$) and agency ($p = .017$), but not the affective experience ($p = .886$) (see Figure 5.5E) or in the responses to the control question ($p = .308$) (see Figure 5.5F).

As suspected, the susceptibility of the illusion was highest after the stretch-illusion, which was significantly different from contextual control ($p < .001$), but not the hand only condition ($p = .253$) (see Figure 5.5A). Ownership

of the hand was the lowest after the stretch-illusion and significantly lower compared to the hand only condition ($p < .001$), with no significant difference between contextual control ($p = .112$) (see Figure 5.5B). There was a significant loss of agency after the stretch-illusion compared to the own hand condition ($p = .03$) (see figure 5.5C). However, this was not significantly different from contextual control ($p = .059$), suggesting that agency was overall lower in the illusion condition compared to the hand-only visit. Participants reported their hand/finger as feeling longer after illusory stretching of the finger compared to contextual control ($p < .001$) and hand only ($p = .012$), suggesting that the stretch-illusion, but not pulling the finger alone, was sufficient for experiencing physiological changes (see Figure 5.5D).

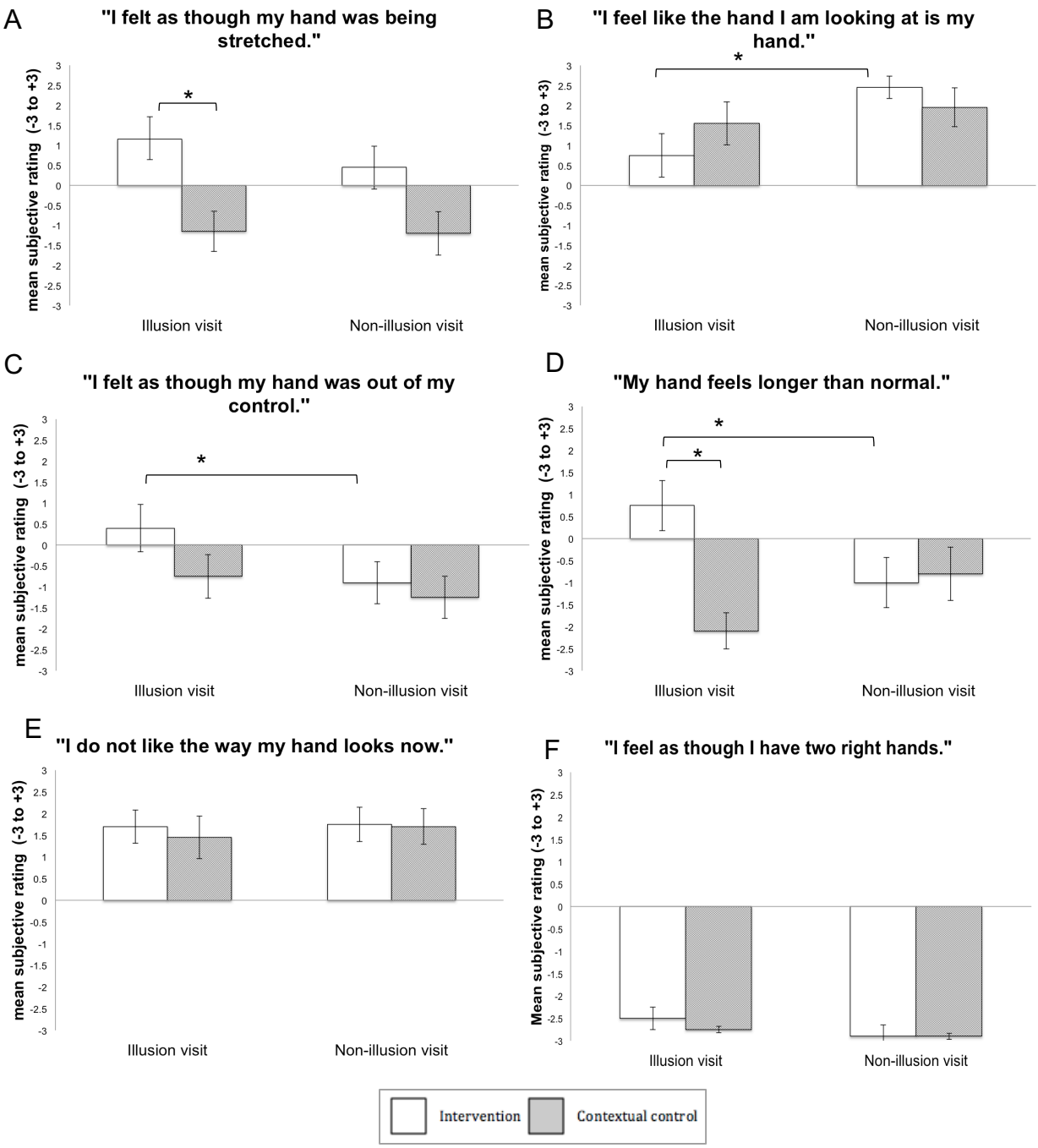


Figure 5.5 Mean objective ratings of the statements for the illusion-visit and the hand-only visit, between interventions and contextual controls. Error bars are standard error. * represents statistically significant difference between conditions after Bonferroni correction. -3= no, not at all, +3= yes, lots and lots.

5.3.5 Grip Strength

The Shapiro-Wilks test suggested a highly-skewed distribution for the grip-strength data. Neither Log transformation nor square-root transformation helped to normalize the data. Therefore, non-parametric statistics were used on the non-transformed data. There was no statistically significant effect of condition on mean average force, $\chi^2(5) = 10.127$, $p = .072$ (see Figure 5.6B). However, there was a statistically significant difference in maximum peak force, $\chi^2(5) = 12.580$, $p = .028$ (see Figure 5.6A) and time to peak force, $\chi^2(5) = 13.704$, $p = .018$ (see Figure 5.6C). Follow up Wilcoxon signed rank tests were conducted per visit (stretch-illusion visit, hand-only visit) with a Bonferroni correction applied, resulting in a significance level set at $p < .017$.

For the stretch-illusion visit, no statistically significant differences were found between baseline max grip strength (*Mdn* = 3.56) and max grip strength after the stretch-illusion (*Mdn* = 4.1), $Z = -1.144$, $p = .253$, or between stretch-illusion and contextual control (*Mdn* = 4.41), $Z = -1.714$, $p = .086$. In the hand-only visit, max grip strength was smaller after the hand-only condition (*Mdn* = 3.92) compared to baseline (*Mdn* = 4.3) however this was not significant, $Z = -.532$, $p = .595$. There was no statistically significant difference between baseline and contextual control (*Mdn* = .4.04), $Z = -1.947$, $p = .052$, or between hand-only and contextual control after controlling for pairwise comparisons, $Z = -2.190$, $p = .029$.

In the stretch-illusion visit, time to peak force was significantly faster after the stretch-illusion (*Mdn* = 0) compared to baseline scores (*Mdn* = .400), $Z = -2.421$, $p = .015$. There was no significant difference in peak time between baseline and contextual control, $Z = -1.351$, $p = .177$, nor any statistically

significant difference in peak time between stretch-illusion and contextual control (*Mdn* = .150). For the hand-only visit there were no statistically significant differences in time to peak between the different conditions, with all indicating p > .05 (see Figure 5.6C).

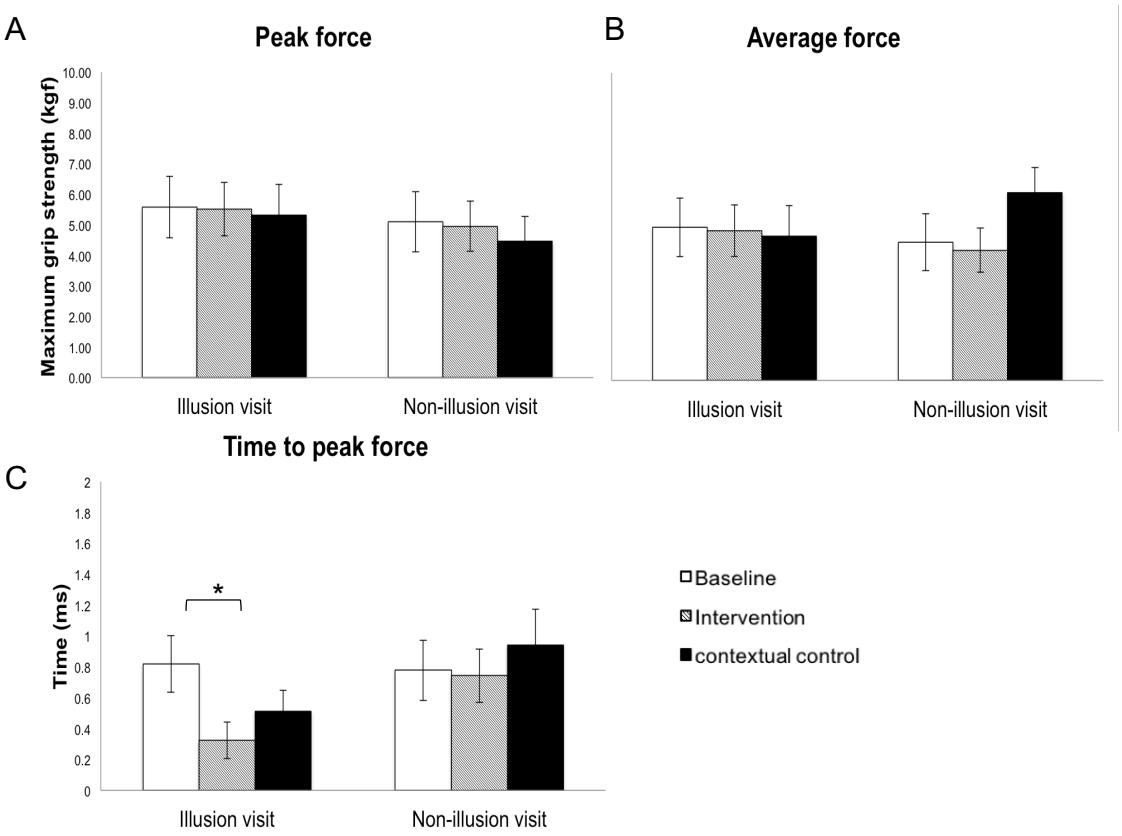


Figure 5.6 Changes in the Peak force (**A**), Average peak force (**B**) and Time to peak force (**C**). Intervention refers to the stretch-illusion and hand-only in the stretch-illusion visit and hand-only visit respectively. Error bars represent standard error. * Represents significant difference between the conditions after Bonferroni correction ($p < .017$)

5.3.6 FIHOA

There was no effect of visit, $F(1,24) = 1.20$, $p = .733$, or time, $F(1,24) = .210$, $p = .651$, on FIHOA scores and no interaction between visit and time, $F(1,24) = 1.231$, $p = .278$.

5.3.7 Follow up

Follow up questionnaire data were collected from 26 of the 28 participants after the stretch-illusion visit and 25 participants after the hand-only visit. For the majority of participants, any reduction of pain only lasted for the duration of the experiment. Some participants reported a decrease in pain lasting up to 60 minutes after the visit and a small percentage of participants experienced an increase in pain after the visit (see Table 5.2).

Table 5.3 Change in subjective pain ratings after both visits

	No change in pain at all	**Decrease <15 min. after visit**	**Decrease <30 min. after visit**	**Decrease <60 min. after visit**	**Decrease <90 min. after visit**	**Decrease <24h after visit**	**Increase after visit**
Follow up Stretch-illusion visit	23/26 (88%)	1/26 (4%)	-	1/26 (4%)	-	-	1/26 (4%)
Follow up hand-only visit	21/25 (84%)	2/25 (8%)	1/25 (4%)	-	-	-	1/25 (4%)

5.3.8 Correlations between baseline pain and other outcome measures

Pearson's Correlation Coefficients were calculated to examine the relative test-retest stabilities of the individual pain measures between the two visits and between current pain at the start of the visit and various other measurements on the day. Current pain at the start of the stretch-illusion visit (C1) and current pain at the start of the hand-only visit (C2) were strongly correlated (all *ps* < .01, see Table 5.3), suggesting a high test-retest stability and reliability of the individual pain measures and a high degree of stability between the two visits within subjects. C1 strongly correlated with all other pain and function ratings made on the day (all *ps* < .05). C2 strongly correlated with all other measurements made on the day (all *ps* < 0.01), except for hand pain/aching or stiffness over the last month ($p > 0.05$). C2 did not significantly correlate with hand function or FIHOA scores (all *ps* > 0.05).

5.3.9 Correlations between baseline pain, illusion strength and PPT

There was no significant correlation between C1 and change in pain after the stretch-illusion, Pearson's $r(20) = .220$, $p = .16$. This was the same for C2 and change in pain after the hand-only condition, Pearson's $r(26) = -.241$, $p = .11$. C1 (all participants) was negatively correlated with ownership of the hand after the stretch-illusion ("I feel like the hand I am looking at is my hand", Pearson's $r(30) = -.41$, $p = .01$. That is, the greater the pain ratings at baseline, the lower the ownership of the hand after stretch-illusion. There was no significant correlation between C2 (all participants) and ownership after the hand-only condition in the hand-only visit Pearson's $r(27) = -.10$, $p = .29$.

There was a small positive correlation between C1 and susceptibility to the stretch-illusion (“I feel as though my hand was being stretched”, Pearson’s r (28) =-.30, p = .05, in that the greater the pain ratings at baseline, the higher the susceptibility to the stretch-illusion. There was a moderately positive relationship between current pain and the feeling that the hand/finger was stretched after the hand-only condition, Pearson’s r (24) = -.43, p = .027. Finally, there was a negative correlation between ownership and susceptibility, in that higher ownership (“I feel like the hand I am looking at is my hand’’) was related to lower susceptibility to the illusion (“I feel as though my hand was being stretched’’, Pearson’s r (28) = -.32, p = .038.

Table 5.4.Pearson Correlations between subjective pain ratings baseline 1st visit and baseline 2nd visit n=28. (significant correlation is highlighted in bold).

Measure	**Correlation (*r*)**	***p***
	Visit 1&2	
Single pain intensity ratings		
Current pain most painful joint	**.31***	**.049**
Overall hand pain last 2 weeks	**.752****	**<.001**
Overall hand pain last 48h	**.709****	**<.001**
Most painful joint 48 hours	**.666****	**<.001**
Most painful joint last 2 weeks	**.607****	**<.001**
Activity arthritis 48 hours	**.765****	**<.001**
Thumb pain 48 hours	**.752****	**<.001**
Pain in all joints 48 hours	**.693****	**<.001**
Hand function		
Satisfaction with function 48 hours	**.372***	**.025**
Hand pain/aching or stiffness over the last month	**.573****	**<.001**
FIHOA	**.737****	**<.001**

** Correlation is significant at the .01 level
* Correlation is significant at the .05 level

5.4 Discussion

The current study aimed to investigate previously observed analgesic effects of multisensory body illusions and their effects on pain, body representation and hand function in people with painful HOA. Participants viewed their most painful hand through MIRAGE under a number of conditions, with illusory stretching of the hand and changes in sensory input. The primary outcome measures were participants' subjective pain ratings, pressure pain thresholds (PPTs), and subjective experience of the illusion measured on an eight-item questionnaire. Secondary outcome measures included a measurement of grip strength and questionnaires assessing hand pain, stiffness, and hand function.

Although an effect was not found on average pressure pain thresholds between the conditions and compared to the baseline, nor any effect on hand function, the results provide evidence for a change in pain ratings and changes in perceived hand size, ownership, agency and grip strength after stretching both the real and virtual body. A decrease in pain ratings was found in both stretch conditions (stretch-illusion and hand-only) compared to the baseline, with no differences between conditions. Thus, both illusory stretching and tactile stretching resulted in a statistically significant reduction of pain compared to the baseline.

The finding that both actual and virtual views of the painful hand led to a reduction in pain, suggest that the analgesic effects after the stretch-illusion condition are not merely due attention or expectation alone, or being immersed in the virtual environment. Instead, it suggests, in line with previous findings, that the specific multisensory context in which pain occurs is important (Mancini et al., 2011). More specifically, viewing the body can modulate the

sensory processing of pain, but has been shown to depend on the specific visual context in which it occurs, depending on whether the painful body is presented smaller or larger (Mancini et al., 2011; Romano & Maravita, 2014). The findings of the current study go beyond previous findings as they demonstrate that both actual and virtual views of the painful hand can be analgesic.

The finding of an analgesic effect after both stretch conditions is in line with recent findings showing that vision of the body is found to reduce pain (Longo, Betti, et al., 2009; Longo et al., 2012; Sadibolova & Longo, 2014) and that this is specific to viewing one's own body (Haggard et al., 2013). One could argue that the analgesic effects found in the current study could be explained by contextual factors such as participant/experimenter interaction or the experience of touch/expectation (Abhishek & Doherty, 2013; Haggard et al., 2013). Indeed, pain is a multidimensional experience influenced by several top-down factors including prior experiences, beliefs, social factors, attention, expectations, and emotion (Melzack & Wall, 1965). Moreover, although there was a significant reduction in pain after the intervention conditions compared to baseline, the intervention conditions did not significantly differ from contextual control further suggesting that the reduction in pain might not be specific to the multisensory illusion. The effects of the stretch-illusion compared to viewing an object and the effects of tactile input will therefore be further investigated Chapter 6.

To date, there has been limited research investigating the effects of multisensory illusions on pain sensitivity in chronic pain. The results of the present study are in line with studies finding no change in pain sensitivity

following multisensory illusions in healthy controls (Foell et al., 2013; Moseley, McCormick, Hudson, & Zalucki, 2006). There were, however, differences in PPTs for the different body sites, showing a decrease in PPT for the most affected (and experimental) hand after the stretch-illusion. However, as there was no effect on PPT between conditions, it is difficult to determine whether this effect is specific to the stretch-illusion condition or whether it represents a general difference in PPT levels depending on the anatomical location of the measurement taken (Fernández-De-Las-Peñas et al., 2010). Instead, it suggests that if there was indeed an effect of the illusion on pain sensitivity, that this would be comparable with that of seeing one's own hand (Hegedüs et al., 2014).

Another intriguing finding of the present study is the effect of the stretch-illusion on body representation and in particular, its effects on body ownership and agency. The results demonstrate a loss of ownership and agency after illusory stretching of the hand compared to the tactile stretch outside of MIRAGE. The idea that levels of ownership might directly modulate pain is supported by findings in experimental studies where visually changing the size or shape of the affected limb can reduce and increase pain and swelling associated with a reduction of ownership over that limb (Moseley, Parsons, et al., 2008), as well as physical symptoms (Barnsley et al., 2011; McKenzie & Newport, 2015). It has been suggested that some of the analgesic effects of multisensory illusions could be explained by the resultant loss of ownership of the painful hand (McCabe, 2011). However, this would not entirely explain why ownership ratings remained high in the contextual control condition, in which pain ratings were similar to the intervention.

The findings demonstrate a positive correlation between the amount of pain at baseline and the susceptibility to the illusion, in that the greater the pain ratings, the greater the perceived feeling of stretch after the stretch-illusion. Variability in susceptibility to bodily illusions has been reported previously (Haans, Kaiser, Bouwhuis, & Ijsselsteijn, 2012; Preston & Newport, 2011) and has been related to the efficacy of the illusion, in that the higher the susceptibility to the illusion the greater the analgesic effect (Mercier & Sirigu, 2009). This might also explain the variability found in the lasting effects of the illusion (see Table 5.2). Future research should focus on establishing, or perhaps even increasing susceptibility before starting the experiment in order for the illusion to be more effective. This is something that is common practice in non-virtual visual exposure paradigms, such as the rubber hand illusion (Botvinick & Cohen, 1998).

Contrary to the predictions, there was no effect of the stretch-illusion on hand function in terms of maximum or average grip strength, or in terms of scoring on the FIHOA questionnaire. There was, however, an effect on time to peak force after the stretch-illusion, suggesting that participants were adopting a different motor strategy after this condition. Differences in adopting motor strategies have been reported in subgroups of chronic pain, which in some cases have been thought to be mediated by fear-avoidant behaviour (Tsay et al., 2015). Although measurement of grip strength is one of the most commonly used measurements of hand function in clinical and research settings, it has been argued to be an insufficient measure of the different attributes of hand strength (Dias et al., 2013). Hence, I cannot conclude that the stretch-illusion

improved whole hand function and future work should aim to incorporate more functional measures of hand function.

Based on previous findings it was hypothesised that the affective experience of the illusion (like/dislike) would be strongest after the stretch condition. However, the findings show no differences between the different conditions, showing a strong dislike of the hand across all conditions. There is a growing body of evidence suggesting that body image – that is, a person's perception of their body - is disrupted in many chronic pain conditions, including osteoarthritis (Gilpin, Moseley, et al., 2014). Another important factor impacting on body image is the deformities often associated with hand osteoarthritis. Furthermore, the body dissatisfaction experienced by individuals living with this condition has been found to have a major functional and psychological impact on everyday live (Hodkinson et al., 2012). Experience of pain and of the bodily self are closely linked, and there is an important need for the development of interventions that improve satisfaction with body image in chronic pain (Hodkinson et al., 2012). Future work should therefore address the significant body dissatisfaction in these conditions and how this might contribute to body image and the maintenance of persistent pain.

Limitations

Several limitations of the methods and results deserve consideration, each of which point to directions for future research. First, to minimize the burden on participants, the number of conditions and repetition of PPT testing was minimized. Although the current design allowed for a comparison between

view of the hand in or outside the virtual environment and with or without any tactile and visual manipulation, it is difficult to disentangle the tactile contribution and experimenter interaction from the observed analgesic effects. Furthermore, it is possible that simply viewing an image being stretched is in itself distracting. Similarly, an alternative explanation for finding limited effects of the conditions on PPT is that simply viewing the hand was itself analgesic. The effect of viewing one's own hand compared to viewing a non-corporeal object will be investigate further in Chapter 5.

5.5 Conclusions

The current study provides a thorough and controlled examination of the effects of the stretch-illusion on pain ratings, pain sensitivity and body representation in HOA. The study found support for analgesic effects of illusory stretching of the painful hand in HOA, which were similar to the analgesic effects observed after stretching and viewing the real hand. Furthermore, in keeping with previous findings, evidence was presented that further demonstrated that multisensory illusions can alter body representation and body ownership in people with HOA. Not only did the stretch-illusion decrease pain, but subjective pain ratings at baseline significantly predicted illusion strength, which might explain the large variability in responses to the illusion and those observed in other body-illusion paradigms. The current study highlights the importance of the context in which pain is experienced; in this case, virtual and physical stretching modulating pain, but not viewing the hand alone. The following chapter will further investigate the several multisensory components by manipulating different types of multisensory input.

Chapter 6 The effects of multisensory illusions on pain and body perception in people with hand osteoarthritis and healthy controls

6.1 Introduction

Multisensory illusions, including rubber- and virtual-hand illusions, can alter body perception as well as the feeling of perceived body ownership over different objects (Ma & Hommel, 2015). The observed perceptual and analgesic effects of these illusions often occur in reference to the body, and in particular to one's own body. More specifically, viewing one's own body has been found to modulate pain, whereas viewing something else, such as someone else's body or an external object, can diminish these effects (Martini, Kilteni, et al., 2015). For this reason, it has been questioned whether some of the analgesic and perceptual effects found in previous studies using virtual illusion paradigms, are indeed specific to viewing one's own limb or whether they would also occur when viewing a non-corporeal object. Indeed, as mentioned in Chapter 2 the effect of viewing the virtual body, with or without distortions, is especially pronounced when comparing body-specific with non-corporeal objects (Mancini et al., 2011).

In addition, it has been argued that due to the powerful attentional modulation of being immersed in virtual reality, it is difficult to disentangle the contribution of this effect from the suggested analgesic effects of viewing a virtual representation of one's hand (Gilpin, Bellan, et al., 2014). The aim of this Chapter is to re-examine the effects of the stretch-illusion delivered to both the hand and non-corporeal objects on subjective and objective aspects of body perception using a hand size estimation task.

Given that chronic pain is associated with large distortions in perceived shape and size of the body, it is intriguing to consider how participants with painful HOA would perform on a hand size estimation task. Previous research has shown that compared to healthy controls, people with HOA tend to underestimate the size of their hand. Furthermore, as mentioned in Chapter 5, illusory enlarging of the hand has been shown to lead to perceptions of increased hand size in people with OA (Gilpin, Moseley, et al., 2014). This was taken as evidence that people with HOA present with a distorted mental representation of the hand. However, these observations are often interpreted with the assumption that healthy controls do present with an accurate representation of the body (Fuentes et al., 2013).

As mentioned in Section 1.1.3, there is evidence to suggest that healthy controls may actually present with a disruption in body representation. That is, healthy participants present with systematic body perception distortions in implicit measures of body image (Fuentes et al., 2013), as well as in terms of perceived distance of tactile stimuli on the body and position sense (see Longo (2017) for a review). Indeed, Gilpin et al. (2014) demonstrated that people with OA are actually more accurate in estimating hand size compared to controls, which they say, is in itself atypical. In their study, participants were asked to view a picture of their hand, either presented at 150%, normal, or 75% of actual hand length which they then had to match to their actual hand size using an adaptive stairway procedure after the hand was shrunk or stretched in size (Gilpin, Moseley, et al., 2014). The authors reported an overestimation in hand size for both OA participants and healthy controls.

However, this task can be considered as an explicit measure of the conscious body image (Gandevia & Phegan, 1999; Longo & Haggard, 2012), and although similar distortions are generally found using different tasks (Longo, 2017) it would be interesting to investigate whether distorting the hand affects implicit body representations in a similar way. As previous studies in osteoarthritis have only looked at the general effects of visual distortions on perceived hand size, it would be valuable to investigate whether the illusion in fact disrupts the whole hand or whether this is specific to part of the hand that has actually been stretched.

This study will further re-examine the effects of the stretch-illusion by further disentangling the contributions of several factors thought to contribute to the observed perceptual and analgesic effects of the illusion. More specifically, the stretch-illusion will be delivered to a non-corporeal object (in this case, a foam block) placed inside the MIRAGE within the peripersonal space, controlling for any attentional effect specific to the mediated-reality set-up. Furthermore, a hand size estimation task will be included to provide a more objective behavioural measure of the perceptual effects of the illusion. Notably, this is not an investigation into the effects of non-corporeal objects on body representation that are under the participant's control, as this might influence the perceived sense of body ownership. Indeed, recent studies have shown that participants can perceive ownership over a non-corporeal object when it moves in synchrony with the participant's hand (Ma & Hommel, 2015). Finally, these effects will be investigated in both participants with HOA and healthy individuals to allow for a direct comparison of clinical and control performance.

Overall this study has three aims. The first aim is to replicate and extend the effects of the stretch-illusion reported in Chapter 2, 4 and 5 on the subjective experience of the illusion (measured by questionnaire items), and test whether these effects differ between HOA participants and healthy controls. If participants with HOA are as susceptible to the stretch-illusion as healthy controls (HC), I would expect to find similar response to the questionnaire items measuring illusion strength. However, based on findings in Chapter 5 I would expect to find differences in the affective experience of the illusion, resulting from a greater body dissatisfaction in the HOA group at baseline. Furthermore, based on previous findings I would expect to find analgesic effects of the stretch-illusion in the HOA group, with no modulation of pain in the HC group.

The second aim is to test the effects of the stretch-illusion on objective and subjective measures of hand size (estimation judgements and questionnaire items), and whether this differs between HOA participants and healthy controls. Based on the perceptual findings after the stretch-illusion in the previous chapters, I expect to find a distal localisation error after the stretch conditions. Furthermore, as bodily illusions with multiple sensory inputs are thought to induce stronger illusion effects (Gilpin, Moseley, et al., 2014), it is expected that the highest amount of bias will occur after the illusion condition. Also, I would expect to see an effect of condition for the distal bias of the top of the index finger, but not for the knuckle (distal bias remains the same across conditions). That is, the objective perceptual changes would be specific to the location of the visual stretch (fingers) and not simply reflective of a shift in hand size.

Based on previous studies (Gilpin, Moseley, et al., 2014), I would expect to find a difference in the mental representation of the body between people with HOA and healthy controls, but this difference would become smaller after the stretch conditions. Finally, based on previous findings (Mancini et al., 2011; Martini et al., 2014) if the perceptual and analgesic affects for the HOA group are specific to one's own body, I would expect to see very little perceptual changes when viewing a non-corporal body being stretched.

6.2 Materials and methods

6.2.1 Participants

Two groups of participants took part in this study. The first group consisted of seventeen participants with confirmed HOA (mean age 70.7 years, SD = 8.7, 15 female) and 17 healthy controls (mean age 63.6 years, SD = 3.75, 6 female). Participants were recruited through the University of Nottingham's community volunteer lists and through advertisement in local newspapers. All participants provided informed consent and the study was approved by the School of Psychology ethics committee.

6.2.2 Design

A mixed design was used with condition (baseline, illusion, vision-only, tactile-only and control) as the within-subjects factor and group (HOA and HC) as the between-subjects factor.

Table 6.1 Participant demographics

#	Group	Age	Gender	Handedness	Pain location	Most affected hand	Occurrence hand pain 12m	Chronicity	Pain intensity			Function	
									Current pain 0-10	Pain all joints >48h	Pain most painful hand > 48 h	Satisfaction with function 48 h [b]	FIHOA (0-30) [c]
1	HOA	62	Female	Right	Both hands	Right	>3 months	>10 years	1	1	2	1	3
2	HOA	78	Male	Right	Right hand	Right	>3 months	5-10 years	1	4	4	5	11
3	HOA	67	Female	Right	Both hands	Right	>3 months	<12 months	1	4	4	4	0
4	HOA	64	Female	Right	Both hands	Left	>3 months	<12 months	0	4	5	4	6
5	HOA	85	Male	Right	Both hands	Right	1-4 weeks	>10 years	0	0	0	5	9
6	HOA	60	Female	Right	Both hands	Right	>3 months	>10 years	7	7	9	8	16
7	HOA	71	Female	Right	Both hands	Left	>3 months	5-10 years	3	6	8	3	16
8	HOA	70	Male	Right	Both hands	Right	Missing	Missing	0	Missing	Missing	Missing	Missing
9	HOA	62	Female	Right	Both hands	Right	>3 months	5-10 years	5	4	4	5	5
10	HOA	72	Female	Right	Both hands	Right	>3 months	5-10 years	3	5	5	7	5
11	HOA	71	Female	Right	Both hands	Right	>3 months	5-10 years	0	2	3	6	8
12	HOA	69	Female	Right	Right hand	Right	1-3 months	<12 months	1	1	1	1	0

13	HOA	73	Female	Right	Both hands	Left	>3 months	1-5 years	1	3	4	5	3
14	HOA	71	Female	Right	Both hands	Left	>3 months	1-5 years	3	2	2	5	4
15	HOA	90	Female	Right	Both hands	Right	>3 months	>10 years	0	2	0	10	21
16	HOA	83	Female	Right	Right hand	Left	>3 months	>10 years	5	6	6	10	20
17	HOA	64	Female	Right	Both hands	Right	1-4 weeks	>10 years	1	0	0	2	5
18	Control	64	Female	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a
19	Control	64	Male	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a
20	Control	65	Female	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a
21	Control	60	Female	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a
22	Control	66	Female	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a
23	Control	58	Male	Left	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a
24	Control	61	Male	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a
25	Control	65	Male	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a
26	Control	66	Male	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a
27	Control	69	Male	Left	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a
28	Control	61	Male	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a
29	Control	65	Male	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a
30	Control	58	Male	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a
31	Control	60	Male	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a
32	Control	68	Male	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a
33	Control	70	Male	Left	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a
34	Control	68	Male	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a
35	Control	66	Female	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a
36	Control	65	Female	Right	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a

= participant number. [a] Pain intensity measured on a 0-10 numerical rating scale (NRS) rated from 0=no pain at all to 10=worst pain imaginable. [b] 0=very satisfied, 10= not at all satisfied. [C] higher scores denote decreased hand.

6.2.3 MIRAGE system

The apparatus (MIRAGE) was identical to that used in the previous chapters, with a few slight adjustments in the experimental set-up and the conditions used. In the current study, both HOA and HC participants were asked to place their hand (most affected or dominant, respectively) flat inside MIRAGE and keep it flat during the conditions. There were five conditions in total. In the no-illusion (baseline) condition, participants viewed their hand inside MIRAGE without any additional input (see Figure 6.1A). The stretch-illusion condition, vision-only and tactile-only conditions were identical to those described in Chapter 5. An additional non-corporeal control condition was included using a piece of grey foam with no visual resemblance to the real hand (see Figure 6.1). This object was place underneath the participants' hand, with one-third of the foam block extending beyond the tips of the fingers of the participants. In this condition, the foam block was subject to an illusory stretch in the same way as during the stretch-illusion condition: holding the ends of the foam block whilst visually stretching the image of the foam to twice its normal length, without the experimenter touching the participants hand.

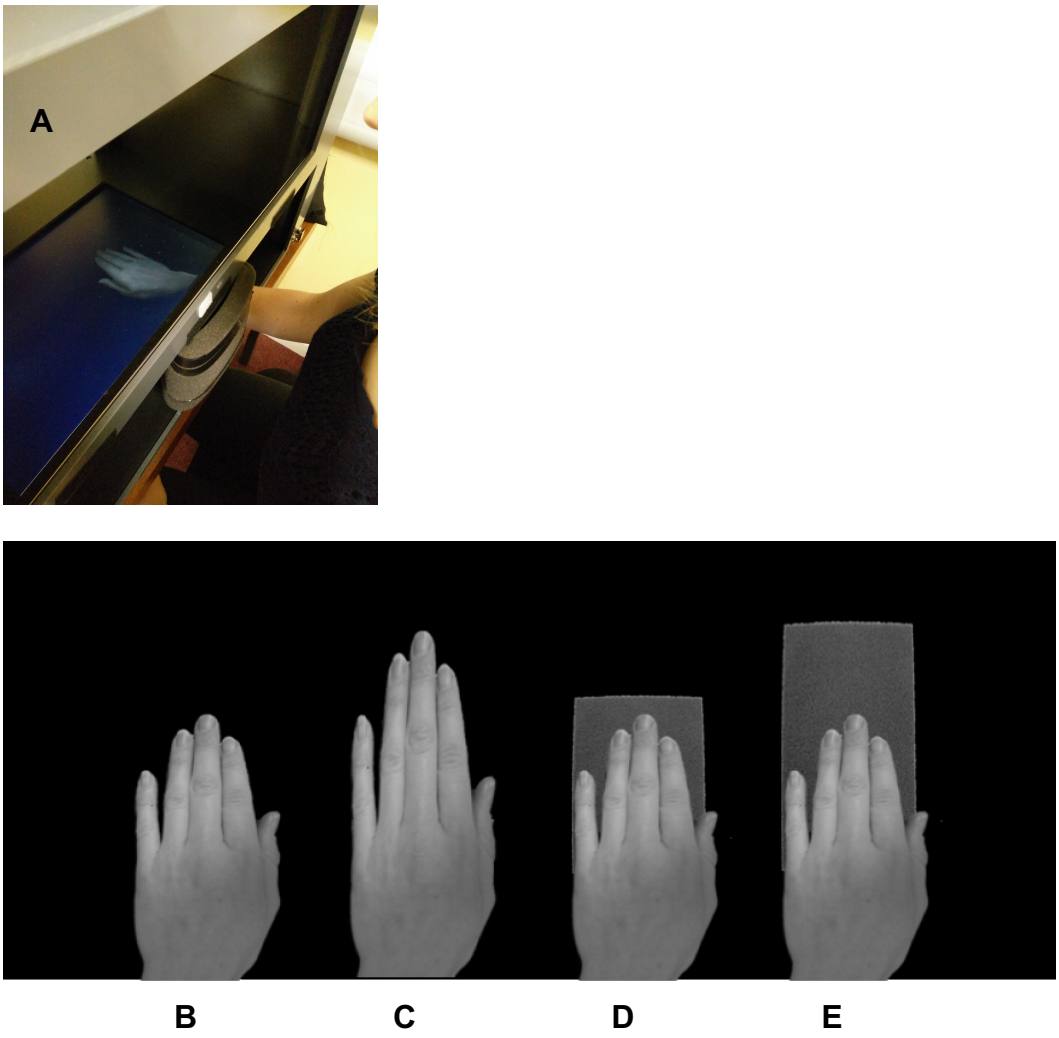


Figure 6.1 Experimental set-up and example stimuli. Participants were asked to place their hand on the MIRAGE surface (A). Example experimental stimuli showing view of the hand before (B) and after (C) illusory or visual stretch, and (D) view of the hand placed on the non-corporeal object (D) before and (E) after the foam block was subject to an illusory stretch. Note: In both the stretch-illusion condition and the non-corporeal condition, the experimenter took hold of the hand or foam block, respectively, and gently pulled the hand (in the stretch-illusion) or the foam block (in the non-corporeal condition) at the same time as the image of the hand stretched.

6.2.4 Finger-length estimation task

Finger-length estimations were performed using the MIRAGE system and the task was created using a LabVIEW (National Instruments, Austin, TX) script. The main knuckle, or metacarpophalangeal joint, was localised by asking participants to make a fist with their hand, and marked with a pen, invisible to the participant. In the finger-length estimation task, vision of the hand was removed before a moving horizontal line appeared across the screen from either the top or the bottom whilst moving away or towards the participant. The hand was in the same position on the x-axis, as during the experimental conditions.

Participants had to indicate the position of their finger by saying “stop” when the red line aligned with the perceived position of the top of their middle finger, after which the line changed direction from the start position. The process was repeated six times, three times for the index finger and three times for the knuckle. The order was counterbalanced across participants, with two practice trials preceding the first conditions. The actual, seen and estimated hand positions were recorded in pixels and converted into cm (1 pixel = 0.73mm). Finger length estimations were calculated by subtracting the localisation error of the knuckle from the localisation error of the finger expressed as a percentage of the actual finger length. The average of the three trials was used for analysis (see Figure 6.2). The participant’s other hand was out of sight for the duration of the experiment.

6.2.5 Subjective experience of the illusion

The same six-item questionnaire and measurements of subjective pain ratings as those described in Chapter 4 and 5 were used to measure the subjective experience of the illusion (See table 3.2).

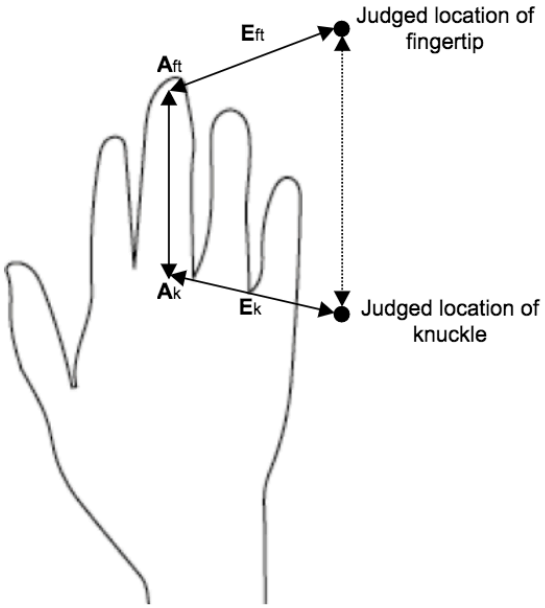


Figure 6.2 Finger length estimations used for analysis. Finger length estimations were calculated by subtracting the localization the error of the knuckle (**E**k) from the localization error of the fingertip; (**E**ft) expressed as a percentage of the actual finger length. **E**k= Estimated knuckle position, **A**k= Actual knuckle position, **E**ft= Estimated fingertip position, **A**ft= Actual position fingertip. Based on Longo & Haggard 2010.

6.2.6 Procedure

The HOA participants completed a functional questionnaire at baseline as described in Chapter 5. For each condition, the participants placed their hand in an unseen start position. For the OA group, the experimental hand was the most painful hand and for the control group, the experimental hand was the dominant hand. After each condition, including the baseline, participants started with either responding verbally to the questionnaire or with the hand

position task. Participants were reminded to keep looking at their hand throughout the experiment. After the experiment participants were asked what they would use the foam object for and no one reported that they would use it as a tool. This was important to establish, as tools might be cooperated into the body schema (Maravita & Iriki, 2004).

6.2.7 Data analysis

Subjective pain ratings, finger-length estimation scores and questionnaire responses were entered in a two-way mixed ANOVA with the within-subjects factor of condition (baseline, illusion, vision-only, tactile-only, and control) and the between subjects factor of group (HC or HOA). Similar to the study discussed in Chapter 5, Pearson correlations were used to examine the relationship between current pain and illusion strength on the ownership, susceptibility and affective experience subscales for the HOA group.

6.3 Results

6.3.1 Subjective ratings of pain

The main effect of group showed that there was a statistically significant difference in pain ratings, with higher pain ratings in the HOA group (M = 2.12, SE = .407), compared to the HC group (M = .071, SE = .383), $F(1,30) = 13.456$, $p < .001$, $\eta^2 = .310$. There was no main effect of condition, $F(2.339,70.164) = .439$, $p < .677$, $\eta^2 = .014$, and no two-way interaction between condition and group, $F(2.339,70.164) = 1.131$, $p < .335$, partial $\eta^2 = .036$, as illustrated in Figure 6.3.

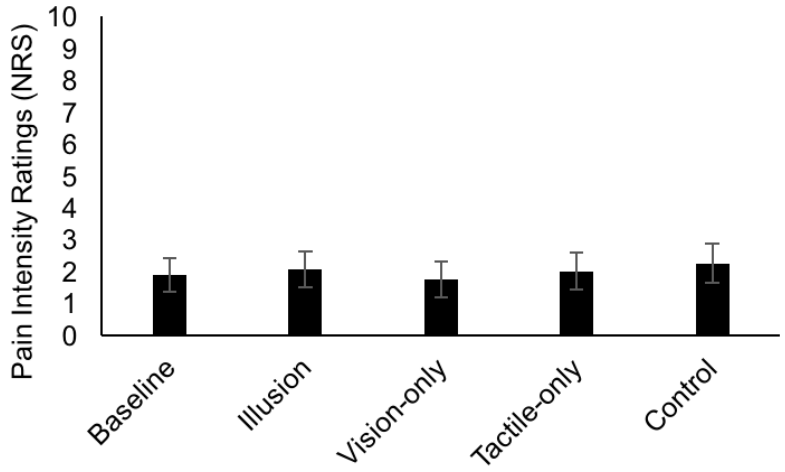


Figure 6.3 The mean effect of condition on pain intensity (NRS ratings) for the HOA group only, with error bars representing standard error.

6.3.2 Finger-length estimation task

Results from the estimation task are shown in Fig. 6.4. As can be clearly seen from Figure 6.4A and 6.4B, participants misallocated their finger after the stretch-illusion and vision-only condition, whereas knuckle estimations stayed approximately the same across conditions. This is important as it shows that participants do not simply perceive their whole hand to be placed further forward. Figure 6.4C shows the mean finger length estimations (cm) after subtracting the knuckle estimation error from the finger estimation error. Finger length estimations as percentage of actual finger length for each group are presented in Figure 6.4D.

The two-way mixed ANOVA showed a trend for an effect of group, $F(1, 30) = 3.362$, $p = .077$, $\eta 2 = .101$, with HOA participants being more accurate on the finger length estimation task at baseline ($p = .086$) and after the tactile-only condition ($p = .083$) (see Figure 6.4D).

The main effect of condition (for both groups) showed a statistically significant difference between the different conditions on the mean finger

length estimations, $F(4, 120) = 22.620$, $p < .001$, $\eta 2 = .430$. There was no statistically significant interaction between the conditions and group on finger length estimations, $F(4, 120) = .733$, $p = .571$, $\eta 2 = .024$.

Bonferroni corrected post-hoc analysis of the main effect of condition showed that mean finger length estimation was greatest after the stretch-illusion (M = 129%, SD = 39.22),which was significantly higher compared to the baseline (M = 77.58%, SD = 22.84), tactile-only (M = 92.16%, SD = 26.2) and the control condition (M = 82.85, SD = 34.03), all ps < .005, ds ≥ 36.56. There was no significant difference found between stretch-illusion and vision-only, but vision-only (M = 128.60%, SD = 37.19) was significantly higher compared to the baseline, tactile-only and control conditions (for all, $p's < .001$, d's ≥ 36.43). However, there were no significant differences in finger length estimations between tactile-only and baseline or control and baseline (all $ps > .05$, d's ≥ 14,64).

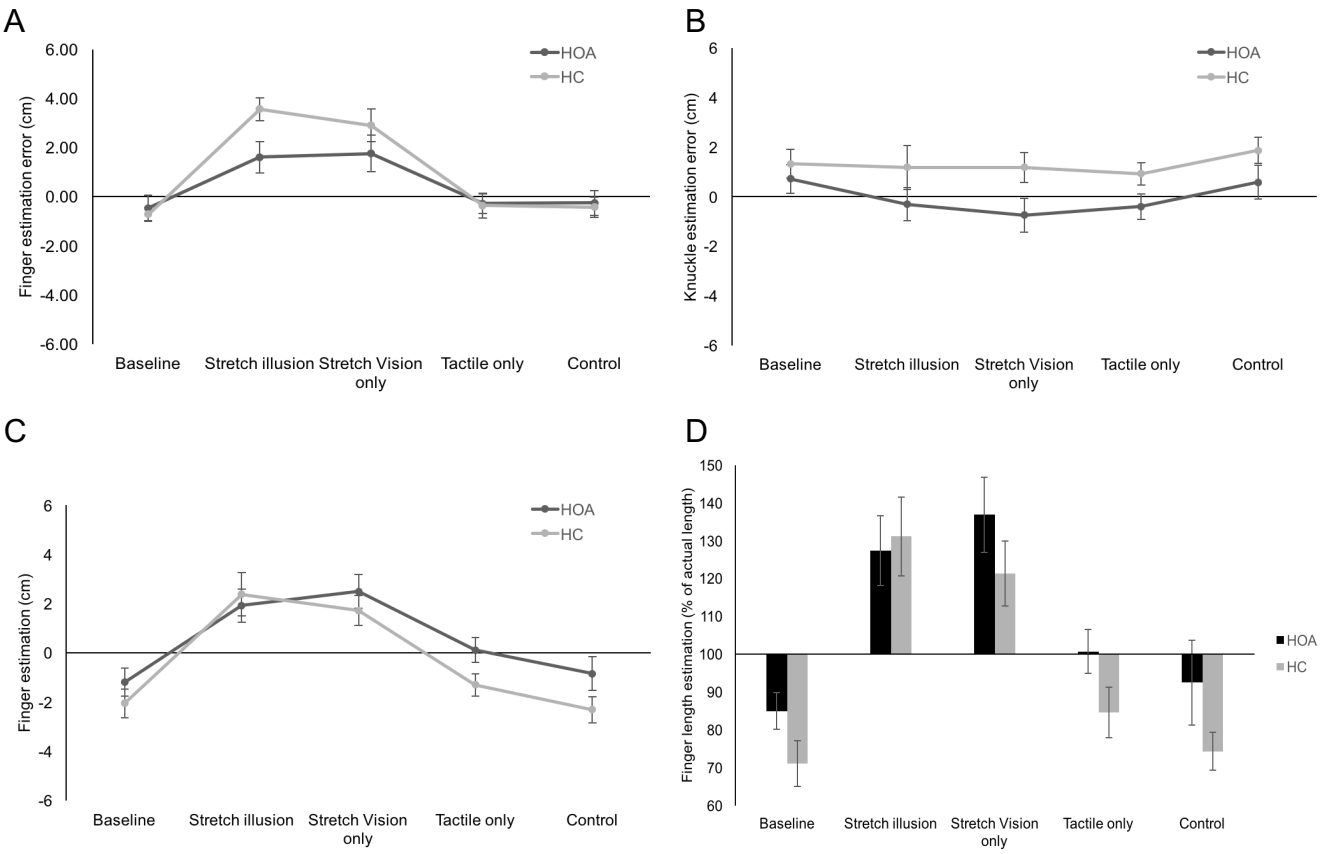


Figure 6.4 Results from the estimation task in which people estimated the location of A) the top of their finger and B) the knuckle. Panel C shows the finger estimations expressed in centimetre after subtracting the knuckle estimation error (B) from the finger estimation error (A) to control for a general shift in hand size. A value of Zero equites to no error/actual finger length. Panel D shows the mean finger length estimations expressed as % of actual finger length after each condition. Error bars represent standard error.

6.3.3 Subjective experience of the illusion

Susceptibility ("It felt as though my hand was being stretched")

The main effect of condition showed a statistically significant difference in mean susceptibility after the different conditions, $F(2.785, 86.348) = 15.308$, $p < .001$, $\eta^2 = .331$. Mean susceptibility ratings were greatest after the stretch-illusion ($M = 1.18$, $SD = 1.509$), which was significantly higher compared to the baseline ($M = -.94$, $SD = 2.41$), vision-only ($M = 1.15$, $SD = 2.43$), tactile-only ($M = .70$, $SD = 2.32$) and control ($M = -1.03$, $SD = 2.27$), (all *ps* values <.05,

d's ≥ 1.05). Ratings for vision-only were significantly higher compared to the baseline, illusion, and the control conditions (all *ps* < .05, d ≥.05), but not different from tactile-only (*p* > .05, *M* = .423). There were no significant differences in susceptibility ratings between tactile-only and baseline, or the control condition and baseline (all *ps* > .05, d ≥.1.631). There was no main effect of group, *F(*1,31) = .110, *p* < .742, η^2 = .004, and no two-way interaction between condition and group on ratings of physiological changes, *F(*2.785,86.348) = 1.821, *p* < .129, η^2 = .055). These findings are illustrated in Figure 6.5A.

Ownership ("I feel like the hand I am looking at is my hand")

The main effect of condition showed a statistically significant difference in mean ownership ratings for the different conditions, *F(*4, 124) =14.749, *p* < .001, η^2 = .322. Ownership ratings after the stretch-illusion were low (*M* =-.18, *SD* = 2.311), which was significantly lower compared to the baseline (*M* = 1.97, *SD* = 1.63), tactile-only (*M* = -1.85, *SD* = 2.00) and control (*M* = -1.73, *SD* = 1.90) (all *ps* <.001, *d* ≥ 1.92). There was no significant difference between stretch-illusion and vision-only, but ownership was lowest after vision-only (*M* = -.42, *SD* = 2.91) and was significantly lower compared to baseline, tactile-only and control (all *ps* <.001, d ≥ 2.0). However, there were no significant differences in ownership ratings between tactile-only and baseline or the control condition and the baseline (all *ps* > .05, d ≥ .112). There was no main effect of group, *F(*1,31) =1.088, *p* < .305, η^2 <.034, and no two-way interaction between condition and group on ownership ratings, *F(*4,124) = .607, *p* < .607, η^2 = .658. These findings are illustrated in Figure 6.5B.

Agency ("It feels as though my hand is in my control")

There was a loss of agency after the stretch-illusion (*M* = .91, *SD* = 2.082), which was significantly higher compared to baseline (*M* = -1.24, *SD* = 1.90), and the control condition (*M* = -1.21, *SD* = 2.16) (all *ps* < .001, *d* ≥ 2.15). There were no statistically significant differences in agency between stretch-illusion and tactile-only (*M* =-.48, *SD* = 2.399) or between stretch-illusion and vision-only (*M* = 1.45, *SD* = 2.017).

Loss of agency was highest after vision-only, which was significantly greater compared to baseline, illusion, and the control condition (all *ps* <.001, *d* ≥ 1.93). There were no significant differences in agency ratings between tactile-only and baseline or the control and baseline condition (all *ps* > .05, *d* ≥ .764), nor any significant main effect of condition, $F(1,31) = 1.086$, $p < .305$, $\eta^2 = .034$, or two-way interaction between condition and group on agency ratings, $F(4,124) = .432$, $p = .785$, $\eta^2 = .014$. These findings are illustrated in Figure 6.5C.

Change in perceived shape ("My finger feels longer than normal")

The main effect of condition showed a statistically significant difference in mean change in shape ratings after the different conditions, $F(3.110, 96.401) = 31.559$, $p < .001$, $\eta^2 = .501$. Mean change in shape ratings were greatest after the stretch-illusion (*M* = 1.55, *SD* = 2.166) which was significantly higher compared to the baseline (*M* = -1.39, *SD* = 2.12), tactile-only (*M* = -1.67, *SD* = 1.80) and Control (*M* = -1.76, SD = 1.733) (all *ps* < .001, d ≥ 2.9). There was no significant difference between stretch-illusion and vision-only, but vision-

only (M =1.48, *SD* = 2.307) was significantly higher compared to the baseline, tactile-only and control (all *ps* <.001, *ds* ≥ 2.87). However, there were no significant differences in finger length estimations between tactile-only and baseline or the control condition and baseline (all *ps* > .05, d's <.366).

There was no significant main effect for group, *F(*1,31) > .001, *p* < .984, η^2<.001, and no two-way interaction between condition and group on ratings of physiological changes, *F(*1,31) > .001, *p* < .984, η^2 <.001. The findings are illustrated in Figure 6.5D.

Affective experience ("I do not like the way my hand looks now")

There was a significant main effect of condition, *F(*2.881, 89.317) =5.461, *p* < .001, η^2 = .150, and a statistically significant interaction between condition and group on mean ratings of affective experience, *F(*2.881, 89.317) = 4.104, *p* < .001, η^2 = .117. There was a statistically significant effect of condition on the affective experience for the HC group, *F(*2.772, 44.352) = 9.269, *p* <.001, η^2 = .367, with body satisfaction significantly reduced at stretch-illusion compared to tactile-only (*M* = 2.41, SE = .607, *p* = .011) at stretch-illusion compared to control (*M* = 2.529, SE = .631, *p* = .010), at vision-only compared to tactile-only (*M* = 2.47, SE = .631, *p* = .012) and at vision-only compared to control (*M* = 2.588, SE = .713, *p* = .022). There was no statistically significant effect of conditions of affective experience for the HOA group, *F(*2.450, 36.747) = .077, *p* < .952, partial η^2 = .005. The relationships are illustrated in Figure 6.5E.

Control ("I feel as though I have two right hands")

There was no significant main effect of condition, $F(2.986,92.569) = 14.749$, $p < .053$, $\eta^2 = .079$, or group, $F(1,31) = 5.241$, $p = .325$, $\eta^2 = .031$, and no two-way interaction between condition and group on the control question ratings, $F(2.99,92.569) =$, $p = .349$, $\eta^2 = .035$. The findings are illustrated in Figure 6.5E.

6.3.4 Correlations between baseline pain and illusion strength

Pearson's Correlation Coefficients were calculated to examine the relationship between pain and illusion strength for the HOA group. Pain scores following each condition did not correlate with the perceived feeling of ownership, all Pearson's $r \leq .41$, $p > .05$, and pain measured at the baseline did not predict ownership following the different conditions (all Pearson's $r \leq 38$, $p > .05$. There was a positive relationship between pain measured at the baseline and susceptibility (the feeling that the hand was stretched) after tactile-only condition Pearson's $r(15) = -.44$, $p = .039$, but not for the other conditions, all Pearson's $r \leq .37$, with all $ps > .05$. Finally, pain measured at the baseline did not correlate with the affective experience ("I do not like the way my hand looks now") following the different conditions, Pearson's $r = .35$, $p > .05$.

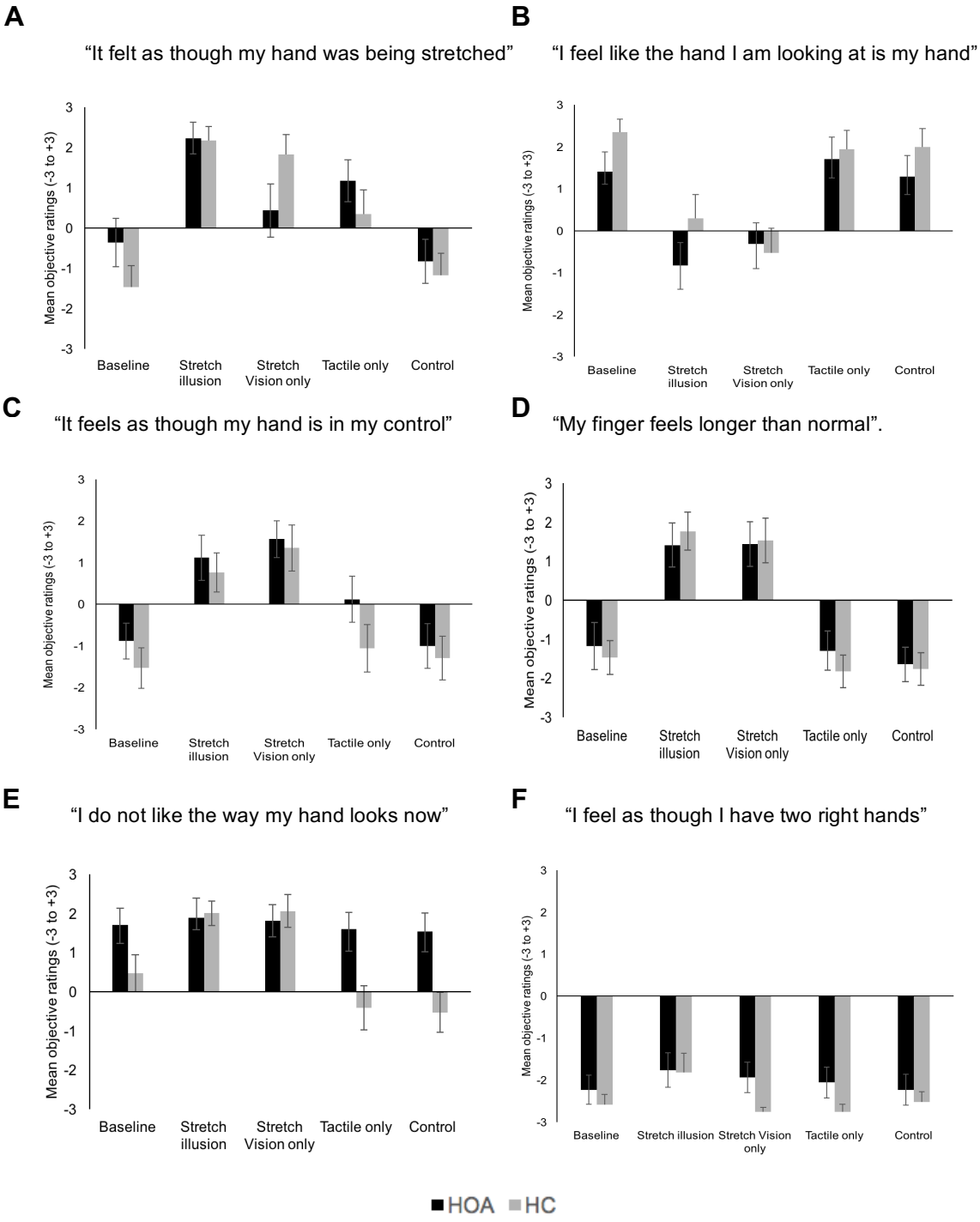


Figure 6.5 Mean objective ratings of the responses to the statements investigating the subjective experience of the illusion taken after every condition. Error bars represent one standard error of the mean. A= susceptibility, B= ownership, C= agency, D=change in perceived shape, E=dislike, F=control question.

6.4 Discussion

The present study examined the effects of the stretch-illusion in people with and without HOA. There are a number of noteworthy findings. First, the stretch-illusion changed the perceived feeling of ownership, changes in body representation and agency. These effects were similar for both HOA participants and healthy controls. Second, although participants with HOA were marginally more accurate than HC participants at estimating finger length at baseline and after the tactile-only (control) condition, they were as accurate at estimating finger length after the illusory conditions. Thus, the first hypothesis was partially supported. The main difference between groups was that illusory stretching significantly negatively impacted on body satisfaction in healthy controls, whilst it did not modulate body satisfaction in HOA. Interestingly, however, HOA participants expressed abnormally high levels of body dissatisfaction. Furthermore, no effect of condition on pain was found in the HOA group. In addition, it was found that illusory stretching of the hand changed perceptions of hand size in both groups, measured by objective and subjective methods and thus supporting the second hypothesis. Third, viewing a non-corporeal object being stretched did not affect any subjective or objective perceptual changes, supporting the third hypothesis. The results will now be discussed in relation to previous findings and the main hypothesis.

The findings show that the stretch-illusion modulates both subjective and objective aspects of body perception and lends further support for the idea that multisensory paradigms can be used to alter body representation and the sense of body ownership in clinical groups (Botvinick & Cohen, 1998; Kammers et al., 2009; Newport et al., 2015; Preston & Newport, 2012). The

high level of perceived ownership at baseline is in line with previous studies showing high ownership ratings over an virtual hand (Newport & Preston, 2010; Schmalzl & Ehrsson, 2011). Furthermore, the amount of perceived ownership reduced after both illusory and visual stretching of the hand, replicating the findings from Chapter 5.

Given that both Illusory stretching and visually stretching of the hand increased perceived finger length suggests that there are no additive effects of tactile information on the strength of the illusion. This finding is intriguing, as it has been suggested that the strongest illusions occur when there is a combination of synchronous vision, touch and proprioception (Newport et al., 2015), or should be more effective with input from multiple modalities, such as vision and touch (Senkowski & Heinz, 2016). Instead, the findings demonstrate that a visual change in body size is sufficient for the illusion (change in perceived finger length) to occur. These observations could be explained by the dominance of vision over proprioception, also known as visual capture (Farnè et al., 2000), and are consistent with the findings reported in Chapter 2 observing no differences between the illusory stretch and the visual stretch.

The present findings have important implications for future work, as it raises the possibility for visual feedback training in clinical practice that do not require experimenter interactions, such as touching the finger of the participant. This is discussed in more detail in Chapter 7. That there was no effect of tactile stretching on the hand or visually stretching an object suggests that the observed effect cannot merely be explained by attentional or proprioceptive factors (Martini, Perez-Marcos, et al., 2015).

Based on previous findings, it was hypothesised that there would be a significant difference in finger-length estimations between groups, which is indicative of a disruption of body representation in the HOA group. This hypothesis was partially supported. The HOA group was generally more accurate in both estimating the position of the finger and the position of the knuckle relative to the actual position. This is in line with findings from Gilpin, Moseley, et al., (2014), who showed that people with HOA are better at estimating the size of their painful hand compared to healthy controls. Furthermore, under normal conditions, HOA participants perceive their hand to be smaller compared to controls which is, in itself, atypical. The authors propose that people with osteoarthritis might be relying on different mechanisms for estimating the size of their painful hand, indicative of a distorted mental representation of the hand (Gilpin, Moseley, et al., 2014). That healthy controls were inaccurate at estimating finger length is in line with previous findings showing that unlike the hands, healthy participants consistently underestimate finger length (Longo, 2015b; Longo, Mattioni, & Ganea, 2015).

However, HOA participants performed similarly on a finger estimation task compared to HCs after illusory stretching of the finger. Indeed, although the HOA group was generally more accurate in both estimating the position of the finger and the position of the knuckle relative to actual position and in line with previous findings (Gilpin, Moseley, et al., 2014), there were no significant group differences after the experimental conditions. These findings are consistent with previous studies showing that the strength of bodily illusions is not necessarily influenced by pain (Giummarra, Georgiou-Karistianis, Nicholls,

Gibson, & Bradshaw, 2010). This suggests that HOA participants are susceptible to the illusion to the same extent as the healthy participants and that the mental representation of their most affected hand is malleable and can be modulated via multisensory illusions (but see: Braithwaite, Broglia, & Watson, 2014).

The current experiment investigated the effect of the illusion on perceived hand size specific to the location of the visual stretch. That is, participants were asked to estimate the position of their finger in relation to the non-stretched hand. By measuring both the perceived location of the knuckle and the fingertip and subtracting the error in finger estimation from that of the knuckle, it was possible to control for a general shift in hand position. Indeed, as can be seen from Figure 6.4B and the findings, there was no effect of condition on the estimated location of the knuckle. In contrast, fingertip estimations were heavily influenced by the stretch-illusion and the vision-only condition, suggesting that the perceived change in size was specific to the location of stretch.

Both illusory and visual stretching of the hand resulted in subjective changes in body representation, body ownership and agency, with no differences between groups. In contrast, whilst illusory and visually stretching decreased body satisfaction in healthy participants, no such effect was observed in the HOA group, indicating that HOA participants may present with abnormally low body satisfaction under normal conditions. Indeed, the findings indicate that even at baseline, people with HOA present with a high level of body dissatisfaction. As mentioned in Chapter 5, people with HOA often

experience high levels of body dissatisfaction which can have a significant impact on everyday live (Hodkinson et al., 2012).

Research into the link between body perception and the affective experience of the body is now emerging (Martini, Perez-Marcos, et al., 2015; Martini et al., 2014; Osumi, Imai, Ueta, Nakano, et al., 2014). As discussed in Chapter 2, there are a growing number of studies using the virtual reality paradigm for changing body satisfaction in clinical and non-clinical conditions, such as eating disorder psychopathology (Osumi, Imai, Ueta, Nakano, et al., 2014; Preston & Ehrsson, 2014; Serino et al., 2016). However, the current study appears to be one of the first to examine the effect of virtual distortions of the affected body part on body satisfaction in chronic pain. Future work should investigate the link between body perception, body satisfaction and pain using multisensory illusions, with a particular focus on improving negative perceptions towards the body.

Based on previous findings it was expected that illusory stretching of the hand would be analgesic in people with HOA (Preston & Newport, 2011). Although HOA participants presented with higher pain scores in the baseline condition, there was no significant effect of Group or Condition x Group interaction on subjective pain ratings. These results contrast with the findings reported by Preston and Newport (2011a) and those found in Chapter 5. There are several reasons that could explain the differences in findings. Although at screening all participants reported to experience pain in one or both of their hands due to HOA, participants did not necessary experience pain on the day of testing. Indeed, of the 17 participants with HOA included in this study, only 35% of participants experienced pain more than 3 out of 10 on a 10-point

numerical rating scale (NRS). Thus, it is possible that generally low pain ratings at baseline resulted in a floor effect.

However, despite the low pain ratings at baseline, there was a marginal effect of group on the finger length estimation task, with the HOA group being more accurate at estimating finger length under normal conditions. Despite the lack of group differences in pain ratings, it is important to note that the current study also found a significant group difference in the affective experience of the illusion and body satisfaction towards the hand and that pain did not predict the abnormal levels of body satisfaction. Further testing of the effect of current pain on representation of body size and shape would be valuable. One way to investigate the specific effect of current pain on perceived body shape would be to look at the differences in mean hand shape between the most painful hand and the other hand.

6.5 Conclusions

The current study demonstrates that body representation can be modulated by multisensory illusions, even when controlling for contextual effects. In line with previous findings, people with HOA are more accurate at estimating body size using objective measures of body representation, which is, in itself, atypical. This suggest that HOA participants may present with an abnormal mental representation of their affected limb. Very few differences were found between HOA and healthy participants in other objective and subjective measures of body representation and perceived body ownership. These findings suggest that multisensory illusions can be used to alter the representation of the affected body part in HOA. However, as discussed in

more detail in the General discussion, HOA participants present with abnormal levels of body dissatisfaction, which contrary to healthy participants does not appear to be influenced by multisensory illusions.

Chapter 7 General discussion

7.1 Summary of experimental results

This thesis had two main objectives. First, it aimed to investigate the effects of multisensory illusions on body representation, sense of body ownership and pain in healthy participants. Work in this field has mainly focused on ownership illusions such as the Rubber Hand Illusion and it is only recently that research started to investigate virtual illusion paradigms and their potential use as clinical tools. As a result, there is a growing body of evidence suggesting that pain and body perception can be modulated using virtual- or mediated-reality paradigms, in which people take ownership over a virtual limb. However, the findings across studies are not unequivocal (Romano & Maravita, 2014), which could be due to differences in methods and experimental designs used. A greater understanding of how these techniques might alter body representation and modulate pain in healthy participants would elucidate the possible applications of these techniques for clinical conditions where body representation distortions and pain might be present, such as chronic pain.

The second aim of this thesis was to investigate the effects of multisensory illusions on body representation, sense of body ownership and pain in individuals with osteoarthritis. More specifically, I examined which factors might contribute to the previously observed analgesic effects of these multisensory illusions. A growing body of evidence suggests that bodily illusions might be used to alleviate chronic pain (Boesch et al., 2015; Moseley & Flor, 2012; Wittkopf & Johnson, 2016). However, existing evidence for the analgesic effects of multisensory illusions in chronic pain is mixed, and these

illusions are sometimes found to worsen the pain experience (Martini et al., 2013). It is important to investigate the interaction between the pain and the body, as it is well known that pain can be modulated through somatosensory modalities (Haggard et al., 2013). This thesis draws on a range of behavioural and psychophysiological methods to investigate the interaction between pain and body representation. The following section will provide a brief summary of the findings from each of the studies and discuss the implications of these findings in relation to the literature of body representation and chronic pain.

7.2 The effect of multisensory illusions on body representations, body ownership and pain in healthy individuals

The experiments described in Chapters 2 and 3 investigated the effects of the stretch and shrink-illusion on body representation, body ownership and pain in healthy participants. Research suggests that body ownership illusions can be used to alter perceived body shape and modulate pain (Mohan et al., 2012). The feeling of body ownership is generally thought to be the result of synchronous multisensory inputs (Jeannerod, 2003). However, the optimal methods for adapting body representations and body ownership and how these might relate to pain in healthy individuals are less clear.

Chapter 2

The main aim of Chapter 2 was to investigate the link between body image and the sense of body ownership. In particular, this study investigated the extent to which distortion of the virtual body impacts upon the feeling of body ownership, with the aim of establishing that distorting the virtual hand can alter

perceived body shape (body image) whilst retaining ownership. Participants viewed their dominant hand through a virtual reality device under different conditions, with four relating to illusory stretching and four to illusory shrinking of the hand, with changes in sensory input. Perceived ownership, body image and experience of somatosensations were measured.

Results showed that the stretch/shrink-illusion led to changes in perceived body shape and body satisfaction, without losing ownership. Furthermore, the results showed a higher amount of somatosensory sensations in the multisensory conditions which was related to the amount of perceived body ownership. Previous work has reported that it is relatively easy to change the perceived body in terms of shape and size, and that this can be readily induced using illusions such as the rubber hand illusion (Ehrsson, Wiech, Weiskopf, Dolan, & Passingham, 2007; Makin et al., 2008). The feeling of ownership over a fake body is generally thought to be the result of synchronous multisensory correlations.

More recent studies have shown that this feeling of ownership over an external body can extend to virtual hands (Martini, Perez-Marcos, & Sanchez-Vives, 2013; Romano, Llobera, & Blanke, 2016; Slater, Perez-Marcos) and virtual bodies (Preston & Ehrsson, 2014; Preston et al., 2015; Romano et al., 2016; Slater et al., 2010). The findings from Chapter 2 add to this literature by demonstrating that people can experience ownership over a virtual hand when the hand is placed within the same spatial reference frame, even when it is displayed in an anatomical implausible configuration. In addition, vision alone is sufficient for a feeling of ownership over or a change in perceived body shape to occur. The findings of Chapter 2 provide further evidence for the

notion that the representation of the body in terms of size, shape, and ownership, is a dynamic process that can easily be altered. This is consistent with the idea that the feeling of ownership is the result of an interplay between top-down and bottom-up factors (Longo, Cardozo, et al., 2008).

The results of Chapter 2 further suggest a link between body ownership, body perception and body satisfaction. This is evidenced by a significant reduction in body satisfaction of the virtual hand in the conditions in which a change in body shape was experienced. It was proposed that the finding that perceptual changes of the (virtual) body can alter affective body representations may be of great importance for conditions where body image disturbances and body dissatisfaction may be apparent. This finding was further investigated in Chapters 5 and 6.

Chapter 3

Having established that the stretch and shrink-illusion can alter perceived body shape as well as body satisfaction, the study in Chapter 3 was designed to investigate whether these illusions could be used to modulate pain. More specifically, it was tested whether distorting the size and shape of the virtual hand would influence pain ratings and pain sensitivity. Research into this area stems from findings of a cross-modal interaction between vision of the body and somatosensation, showing that visual input can alter the perception of different modalities (Longo, Betti, et al., 2009; Martini, 2016). Furthermore, recent studies have demonstrated that vision of the body can have modulatory effects on the perception of pain (Longo, Betti, et al., 2009; Mancini et al., 2011; Martini, 2016).

In Chapter 3, pain sensitivity was measured using Pressure Pain Thresholds (PPT). The study replicated the findings from Chapter 2, showing that visually distorting the virtual body changes perceived body shape and the affective experience of the body. Additionally, participants showed a significant loss of ownership in the conditions in which they experienced a change in perceived hand shape. Contrary to previous studies (Longo, Betti, et al., 2009; Mancini et al., 2011; Martini, 2016; Preston & Newport, 2011), the current study did not find evidence for a modulation of pain following virtual body ownership over a distorted hand. It was therefore argued that PPT or pain ratings are not necessarily affected by the amount of body ownership in healthy participants.

As the aim of the study was to investigate whether a change in perceived body size could affect pain, the study did not compare vision of the virtual body with vision of a non-corporeal object. One explanation for not finding modulatory effects on pain is that all conditions involved vision of the virtual body, which is found to be in itself analgesic compared to viewing someone else's hand or an external object (Longo, Betti, et al., 2009; Mancini et al., 2011). In Chapter 6 vision of the body was compared to vision of a non-corporeal object in order to investigate these differences more closely in both healthy controls and people with HOA.

7.3 The effect of multisensory illusions on body representations, body ownership, and pain in individuals with osteoarthritis

The experiments described in Chapters 4, 5 and 6 examined body representation, body ownership and pain in individuals with HOA. These studies built upon the findings of Chapter 2 and 3, having found support for the

idea that multisensory illusions can alter body perception and the affective experience of the body.

Chapter 4

This chapter investigated whether people with HOA performed differently on a hand laterality motor task. It has recently been suggested that the body schema is disrupted in some chronic pain states (Giummarraa, Gibson, Georgiou-Karistianis, & Bradshaw, 2008; McCabe, 2011; Moseley, 2011; Tsay et al., 2015). The ability to recognise body parts and distinguish between the self and others is thought to rely on an intact body schema, as well as for action and maintaining posture (Longo, Schüür, et al., 2009; Newport et al., 2010; Schwoebel & Coslett, 2005). Hand laterality judgments enable an investigation into the integration between the processing of visual information, the working body schema and premotor processes (Tsay et al., 2015).

The results showed that mental rotation was similar between people with HOA and healthy controls. However, when pain in one of the limbs was present, participants with HOA demonstrated an effect of displayed hand size on body recognition. That is, they demonstrated particular difficulty in recognising the hands when they were displayed larger than normal, and were most accurate when the hand is displayed smaller as normal. Gilpin et al., (2014) demonstrated that people with osteoarthritis tend to perceive their hand to be smaller than actual hand size. It was therefore argued that it is possible that the general perception of body size is important for self-recognition and recognising other bodies.

Furthermore, the findings indicate that participants with HOA present with an effect of the magnitude of mental rotation on motor imagery performance and take longer to process other body information than their own body information, which did not differ from healthy participants in this regard. The finding of an effect of perspective (mental rotation) on reaction times, consistent with the biomechanical constraints of the body on movement, further supports the involvement of the body schema in this task (Parsons, 1987a; Schwoebel & Coslett, 2005). Indeed, these findings indicate that people with HOA use similar processes for body recognition to healthy controls.

The findings show that performance on this task is mediated by the presence of pain, and is dependent on the size and perspective of the body part in view. Thus, although I did not find support for an impairment on this task as a general result of having HOA, the findings provide some support for a distorted representation of the painful body part.

Chapter 5

This chapter examined the effects of the stretch-illusion on pain and pain sensitivity in people with HOA. In particular, it builds upon the findings of Chapter 4, in which support was found for a disruption of the working body schema in chronic pain and previous studies showing an analgesic effect of multisensory illusions in HOA (Preston & Newport, 2011). There is mixed evidence for the use of visual and multisensory feedback for the modulation of chronic pain, mostly due to inconsistent findings in analgesic effects to do with the direction of effect of the visual manipulation (Boesch et al., 2015).

Furthermore, other factors that might contribute to the observed analgesic effects are frequently overlooked.

The study reported in this chapter aimed to investigate how these factors might contribute to the analgesic effects of the illusion by directly comparing the stretch-illusion with other means of visual inputs. Participants viewed their most affected hand through MIRAGE under a number of conditions over two visits, using a cross-over design. The stretch-illusion visit consisted of a stretch-illusion condition and a contextual control, and the hand-only visit consisted of a hand-only condition and the same contextual control. In the stretch-illusion condition, participants viewed their most painful hand inside MIRAGE whilst it was visually and physically stretched. In the hand-only condition, participants viewed their hand outside MIRAGE, whilst it was physically stretched. In both contextual control conditions, participants viewed their hand inside MIRAGE without any tactile or visual manipulation.

The findings demonstrated an analgesic effect of stretching the hand, both virtually and outside of MIRAGE, suggesting that viewing the affected limb can modulate pain. As there was no effect of simply viewing the virtual hand inside MIRAGE, it was argued that in accordance with previous findings in healthy controls, the specific context in which pain occurs is important (Mancini et al., 2011). Furthermore, as participants viewed their own hand in all conditions it was argued that it is difficult to disentangle the contextual and experimenter effects from the visual-tactile inputs to the observed analgesic effects. The contribution of several multisensory and contextual components was further assessed in Chapter 6.

Another finding to emerge from this study was the effect of the stretch-illusion on body representation, body ownership, and agency, and specifically, the reduction of ownership following the stretch condition. A loss of body ownership over the painful limb has been suggested as a possible mechanism for the analgesic effects of the illusion (McCabe, 2011). The finding of no analgesic effect in the contextual-control condition in which ownership remained high lends further support for this theory. However, as further discussed in Section 7.2, ownership over a virtual limb does not necessarily lead to a loss of ownership over the actual limb (Newport & Preston, 2011).

These findings of a change in body size were consistent with the findings in healthy controls reported in Chapter 2 and 3 of this thesis. However, unlike the findings reported for healthy participants in Chapter 2 and 3, the stretch-illusion did not affect the affective experience of the hand in individuals with HOA. As there were slight methodological differences between the study reported in Chapter 5, and it is clear from previous findings that healthy controls might also present with a distorted body representation, it could be informative to directly compare the effect of the illusion on pain and body representation between clinical and non-clinical groups. This was further investigated in Chapter 6, in which participants with HOA were directly compared to a group of healthy participants.

Chapter 6

This chapter aimed to examine the effects of the stretch-illusion on subjective and objective aspects of body perception in people with and without osteoarthritis of the hand(s). A similar paradigm was used to that in the

previous studies except for a few adjustments. The first difference was that both groups placed their hand resting flat inside MIRAGE so to control for any effect of posture between groups. Second, an objective measure of body perception was included in which participants had to decide on the location of their fingertip and knuckle after each condition without viewing their hand. Third, all testing took place in a single visit but in order to limit participant burden, no measures of pain sensitivity were taken.

Consistent with previous findings, people with HOA were better at estimating the size of their painful hand using objective measures of body representation, compared to healthy controls. This suggests that HOA participants may present with an abnormal mental representation of their affected limb. No significant differences were found between groups on the feeling of perceived body ownership, susceptibility, agency, physiological changes or pain. Furthermore, no differences were found on the finger-length estimation task. The findings demonstrated an effect of the illusion on subjective and objective measures of body perception in both groups. These results suggest that people with HOA are not more or less susceptible to the stretch-illusion compared to healthy controls. This is in line with previous findings showing no effect of pain on susceptibility to body illusions (Giummarra et al., 2010).

There was no effect of viewing a control object placed in the peripersonal space being stretched, thus the results cannot be explained by an effect of attention or contextual factors, such as being immersed in the virtual environment. Despite the lack of group differences, the results are still intriguing as they clearly demonstrate an effect of the illusion on an objective

measure of body perception. Furthermore, that there were no differences between the stretch-illusion and the vision-only conditions suggests that vision alone is sufficient for a change in shape to occur and demonstrates no additive effect of tactile input on illusion strength, replicating the previous findings in this thesis.

A second aim of the study was to compare the effects of the stretch-illusion to other means of visual input. The results demonstrated no effects of viewing a non-corporeal object undergoing the same stretch-illusion and placed in the participants' peripersonal space. Thus, it was argued that the effects of the stretch-illusion are not the result of mere attention/contextual factors alone.

Another difference between groups was the finding that the illusion clearly modulated the affective experience (liking) of the hand in healthy controls, but not in people with HOA who reported high levels of body dissatisfaction across conditions. These results suggest that people with HOA may have an abnormally high body dissatisfaction that cannot readily be altered by multisensory illusions.

The findings from these chapters clearly demonstrate that multisensory illusions modulate body perception, in both people with HOA and healthy subjects, which is in line with previous findings (Kilteni et al., 2015; Preston & Newport, 2011, 2012). Furthermore, mixed support was found for the analgesic effects of multisensory illusions, suggesting that the specific context in which the illusion occurs may be important for modulation of pain in people with osteoarthritis, as it has been suggested for healthy participants (Mancini et al., 2011). They also demonstrate that the affective experience of the illusion

significantly differs between people with OA and healthy controls. The core findings of these studies will be discussed in more detail in the following sections.

7.4 Research contributions

In the introduction of this thesis, several processes related to body representation and pain were presented. It was discussed that pain can inform us about the state of our body and that the body and pain are intrinsically linked. It was also argued that body illusions may potentially lead to analgesic effects in chronic pain. Which factors might contribute to reduction of pain remained unclear. The studies in Chapters 4 and 5 suggest that multisensory illusions can lead to a reduction of pain and alter body perception in individuals with HOA. This is consistent with recent experimental evidence and extends the findings of Gilpin, Moseley, et al., (2014) and Preston & Newport (2011b). However, the findings in Chapter 6 found no evidence of this in a different cohort of people with HOA, suggesting the importance of contextual factors for the analgesic effects to occur.

The data presented in the empirical chapters has contributed towards a richer understanding of some of the factors that may be important for the modulation of pain. These included: the role of vision of the body, the feeling of ownership, the alteration of body image and body schema, attention and contextual factors and finally, the affective experience of the body. The following sections will now discuss the implications of the findings presented in the empirical chapters of this thesis.

Modulation of pain and body perception through multisensory illusions

As described above, Chapter 6 did not find an effect of the illusion on pain in people with HOA, though the findings in Chapter 5 showed an analgesic effect of the illusion compared to viewing the virtual hand without any visual distortion. The reduction in pain after the stretch-illusion was similar to the analgesic effect of viewing the actual hand. As outlined in the introduction of this thesis, pain is a multidimensional experience influenced by several physiological and top-down cognitive factors, including prior experiences, beliefs, social factors, attention, expectations, and emotion (Melzack & Wall, 1965). These results further highlight the different ways in which view of the body may modulate pain and that the visual context in which pain occurs is important (Beck, Làdavas, & Haggard, 2016; Mancini et al., 2011).

It has been suggested that for any analgesic effects to occur, people need to perceive ownership over the body presented (Martini et al., 2014). In the introduction of Chapter 2 it was discussed that ownership over an artificial limb can lead to changes in the perceived shape and size of the actual hand and that the illusion of ownership is classically thought to be the result of synchronous multisensory correlations, in particular synchronous visual, tactile and proprioceptive information (Jeannerod, 2003). Although body illusions have been used to investigate the neural and behavioural aspects of the feeling that our body belongs to us, less is known about the ability of virtual- or mediated-reality paradigms to induce the feeling of body ownership, or embodiment.

Recently, it has been suggested that visuotactile input might not be necessary for the feeling of ownership, and that synchrony between visual,

proprioceptive and motor activity is sufficient for the feeling of ownership over an virtual arm (Sanchez-Vives, Spanlang, Frisoli, Bergamasco, & Slater, 2010). The findings presented in this thesis further support this notion by showing that vision and proprioceptive input alone, and arguably motor input, is sufficient to induce the feeling of ownership over a virtual limb. In addition, the findings extend previous results by showing that ownership over a virtual limb can occur even when the hand violates the anatomical constraints of the body (Maselli & Slater, 2013).

Kilteni et al., (2015) present a causal inference model demonstrating that the sense of body ownership could be explained by the processing of multisensory and sensorimotor information that is currently present, and not necessarily the type of sensory information (i.e. only visuotactile cues). Although recent evidence suggests that ownership illusions can still be induced despite violating anatomical and spatial constraints of the body (Maselli & Slater, 2013; Schmalzl & Ehrsson, 2011), Kilteni et al., (2015) propose that these violations might be adapted after the start of the illusion. That is, once the illusion of ownership is elicited, any gradual anatomical or spatial changes, such as altering the size of the fake hand or moving it outside of the hand-centred spatial reference frame, might not abolish the illusion due to the likelihood that the seen and felt signals still originate from the participant's hand instead of it being someone else's hand.

Kilteni et al., (2015) draw from a recent study to support their model, showing that illusory ownership over the rubber hand remained even when spatial or semantic violations were introduced (Hohwy & Paton, 2010). This would explain why in the current thesis, asynchrony did not abolish the illusion

and ownership remained high even though the anatomical constraints of the body were violated. Future work could investigate whether the illusion of virtual ownership can be induced even when the hand is presented with semantic constraints such as a stretched finger from the onset, and whether ownership and susceptibility to the illusion remains constant throughout the duration of the illusion. Indeed, it has been recently suggested that even with high ownership-ratings at the start of the illusion, people might still experience 'breaks' in illusory ownership during the experimental condition (Kokkinara & Slater, 2014).

There were no differences in body image in terms of size and shape between people with and without HOA, which was consistent across the experimental studies. Indeed, for both groups modulating the appearance of the virtual hand resulted in a perceived change in shape and size of the hand, whilst maintaining ownership. This was demonstrated by both subjective ratings of the experience of the illusion and objectively through a finger localisation task. These findings suggest that people with HOA are no more or less susceptible to the illusion, which is in keeping with the findings of Giummarra et al., (2010), who showed that pain does not affect the susceptibility to bodily illusions.

Furthermore, the findings suggest that both healthy individuals and individuals with chronic pain present with several distortions of body image and that the mental representation hand is malleable in both groups. However, under normal conditions people with HOA are more accurate at estimating finger length compared to healthy controls, which is in line with previous findings (Gilpin, Moseley, et al., 2014). Thus it was argued that people with

HOA may present with an abnormal mental representation of the affected body part.

The findings in Chapter 5 demonstrated that pain at baseline predicted illusion strength, as measured by perceived change in shape, which could possibly explain the large variability to the illusion and the variability in illusion strength observed in this thesis and in other body ownership paradigms (Haans, Kaiser, Bouwhuis, & Ijsselsteijn, 2012; Preston & Newport, 2011). This finding has been explained through an emphasis on differences in information processes or cognitive demand (Haans et al., 2012)

Previous studies have demonstrated that the higher the susceptibility to visual illusions, the greater the analgesic efficacy (Mercier & Sirigu, 2009). This stresses the need for future research to investigate the differences in individual susceptibility to the illusions which may lead to greater analgesic effects and lasting changes in body image. Future studies should examine the role of pain at baseline and how this relates to susceptibly to the illusion, not only the one used in this thesis but to body ownership illusions in general. It would seem useful to compare the susceptibility of an individual to several body ownership illusions to establish whether the individual differences reflect differences in the methods used or whether they are more reflective of individual abilities and experiences.

This thesis found evidence for a disruption of the working body schema in people with HOA. These findings are consistent with previous studies suggesting a disruption of body schema in several chronic pain conditions, which has been linked to cortical reorganization in areas associated with body perception (Giummarraa et al., 2008; McCabe, 2011; Moseley, 2011; Tsay et

al., 2015). Although pain seems to contribute to the cortical representation that underlies the body, the causal direction of this relation remains mostly unclear (Haggard et al., 2013). From the findings in this thesis it is impossible to confirm the direction of the relationship between a disruption of the body schema, or distorted body representation in general, and pain. However, recent findings suggest that pain might be a consequence rather than cause of distorted body representation (Bultitude & Rafal, 2010; Moseley, Parsons, et al., 2008). Future studies should address the relationship between body perception disturbances and the experience of pain. Furthermore, it would be interesting to investigate whether repeated exposure to a motor imagery task, as used in Chapter 3 of this thesis, would improve or restore these disturbances.

7.5 Limitations and future research

A number of limitations are considered in relation to the experimental studies conducted in this thesis. The first is concerned with the duration of the analgesic effects of the illusion. This thesis mainly focused on the immediate effects of multisensory illusions on pain and body representation. Although the findings in Chapter 5 suggest that for some individuals the stretch-illusion may have analgesic effects beyond exposure to the stretch-illusion lasting up to 24 hours, for the majority of participants the analgesic effects lasted for the duration of the experiment. Future work could focus on the lasting effects of the illusion on body perception and pain, and investigate whether repeated exposure and training would reduce pain in the longer-term.

The second limitation relates to the assessment of functional disability in people with HOA. Though pain is a very prominent and often debilitating complaint of people with HOA, and indeed was the main focus of this thesis, people with HOA often experience many other functional impairments (Hill, Dziedzic, & Ong, 2010). Previous studies have anecdotally reported an effect of the stretch or shrink-illusion on hand function (Preston & Newport, 2011). The study in Chapter 5 included a self-report hand function test (FIHOA), which is commonly used in clinical and experimental studies in people with rheumatic conditions and has robust psychometric support (Poole, 2011). Although this thesis included several objective and subjective measures to assess hand function in terms of weakness and deformities in Chapter 5, it could be argued that they do not provide an appropriate measure of how it affects other important daily activities, such as self-care and work (Poole, 2011). Future studies could include a performance-based hand function test, such as the Arthritis Hand Function Test (AHFT) or the Cochin Hand Function scale (see Dziedzic, K, Thomas, & May, E, (2005) for a review) to directly investigate whether the illusions affect functional ability in the hand.

The third limitation is concerned with feelings of ownership over the virtual body. As well as ownership over the “fake” limb, it has been suggested that the analgesic effects of multisensory illusions may result from a loss of ownership over the painful limb (McCabe, 2011; Petrini & Arendt-Nielsen, 2016). It has been shown that individuals retain normal levels of ownership over the real hand (displayed in the same position as the actual hand) when virtual feedback of the fake hand is synchronous (Newport & Preston, 2011). This was consistent with the findings presented in Chapter 5 and Chapter 6.

Furthermore, it has been shown that ownership over an artificial or virtual body alone is not sufficient for the analgesic effect to occur (Martini et al., 2014; Mohan et al., 2012).

However, the question of whether ownership over a fake body affects the embodiment over the affected painful limb still remains. Future research should investigate what happens to the 'real' affected painful hand in terms of body ownership and whether this affects the experience of pain. Future studies could investigate this, for example, by focusing on the salience of stimuli delivered to both the 'real' affected hand as well as the embodied hand, and investigate the effects on the experience of pain and arousal responses. If stimuli delivered to the affected hand would become less salient and/or individuals report a reduction of ownership over the actual hand, this would provide support for the theory that the analgesic effects might result from, or be influenced by, a loss of ownership over the affected and painful hand.

The final limitation is concerned with the degree of variability across HOA participants between the different chapters (Chapter 4, 5, and 6). Although steps were taking to minimise variation in pain levels by screening all HOA participants prior to study participation, participants did not necessarily experience pain on the day of testing. This was especially the case in the study reported in Chapter 6. However, despite the group differences in pain ratings between chapters, the effects of multisensory illusions on body perception and the high levels of body dissatisfaction in HOA were consistent between studies.

7.6 Clinical implications

It is estimated that around 7.8 million people in the UK suffer from moderate-to-severe chronic pain, making it a major social and economic burden (Hiligsmann et al., 2013). Chronic pain is extremely debilitating and notoriously difficult to treat, resulting in a pressing need for effective rehabilitation treatments. There is growing support for the idea that multisensory illusion approaches can be used for the treatment of chronic pain. Mirror visual feedback training is a commonly used approach and has been shown to be beneficial for the reduction of Phantom Limb pain (Ramachandran & Rogers-Ramachandran, 1996). However, whereas prolonged mirror treatment lasting for between four to six weeks has generally been shown to be beneficial (Boesch et al., 2015), the effectiveness of a single session of mirror therapy for other chronic pain conditions is mixed (Boesch et al., 2015; Moseley, Gallace, et al., 2008),

Given the well-known interaction effects between pain and several (somato)sensory modalities, there is considerable support for the idea that multisensory illusions could be used as a therapeutic intervention. The findings of this thesis and the effects on body representation and chronic pain certainly lend support for this suggestion and, as discussed in Section 7.3, there is a need for future research to systematically investigate the effects of repeated exposure to the illusion. Future work could use the available protocols on prolonged mirror treatment, such as that used by Ramachandran & Altschuler (2009), as a guideline for developing a multisensory feedback training program suitable for individuals with chronic pain.

A consistent finding throughout this thesis is that vision of the virtual body alone is sufficient for any perceptual and analgesic effects to occur. Future work should take this in consideration when designing multisensory feedback paradigms and focus on the equipment and software used. In recent years, virtual reality technology has become more accessible for clinical use through the development of virtual reality techniques for home-entertainment. Thus, future research should focus on making multisensory techniques more accessible by developing interventions that are more portable, less costly and consequently more appropriate for clinical- and home-use. For example, the delivery of these illusions could be implemented through portable devices, such as tablets and mobile phones.

In addition to understanding the relationship between body representation and pain, this thesis also focused on the relationship between the perceptual and affective representations of the body. Previous studies have shown a link between perceptual and affective body representations, illustrating that they can directly affect each other (Preston & Ehrsson, 2014). In Chapter 2 of this thesis, the relationship between the affective experience of the body and pain was highlighted. The study in Chapter 6 demonstrated that people with HOA present with high levels of body satisfaction and that, unlike healthy controls, the stretch-illusion did not modulate the amount of body satisfaction.

One explanation for this finding is that the effects of body ownership illusions seem to depend on the visual context of one's own body (Haggard et al., 2013). It is therefore possible that visually changing the appearance of the painful hand to a more idealized appearance of one's body could lead to

changes in body satisfaction. Indeed, previous studies have shown that ownership over an 'ideal' body can increase body satisfaction, whereas ownership over an less 'ideal' body can decrease body satisfaction (Preston & Ehrsson, 2014).

The findings of this thesis underscore one of many ways in which living with an often visible chronic condition such as arthritis can have a major impact on how I perceive ourselves (Hill et al., 2010). Given the apparent link between perceptual and affective body representations, and the fact that emotion can directly influence or exacerbate pain (Melzack & Wall, 1965), a core focus of future work needs to be upon developing interventions that are aimed at modulating negative perceptions towards the body as part of a broader focus on developing interventions that can modulate pain.

The deformities seen in HOA are generally irreversible and, when asked to look at their hands in a research setting, participants have reported rarely looking at their hands for the equivalent length of time in everyday life (Themelis et al., in preparation). Therefore, visual exposure using similar methods to that used in this thesis, might help reconnect the person with their own body and emotions through an alternative way of viewing their deformities (Hodkinson et al., 2012). This corresponds with the idea that the use of multisensory illusions opens promising avenues for altering perceptions of hand size and shape, and potentially modulate negative perceptions towards the hands.

Finally, the findings of this thesis highlight the many contextual factors that can shape pain. The thesis has mainly focused on the perceptual factors such as specific visual contexts and variety in multisensory inputs, but

acknowledges the role of a whole variety of top-down cognitive factors that may influence pain. Indeed, contextual factors such as participant interactions, patient expectation and beliefs, and treatment factors have all been found to enhance treatment outcomes in patients with osteoarthritis (Abhishek & Doherty, 2013). It has been suggested that health care professionals should consider optimizing contextual effects in order to enhance treatment outcomes and minimize side-effects, whilst considering the ethical issues associated with the use of placebo and adhering to ethical guidelines (Doherty, Bijlsma, Arden, Hunter, & Dalbeth, 2016). Although the use of placebo remains controversial, future research should consider the use of contextual factors in a research context in chronic pain conditions, as contextual effects occur with any participant-experimenter interaction and could potentially lead to significant improvement in treatment outcomes.

7.7 General conclusions

The research presented throughout this thesis has found the following key findings. First, multisensory illusions can alter body representation in both individuals with HOA and healthy groups. Furthermore, the findings demonstrate that participants can experience ownership over a virtual body even when anatomical constraints are violated, arguing against a purely top-down account for the feeling of body ownership. Under normal conditions, individuals with HOA perceive their affected hand to be different in size, which suggest that, in line with previous findings, people with HOA have an abnormal representation of their affected body part. Furthermore, people with HOA perform worse on a motor imagery task compared to healthy participants which

may, in line with previous research, be indicative of a disruption of the working body schema. However, the causal relationship between disruptions in body representation and pain remains unclear, and future studies should investigate whether prolonged and/or repeated exposure to the illusions causes any of the effects to endure for longer.

While the results of this thesis suggest that the effectiveness of multisensory illusions on the reduction of pain in HOA is mixed, the findings may still be clinically important. Specifically, the findings here suggest that baseline pain might be an important predictor of susceptibility to the illusion. Furthermore, they demonstrate that the specific context in which pain occurs is important and highlight the many perceptual and cognitive factors that may contribute to previously observed analgesic effects. Although it is often taken for granted, the experience of pain is shaped by numerous contextual factors and occurs with every participant-experimenter interaction. As such, they should be taken into account as an additional feature for understanding the variability in treatment effects between individuals.

The findings further support recent evidence for a link between body perception and body satisfaction (Preston & Ehrsson, 2014) by showing that multisensory illusions can alter the affective experience of the body. In contrast, illusory ownership over a distorted hand did not alter body satisfaction in individuals with HOA, which could be explained by abnormally high levels of dissatisfaction towards the body. There is a pressing need for interventions to address some of the common yet understudied concerns that are associated with living with a chronic and often visible condition such as HOA.

As discussed in the previous section, the findings in this thesis have important implications for future research and the development of visual feedback interventions not only for HOA, but also for a range of similarly visible chronic conditions where pain, body image disturbances and body dissatisfaction may be apparent, such as Complex Regional Pain Syndrome (CRPS) and burn injuries. Specifically, building on the findings that visual feedback alone is sufficient to modulate body perception, and to some extent pain, future work should focus on the development of interventions that are more portable and accessible for home use, and focus on developing research around the effects of repeated and prolonged exposure to multisensory illusions on pain and body image disturbances.

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