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How the Body Can Feel Wrong : : Sensory Processing and Neural Body Representation in Transsexuality and Anorexia Nervosa

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# UNIVERSITY OF CALIFORNIA, SAN DIEGO

How the Body Can Feel Wrong: Sensory Processing and Neural Body Representation in

Transsexuality and Anorexia Nervosa

A dissertation submitted in partial satisfaction of the requirements for the degree Doctor of

Philosophy

in

Psychology and Cognitive Science

by

Laura Kristen Case

Committee in charge:

Professor Vilayanur S. Ramachandran, Chair Professor Nicholas Christenfeld Professor Eric Halgren Professor Walter Kaye Professor Amanda Roberts Professor John Serences

2013

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The Dissertation of Laura Kristen Case is approved, and is acceptable in quality and form for

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Chair

University of California, San Diego 2013

# DEDICATION

I would like to dedicate this dissertation to my parents, who taught me to observe and question everything. To my dad, who studies the "unconscious" from a different angle, and to my mom, who always asks the hardest and most important questions.

# EPIGRAPH

In most public and most scientific discussions, sex and nature are thought to be real, while gender and culture are seen as constructed. But these are false dichotomies.

Anne Fausto-Sterling, Sexing the Body

In a sense, when we look at the world, we are hallucinating all the time. One could almost regard perception as the act of choosing the one hallucination that best fits the incoming data.

VS Ramachandran, The Tell-Tale Brain: A Neuroscientist's Quest for What Makes Us Human

Never lose a holy curiosity.

Albert Einstein

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Chapter 3, in full, is a reprint of the material as it appears in Experimental Brain Research. Case L, Wilson RC, & Ramachandran VS (2012). Diminished Size-Weight Illusion in Anorexia Nervosa: Evidence for Visuo-Proprioceptive Integration Deficit. Experimental Brain Research, 217(1), 79-87. The dissertation author was the primary investigator and author of this paper.

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### PEER-REVIEWED PUBLICATIONS

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**Case L**, Ramachandran VS, & Pineda J (In preparation). Mu Suppression Indicates Preference of Human MNS for Egocentric Visual Viewpoint on Goal-directed Hand Movement.

### SELECTED ABSTRACTS AND INVITED PRESENTATIONS

**Case L**, Gosavi R, & Ramachandran VS. Heightened Motor Referral and Sensory Referral Induced by Nerve Block or Topical Anesthetic. Cognitive Neuroscience Society 20th Annual Meeting, San Francisco, April 2013.

**Case L**. Alternating Gender: A Window into the Plasticity of Sex and Gender? UCSD Interdisciplinary Collaboratory on Gender Inequality, San Diego, February 2013.

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### ABSTRACT OF THE DISSERTATION

How the Body Can Feel Wrong: Sensory Processing and Neural Body Representation in Transsexuality and Anorexia Nervosa

by

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Doctor of Philosophy in Psychology and Cognitive Science

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While most people take identification with their bodies for granted, conditions like phantom limb pain, alien hand syndrome, and Xenomelia demonstrate that feelings of bodily congruence or incongruence are tied to neural construction of body image. Individuals with Xenomelia, for example, show reduced right parietal representation of body parts they find overpresent and aversive. Similarly, transsexual individuals often find their untreated sexed body parts incongruent and aversive. Could differences in representation of these body parts in the right parietal lobe underlie this sense of bodily incongruity? Moreover, could a similar mechanism be involved in the counterfactual feelings of fatness in patients with anorexia nervosa (AN)? In this dissertation I investigate sensory processing and neural body representation of congruent and incongruent-feeling body parts in presurgical female-to-male (FTM) transsexual individuals, and dysphoric and neutral-feeling body parts in people with AN. Experiment 1

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demonstrates heightened skin conductance response to tapping of the breast in presurgical FTM individuals, suggesting that aversion to body parts that feel incongruent extends to the level of automatic sensory processing. Utilizing magnetoencephalography (MEG), Experiment 2 demonstrates different integration of sensation from a body part that feels incongruent with one's gender. Experiment 3 reports diminished visual-tactile integration in individuals with AN, suggesting either greater reliance on somatosensory information or deficits in multisensory integration. Experiment 4 discusses differences in the somatosensory response (measured through MEG) to sensation from the abdomen between individuals with and without AN. Experiment 5 reports preliminary research on the use of allocentric mirror viewing strategies to correct body image distortion. I also report within-subject effects of body satisfaction on visual and tactile estimates of body size, suggesting rapid top-down modulation of sensory body representation. In summary, these studies demonstrate the presence of low-level differences in somatosensory processing for body parts that feel incongruent or dysphoric, suggesting strong connections between lower-level sensory representations of the body and higher-level, explicit body image and body dysphoria. This work advances our understanding of the involvement of sensory processing and sensory integration in the construction of experiences of body and self.

# INTRODUCTION

As humans, we intimately identify with the bodies we inhabit. Yet these bodies are never stable; they grow and change over time. Typically the brain keeps pace with these changes; most people identify with their body in its current form. Amputees with phantom limbs, stroke patients with alien hand syndrome, and individuals with Xenomelia, however, do not. These patients experience the presence of a limb that no longer exists, movements of an arm that feel eerily unpredictable and avolitional, or the overwhelming sense that one of their normal, healthy limbs should not be a part of their body. In other cases, such as Body Dysmorphic Disorder or various eating disorders, a body that appears normal to others is perceived by its owner to be grossly insufficient or "wrong". How could a physically normal body feel overwhelmingly "wrong" to its inhabitant, given that the brain and body are developmentally interconnected from the earliest moments of life? These conditions demonstrate the potential for dysfunction- and thus the central importance- of brain mechanisms that allow us to identify with and feel ownership of our bodies.

#### Xenomelia

A particularly striking example of seemingly irrational feelings of bodily wrongness is Xenomelia- a form of Body Integrative Integrity Disorder also known as "apotemnophilia." Individuals with Xenomelia desire the amputation of a completely healthy limb because the limb feels as if it should not be a part of their body; it feels wrong. This desire does not result from negative experience with the limb or from any real or perceived defect of the limb (First 2005). How could one healthy, normal-looking arm or leg (but not the other) feel unbearably out of place to its owner?

A clue to Xenomelia's neurological basis comes from the fact that patients describe a precise and consistent line for their desired amputation; in addition, patients who proceed with amputation are overwhelmingly relieved and satisfied with the outcome of their decision

(Ramachandran & McGeoch, 2007). Might abnormalities in neural representation of the body lead to dysphoria for a particular body part? McGeoch et al. (2011) used magnetoencephalography (MEG) to study activity in the right superior parietal lobe (rSPL), a part of the brain involved in multisensory construction of body image, in response to tactile stimulation of patients' affected (disliked) and unaffected (liked) limbs. They found significantly less sensory-evoked response to the affected limb in the rSPL, suggesting that the desire for amputation may stem from an insufficient representation (or functional activation) of the affected limb in the rSPL. Interestingly, Xenomelia patients sometimes describe their affected limb as feeling "over-present" (Giummarra et al., 2011). Since primary sensory processing of tactile stimulation seems to be preserved in Xenomelia, might this sense of over-presence arise from a discrepancy between magnitude of primary sensory response to the limb and insufficient integration in higher-level body integration areas like the rSPL? A discrepancy between sensory perception and body representation might tell the brain that incoming sensation cannot be categorized or integrated, sending an alarm signal leading to anxiety and discomfort. Indeed, heightened sympathetic nervous system response has been observed to tactile stimulation of the affected limb in Xenomelia (Brang et al., 2008).

#### Neural Respresentation of Body and Self

Xenomelia highlights the extent to which body and self are phenomenologically entwined: typically, body and self are experienced in unity. A unitary percept of body and self, however, reflects a complex orchestration of body representation, integration of multisensory experience, sense of agency, and phenomenological embodiment (Giummarra et al., 2011). Research on the neural bases of these components of body representation provides insight into the construction of the perceptual experience of body and self. Beyond Xenomelia, a number of other strong and unusual feelings about the body have been linked to damage of the rSPL, including neglect or hatred of the left side of the body (Critchley 1953), denial of paralysis of the body (Babinski 1914), personification of a paralyzed limb (Critchley 1955), perception of supernumerary phantom limbs (Critchley 1953), and sizedistortions of body parts (e.g. Frederiks 1969). In addition, Gerstmann described an interesting delusion he called 'somatoparaphrenia' in which a patient with a right parietal lesion misattributes ownership of a paralyzed left arm or leg to another person (1942). These conditions suggest that the rSPL contributes to a normal sense of body ownership, liking, and understanding of the body's shape, size, and sensorimotor condition. The rSPL is likely part of a 'body-matrix' such as that proposed by Moseley et al. (2012), including brain areas that represent both somatotopic and peripersonal sensory data as well as body-centered spatial sensory data. Representation of the form of the body in the rSPL and early sensory regions may be largely hard-wired, as evidenced by some patients who congenitally lack one or more limbs yet nonetheless report phantom sensations (Saadah & Melzack, 1994; Ramachandran & Hirstein, 1998; Brugger et al., 2000).

Body representation is not a fixed entity, however: sensory input plays a strong role in modifying online representation of the body. Indeed, changes in afferent sensation due to post-amputation phantom limb pain and local anesthesia have been found to modify the somatotopy of primary sensory cortex (Flor et al., 1998; Waberski et al., 2007). After initial activation of contralateral primary sensory cortex, sensory input is processed and integrated with body representations in a number of parietal and insular regions in addition to the rSPL. Tsakiris (2010) proposes a neurocognitive model of body-ownership in which (1) a structural model of the body in the right temporo-parietal junction (rTPJ) checks incoming sensory data for structural compatibility with the incoming sensation, (2) primary sensory cortex (S1) and secondary somatosensory cortex (S2) work to integrate multisensory data into egocentric coordinate

systems, creating an online representation of the body, and (3) a sense of body-ownership arises based on the sensory input successfully onto one's body. This final step includes the rTPJ and S2 as well as the right posterior insula. Indeed, the rTPJ is implicated generally in self-other distinction and with inference of self-agency and interaction with the outside world (Decety & Lamm, 2007), and the posterior insula appears to underlie subjective experience of body ownership; an fMRI study of the rubber hand illusion<sup>1</sup> found that increased experience of a rubber hand as one's own was correlated with heightened activation of the posterior insula (Tsakiris 2007).

In addition to the areas included in Tsakiris's model, other areas including the angular gyrus, insular cortex, precuneus, and cingulate gyrus may also play a role in the sense of self and embodiment. Stimulation of the angular gyrus has been shown to elicit out-of-body experiences (Blanke et al., 2002). Because Blanke et al., also found stimulation of the angular gyrus to cause illusory transformations of the arms and legs, and whole-body displacements, they suggest that out-of-body experiences may be tied to difficulty integrating complex somatosensory and vestibular feedback. Insular cortex also plays an important role in body perception, especially in the perception of visceral sensation, pain, and emotion. In addition to its role in the sense of body ownership, the posterior insula balances sensory and visceral input to maintain bodily homeostasis. The anterior insula is strongly implicated in affective processing of interoceptive and other somatic stimuli, bodily- and self-awareness, emotions, and pain (Craig 2009). On the medial surface of the parietal cortices, activity in the precuneus and cingulate gyrus is tied to conscious awareness of sensation and pain, as well as self-related attention and introspection (e.g. Boly et al., 2007). These regions likely work in concert to determine embodiment and ownership

<sup>&</sup>lt;sup>1</sup> In the Rubber Hand Illusion a participant's hand is occluded and he or she views only a rubber hand. Spatiotemporally synchronized touch to the rubber hand and the participant's hand frequently gives the participant the illusory feeling that their sensation is arising from the rubber hand, and/or that the rubber hand is part of their body.

of incoming sensation, updates to online representations of body structure and position, and selfrelevance and emotional valence of the bodily sensation.

#### **Current Studies: Anorexia Nervosa and Transsexuality**

Conditions like Xenomelia suggest that sensory integration and multimodal body representation are critical to feeling that one's own body is coherent and "correct." Could differences in sensory integration in the rSPL or other body integration areas underlie (in part) other conditions in which the body is perceived to be wrong? For example, how does an irrational feeling of obesity, or a sense that one's body is of the wrong sex, relate to multimodal construction and representation of the body in the parietal and insular cortices? The current work investigates anorexia nervosa and transsexuality, two conditions involving atypical body image whose neurological bases are still obscure. In each of these conditions past research and clinical symptomatology suggest involvement of differences in parietal lobe sensory processing and body representation, but the mechanisms underpinning each disorder's unique body image conflicts are unknown.

Historically, anorexia has been viewed biologically as a problem with appetite regulation, or socially as a problem of higher-level body-image and self-esteem. Only recently have neuropsychological theories emerged identifying cognitive traits and sensory differences associated with this disorder (e.g. Braun & Chouinard, 1992; Lopez et al., 2008). Similarly, transsexuality has been conceptualized biologically as a result of abnormal hormone levels during brain development, or socially (and often pejoratively) as a disorder of gender or sexual identity development. Only quite recently has the neural basis of sexed body representation in transsexuality been discussed (e.g. Giummarra et al., 2011).

In the current work, Chapters 1 and 2 present studies of body representation in female-tomale (FTM) transsexual individuals based on the aforementioned studies of Xenomelia performed in our laboratory (Brang et al., 2008; McGeoch et al., 2011). Chapter 1 investigates whether somatosensation from a body part that feels wrong causes consistent sympathetic nervous system arousal. Specifically, we measure skin conductance response to mildly painful sensory tapping of the chest and lower leg in presurgical female-to-male (FTM) transsexual individuals and cissexual female individuals (control participants whose gender and body sex align in the traditional fashion). Chapter 2 presents the results of a magnetoencephalography (MEG) study on how sensation from the chest- a body part that feels incongruous to the presurgical FTM male participants, but not the cissexual female controls- is integrated in body representation areas.

Chapters 3-5 describe research on sensory integration and body representation in anorexia nervosa. Chapter 3 investigates whether patients with anorexia show any differences in their integration of visual and somatosensory information in judgments of mass. Similar to Chapter 2, the study described in Chapter 4 investigates sensory processing of a disliked body part (the abdomen) in parietal and insular body representation areas in patients with anorexia nervosa and in healthy controls, using magnetoencephalography (MEG). Finally, an exploratory case series summarized in Chapter 5 investigates interactions between explicit body image and lower-level sensory body representation. In addition, we test the effects of allocentric mirrorviewing on the body image of patients with eating disorders and its effect on patients' visual and tactile estimates of body size.

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# CHAPTER 1

Skin Conductance Response to Somatosensation from Body Parts that Feel Congruent or

Incongruent with Gender

### Abstract

Brain-based body representation is a neglected topic in the study of transsexuality. Most transsexual individuals desire to change the sex of their body not only because of how others perceive them, but also because the sex of their internal body image differs from their external anatomy. The presence of phantom sensations for desired body parts that are congruent with gender identity and an absence of phantoms for incongruous-feeling body parts (after their removal) suggests that transsexual individuals may have sensory body maps biased to represent the anatomy they identify with. If an incongruous-feeling body part were poorly represented in the brain, sensation from that body part might cause alarm and heightened skin conductance response (SCR), as seen in individuals who desire amputation of a limb (Xenomelia). Would SCR reveal a similar pattern of autonomic response in transsexual individuals? In the present study we compare SCR to nonsexual tactile stimulation of the breast and of the leg in pre-surgical FTM individuals and cissexual female controls to see whether SCR response is heightened for the incongruent-feeling body part- the breasts- in FTM individuals. We report heightened SCR to the breast in the FTM group, suggesting that aversion to gender-incongruent body parts extends to the level of automatic sensory processing. This difference in sensory response suggests low-level differences in body representation associated with transsexuality.

### Introduction

How could sensation from a person's own body feel alien, or out of place? Most research on bodily identification focuses on changes in bodily awareness that occur with brain damage, or on the induction of bodily illusions in healthy adults (Hilti et al., 2013). Xenomelia, Hilti et al., argue, is a unique exception to this rule: patients with Xenomelia are neurologically and psychiatrically healthy, yet experience one of their limbs as consistently foreign-feeling and overpresent. Their sense of bodily wrongness is so strong that they desire to amputate the offending limb.

Is sensation from a body part that feels "wrong" integrated differently than sensation from other body parts? Indeed, one study of patients with Xenomelia found that somatosensory stimulation of the incongruous-feeling limb resulted in heightened skin conductance response (SCR) compared to stimulation of the unaffected, yet seemingly identical, limb (Brang et al., 2008; Brang et al., 2009). In addition, differences have been observed in Xenomelia in brain areas involved in integrating somatosensation into representations of the body (McGeoch et al., 2011; Hilti et al., 2013).

We suggest that there is another population of neurologically and psychiatrically healthy individuals who experience such bodily incongruity. Individuals who identify as transsexual overwhelmingly experience their sexually dimorphic body parts as inappropriate and incongruous with their body image. Giummarra et al. (2011) point out that Xenomelia and transsexuality both involve "profound discontent with embodiment/identity, and onset in childhood/early adolescence; reduction of desire following surgery or when mimicking the desired identity.... ; and in some sexual arousal in relation to acquiring the desired identity, or others with the desired identity." In addition, research suggests that there are significantly more male-to-female than female-to-male transsexual individuals- and most individuals with Xenomelia are genetically male (Landen et al., 1996; Hilti et al., 2013).

The similarities, however, extend further. For most transsexual individuals, the discontent is not mere cognitive discomfort: many transgender and transsexual individuals experience their breasts or genitals as unwanted, uncomfortable, or even alien. In "Second Skins: The Body Narratives of Transsexuality," Prosser describes sex reassignment surgery "as a nostalgic return to the sexed contours that should have been" (84). He applies the work of Oliver Sacks on body agnosia and phantom limbs to transsexuality, suggesting a degree of agnosia for incongruous-feeling body parts, and "phantomization" of desired body parts of the "idealized somatotype" (84). Prosser argues for an embodied understanding of transsexuality:

My contention is that transsexuals continue to deploy the image of wrong embodiment because being trapped in the wrong body is simply what transsexuality feels like... It suggests how body image is radically split off from the material body in the first place, how body image can feel sufficiently substantial as to persuade the transsexual to alter his or her body to conform to it. The image of wrong embodiment describes most effectively the experience of pre-transition (dis)embodiment: the feeling of a sexed body dysphoria profoundly and subjectively experienced (Prosser page 69).

### Transsexuality

Transsexuality falls under a broader spectrum of transgender identities. Most transgender individuals experience their combination of gender and sex to fall outside of western society's binary categories of "male" and "female," while others actively choose to transgress these binary cultural categories. Transsexual individuals perceive the sex of their anatomical body to be wrong or incongruent with their sense of gendered self, or gender identity. Currently, transsexuality is classified as a form of Gender Dysphoria in the Diagnostic and statistical manual of mental disorders (DSM-5; American Psychiatric Association, 2000). The DSM-5 emphasizes that it is not the individual's gender identity that is the clinical problem, but rather the individual's dysphoria about the gender they identify with versus the gender assigned to them; this dysphoria is typically treated through hormones and surgery to align the body's appearance

with the individual's identity (American Psychiatric Association Gender Dysphoria Fact Sheet). In the present work the term "transsexual" is utilized because it is used widely in both the scientific community and in the transgender and transsexual communities. (For the purposes of this work a transsexual individual is a person who perceives their body to be incongruous with their gender identity and sense of self and wishes that their body were differently sexed. Broader transgender experiences of body and self, including nontraditional combinations of body and gender that do not feel dysphoric or incongruous to the individual, do not fall within the scope of the current work.)

#### **Body representation in transsexuality**

Brain-based body representation is a neglected topic in the study of transsexuality. As previously mentioned, many transsexual individuals describe their clash of sex and gender in an immediate, embodied manner. They desire to change sex not only because of how others perceive them, but also because the sex of their internal body image differs from their external anatomy. A neurological perspective on body image lends particular credence to this point of view. Indeed, many transsexual individuals experience phantom body parts of the other sex; 18 of 29 transsexual men (62 percent) reported experiencing a phantom penis long before undergoing sex "reassignment" surgery (Ramachandran 2008). This phenomenon parallels sensations reported by amputees with phantom limbs (Ramachandran 1998); after deafferentation, the cortical representation of the limb continues, combining sensory signals from the stump and nearby body parts to form a confabulatory representation of the limb's sensorimotor state. If congruent-feeling body parts generate phantom sensations, then incongruent body parts should produce fewer phantom sensations after their amputation, due to their lesser cortical representation. Indeed, Ramachandran found that a third to half of cissexual

women experienced phantom breasts after mastectomy, but only 3 out of 29 transgender men (who had experienced their breasts as incongruent) did (Ramachandran 2008).

If phantom body parts resulted merely from desire and imagination, they should not occur against a person's will. Yet painful phantom limbs are a notorious medical problem, and phantom body parts can even conflict with gender identity, as seen in the case of a recurrent, unwanted phantom penile erection after removal of the penis in a sex "reassignment" surgery (Namba et al., 2008). This raises the interesting question of how body parts come to be experienced as "correct," or congruous with identity. Do most people experience the sex of their body as "correct" solely through experience with their own body and feedback from society—or does the brain contain a genetically wired (or hormonally shaped) template that expects to receive input from a male or female body?

Brang et al. (2008) propose that congenital dysfunction of body representation and integration areas in Xenomelia leads to mismatch between external anatomy and internal body image, which in turn leads to abnormal sympathetic outflow (and heightened SCR) via the insula. Critically, a discrepancy between S1 representation of the body part (normal) and representation of the body part in areas like the rSPL (abnormal) leads to the alarm response that heightens the SCR. Indeed, SCR is strongly modulated by prefrontal and parietal cortices as well as the insula, cingulate cortex, and amygdala, all areas involved in representation of body and self (Critcheley 2002). Control of the autonomic nervous system and SCR, like body representation, is lateralized to some degree to the right hemisphere (Critcheley 2002; Oppenheimer et al., 1992).

The presence of phantom body parts for the congruous sex, and absence of phantom body parts after amputation of incongruous-feeling body parts, suggests that transsexual individuals may have sensory body maps arranged according to the sex they identify with. If transsexuality, like Xenomelia, involves low-level differences in neural body representation, we might expect sensation from an incongruous-feeling body part to also cause heightened SCR relative to a congruous-feeling body part. In the present study we compare SCR to nonsexual tactile stimulation of the breast and of the leg in pre-surgical FTM individuals and cissexual (nontranssexual) female controls to see whether SCR response is heightened (as in Xenomelia) in individuals who feel their breasts are incongruent with their body image. If SCR were heightened for the breast (relative to the leg) in the transsexual group, this would provide evidence that the sense of bodily incongruity in transsexuality extends to low-level sensory mapping of sexed body parts, suggesting differences in sexed sensory body representation in transsexual individuals.

### Methods

### **Participants**

This study was conducted in accordance with approval from the University of California, San Diego Human Research Protections Program. FTM participants were recruited through fliers and email announcements distributed to local LGBT centers and groups and cissexual participants were recruited through email and word-of-mouth advertisement. Ten preoperative FTM transsexual (TR) individuals (age M = 27.8, SD 8.2) and ten cissexual (CIS) females (age M = 26.3, SD 9.3) participated in the current study. Age did not differ significantly between the groups (two-tailed t(18) = 0.38, p = 0.71). 7 of the transsexual participants reported phantom penises and an additional 2 who did not experience full phantoms still reported infrequent sensory events such as phantom erections. 5 of the 10 FTM participants were taking testosterone.

### **Data collection**

Participants were seated in a chair and asked to keep their eyes closed during data collection. A research assistant blind to the hypothesis of the study poked the participant's left breast (through one thin layer of clothing) and left leg (typically unclothed) 40 times each in a

pseudo-random order using a Neurotip<sup>®</sup>. The intensity of pokes to the breast and leg were subjectively equated before beginning data collection by poking each body part several times until the participant reported that they felt the same level of pressure and pain at each site. Skin conductance response (SCR) was recorded continuously using a pair of Ag-AgCl electrodes attached to the palmar surface of the index and middle fingers (proximal phalanges) of the right hand. SCR was measured using a Biopac System (MP100A-CE) and recorded in AcqKnowledge 4.1. Trials were separated by a minimum of ten seconds; after each trial, the experimenter waited for the participant's skin conductance to return, approximately, to the pre-trial baseline before initiating the next trial.

## Analysis

Because of significant habituation across the session in most participants, only the first 20 of the 40 pokes in each condition were included in analysis. The raw data were high-pass filtered (IIR) above 0.05Hz to remove baseline drift across the session. SCR Max-Min values were calculated for each 5-second baseline period (BASE) preceding each poke, and for each 5-second response period (STIM) following stimulus onset. Max-Min values were z-score transformed within each subject based on the subject's mean and standard deviation for the BASE trial period (collapsed across chest and leg). STIM z-scores for breast and leg were averaged separately and an average breast-leg difference score was computed for each participant. A subtraction, rather than a percent change statistic, was utilized because no correlation was observed between average SCR and difference score. Finally, a student's t-test was conducted to compare Breast-Leg difference scores between groups for the first 20 trials. To further remove the effect of habituation, a second t-test was conducted to compare the same scores for only the first 10 trials at each body part.
## Results

Averaged across chest and leg trials, the TR and CIS participants showed similar overall z-scored skin conductance responses to Neurotip® stimulation (versus baseline; two-tailed t(18) = 0.54, p = 0.60). The Chest-Leg difference score for the average of the first 20 responses was marginally higher in TR than CIS individuals (two-tailed t(18) = 1.93, p = 0.07). The difference score for the average of the first 10 responses at each site, however, was significantly higher in the TR participants than in the CIS participants (two-tailed t(18) = 2.73, p = 0.01; see Figures 1.0 and 1.1). The effect size for the difference between chest and leg was large for both the first 10 trials (Cohen's d = 1.22) and for the first 20 trials (d = 0.86). TR participants taking and not taking testosterone showed similar differences scores on the first 10 trials (t(8) = 0.94, p = 0.37).

Insert Figure 1.0 about here Insert Figure 1.1 about here

#### Discussion

Though the discrepancy between internal body image and the external body is central to the experience of most transsexuals, its basis has not been explored at a sensory or neural level. We compare SCR to nonsexual tactile stimulation of the breast (incongruous-feeling) and leg (congruous-feeling) in pre-surgical FTM individuals and cissexual female controls. The results of this study show heightened SCR to noxious tactile stimulation of the breast, relative to leg, in preoperative FTM transsexual individuals. This effect was statistically significant only at the beginning of the session, during the first 10 trials at each body site, consistent with the strong effect of habituation to somatosensory stimuli (e.g. De Pascalis et al., 1999). We suggest that this heightened SCR is a physiological correlate of bodily incongruity and aversion in transsexuality, representing differences in the integration of afferent sensation from the disliked body part.

We propose that- as theorized in Xenomelia- insular over-activation in response to underintegration of incoming tactile information causes heightened SCR in transsexual individuals. However, SCR is a general indicator of sympathetic arousal and is modulated by a wide range of cognitive and emotional processes that affect subjective salience, motivation, and attention (Critcheley 2002). While we interpret heightened SCR in the current study to reflect alarm and anxiety in response to mismatch of sensation and body representation, other explanations are possible, including heightened attention or learned emotional response to sensation on the chest; indeed, SCR can be quickly transferred to new stimuli through classical conditioning (Critcheley 2002). Aversion to the body likely increases over time with increased identification as transsexual. Speaking about differences in cortical thickness in Xenomelia, Brugger et al. (2013) recently suggested that the neural differences could result from bottom-up differences in neural body representation- or, equally plausibly, from "years, if not decades, of a hostile attitude directed to a part of the body." The same could be true for transsexual individuals. Higher-level body image differences in gender-identification could drive social comparisons that lead to an acquired aversion to sex-specific body parts, and over time could modify sensory representation of that body part. The current finding thus likely reflects a physiological alarm response to sensation from a body part perceived as incorrect, the ultimate causal origin of which is not known.

While we hypothesized heightened SCR response to gender-*incongruous* body parts based on the findings from Xenomelia (Brang et al. 2008 and 2009), in other studies heightened SCR has been interpreted as an index of embodiment and ownership. For example, greater rubber hand illusion leads to higher SCR upon observing painful somatosensory stimuli applied to the rubber hand (Armel & Ramachandran, 2003). Body ownership is not quite the same as a feeling of congruence, however. In the current study TR participants were adamant that their breasts should not be on their body (M = 1.25, SD 0.46 for "Body should have breasts (1-5)?"), but more mixed about whether they felt ownership of them (M = 2.31, SD 1.39 for "Breasts belong to you? (1-5)").

The current study is also limited by lifestyle differences between TR and CIS individuals. For example, some of the TR individuals engaged in chest binding (to reduce the visibility of breasts), which could affect sensory acuity or sensitivity of the breasts. We attempted to eliminate this confound by equalizing subjective pain and pressure at each body site for each individual (in a blind manner), but transsexual individuals may also dissociate from sensation from incongruous-feeling body parts (somehow down-regulate conscious awareness of it), leading to differences in subjective report of sensation. The expected result of this would be for TR participants to report less sensation than CIS participants for an equivalent level of stimulation, and thus for us to poke them harder than the CIS participants. This would presumably lead to heightened GSR response in *all* blocks of the data, an outcome we did not find. The effect of exogenous testosterone is another factor that could plausibly influence SCR in TR individuals (Dart et al., 2002), though no overall differences in SCR were found between TR and CIS individuals in the current study, nor between those who had taken testosterone and those who had not.

While the current study cannot discriminate the origin (genetic, hormonal, sociological, etc) of differences in body representation in the brain in transsexuality, our results demonstrate that aversion to gender-incongruous body parts is instantiated at an early, automatic level that likely reflects differences (either innate, or acquired, involving plastic reorganization) of sensory body maps in the brain. The brain areas involved in this putative difference will be explored in Chapter 3.



**Figure 1.0: Average z-scored skin conductance response for breast and leg.** TR and CIS participants were poked on the breast and leg with a Neurotip® while skin conductance was measured continuously. Left plot shows data for first ten trials at each body site and right plot shows data for trials 11-20.



**Figure 1.1: Breast-Leg mean z-scored skin conductance response difference scores.** TR and CIS participants were poked on the breast and leg with a Neurotip® while skin conductance was measured continuously. Breast-Leg difference score of average z-scored skin conductance responses for the first 10 trials at each body location are shown.

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# CHAPTER 2

Magnetoencephalography Recording of Somatosensory Evoked Fields in Body Parts that Feel

Congruent or Incongruent with Gender

#### Abstract

While most people take basic identification with their bodies for granted, conditions like phantom limb pain, alien hand syndrome, and Xenomelia demonstrate that this feeling of bodily congruence is a result of neural construction of body image. Individuals with Xenomelia show reduced right parietal representation of the body parts they find over-present and aversive (McGeoch et al., 2011). Similarly, transsexual individuals often describe their untreated sexed body parts as incongruent and aversive, and many experience phantom body parts of the sex they desire to transition to (see Chapter 1). Could differences in representation of incongruent-feeling body parts in the right superior parietal lobe (rSPL), or other body integration areas, underlie this sense of bodily dis-identification? In the current study we utilize magnetoencephalography (MEG) imaging to record brain activity during somatosensory stimulation of the breast- a body part that feels incongruent to pre-surgical female-to-male (FTM) transsexual individuals, but not to female controls– and the hand, a body part that feels congruent to both groups. We measure the sensory evoked field (SEF) response in eight right hemisphere somatosensory and bodyrelated brain areas and find significant interactions between group and time in the chest condition in secondary somatosensory cortex and in the medial temporal lobe (without or without the hand data as a covariate), but no significant interactions in the hand condition. These findings suggest that the dysphoria related to gender-incongruent body parts in FTM individuals may be tied to differences in neural representation of the sexed body. Our study is the first to link parietal-based body representation to subjectively experienced gender identity. More broadly, these findings advance our understanding of the relationship between sensory processing and neurological body image.

#### Introduction

Transsexual individuals experience a strong sense, often beginning in childhood, that their body is of the "wrong" sex (Lindgren & Pauly, 1975; also see introduction to Chapter 1). The criteria in the 4th edition of the Diagnostic and Statistical Manual of Mental Disorders (text rev; American Psychiatric Association, 2000) for transsexuality– classified as a "Gender Identity Disorder"– include "preoccupation with getting rid of primary and secondary sex characteristics, or belief that he/she was born the wrong sex." "Gender Dysphoria" is the new DSM-5 diagnostic category for individuals experiencing distress regarding their gender identity (DSM-5; American Psychiatric Association, 2013). In the DSM-5 classification criteria are broadened to include either the feeling of belonging to the other gender, or strong desires to be treated as the other gender. What are the neural mechanisms underlying the feeling that the sex of one's body is incorrect? If we look for a neurological "cause" of transsexuality, we may fall prey to reductionist models of sex and gender identity. We can, however, inquire into the neural correlates of *one* aspect of gender identity- specifically, the neural correlates of sexed body image.

## **Biological Correlates of Gender Identity**

Before exploring the neural correlates of sexed body image, we will briefly review more general research examining biological contributions to gender identity. Gender identity refers to a person's sense of being a man or a woman. Comparison of transsexual (TR) and cissexual (CIS; gender and sex aligned in the traditional way) individuals allows for direct comparison of different gender identities in individuals with the same anatomical sex. The biological basis (proximate neural correlates, as well as biological causal factors) of gender identity is not known, but biological differences have been identified between TR and CIS individuals. For example, a number of familiality studies show some heritability of transgender identity (e.g. Gómez-Gil et al., 2010), and a number of genetic studies have shown certain chromosomal variations to occur at a higher rate in TR populations than CIS, although these variations are quite uncommon in both populations (Erickson-Schroth 2013). One consistent bio-behavioral finding in male-to-female (MTF) populations is a heightened rate of left-handedness, as compared with cissexual males. Heightened left-handedness is often found in FTM populations as well, indicating possible, but not well circumscribed, differences in developmental lateralization of the brain in TR individuals (Erickson-Schroth 2013).

In the brain, differences in white matter microstructure pattern according to gender identification have been found; Rametti et al. (2011) found that the pattern in non-medicated, presurgical MTF individuals fell halfway between the pattern in CIS men and women, suggesting a lesser degree of masculinization during brain development. One recent study of 24 hormonally untreated MTF individuals and 24 CIS control males demonstrated sex-atypic, increased cortical thickness in the TR group (Luders et al., 2012). Luders et al. (2009) reported that gray matter volume in MTF individuals more closely resembled that seen in CIS men, but found higher volumes of gray matter in the right putamen of the MTF individuals. Sex-atypic differences between TR and CIS individuals have also been reported in the size and shape of parts of the stria terminalis and the hypothalamus, brain regions with strong links to sexual behavior (Zhou et al., 1995; Bao & Swaab, 2011; Kruijver et al., 2000; Cohen-Kettenis & Gooren, 1999). Finally, Berglund et al. (2008) found that MTF individuals show sex-atypical hypothalamic activation when smelling odorous steroids, suggesting possible differences in circuitry of the anterior hypothalamus. Many of these studies are limited, however, by small and frequently-overlapping sample sizes, as well as confounding factors such as hormonal treatment and, in the case of postmortem tissue analysis, age and disease (Erickson-Schroth 2013).

A leading biological theory of gender identity posits that differences in prenatal hormone exposure lead to differences in hormonally mediated brain development. Despite much research, consistent differences in adult hormone levels have not emerged between TR and CIS individuals, and indirect measures of prenatal hormone levels (e.g., finger length ratio) have also not shown consistent patterns across studies (Erickson-Schroth 2013). The most comprehensive study to test the hypothesis of increased rates of Polycystic Ovary Syndrome (PCOS, a hyperandrogenic condition) in FTM individuals, however, *did* find significantly elevated levels of androgens in FTM individuals, compared with CIS women (Mueller et al., 2008). Bao & Swaab (2011) maintain that gender identity (and sexual orientation) are primarily determined by organizational effects of testosterone in utero and by activating effects of testosterone at puberty. Indeed, fetal and neonatal surges in testosterone in male children follow sexual differentiation of the genitals, leaving open the possibility of dissociation between sexual differentiation of the brain and of the genitals- and thus the development of transsexuality and other transgender identities. In support of this theory, girls with Congenital Adrenal Hyperplasia, who have abnormally heightened androgen levels during early development, have a heightened prevalence of transsexual identity in adulthood (Bao & Swaab 2011). Bao & Swaab also argue that gender identity is "irreversibly programmed" based on cases of failed attempts to socialize children as the "other" gender after medical incidents or abnormalities (e.g. Colapinto 2001).

Few functional imaging studies comparing transsexual and cissexual individuals have been conducted to date. One functional magnetic resonance imaging (fMRI) study (Gizewski et al., 2009) found that MTF transsexual individuals responded to erotic stimuli most similarly to people of the gender they identified with. Unfortunately this study conflates transsexuality with homosexuality, and reveals little to nothing about gender or body identity. Sommer et al. (2008), Carrillo et al. (2010), and Schöning et al. (2010) each examine the effects of cross-sex hormone treatment of transsexual individuals on brain activation during language and/or mental rotation tasks. Schöning et al. find differences in the network involved in mental rotation between TR and CIS individuals that remain stable over the course of hormonal treatment, suggesting differences in cognition associated with gender identity. Carillo et al. find differences in MTF transsexuals but not in FTM transsexuals, while Sommer et al. do not find any group differences. In contrast, Ye et al. (2011) find differences in networks related to empathy and mentalizing in FTM individuals only *after* administration of androgens. Finally, a Position Emission Tomography (PET) study comparing resting-state brain activation between transsexual and cissexual individuals found decreased blood flow in the left anterior cingulate cortex and heightened blood flow in the right insula in FTM individuals (Nawata et al., 2010). In an fMRI case study of an FTM individual, however, no significant differences in resting state activation were found from CIS women (Santarnecchi et al., 2012).

## Neurological Sexed Body Image

The sensation of bodily incongruity in TR individuals can begin quite early in life; indeed, it may be voiced as early as the age of two or three (Devorak 2012). Research suggests that TR individuals overwhelmingly feel more like "themselves" and have a much more positive body image after sex reassignment/ affirmation surgeries (Kraemer et al., 2008). In addition, as discussed in Chapter 1, many presurgical female-to-male transsexual individuals experience a "phantom" penis– the sensation of having a penis in the absence of this physical body part (Ramachandran & McGeoch, 2007)– suggesting possible differences in neurological body representation. FTM and MTF individuals who undergo sex reassignment surgery also have a lower incidence of phantom breasts and penises, respectively, than people who undergo such surgery for other reasons, suggesting weak neural representation of these body parts prior to their removal (Ramachandran & McGeoch, 2007). Interestingly, however, no functional brain imaging studies to date have explored body image or body perception in transsexuality. Any brain-based account of transsexuality will fail if it cannot explain this discrepancy between bodily morphology and body image that is a central feature of most transsexual experiences.

How could such a striking discrepancy between body image and body morphology arise at the neural level? As detailed in the Introductory chapter of this dissertation, strong and unusual feelings about the body are often linked to damage of the right superior parietal lobe (rSPL), a part of the brain involved in multisensory construction of body image. Neglect or hatred of the left side of the body (Critchley 1953), denial of paralysis of the body (Babinski 1914), personification of a paralyzed limb (Critchley 1955), perception of supernumerary phantom limbs (Critchley 1953), size-distortions of body parts (e.g. Frederiks 1969), and somatoparaphrenia (Gerstmann 1942) have all been documented in relation to right parietal lobe damage. These conditions suggest that the rSPL underlies a normal sense of ownership, liking, and general understanding of the body's shape, size, and sensorimotor condition, forming part of a 'bodymatrix' (Moseley et al., 2012) representing sensory and spatial data about the body in egocentric coordinates. Indeed, representation of the form of the body may be largely hard-wired in rSPL, as evidenced by some patients who congenitally lack one or more limbs yet nonetheless report phantom limb sensations (e.g. Saadah et al., 1994; Ramachandran & Hirstein, 1998; Brugger et al., 2000).

As discussed in Chapter 1, Xenomelia, like transsexuality, is a condition in which body image and body morphology differ in the absence of known brain injury or pathology. Individuals with Xenomelia desire to remove a limb that feels inexplicably "over-present" and unwanted. A clue to Xenomelia's neural basis comes from the fact that patients describe a precise and consistent line for their desired amputation; further, patients who proceed with amputation are overwhelmingly relieved and satisfied with the outcome of their decision (Ramachandran & McGeoch, 2007). Patients with Xenomelia respond to touch on their affected limb with heightened physiological arousal (Brang et al., 2008; McGeoch et al., 2009), but sensation from the affected limb activates the rSPL (40-140ms post-stimulation) significantly *less* than touch from the patient's unaffected arm or leg (McGeoch et al., 2011). Processing of tactile stimulation in primary sensory cortex (S1) seems to be preserved in Xenomelia, suggesting that the patient's feeling of over-presence of the limb may arise from a conflict between normal sensory registration of the limb in S1 and insufficient representation (or functional activation) of the limb in the rSPL. Feeling touch in the relative absence of rSPL activation may lead to sympathetic arousal and discomfort due to inability of the brain to "map" or integrate this sensation into the rSPL body image. Similarly, Hilti et al. (2013) found that individuals with Xenomelia exhibit decreased cortical thickness in the rSPL.

In the absence of brain injury, could congenital or developmentally acquired differences in the rSPL or other brain areas underlie abnormalities in body perception in transsexuality? In the current study we conduct magnetoencephalography (MEG) recordings during tactile stimulation of the breasts and hands of presurgical FTM transsexual individuals and CIS female controls. We aim to determine whether body representation areas are less activated in FTM individuals than in CIS females by tactile input from the breasts, a body part that felt highly incongruent to all FTM participants in the current study. We examine the early sensory response (40-140ms) in S1 and the rSPL, as well as in six other brain regions implicated in processing sensory information and integrating it with representations of the body.

The numerous parallels between Xenomelia and transsexuality, discussed in Chapter 1, led us to predict reduced rSPL activation to incongruent-feeling body parts in transsexuality. Transsexuality is a different condition than Xenomelia, however, and different brain regions involved in sensory integration and body representation might be involved. For example, S2, the posterior insula, and the supramarginal gyrus have been shown to relate to conscious perception of sensation, body ownership, and attribution of sensation to the self, respectively (Dijkerman & de Haan, 2007; Tsakiris et al., 2007; Blanke et al., 2005), and these areas might be less engaged for incongruent-feeling body parts. The intraparietal sulcus (IPS), similarly, might show reduced activation due to its role in sensory integration and multimodal body representation (e.g. Mauguière et al., 1997; Ehrsson et al., 2005). In contrast, we predicted heightened activation to the incongruent-feeling body part in the medial temporal lobe, due to an alarm response in the amygdala (also suggested by the heightened skin conductance response observed in Chapter 1), and in the anterior insula, due to disgust towards an incongruent-feeling body part (e.g. Craig et al., 2009). We did not predict differences in S1 activation between groups, as there is no evidence of differences in sensory acuity in transsexuality (however, binding of the chest, as practiced by some FTM individuals, could affect sensory acuity, and has not been researched to our knowledge).

#### Methods

# **Participants**

This study was conducted with approval from the University of California, San Diego Human Research Protections Program. FTM participants were recruited through fliers and email announcements distributed to local LGBT centers and groups, and CIS participants were recruited through email and word-of-mouth advertisement. Study inclusion was based on two screening questions: "I feel my biological sex (e.g. anatomy) feels inconsistent with who I feel I am," and "I feel like my body should have breasts on it." TR participants who agreed and disagreed, respectively, with these questions, were invited to participate in the study (the opposite responses were selected for CIS participants). Eight female-to-male transsexual (TR) individuals and eight female cissexual (non-transsexual; CIS) control individuals were enrolled in the current study. The mean age of participants was 29 (range = 20-50) and did not differ by group (t(14) = 0.06, p= 0.96). Participants varied in self-identification from "male" to "transsexual female-to-male" to "genderqueer and primarily male." All agreed that they could be considered transsexual for the purposes of the study: they felt male or predominantly male in gender, desired a male or mostlymale anatomy, and strongly desired to have their breasts removed. All individuals in the CIS group identified strongly as female and rated their breasts as congruent with their internal body image. In response to the question "Should your body have breasts? (1-5)," all CIS participants marked "5" and all TR participants marked either 1 or 2 (*mean* = 1.3). All TR participants wished to have their breasts surgically removed (though one expressed uncertainty). All participants were right-handed. Four of the eight participants in the TR group were taking testosterone, but none had undergone any type of surgery related to their gender identity (see Table 2.0 for participant characteristics).

Insert Table 2.0 about here

# Magnetoencephalography Recordings

Magnetoencephalography (MEG) recordings were conducted at the Radiological Imaging Laboratory at the University of California, San Diego using a whole-head Elekta Neuromag Vectorview 306-channel system in an enhanced multi-layer magnetically shielded room. Head position was digitally recorded using four non-magnetic head position indicator coils. The magnetic field surrounding the participant's scalp was measured continuously at a sampling rate of 1000Hz. A structural MRI (T1- and T2-weighted imaging, gradient echo sequences, fluid attenuated inversion recovery and diffusion-weighted imaging) was collected after the MEG in order to apply anatomical constraints to the source localization of the recorded signal.

Somatosensory evoked fields (SEFs) were recorded in the MEG scanner for each participant during two primary conditions: tactile stimulation (tapping) of the palmar surface of

the hand near the base of the thumb (eyes closed; left and right hands in separate conditions), and tapping of the breast approximately 1-2 inches above the nipple (eyes closed; left and right chest in separate conditions). Two separate blocks were collected in both the hand and chest conditions, except only one hand block was collected in two of the TR participants and only one chest block was obtained in two other TR participants. As time permitted, some participants also received electrical stimulation of the median nerve over the volar aspect of each wrist (eyes closed; left and right tapping intermingled in random order), and tapping of the left hand and left breast with the participant watching the tapping; these conditions are not analyzed in the current study. Tapping was conducted in single-condition blocks, between which the participant rested. Head position was digitally measured at the start of each block. During each block a research assistant blind to the hypothesis of the study tapped the participant's body part at approximately 1Hz intervals using two bundled fine fiber-optic filaments. A low-energy laser beam emitted from one of the filaments scattered upon contact with the body and the scatter was detected by the second filament, triggering an optical switch to timelock each tap to the MEG recording. To assist the scattering of the laser, white tape was placed over the body part being tapped (over a single layer of clothing; see Figure 2.0). Median nerve stimulation was started at 5mA and, if necessary, increased in 1mA increments until perceptible movement of the thumb was observed. During each block of tapping or median nerve stimulation the participant was instructed to relax but to remain aware of the tapping (not meditate or fall asleep).

Insert Figure 2.0 about here

## **Data Analysis**

Each participant's cortical surface was reconstructed from his or her structural MRI in FreeSurfer and the anatomical head digitization from the MEG session was manually aligned to

the MRI in mrilab (Neuromag software). An inner skull surface boundary element model was calculated in seglab (Neuromag software) from the MRI for use in the forward solution. MEG data from each condition were spatially filtered in maxfilter (Neuromag software). A bandpass frequency filter was then applied between 0.1-50Hz. Next, the data were downsampled to 250Hz and epoched from -100ms to 400ms. Individual trials were reviewed and outlier trials were deleted based on overall magnitude of sensor activity. Automatic rejection thresholds for the gradiometers, magnetometers, and EOG channel were then raised iteratively until all but 200 (+/-3) trials remained. Several participants had only 160-180 available events instead of 200 (1 hand block for one TR participant, 1 hand block for one CIS participant, and two hand blocks and two chest blocks for one CIS participant). Epoched data were then averaged in matlab (see Figure 2.1 for sample filtered average waveforms in sensor space). Individual distributed statistical parametric maps (dSPMs; Dale et al., 2000) were constructed for each block for each participant. Due to greater involvement of the right hemisphere in representation of body and self, we analyzed only the right hemisphere (contralateral to the left-sided sites of stimulation). Only the left hand and left chest blocks were included in the analysis carried out in this paper. Labels were hand-drawn in FreeSurfer on the FreeSurfer fsaverage brain, based on functional activation and guided by the FreeSurfer atlas for eight brain areas in the right hemisphere: primary sensory cortex (S1), secondary sensory cortex (S2), the superior parietal lobule (SPL), the intraparietal sulcus (IPS), the supramarginal gyrus, the posterior insula, the anterior insula, and the medial temporal lobe (see Figure 2.2) and morphed onto each individual participant's brain using spherical morphing (Fischl et al., 1999). For each of these brain areas for each participant, waveforms were extracted from the dSPM and averaged across blocks within each condition (hand and chest). For two CIS participants, only chest block 2 was included in analyses because of very noisy raw waveforms in block 1 (confirmed by a blind rater). The results were not affected by the exclusion or inclusion of these blocks.

Insert Figure 2.1 about here Insert Figure 2.2 about here

To examine interactions between group, brain region of interest (ROI), and time, a repeated measures mixed model ANOVA was conducted using a full factorial of four fixed factors: group (TR vs CIS), ROI (all ten), time (continuous for 5 time steps; data averaged within each 20ms bins between 40-140ms)<sup>2</sup>, and body site (hand versus chest). Subject and within-subject factors (the interactions of subject with ROI, time, and body site) were included as random factors. Next, repeated measures ANOVAs were conducted separately for hand and chest, and also separately in each of the eight ROIs, to examine the interactions of group, time, and body site. We also conducted a repeated measures ANOVA in each ROI for the chest and hand conditions alone. A Bonferroni-corrected *p*-value of 0.006 (based on eight ROIs) was applied for these analyses.

Because of the low power in the study, we also computed Monte Carlo *p*-values for each timepoint to test the times at which the groups significantly differed in each ROI. Monte Carlo *p*-values were computed from 1000 random assignments of group to individual subjects at each timepoint. Finally, Monte Carlo t-tests were computed to determine whether TR participants taking testosterone differed from those not taking testosterone in any ROI where significant differences were identified.

<sup>&</sup>lt;sup>2</sup> Time was included as a continuous variable because the study appeared to not have enough power to examine differences between time windows.

## Results

No interaction was observed between group (TR versus CIS), body site (chest versus hand), time (40-140ms in 20ms average bins), and ROI (eight ROIs), F(7, 866) = 1.62, p = 0.13, nor between group, body site, and ROI F(7, 98) = 0.39, p = 0.91), group, time, and ROI (F(7, 98) = 0.88, p = 0.52), or group, time, and body site (F(1, 14) = 0.20, p = 0.66) were found. There was no main effect of group (F(1,14) = 0.19, p = 0.67) and no interactions between group and ROI (F(7, 98) = 1.47, p = 0.19), group and body site (chest vs hand; F(1, 14) = 0.05, p = 0.82), or group and time (F(1, 14) = 0.01, p = 0.92). See Figure 2.3 for average group contrasts in the chest condition and Figure 2.4 and Figure 2.5 for dSPM mean timecourses for TR and CIS for chest and hand.

Unexpectedly, however, the groups appeared to have different spatiotemporal patterns of activation in *both* the chest and hand conditions when analyzed separately (group × ROI × time interactions: chest (F(7, 482) = 2.05, p = 0.048; hand F(7, 480.7) = 2.28, p = 0.027), suggesting problems in using the hand condition as a control condition. We therefore explored the interaction between group and timecourse in the chest and hand conditions separately. A 2-way interaction between group and timecourse was statistically significant in two of the eight ROIs: the medial temporal lobe (F(1, 62) = 3.99, p = 0.049), and secondary somatosensory cortex (S2; F(1, 62) = 4.44, p = 0.039). In the medial temporal lobe, activation appeared to increase more over time in the TR group (see Figure 2.4). When the hand condition was entered as a covariate, to look at differences associated with the chest above and beyond those associated with the hand, S2 remained statistically significant at the multiple comparison-corrected p-value of 0.006. In the hand condition, no ROI showed statistically significant interactions between group and time

below either the corrected or uncorrected thresholds and either with or without the chest condition as a covariate.

> Insert Figure 2.3 about here Insert Figure 2.4 about here Insert Figure 2.5 about here

Monte Carlo *p*-values below 0.05 were found in contiguous clusters only in S2: two timepoints were found at 20-24ms and two at 68-72ms that showed significant differences between TR and CIS, but did not survive correction for comparison of multiple timepoints. Comparison of activation in S2 between 68-72ms between TR participants taking and not taking testosterone did not yield statistically significant differences, but did show a trend for participants on testosterone to have lower S2 activation than those not on testosterone (t(6) = 1.47, p = 0.19).

## Discussion

In the current study we do not find any differences in the overall magnitude or temporal dynamics of sensory-evoked responses in pre-surgical female-to-male transsexual individuals (FTM) and cissexual females (CIS), either overall, or between body parts that feel congruent or incongruent with gender. We do, however, find significant differences in the spatiotemporal dynamics of the sensory response to the breast (incongruent body part) and hand (congruent body

part) between FTM and CIS individuals within certain ROIs. We also find a significant group × ROI × time interaction in both the chest and the hand conditions separately (but no main effects of ROI or timecourse), suggesting differences in integration of sensation from *both* congruent and incongruent-feeling body parts between FTM and CIS individuals. It is unclear why SEFs should differ between groups for the hand, a body part that feels congruent to both groups. Because of greater cortical representation of the hand than of the chest, overall differences in body integration between groups may be amplified in the hand condition, suggesting that the hand is not a good control condition for the chest. These results suggests that TR individuals integrate sensation from their body differently overall than CIS individuals. This could relate to general effects of attention– or, as we argue, to lesser integration of sensation into their body representation in some ROIs. These alternative explanations are discussed later in the chapter.

Within individual ROIs, interactions between group and timecourse are found in the breast condition but not in the hand condition. We will discuss the differences in temporal pattern of activation for the breast SEF observed between TR and CIS individuals within S2 and the medial temporal lobe, and then consider implications of the current findings for theories of body representation in the brain.

#### **Integration of Sensation from a Body Part that Feels Incongruent**

#### **S1**

In order to consider group differences in individual ROIs meaningful, we must demonstrate that the TR and CIS participants received equal intensity of somatosensory stimulation. Indeed, when we compare the early sensory response of TR and CIS participants to chest tapping, there are no statistical differences between groups, and the responses look very similar in each group, suggesting equal registration of the somatosensory stimulus in S1 (see Figures 2.3 and 2.4). Similarly, there are no differences in S1 in overall magnitude of activation, or activation over time. This suggests that differences observed between groups in other ROIs are not due to differences in sensory sensitivity or intensity of sensory stimulation.

**S2** 

S2 lies along the parietal operculum (the ceiling of the lateral sulcus). Neurons in S2 show somatotopy, but have larger receptive fields than those in S1 (Zhu et al., 2007). S2 responds to touch as well as to pain and to isometric contraction of body parts (Lin & Forss, 2002). Lesions to S2 cortex can disrupt perception of body schema (Lin et al., 2002) and ability to perceive pain intensity (e.g. Lockwood et al., 2012). We observed reduced activation in S2 in the later part of the sensory response in the chest in TR participants relative to CIS participants. Diminished S2 activation for the chest in TR participants may reflect diminished integration of the chest into body schema and diminished conscious awareness of the sensation, either through top-down regulation or through reduced representation of the chest in S2; activation of S2 has been shown to relate to conscious perception of touch (Dijkerman & de Haan, 2007).

Another possibility, however, is that S2 exhibits sexual dimorphism, and the brains of the FTM participants may be more male in structure and function than the brains of the CIS female participants. Interestingly, a decrement in SEF in S2 has been observed to median nerve stimulation in males relative to females (Stephan et al., 2006; see Figure 2.7). If the FTM participants have brains with more male structural or functional characteristics, we might expect a male-looking sensory response in S2. However, the decrement in SEF in cissexual males in the study by Stephan et al. (2006) was at 28 and 51ms, earlier than observed in the current study. Still, it is possible that the diminished later response in S2 in the FTM group could reflect gender differences in the general function of S2, either inborn or acquired, rather than a specific response to disliked body parts.

A limitation of the S2 finding is that localization of source activity to S2 is difficult with MEG. Intracranial electric recordings show a strong radial somatosensory source in S2 that is not captured in MEG (Frot & Mauguière, 1999). However, the temporal pattern of the S2 effect in the current study (greater differences between groups over time, and visually peaking around 70ms) is consistent with converging evidence suggesting that the S2 sensory response begins around 60 or 70ms. Zhu et al. (2007) find distinct sources of activity driving early and late sensory response to finger tapping: in the early response period between 30-70ms, activation originates primarily in S1; in the later response, between 70-130ms, S2 is the primary contributor. Similarly, Cheyne et al. 2000 (in Aine et al) find a strong field reversal in MEG sensory evoked responses at 50-60ms (localized to S1) and a slower component at 70-90ms (localized to S2), and Frot & Mauguière (1999) find an N60 and P90 in S2 from electric median nerve stimulation using intracranial EEG. Other groups have reported onset of S2 response as early as 45-60ms (Stephan et al., 2006). In their paper, however, their data show a third, longer peak at roughly 70-120ms.

S2 was the only ROI where Montecarlo simulations found a significant window of group differences, at 68-72ms, suggesting lower S2 activation in TR than CIS. We did not find a significant relationship between S2 activation and treatment with testosterone in the TR participants, but the direction of the trend found (lower S2 in those taking testosterone) suggests that differences between TR and CIS could relate to hormone treatment. This trend may reflect biological effects of testosterone– or it may indicate that individuals who feel more strongly about their gender-body incongruence (and are thus more likely to already be taking testosterone) show more discrepant processing of sensation from the chest. We believe the reduced response over time in S2 reflects differences in somatotopic representation of the chest in S2. Indeed, S2 was one of the right parietal regions found by Hilti et al (2013) to show reduced cortical thickness in patients with Xenomelia, suggesting underrepresentation or under-integration of the body in S2 and consequent dysphoria.

#### **Medial Temporal Lobe**

In contrast to the effect observed in S2 and the trends visually apparent in the other ROIs, we observed *greater* increase in activation over time in the medial temporal lobe in the TR group versus CIS group during the chest condition. This heightened activation likely reflects an anxiety or alarm response in the amygdala/ periamygdaloid cortex to somatosensation from an incongruous-feeling body part, consistent with the heightened skin conductance response seen in Chapter 1 to tapping of the chest. While further from the cortical surface and thus difficult to record from using MEG, periamygdaloid activity related to negative emotion has been reported; Cornwell et al. (2008) report the greatest amygdala-related activation between 100-250ms after presentation of negative emotional faces. Similarly, in an MEG study involving priming with negative words, intensification of amygdala-related response was seen 150-400ms after stimulus presentation (Garolera et al., 2007).

Insert Figure 2.6 about here Insert Figure 2.7 about here

#### **Superior Parietal Lobule (SPL)**

Based on the findings in individuals with Xenomelia, we hypothesized that TR individuals, relative to CIS controls, would show less increase in activation in the SPL over the 40-140ms timecourse for chest sensation. We did not find any significant differences between groups in this ROI, however. The SPL is often characterized as a convergence zone for somatosensory, visual, and vestibular signals (Wolpert 1998, in Hilti et al., 2013). It has also been characterized as an area that binds sensory and motor representations, creating a unified sense of body in space (Tsakiris 2000, in Hilti). Indeed, the rSPL has been found to monitor illusory displacement of a limb (Naito et al., 2005, in Hilti). Since breasts do not have motor innervation, the visual-somatosensory binding seems the most likely explanation of the functional activation obtained in the present study. This may explain why we did not observe differences in the current study. Activity in the SPL appears to be a prerequisite for a body part feeling owned and familiar (Hilti & Brugger, 2010), suggesting that TR individuals may in fact feel familiar with their breasts, and that other regions of the brain may more directly relate to the dysphoria they experience. It is also possible that with more participants we would be able to detect differences in the SPL; we did observe a slight trend towards less activation over time in the TR group (p = 0.11).

# **Posterior Insula**

Activation of the posterior insula is tied to dynamic updating of body ownership, as seen in the modulation of activity in this region by the rubber hand illusion (Tsakiris et al., 2007). The right posterior insula has also been related to egocentric representation (Fink 2003), selfrecognition (Devue et al., 2007), and body ownership (Baier & Karnath, 2008). Tsakiris et al. found that greater proprioceptive drift in the rubber hand illusion (indicative of greater illusion) correlated with reduced S1 and S2 activity but heightened right posterior insula activation, suggesting that the posterior insula activity reflects the degree of perceived ownership of a body part. If FTM individuals showed reduced posterior insula activation over time, this would suggest lesser mapping of the chest sensation into egocentric body space, and thus lesser recognition of breasts as "self." We did not observe any significant differences in this ROI, but the visual trend in the data suggest that differences might be found with a larger number of participants.

## Supramarginal Gyrus, Anterior Insula, and Intraparietal Sulcus

We did not find differences between TR and CIS participants in the temporal dynamics of the response to hand versus chest activation in the supramarginal gyrus (SMG). The supramarginal gyrus is multimodal (Jones and Powell, 1970) and has been shown to have strong involvement in body image and attributions of agency (Blanke et al., 2005). It receives input from the visual, somatosensory, and auditory modalities, and appears to show crossmodal integration effects after 150ms (e.g. Quinn et al., in preparation). Lesions of the supramarginal gyrus can produce hemi-neglect for stimuli in multiple modalities (Sarri et al., 2006). The TPJ, which partially includes the supramarginal gyrus, is broadly implicated in self-other distinctions and inference of self-agency (Decety & Lamm, 2007). Electrical stimulation of the angular gyrus, just posterior to the supramarginal gyrus, has been found to elicit out-of-body experience (Blanke et al., 2002). Our results suggest that sensation from the chest do map on to the SMG normally, suggesting that the hands and breast are identified as self. This accords with the midrange ratings of TR individuals for feeling ownership for their breasts: the sensation is aversive or incongruent-feeling, but still feels like part of their body.

Activation of the right insula broadly correlates with subjective experience of interoception, and the insula becomes more active when participants are made aware of interoceptive sensations (Craig et al 2009). The anterior insula shows response to anxiety, risk, and aversive events, and shows a heightened response to oddball stimuli embedded amid continuous stimulus streams (Simmons et al., 2012). The anterior insula is also involved in the perception of disgust (Craig et al 2009). We thus expected relatively greater activation of the anterior insula in the TR group for the chest than for the hand, but did not obtain these predicted

results. This is interesting, as it suggests that disgust is not the primary neural process involved in the aversion to a body part that feels incongruous with gender. Though some individuals feel disgust to such parts, this was not the primary way that our participants described their aversion to their breasts.

We also did not find differences in the intraparietal sulcus (IPS) in the current study. The IPS is one of the main sources identified in somatosensory processing, activating along with S2 in the 70-140ms time window, though it is also difficult to distinguish its activation from that of the superior parietal lobule. The IPS has been found to be involved in perceptual correlates of multimodal body representation, at least for body part size (e.g. Mauguière et al., 1997, Ehrsson et al., 2005).

# **Body Representation versus Attention**

Do the SEF timecourse differences observed in the current study reflect long-standing differences in body representation in TR versus CIS individuals? This is difficult to know. The sensory system is much more malleable than previously realized; indeed, Schaefer et al. (2007) demonstrate that illusory elongation of a person's arm shrinks the distance between the cortical representations between the 1st and 5th digit in proportion to the subjective strength of the illusion. The current study, however, was conducted without visual input, and in the absence of any illusion, suggesting that differences in the sensory response were based on differences in internal representation of body form. The differences in temporal dynamics visually appeared to be driven primarily by increases in activation emerging around 70ms, consistent with simultaneous SEF activity observed in the parietal operculum and posterier parietal cortex in the 70-140ms range in similar studies (e.g. Mauguière et al., 1997).

Could differences in attention to sensation be the cause of group differences in the current study? If FTM participants are uncomfortable with their breasts, might they employ automatic

strategies to diminish conscious perception of them? Certainly, attention can alter sensory response in a number of brain regions, including S1: Noppeney et al. (1999), for example, found that S1 representation of a digit shifted spatially when attention was directed to either neighboring finger. Similarly, Schubert et al. (2008) find amplitude of S1 activation (measured using fMRI) to covary with the modulation of sensory evoked potentials by spatial attention– as early as 50ms. Behrmann et al. (2004) discuss efforts to localize an attentional biasing signal, a source of enhancement of a sensory response. Bottom-up attentional biasing in the sensory domain may be driven by the temporo-parietal junction, while top-down processing appears to be driven by the SPL and precuneus. However, in the current study, we did not find significant differences in S1 or in the SPL, and our goal is to explain why TR individuals showed *reduced* sensory processing over time in S2, yet *heightened* processing over time in the medial temporal lobe; the CIS individuals, as our baseline control group, had no special interest or aversion to the sensation.

Could active inhibition or mental distraction in the TR group explain reduced sensory processing over time for the chest in TR individuals (in S2, as well as a visual trend in the other ROIs)? Yamasaki et al. (2000) record pain-related electric and magnetic evoked responses and found that arithmetic mental distraction tasks did not affect the SEF in S1 or S2, and affected the pain-related evoked potential only after 140ms. Fujiwara et al. (2002), on the other hand, examined SEFs under attended and non-attended (distracter) conditions and found SEF modulation around 77ms originating in S2. They did not find modulation of S1 activity. This result supports results from several other studies implicating S2 in attention (e.g. Hoechstetter et al., 2000, Hamada et al., 2003). Iguchi et al. (2002) even demonstrate attentional regulation of intensity of activation in S1 to finger stimulation. It is possible that TR individuals employ specific distraction strategies, or have learned to diminish sensory integration of sensation from incongruent-feeling body parts over time to avoid negative emotional consequences. Anecdotally we believe participants remained attentive to the sensation from their bodies and did not tune it

out: we instructed them to remain aware of the sensation, and they claimed to do this. In addition, the FTM participants exhibited heightened response in the medial temporal lobe (periamygdaloid cortex) both early and late in the SEF, which is somewhat inconsistent with an account of down-regulated sensory processing, as their emotional response appeared to be stronger than that of CIS individuals.

Pain and goal-directed attention are not the only factors that can bias somatosensory processing. Poliakoff (2007) investigated the effect of visual threat on spatial attention and found that it could modulate concurrent processing of touch. It is thus plausible that a negative emotional response to touch on an incongruent-feeling body part– perhaps a conditioned response over time– could bias sensory processing as well. However, their study showed *heightened* sensory response on the negatively valenced trials, and so does not explain the *decrement* in processing observed in the current study (other than in the medial temporal lobe, which likely reflects the emotional response itself). We believe the results of the current study are thus best explained by a model of early, automatic reduced integration of sensation into body representation areas, either through differently sexed body maps, or a reduction over time in mapping sensation onto the body maps due to conflict with more abstract representations of self or identity and negative emotional associations.

# **Implications for Current Theories of Body Representation**

Paillard (1999) describes three types of body representation: body image (conscious perception/representation of body features), body schema (implicit sensorimotor representation of the body), and body knowledge (cognitive/ semantic knowledge about the body). In support of this theory, Schwoebel & Coslett (2005) report a triple dissociation between measurements of these constructs in a study of 70 stroke patients. An additional aspect of body representation is emotion. The insula appears to underlie a dimension of emotional experience and perception of

bodily ownership that may diverge from superior and posterior parietal representations of body sensation and position (e.g. Dijkerman & de Haan, 2007).

Contemporary theories of body schema, body image, and body ownership/ identification can inform our interpretation of the current results; conversely, these theories can be evaluated in light of the current findings.

Insert Figure 2.8 about here

**Body Schema** 

The superior parietal lobe contains a representation of the spatial configuration of the body that is closely connected to the motor system (Graviano & Botvinick, 2001). This representation may in fact encompass multiple body maps involved in motor planning and in monitoring movement-in-progress (e.g. monitoring discrepancy between an efferent copy of a motor command and feedback from current proprioception). The SPL represents much more than body position, however; it also monitors proprioceptive signals and shows a position-dependent response to touch. Given this special role in motor coordination, it is relatively unsurprising that diminished representation of a limb in the rSPL would relate to a diminished sense of agency and ownership of that limb as seen in Xenomelia. Breasts, however, have little involvement in motor planning. This may be one of the reasons we do not observe significant differences between FTM and CIS individuals in this ROI. However, the SPL is also critically involved in mapping sensation onto an internal structural model of the body. Sensory information is relevant even in the absence of motor capability of a body part (e.g., while one cannot move one's ear, it is still important to sense pain in one's ear and coordinate a movement of the body or hand to remove the source of the pain). We did observe a trend in this ROI towards reduced activation over time in the FTM group, which may indicate diminished integration of sensation into the body schema.

It would be interesting to conduct behavioral work in transsexual individuals to see whether sensorimotor deficits would exist in the spatial representation of incongruent-feeling body parts, or for the body at large.

Differences in spatial representation of the body can also occur based on temporary alterations in sensory input. Vibration of the tendons can create postural illusions by giving the brain false proprioceptive feedback. For example, vibrating the biceps while touching the nose leads to a perception of an elongated nose, as the brain attempts to interpret the sensory information in an anatomically meaningful way (Lackner 1988). Multimodal illusions like the "cutaneous rabbit" or observing synchronized, displaced touch on a fake arm can even modulate representation of the body in S1 (e.g. Blankenburg et a., 2006; Schaefer et al., 2006), suggesting that the brain uses visual and proprioceptive feedback to modify and update body representation, or distort it to resolve conflicts. Differences in the SPL for stimulation of the breasts are unlikely to reflect 'errors' in multisensory integration, as they occurred repeatedly across trials and blocks of somatosensory stimulation. The trend towards diminished activation over time is thus more likely indicative of reduced representation of the breasts in the SPL leading to reduced ability to integrate sensory input into the spatial mapping of the body. It would be interesting to see whether similar effects could be reproduced through simply imagining a novel body anatomy or anatomy of a different sex, or whether illusory sensory feedback (as in the bicep vibration or prism adaptation) is required.

This question also relates to broader debate about the origins of internal body representation. While multisensory feedback can clearly alter spatial body representation, there is also evidence that online multisensory information is insufficient to generate the internal body model (Tsakiris 2010). For example, in a study of the RHI, Longo et al. (2009) found that visual similarity of the rubber hand to the participant's hand did not drive reports of ownership; rather, feelings of ownership drove participants' ratings of visual similarity to the rubber hand. Thus a calculation of bodily ownership may occur that is independent of evaluation of the sensory "fit" of that body part. On the nativist side of this argument, Meltzoff & Moore (1983) demonstrate visual-proprioceptive matching shortly after birth, before sufficient multisensory input could be generated to form a working representation of the infant's body. Similarly, Morgan & Rochat (1997) showed that infants are sensitive to left-right reversals of visual images of their legs, suggesting innate representations of structural and functional characteristics of typical human anatomy.

Some authors postulate an offline model of the body that is not motor or sensory statedependent. Evidence for such an offline normative body template includes the phenomena of phantom limbs and phocomelia (phantom limbs in some individuals with congenital absence of a limb (De Preester & Tsakiris, 2009). Similarly, Longo et al. (2010) argue for a distinction between higher-order representations of the perceptual state of the body, versus longer-term stored knowledge and attitudes about the body. Could such a visual or cognitive model of the body determine sexed body image and body schema? Indeed, the differences between FTM and CIS individuals found in the current study- despite identical sensory stimulation conditionssuggest that spatial, anatomical body representation is constructed from more than online multisensory input. Under nominally identical sensory conditions, TR individuals show differences in SEFs in S2 that seem to reflect differences in body representation, supporting the idea of innate or hard-wired body representation beyond a simple read-out of current sensorimotor status. We may have not had enough power in the current study to identify which regions contributed to this hard-wired body representation, but the differences in S2 suggest differences in integration of sensation and likely a reduction in conscious experience of the breasts in FTM individuals.

#### **Bodily Ownership**

As Tsakiris (2010) points out, one's own body earns special status due to the experience of sensations that feel unique to oneself (see Figure 2.8). This exclusive access to one's bodily sensations likely drives the feeling of bodily ownership. Because the feeling of bodily ownership is normally constant, it has been difficult to study experimentally. The Rubber Hand Illusion (RHI) has recently emerged as a paradigm for studying body ownership because it allows external objects to be perceived as part of one's body through synchronized touch to the rubber hand (seen) and participant's own hand (occluded; Botvinick and Cohen 1998). Inference of bodily ownership effects systemic change in the body at a physiological level; Moseley (2008) found a decrease in skin temperature in the participant's own arm during the RHI that was modulated by the phenomenological feeling of body ownership (not merely the parameters of the illusion).

Tsakiris (2010) presents a neurocognitive model of bodily ownership that accounts for phenomena like the RHI. First, a visual form (e.g., a rubber hand that you see) is compared against an internal model of a human body (Constantini & Haggard, 2007; Tsakiris & Haggard, 2005; Tsakiris, Constantini, & Haggard, 2008). Second, the posture and anatomical features of the visual form are compared to the posture and anatomy of one's own body, and if they align, multisensory input from the body part recalibrates the brain's visual and tactile coordinate systems. Third, sensory input gives rise to a sense of body "ownership" to the extent that the sensory input is integrated into one's egocentric body representation. At the neural level, the first step involves the right temporo-parietal junction, which contains a structural model of the body. The second step, evaluating postural and anatomical similarity/congruity and transforming sensory input into egocentric coordinates, involves the anterior and posterior parietal cortices. Finally, the likelihood of body ownership is evaluated in the posterior insula, the activation of which correlates with the phenomenological experience of bodily ownership during the rubber hand illusion (RHI) as observed in PET imaging (Baier & Karnath, 2008; Tsakiris et al., 2007). Transsexuality, like Xenomelia, demonstrates that despite the success of the RHI, correlated multisensory stimulation and spatial proximity are necessary but not *sufficient* conditions for the experience of bodily identification. FTM individuals experience breasts as part of their body and experience sensation arising from them. Yet their sense of ownership of and identification with this part of the body is reduced. One possible explanation for this phenomenon is that FTM individuals may have an internal body representation that is anatomically male. In the first step in Tsakiris's model- comparison of a viewed body part to the anatomy of one's own body- sensory input from the breasts would be less likely to be integrated into egocentric tactile coordinates and thus not activate a sensation of bodily ownership in the posterior insula. This is consistent with the visual trends toward reduced sensory activations across time in the FTM group in the posterior insula and the superior parietal lobe- regions that might influence processing of bodily ownership and emotion in the posterior insula. More participants would be needed to confirm whether differences are in fact present in these regions.

## **Body Image**

Body image- the explicit representation and perception of one's own body- appears to differ in TR and CIS individuals. Phantom body parts of the congruent-feeling gender are one strong example of this. This could be related to innate or early-acquired differences in anatomical body schema and visual body-form representation. However, it could also plausibly result from abstract aspects of culture, identity or emotion that could influence body image. Some authors suggest visual body form representation in the supramarginal gyrus and the inferior parietal lobe in general (e.g. Carruthers 2008; Tsakiris et al., 2008). It is interesting that we found did not find an interaction between and SEF timecourse in this ROI, given the conflict between physical anatomy and body image in TR.
Finally, the location of chest activation in S1 in the cissexual group is also of interest, as little research has been conducted on the "hermunculus," the female version of the homunculus (Di Noto et al., 2012; see Figure 2.6). In the current study we observed chest activation in S1 on the superior dorsal part of S1. The few studies that have examined the somatosensory representation of the female breast and nipple report the same location for the female breast in S1 as for the male chest (Rothemund et al. 2005; Aurbach et al. 2009; Komisaruk et al. 2011). The location of chest activity we find is in agreement with these studies.

# Conclusion

In sum, we do not find overall differences in neural response to stimulation of the hand or chest in FTM versus CIS female individuals. We do, however, find differences in the temporal pattern of activation in response to sensation from the chest in FTM versus CIS individual in S2 and the medial temporal lobe, and a visual trend in the superior parietal lobe and posterior insula. This suggests that overall level and temporal dynamics of body integration are similar between the two groups, but with significantly reduced integration of sensation in S2 and heightened emotional response in the medial temporal lobe in the FTM group for sensation from the breast. These differences may reflect the incongruence of the physical body with the desired body form, such that overall sensation is integrated less in TR individuals when a body part is perceived to be incongruent with the participant's gender.

# **Limitations and Future Directions**

One limitation of the current study is the variability in rate of manual tapping during each session. However, we confirmed that the tapping intervals were randomly distributed across trials and participants by checking the average interstimulus interval (ISI). On average, participants were tapped every 1.01s (SD 0.13) on the hand and every 1.05s (SD 0.14) on the

chest; average ISI across blocks for each participant did not differ significantly between groups (Hands: t(14) = 0.28, p = 0.78; Chest: t(14) = 1.26, p = 0.23). This ~1Hz rate of tapping was lower than the temporal window for somatosensory integration seen in MEG with ISIs below 50-75ms (Yamashiro et al., 2011); the late response seen at 70-130ms has been found to almost disappear when the ISI is decreased to .33s (Zhu et al., 2007). In addition, this jittered ISI prevents accurate prediction of tap onset, reducing potential effects of attention on the current results.

Another limitation of our design is the blocked stimulation of the hand and chest. Due to technical limitations we could not intermix stimulation of the two sites. Blocked stimulation introduces the possibility that participants had different emotional and attentional regulation states during the different conditions, although the order of blocks was consistent across participants.

A general limitation of MEG is the limit on source localization; MEG records primarily from sulcal neurons. It would be interesting in the future to conduct the study using fMRI and/or simultaneous MEG and EEG to obtain fuller coverage of the cortex. In addition, we did not have enough power in the current study for a full-brain analysis, so differences in additional brain areas may exist that we were unable to detect. We also did not have enough power to identify differences across averaged time windows. The current analysis can describe only linear effects in the data, which is not an ideal model for waveform data.

Future work should study both presurgical FTM and MTF individuals to see whether the penis is similarly under-integrated for transsexual individuals who identify as female. Postsurgical FTM and MTF individuals could also be studied to see whether sensation from the body is better integrated once it corresponds to the individual's internal body image. It would also be interesting to compare cissexual males and females on the current paradigm, to see whether breasts have heightened cortical representation in females relative to males, or whether any of the results in the current study could be explained by gender differences between the TR and CIS participants unrelated to the physical anatomy of the body.

Finally, it would be interesting for future research to examine the sensory-evoked potentials in these body representation areas while the participant was engaged in an unrelated task. Under cognitive load, the sensory responses might be an even more direct reflection of automatic sensory processing and body representation, with less potential for confounds of attention or emotion or other higher-level regulation of sensory processing. Similarly, to test the extent to which the reduced sensory integration is an effect of attention, emotion, or visual-tactile multisensory mapping onto body schema, it would be interesting to conduct the same study and add a condition where a visual illusion is provided of the flat, male chest the TR participants desire. If the visual input matched the participant's body image, would multisensory integration increase? Continued decrement of SEFs in TR relative to cissexual controls in S2 and other ROIs would then suggest hard-wired differences in body representation not fully explainable by online sensory integration.



**Figure 2.0: Illustration of MEG somatosensory stimulation paradigm.** White rectangles show placement of reflective tape where the participant was tapped.









A

В

**Figure 2.2: FreeSurfer average brain displaying the regions of interest (ROIs) analyzed.** A: lateral view of right hemisphere, (1) primary somatosensory cortex; (2); secondary somatosensory cortex; (3) superior parietal lobule; (4) IPS; (5) supramarginal gyrus; (6) posterior insula; (7) anterior insula. B: medial view of right hemisphere, (8) medial temporal lobe. ROIs were drawn based on FreeSurfer atlas and observed functional activation.



Figure 2.3: Mean dSPM values for the Chest condition for the TR versus CIS groups at (A) 40ms; (B) 72ms in CIS group; (C) 140ms. Units of activation amplitude are arbitrary. Yellow: TR > CIS; Blue: CIS > TR





Figure 2.4: Averaged dSPM timecourses for the chest condition for each ROI.









Superior parietal lobule

Intraparietal sulcus



Figure 2.5: Averaged dSPM timecourses for the hand condition for each ROI.



Supramarginal gyrus





Figure 2.5: continued.



Figure 2.6: Figure from Di Noto et al., 2013. One version of the female hermunculus. Both versions position the female breast and nipple on primary somatosensory cortex in the same location as the male chest and nipple.



**Figure 2.7: Figure from Stephan et al., 2006.** The late component of the SEF to median nerve stimulation was found to be reduced in contralateral S2 in males, relative to females (and in the elderly, relative to young adults).



Figure 2.8: Figure from Tsakiris et al., 2010. Model of neural inference of body ownership.

Table 2.0: Eight FTM individuals participated in the current study. Demographic and descriptive data were collected before the MEG and MRI sessions. 1 = strongly disagree; 5 = strongly agree.

	Desired anatomy	No breasts	Anatomic male	Anatomic male	Anatomic male	Anatomic male	Other/ more masculine, no breasts	Anatomic male	Anatomic male
	My body should have breasts (1-5)	1	1	1	1	1	1	2	2
	My breasts belong to me (1-5)	1	1	5	2.5	3	1	3	2
	Self-identification	genderqueer, leaning towards male	male; transgender FTM	transmale	mostly male	male	genderqueer, mostly male	male	transmale, FTM, or transgender
	Hormones			Yes		Yes		Yes	Yes
	Age	20	34	50	22	21	28	20	28
	Participant	1	2	3	4	5	9	L	8

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# CHAPTER 3

Diminished Size-Weight Illusion in Anorexia Nervosa: Evidence for Visuo-Proprioceptive

Integration Deficit

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RESEARCH ARTICLE

# Diminished size-weight illusion in anorexia nervosa: evidence for visuo-proprioceptive integration deficit

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Abstract Individuals with anorexia nervosa (AN) experience pronounced body image distortion in combination with a pernicious desire to maintain a dangerously low body weight. Relatively little is known, however, about the mechanism underlying body image distortion in AN. Despite having normal visual perception, individuals with AN both feel and see themselves as large-bodied and show deficits in interoception and haptic perception, suggesting a potential deficit in visual and tactile integration. The sizeweight illusion (SWI) arises when two objects of equal weight but different sizes are held. Typical individuals experience a strong and robust illusion that the smaller object feels much heavier than the larger object because of an implicit assumption that weight scales with size. The current study compared the strength of the SWI in individuals with AN to healthy control participants. Individuals with AN exhibited a markedly reduced SWI relative to controls, even though their ability to discriminate weight was unaffected. Because the SWI is strongly modulated by visual appearance, we believe our finding reflects decreased integration of visual and proprioceptive information in anorexia. This finding may explain the puzzling observation that visual perception of the body in a mirror does not correct an AN patient's distorted body image. We speculate that methods to correct visuo-proprioceptive integration in constructing body image may help rehabilitate patients' judgments of size and weight regarding their own bodies. We also suggest that a dysfunction in interactions between inferior parietal lobule (concerned with body image), insula, and hypothalamus may underlie AN.

Keywords Anorexia nervosa · Eating disorders · Sensory integration · Size-weight illusion · Parietal lobe

### Introduction

Anorexia nervosa (AN) is a serious—potentially fatal psychiatric disorder, with a standardized mortality rate as high as 10.5 (Birmingham et al. 2005). The average prevalence found in reviews of anorexia is about 0.3% for young females (Hoek and van Hoeken 2003). Prognosis for patients with AN is poor; Zipfel et al. (2000) found only a 50.6% rate of full recovery for patients with AN 21 years after hospitalization, while 10.4% still met full criteria for AN.

Severely distorted body image is a diagnostic feature of AN. Despite exhibiting normal perceptual sensitivity to body size (Smeets et al. 1999), individuals with AN both feel and see themselves as large-bodied. Indeed, body size overestimation in anorexia predicts pretreatment characteristics that are associated with poor outcome, including greater denial of illness (Casper et al. 1979). Current explanations of anorexia propose multifactorial models including genetic, biological, psychological, and socio-cultural risk factors related to disturbances in neurotransmitter and neurocircuit function (Kaye et al. 2009). Differences in serotonin receptors may relate to increased satiety and an anxious, harm avoidant temperament in individuals susceptible to AN. Little is known, however, about the biological basis of the profound body image distortion that is a core symptom of the disorder-or its resistance to correction through sensory feedback.

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Striking parallels between body size overestimation in anorexia and body image distortion in patients with right superior parietal lobule (rSPL) damage have been noted by a number of authors (e.g. Tomasino 1996). The rSPL is associated with multisensory construction of body image. Damage to the right parietal lobule can cause unilateral neglect, denial of paralysis (anosognosia), or misattribution of a paralyzed limb to another person (somatoparaphrenia; Critchley 1953). Right parietal dysfunction has also been associated with hatred of the left side of the body and with the desire to amputate a healthy limb that inexplicably feels over-present or unnatural (McGeoch et al. 2011). Individuals with anorexia similarly exhibit body image distortion and denial about the state of their body.

Indeed, a number of studies have now reported differences in right parietal function in anorexia. Komatsu et al. (2010), for instance, found decreased regional blood flow in the right parietal lobe of AN patients, which was restored after recovery. Nico et al. (2010) compared AN patients to patients with right and left parietal damage, as well as healthy controls, on a task probing implicit body representation. Interestingly, both patients with AN and right, but not left, parietal patients showed selective distortion of their left body boundary when judging whether an approaching visual stimulus would contact their body. Finally, Guardia et al. (2010) found that AN patients had enlarged implicit body schema in a task judging whether they could fit though apertures of various widths. This suggests that distortions of body image in AN are at least in part lower-level distortions of representation and may be related to disturbances of the rSPL.

These findings suggest disturbances in AN in sensory integration related to body image representation. Could basic problems with sensory integration underlie these distortions? How could body representation of the self be selectively distorted, particularly if visual perception of other bodies is normal? A possible answer is that interoception and proprioception are unique to ones own self, so distortions in these somatosensory domains may lead uniquely to distortions of ones own body representation (one has visual access to other bodies, but interoceptive access only to oneself). Indeed, differences have been found in individuals with AN in haptic perception; Grunwald et al. (2002) found that patients with AN had difficulty reproducing angles through haptic perception. Patients with AN have also been found to have reduced interoceptive awareness that is improved with recovery (Fassino et al. 2004; Matsumoto et al. 2006), and reduced interoceptive sensitivity (reduced capacity to accurately perceive bodily signals, e.g. Pollatos et al. 2008).

Yet distortions of proprioception and interoception alone cannot explain why patients with anorexia process visual images of their own body differently from images of other

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bodies. Sachdev et al. (2008) showed abnormal processing of self-images in anorexia using fMRI. Self-image processing lacked activation of the attentional system or insula seen in healthy participants. Similarly, Blechert et al. (2010) demonstrated attentional bias for self-photographs in anorexia. We can explain such differences, however, if we consider disturbances in multisensory integration. Higher-level visual distortions might result from multisensory construction of body image in the right parietal lobule based on distorted proprioception and integration of visual and proprioceptive information. Indeed, patients with AN have difficulty drawing objects that they explore through touch (Grunwald et al. 2001). While the authors explain this finding in terms of deficits in haptic perception, the finding could equally well reflect deficits in tactile-visual transformation. Patients in the same study also show diminished parietal activation during the task, suggesting proprioceptive integrative deficits in the parietal lobes. Similarly, Mohr et al. (2010) conducted fMRI imaging of body size estimation in AN patients and suggest that body size overestimation may relate to difficulty retrieving multimodal body schema in the precuneous/posterior parietal cortex. Difficulties with retrieval might also reflect disturbances of body representation; Epstein et al. (2001) found subtle neurocognitive deficits involving executive functions in addition to body-schema-related functions during acute stages of AN. Interestingly, AN has recently been noted to share many social and cognitive endophenotypes with autism (Zucker et al. 2007), a disorder that involves significant deficits in sensory integration (e.g. Russo et al. 2010; Oberman and Ramachandran 2008). Might disturbed sensory integration involving touch, proprioception, and vision constitute an endophenotype of AN?

We tested visuo-tactile-proprioceptive integration in individuals with AN and healthy control participants through a size-weight illusion (SWI) battery. The SWI, first known as the "Charpentier Illusion," is a powerful demonstration of the predictive power of visual perception. The participant is given two objects of identical shape and absolute weight (mass) but different sizes and asked to compare their weights. Participants consistently estimate the smaller of two equally weighted disks to be heavier (Charpentier 1891). Even when the larger disk is 50% heavier than the smaller one, typical individuals experience a strong and robust illusion that the smaller object feels heavier because of an implicit expectation that weight scales with size. Intriguingly, we have found that the illusion does not diminish even if the participant is explicitly told that the objects are of equal weight; the illusion is thus relatively immune to top-down correction.

The SWI results from higher-level perceptual integration of vision and tactile perception (Flanagan and Beltzner 2000). Previous research has indicated that sensorimotor

(Ross 1966; Ross and Gregory 1970), perceptual (Flanagan and Beltzner 2000; Grandy and Westwood 2006), and cognitive (Ellis and Lederman 1998) components all contribute to the illusion. Disagreement exists, however, as to the relative influence of sensory versus cognitive mechanisms. Flanagan and Beltzner (2000) showed that fingertip force scales to actual weight with practice, suggesting independence of sensorimotor systems from higher-level perceptual systems in which the illusion is preserved. Grandy and Westwood (2006) similarly found that perceived heaviness of objects in the SWI did not change even as participants used sensorimotor feedback to correct their lifting force. Indeed, Buckingham and Goodale (2010) found that looking at objects before lifting them-without actually seeing them during lifting-can create a SWI, demonstrating that visual expectation alone can alter perception of weight and maintain inaccurate lift behavior. Similarly, Kawai et al. (2007) demonstrate that a SWI influenced only by illusory visual cues is sensory based and depends on participants' multimodal sensory integration. Finally, Ellis and Lederman (1993) have documented an SWI arising from haptic perception alone, showing that visual cues are not the only origin of the SWI. Clearly, the SWI can be influenced by tactile sensation, vision, and expectation.

Based on our theory about multisensory body representation disturbances in AN, we predicted decreased SWI in patients with AN. Decreased SWI would suggest diminished multisensory integration between touch, proprioception, and vision.

#### Methods and materials

### Participants

Ten females with *anorexia nervosa* [AN patients; mean age 29.1  $\pm$  11.0 years; mean body weight index (BMI) 17.1  $\pm$  0.9; median illness duration 36 months] and ten females without any eating disorder (control participants; mean age 25.8  $\pm$  9.0 years; mean BMI 21.7  $\pm$  1.6) participated in this study. All participants provided informed consent to participate in the current study.

Anorexia nervosa patients were recruited through local psychologists and eating disorder outpatient providers. Patients had a DSM-IV-TR diagnosis (American Psychiatric Association 2000) of AN made by a licensed clinical psychologist (one patient unwilling to seek treatment was screened by the experimenter, and results were reviewed by a clinical psychologist) and were currently underweight (BMI < 18.5). Participants were excluded if they had any known neurological disorder or psychotic illness. Control participants were additionally screened for any past or present psychological disorder using the MINI (Sheehan et al.

2009). Control participants also participated in an interview to screen their lifetime relationship with weight and food. Participants were included in the study if they showed no psychological disorders past or present, no history of underweight or overweight, a current BMI in the normal range, no history of dieting to lose more than 10 pounds, and a self-reported daily eating pattern than exhibited no restrictiveness or excessive concern about eating. Control participants were also excluded if any member of their immediate family had been diagnosed with an eating disorder.

### Size-weight illusion

The SWI was measured by asking participants to judge the relative absolute weight (heaviness) of sequentially presented pairs of wooden disks painted gray. Participants were presented with one small disk (3.8 cm tall and 5.1 cm diameter) and one large disk (3.8 cm tall and 12.7 cm diameter) on SWI trials, and with two large disks on control trials. The surface area of the large disk was four times greater than the surface area of the small disk. The weight of each disk was evenly distributed about its center, and disks appeared to be of identical material.

Participants were instructed as follows: "during this experiment, you will be asked to compare the weights of two disks that I place on your palms, one in each hand. Please tell me numbers from 1 to 10 that describe the relative weights of the disks; that is, how much they weigh compared to each other. For example, if one is twice as heavy as the other, you could say 'two and one' or 'eight and four.' You can use different numbers on each trial—all that matters is that for each pair of disks you pick numbers that compare their weight. Please keep your eyes on the disks the whole time."

During testing, the experimenter placed two disks simultaneously onto participants' outstretched hands (see Fig. 1). If participants closed their eyes or looked away from the disks, they were immediately reminded to look back at them.



Fig. 1 Presentation of SWI disks. On SWI trials, the participant held a small-sized disk weighing 90 g and a large-sized disk weighing 90–210 g. The participant watched the disks at all times and generated estimates of the weight of each disk relative to the other

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Size-weight illusion trials presented the 90-g small disk to one hand and one of 13 large disks (90–210 g in 10 g increments) to the other. Four blocks were conducted; each contained all thirteen SWI trials in one of five pseudo-random orders. The participant was not informed that the small disk was always the same one. In addition, each block contained four intermixed weight discrimination trials in random order: 100–130, 100–150, 100–190, and 100–210 g. Blocks counterbalanced presentation of the small disk (or lighter disk, on control trials) to the participant's right versus left hand.

### Statistical analyses

For each SWI trial, a SWI ratio was obtained by dividing the number the participant assigned the small disk by the number the participant assigned the large disk. Ratios greater than one indicate that the participant judged the small disk to be heavier than the large disk; in reality, the small disk was always of equal or lesser weight than the large disk. SWI ratios were averaged across blocks for each subject, and the log of each average ratio was calculated for use in subsequent analyses to linearize the distance between the ratios. For one participant with AN, data from the first of the four blocks administered were dropped because the estimates provided by the patient were highly anomalous and inconsistent with the much more consistent responses she provided on the three subsequent blocks.

The control weight discrimination trials were analyzed similarly to the SWI trials by dividing the participant's estimate of the lighter disk's weight by the participant's estimate of the heavier disk and evaluating the log of this ratio. Difference scores were calculated by subtracting actual from estimated average log ratios and compared between groups. The absolute value of this difference score was used as a measure of weight discrimination accuracy. The Pearson product-moment correlation between weight discrimination accuracy and SWI was checked, as some groups have found a positive correlation between weight discrimination and susceptibility to SWI (e.g. Kawai et al. 2007).

Amazeen and Turvey (1996) found that the perceived heaviness of objects decreases with constant mass but increasing volume and increases with increasing mass but constant volume. This suggests that comparison of disks with equal volume but differing mass creates a "reverse" SWI Itself wherein the discrepancy between a visual-based expectation of equivalent mass and an actual mass difference is amplified. In the traditional SWI, the small weight is denser than in appears, causing it to feel heavier; in the reverse case, one disk is less dense than it appears, leading to an illusion that it is lighter than it actually is. We realized post hoc that a comparison of directional error on our

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control weight discrimination task afforded a reverse SWI illusion, and we hypothesized that AN patients would also exhibit a reduced reverse SWI, due to decreased relative reliance of vision. To check this, we compared directional difference scores between groups to determine whether either group tended to globally over- or underestimate mass differences and whether they experienced a "reverse SWI" based on the discrepancy between vision and weight on these trials.

A repeated measures ANOVA (within-subject factor: disk ratio; between-subject factor: group) was conducted to test the prediction that the log of SWI ratios would differ in AN patients and healthy controls. Finally, we also conducted Pearson product-moment correlations to test whether illness duration or current BMI was correlated with SWI.

### Results

### Weight discrimination

Weight discrimination data were missing for two AN patients who participated before these trials were added to the study. Unfortunately, these participants were not available to return to the laboratory in the period of illness during which they met our inclusion criteria. In the remaining participants, we found that the absolute value of average difference scores did not differ between AN patients and controls (t(16) = 0.2129, P = 0.8341). In other words, the groups exhibited similar levels of accuracy in mass discrimination. Weight discrimination errors showed a trend toward positive correlation with SWI in controls Pearson product-moment correlation; (r(8) = 0.564, P = 0.090). In contrast, AN patients showed a negative correlation between weight discrimination errors and SWI (r(6) = -0.681, P = 0.063). These correlations were significantly different from each other (z = 2.51, P = 0.012).

### Healthy subjects

Healthy controls exhibited an SWI profile similar to that found in other studies: the SWI diminished as the actual weight difference between the disks increased. For example, the point of subjective equality (the point at which subjects are equally likely to report that one weight is heavier than the other, and therefore cannot discriminate between the two stimuli; see Gescheider 1997) for healthy participants in the current study was estimated from a moving average trendline to occur at a large disk weight of approximately 177 g; using the same stimuli, Williams et al. (2009) found a point of subjective equality of 174.2 g for nonpsychiatric individuals. Fig. 2 Log of SWI ratios by trial type in AN patients and healthy controls. Higher small to large disk size-weight ratios indicate greater illusion of perceiving the smaller disk as heavier when it actually was not. The higher the log size-weight ratio from the actual log weight ratio of the disks (*dashed line*), the greater the illusion perceived



### AN patients

Like the healthy controls, AN patients showed a SWI on all trials pairs (average SWI ratio grater than actual disk weight ratio on all trials; see Fig. 2). However, their SWI was reduced compared to healthy controls (see Fig. 3). The point of subjective equality for AN patients was approximately 166 g compared to 177 g for the healthy controls. To avoid losing two patient cases, the two missing control trial values were replaced with the mean of all study participants. The (disk weight ratio × group) ANOVA with weight discrimination as a covariate showed a significant main effect of group, F(1,17) = 7.164, P = 0.016. The main effect of group remained significant when the two cases with missing covariate data were excluded from analysis (F(1,15) = 7.587, P = 0.015). The  $\eta^2$  (eta-squared) was 0.219, indicating a very large effect size of group on the SWI. The difference between patient and control participants was larger when the disks were closer in weight (see Fig. 2). Indeed, there was a highly significant interaction between group and disk weight ratio: Greenhouse-Geisser F(5.000) = 5.364, P < 0.001 (P < 0.01 without replacement of missing covariate data). This was driven by controls, whose SWI depended significantly on disk weight ratio F(1) = 81.880, P < 0.01). Disk weight ratio did not affect AN patients' SWI estimates (F(1) = 0.289), P = 0.592).

Within the AN patients, SWI was not correlated with illness duration (r(8) = 0.421, n.s.) or current BMI (r(8) = -0.011, n.s.). Because a number of our patients were actively participating in treatment programs, however, it is possible that other measures of illness severity might be predictive of SWI, as BMI might not accurately



Fig. 3 Log of SWI ratios in AN patients and healthy controls. AN patients and healthy controls estimated the weights of small disk and large disk pairs of varying relative weights. Visual information about disk size creates a "size-weight illusion" that the smaller disk is heavier than it actually is. Estimated weight ratios of the small to large disks were averaged and linearized using a log transform. Higher log size-weight values indicate greater illusion of perceiving the smaller disk as heavier when it actually was not

represent recent illness severity, and illness duration similarly might not predict current severity.

### "Reverse" SWI

Directional difference scores on the weight discrimination trials did differ significantly between AN patients and controls (t(16) = 2.4548, P = 0.0259). The difference for AN patients between log ratios of estimated and actual disk weights did not differ from zero (t(7) = 0.6846, P = 0.5156), demonstrating that the errors AN patients made were bidirectional and not skewed either toward or away from errors expected by visual expectation. Difference scores between estimated and actual log ratios for controls, on the other hand, did differ significantly from zero (t(9) = 3.1156, P = 0.0124); their errors were significantly

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biased in the direction of visual expectation. Thus, while patients and controls did not differ in magnitude of error on weight discrimination trials, the directionality of their errors revealed a reverse SWI in controls.

### Discussion

Individuals with AN exhibit deficits in interoception and haptic perception, yet their overall body image remains highly distorted even if flatly contradictory information is provided through visual feedback (e.g. viewing their body in a mirror). As such, the disorder provides an opportunity to explore how "low-level" sensory operations can influence high-level percepts and even "beliefs" about ones selfimage, and vice versa (Ramachandran et al. 2009).

In the current study, patients with AN exhibited a markedly reduced SWI (and reduced "reverse" SWI) relative to controls-despite normal weight discrimination ability. Could these effects be due to an overall bias in either group to underestimate or overestimate weight differences? One could worry that a general tendency to exaggerate weight differences might drive the differences in SWI. However, controls' errors on the regular SWI trials reflect greater overestimation of the lighter weight than AN patients exhibit; this is the opposite of control trials, where controls underestimate the mass of the lighter weight more than AN patients do. This inconsistency demonstrates that controls do not differ from AN patients in their magnitude of errors or in their sensitivity to mass discrepancies; they differ only in that their errors are consistent those predicted by visual expectation.

The SWI illusion tends to be higher at more equivalent disk masses because the real weight difference is less discriminable and hence the conflict with visual appearance is smaller. Indeed, literature on multisensory processing confirms that multisensory processing is heightened under conditions of sensory uncertainty (e.g. Alais and Burr 2004). In the current study, controls showed higher relative SWI when the disks were closer in weight. AN patients, however, demonstrated a more consistent level of illusion throughout the study. We believe this difference arises because the SWI is stronger for controls and thus also differentially stronger under optimal conditions for the illusion.

We believe that the SWI effects in the current study are best accounted for by cross-modal sensory integration explanations (e.g. Anderson 1970). Because the SWI is strongly modulated by visual appearance, our finding probably indicates reduced reliance on visual input in judgments of weight by AN patients, relative to a greater reliance on proprioceptive information. It is also possible, however, that patients rely to a lesser extent on the tactile cues that also conflict with the mass cues. Indeed, Keizer et al. (2011) recently reported tactile body image disturbances in anorexia; patients overestimated distances between tactile stimuli on both the arm and abdomen. Overestimating the tactile size difference between the weights in the current study, however, ought to increase the SWI rather than decrease it. Further, the SWI tends to remain quite strong even when tactile cues are removed (Kawai et al. 2007). Thus, we suspect that visuo-proprioceptive integration is more likely disturbed and focus our discussion on this theory, but tactile-proprioceptive or visuo-tactile-proprioceptive integration differences are also possible. Abnormality in visuo-proprioceptive integration may mean that AN patients utilize a different strategy than healthy individuals in judging their own weight and size.

Why would patients with AN show a relatively greater reliance on proprioceptive information? One possibility is that visual processing is impoverished in AN. This is unlikely given the lack of basic visual perceptual differences found to date in AN, and the fact that visual body distortion tends to be selective for images of the self. However, it is possible that malnutrition could affect either vision or sensory integration; it has been found that rats undernourished in early adult life exhibit delays in neuronal pruning in visual cortex (Warren et al. 1989). There is one report that right visual field presentation of objects results in a general size overestimation in women, and that this overestimation is much greater for bodies than for objects (Mohr et al. 2007). Such distortion might plausibly be exaggerated in AN but would still not make perception more variable and hence less reliable. Disks in the current study were counterbalanced to the right and left hands of participants, so differences in visual field should not affect the current results. Thus, there is no evidence to our knowledge of diminished consistency of object perception that could explain diminished reliance on this sensory domain in the current data.

Another possibility is a preference for proprioceptive information. This could not be due to increased accuracy of proprioceptive information, as patients and controls were equally good at the weight discrimination task. However, it is possible that patients rely more on proprioception in general due to increased sensitization to feelings of "fatness" or density of the body. Normally sensory processes are relied upon more when they are more accurate, but cognitiveemotional processes can also bias sensitivity to one domain, as presumably occurred in Mohr et al. (2007). If proprioceptive information about the body becomes distorted (along some dimensions, such as body size or density) and is prioritized over information from other senses, this would explain why patients feel fat and why this sensation might dominate body image perception. Another reason why distortion is likelier to occur in proprioception than vision is that we have a proprioceptive sense primarily

of our own bodies, but we have a visual sense of both our own body and that of others. Since anorexia affects primarily the sense of ones own body, proprioception would seem a more likely candidate for sensory disturbance. It is also possible that deficits in interoception (e.g. Pollatos et al. 2008) lead the brain to prioritize this information when it is available.

In contrast to our prediction, but in line with this reasoning, AN patients and controls showed significantly different relationships between weight discrimination accuracy and SWI. Weight discrimination accuracy was negatively correlated with the SWI in controls, suggesting that more accurate proprioceptive information was relied upon more than less accurate proprioceptive information. In contrast, AN patients relied more on proprioceptive information when it was inaccurate, obtaining a lower SWI with reduced weight discrimination accuracy. This could reflect a disturbance in evaluating the accuracy of sensory information in AN patients.

A further possibility is that sensory integration in general is disturbed in anorexia. General sensory integration problems in anorexia could to do with effects of starvation affecting white matter connectivity, or with top-down effect of beliefs about body image biasing normal construction and updating of body image. Finally, SWI differences could be attributed to differences in how AN patients and controls utilize visual and proprioceptive information to generate expectations of heaviness. In other words, sensory integration per se might not be disturbed, but AN patients might have different internal models of heaviness that would lead to different expectations based on visual information. While we favor a sensory interpretation of our data given the previously discussed sensory disturbances found in AN and data favoring sensory interpretations of the SWI (e.g. Kawai et al. 2007), we hope that future work will be able to disentangle the effects of sensory, sensory integration, and cognitive expectation differences that may exist in AN.

A reduced SWI in patients with AN fits with emerging picture of interoceptive and proprioceptive deficits in this population, but our evidence points more specifically to dysfunctional multisensory integration. This would explain how visual body image distortions can occur in the absence of low-level visual deficits and may also explain deficits in implicit body image and body schema found in relation to parietal lobe functioning (e.g. Nico et al. 2010; Guardia et al. 2010; Grunwald et al. 2001). Reduced SWI also implicates the parietal lobes: Jenmalm et al. (2006) found parietal, motor, and cerebellar activation involved in the comparison of predicted and actual sensory input during a lifting task. Right parietal dysfunction has been observed in anorexia (e.g. Nico et al. 2010; Grunwald et al. 2001) and seems to be correlated with illness state (Komatsu et al. 2010). Other brain areas are involved in the SWI as well, however; Chouinard et al. (2009), for example, found the activation of the ventral premotor area in relation to perceived heaviness based on density. AN may reflect dysfunction in interactions between sensory integration in the inferior parietal lobule (concerned with body image), affective processing of bodily states in the insula, and regulation of appetite through the hypothalamus (e.g. Ramachandran et al. 2009). Future work will need to determine whether sensory integration deficits exist between other sensory domains or whether they are restricted, as we would predict, to those involving proprioception and somatosensation.

One potential limitation of the current study is that participants were not explicitly tested on their ability to discriminate the visual size of the large and small objects. Differences in this ability could lead to differences in density expectation based on visual input. However, the lack of crude differences in visual sensitivity to size in patients with AN (Smeets et al. 1999) makes this an unlikely explanation for our finding. Another limitation is that we did not disentangle the contributions of vision and haptic perception to the SWI. While controlling for mass discrimination points toward an effect of vision, the SWI is also affected by haptic size cues. We plan to separate the effects of vision and haptic perception on weight judgments in future work.

The current finding may begin to explain how it is that direct visual perception of the body in a mirror does not correct an AN patient's distorted body image. Of course, the reduction in visuo-proprioceptive integration found in the current study is unlikely to fully account for the magnitude of perceptual disturbance seen in AN with respect to the patient's own body. Our finding may be one of multiple sensory or sensory integration disturbances present in AN, and indeed, we would expect that these differences would be stronger for processing of cues about ones own body, as it is generally self-perception that is most distorted in AN. Future research should examine whether distortions of a similar nature occur for judgments about the patient's own size and weight, and whether these correlate with severity of the eating disorder. If they do, then visual or visuo-tactile integration therapies might help rehabilitate perception of body weight and size in AN patients.

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# CHAPTER 4

Magnetoencephalography Recording of Somatosensory Evoked Fields in Body Parts that Feel

Dysphoric or Neutral in Individuals with Anorexia Nervosa

## Abstract

Anorexia nervosa (AN) is a serious psychological disorder in which individuals dangerously restrict their caloric intake due to a desire for an extremely thin body and, typically, a distortion in judgment of their own size. AN takes common body image concerns and distortions to an extreme, and thus provides an interesting condition in which to study the dissociation between neurological body image and actual body shape and size. Might dysphoric-feeling body parts in AN (like the abdomen) be under-represented in body integration areas like the right superior parietal lobe (rSPL), leading to the type of discomfort felt by those with transsexuality or Xenomelia when sensation is registered but poorly integrated? Or, might sensory processing for dysphoric body parts be heightened, leading to an exaggerated functional brain response in some brain areas, similarly creating a perceptual experience of these body parts being larger than expected? In the current study we conduct magnetoencephalography (MEG) recordings while tapping the abdomen- a body part that feels highly aversive to people with AN (but relatively neutral to healthy controls)- and the hand- and a body part that feels normal to both groups. We find an interaction between group and temporal pattern of activation in the sensory evoked field (SEF) response to the abdomen in S1 and the intraparietal sulcus, as well as an overall difference in AN in the timing of the response to sensation from the hand. This finding suggests that the dysphoria related to body part size in individuals with AN may be correlated with an exaggerated functional representation of the abdomen and diminished representation of the hand- or pathological differences in attention that affect sensory processing. Unlike previous work on AN, we link body image concerns to lower-level sensory-neural body representation. This finding may be useful to understanding the etiology of AN and devising treatments to prevent and reverse the amplification of body-related sensory integration.

# Introduction

Anorexia Nervosa (AN) is an eating disorder characterized by a pathological fear of becoming fat and excessive dieting to a dangerously low weight. Body image distortion is a core feature of AN (*Diagnostic and Statistical Manual of Mental Disorders*, 5th ed., 2013). Like transsexual individuals and people with Xenomelia, people with AN experience extreme dysphoria about their body and wish to alter its form. They differ, however, in that they also display persistent anosognosia about their actual thinness: they both perceive their body to be larger than it is and desire to be thinner than is healthy for their body. What underlies this distorted body image and distorted ideal body form? The extent to which body image distortion relates to distortions in sensory representations of the body in the brain is unknown. The current study aims to uncover whether differences in somatosensory processing in individuals with AN might accompany- or give rise to- the feeling that a body part is uncomfortably large.

## Neurobiology of Anorexia Nervosa

Anorexia is currently conceived of as a complex disorder involving the interaction of genetic, biological, psychological, and sociocultural factors (Kaye et al., 2009). The current work discusses only biological and psychological contributions to the disorder, but this is not meant to downplay the significant role of culture in shaping or adding to biological and psychological vulnerabilities in AN (e.g. Lester 1997). Kaye et al. (2009) propose that AN involves abnormalities in neural processing of somatic, autonomic, and visceral information, which create a disconnect from bodily needs. Increased activity in the orbital and dorsolateral prefrontal cortex may relate to excessive planning and worry, as well as exertion of cognitive control over motivated behaviors like eating that are typically regulated through more automatic, ventral-striatal processes. Disturbances in the serotonin system contribute to behavioral inhibition and anxiety after caloric intake, while disturbances in the dopamine systems alter reward processing
(Kaye et al., 2009). Abnormalities in functional brain activity found in anorectic individuals include impairment of orbito-frontal, somatosensory, and parietal structures as well as subcortical structures including the amygdala, hippocampus, thalamus, hypothalamus, and striatum. Because insular cortex integrates function for these structures, it has been suggested to underlie impairment in anorexia (Nunn et al., 2008). In line with this theory, Strigo et al. (2013) report altered insula activation during anticipation of pain in individuals recovered from AN that appeared to indicate difficulty in accurately perceiving bodily signals. Kaye et al. (2009) also propose strong involvement of the anterior insula in altered interoceptive processing and behavior motivation in anorexia.

# Neurological Correlates of Body Image Distortion and Dysphoria

What is the neural basis of distortions in body perception? Disturbances of the parietal lobe including stroke, epilepsy, or migraine often produce changes in perception of body part size and shape (Ehrsson et al., 2005). In contrast, under local anesthesia– in the absence of somatosensory feedback– surgical patients often experience illusory changes in the size and shape of the anesthetized body part(s) (e.g. Gandevia & Phegan, 1999). Parietal lobe representations of the body are thus shaped by proprioceptive feedback from the body. Changes in somatosensory feedback can also alter multimodal body perception. Lackner (1988), for example, describe an illusion of shrinking or expanding the waist based on vibration of muscles in the wrist when the hand is in contact with the body surface. The vibration activates spindles in the muscle fibers and the brain interprets this false proprioceptive feedback as indicating movement of the hand– and infers a change in shape of the waist, when the hands remain in contact with it. Ehrsson et al. (2005) find that the shrinking waist illusion correlates with activation in the postcentral and anterior intraparietal sulcus.

What is the role of neural body representation in body image distortion in AN? Right parietal cortex and vestibular dysfunction have been suggested to underlie body image distortion in AN (Tomasino 1996). Indeed, in healthy women, body size overestimation has been proposed to relate to difficulties in retrieving multimodal body schema in the precuneous and posterior parietal cortex (Mohr et al., 2010). At the sensory level, individuals with AN exhibit disturbances in sensory processing and body mapping: patients show decreased interoceptive sensitivity (e.g. Pollatos et al., 2008), reduced pain sensitivity (Lautenbacher et al., 1991), deficits in tactilespatial processing (Grunwald et al., 2001), and diminished EEG activity and blood flow in the right parietal lobe (e.g. Grunwald et al., 2001; Komatsu et al., 2010). Patients also show an enlarged implicit body schema (Guardia et al., 2010) and misjudgment of their body boundary (Nico et al., 2010), both suggesting distortions in low-level representations of the body. Furthermore, Mussap & Salton (2006) report a correlation between eating disorder behaviors and the rubber hand illusion (RHI)- an illusory feeling of limb displacement caused by visualsomatosensory cues- suggesting that individuals with eating disorders may have more plasticity in their body representation. It is unclear, however, whether differences in sensory processing could account for, or underlie, distortions in body representation in eating disorders.

Individuals with anorexia do not experience all parts of their body as equally enlarged or aversive. Body parts where more fat tends to be stored, like the abdomen and buttocks, tend to be overestimated and disliked the most in people both with and without eating disorders– at least in Western countries (Gila et al., 2004). In contrast, the hands typically do not feel aversive and are not important contributors to ratings of weight and shape in individuals with eating disorders (e.g. Mussap & Salton, 2006). We wished to see whether we could identify sensory effects of dysphoria for an aversive-feeling body part (the abdomen) versus a neutral-feeling one (the hand). Based on research with Xenomelia (McGeoch et al., 2011), we hypothesized that somatosensory processing in the right superior parietal lobule (rSPL) would differ from that in control participants, because– as in patients with Xenomelia– patients with anorexia often feel that these body parts are over-present and desire to figuratively (or literally) carve off the fat (e.g. Lester 1997). We were not sure whether to expect diminished or heightened activation of the rSPL in AN relative to control participants because it is plausible that body representation could be decreased in AN (such that sensation would overwhelm the reduced maps, as in Xenomelia) or increased (over-integration of sensation, resulting in a feeling of an enlarged body relative to the magnitude of sensation registered in primary sensory cortex). Additionally, we hypothesized differences in seven other brain regions (the same brain areas as in the MEG study in Chapter 2). In general, we predicted that functional body representation would be *either* heightened or diminished for sensation from the abdomen, but not the hand. For the anterior insula and medial temporal lobes, however, we predicted heightened activity in AN patients for the abdomen due to the role of these brain areas in the experiences of anxiety and disgust (e.g. Simmons et al., 2012; Seeger et al., 2002).

#### Methods

## **Participants**

Participants were recruited in accordance with approval from the UCSD Institutional Review Board. Eight females with anorexia nervosa (AN; Mean age = 23.4, SD 6.4, BMI less than or equal to 18.5, M = 16.9) and eight female controls (CON; mean age 25.5, SD 7.9, BMI 18.6-22.9, M =  $20.9^3$ ) participated in the current study (see Table 4.0). The control participants were screened for DSM Axis-1 disorders using the Mini International Neuropsychiatric Interview (Sheehan et al., 2009) and included only if they did not meet criteria for any psychological

<sup>&</sup>lt;sup>3</sup> One CON participant was found to have a BMI in the "underweight" range. She appeared healthy (merely slight in frame) and was found to have healthy attitudes towards eating and weight.

disorder. In addition, control participants were screened and asked about their weight history and current eating patterns, and were included only if their weight history was unremarkable and current eating patterns and attitudes did not reveal any particular attempts to control caloric intake or weight. All participants were right-handed (missing data N = 2).

The AN participants varied in how long it had been since they were first underweight, ranging from 6 months to 11 years; many had histories of recovery and relapse in the intervening time. The average duration of illness was 4.3 years. Participants were asked to rate their overall satisfaction with their body size and shape (1 = extremely dissatisfied; 10 = extremely satisfied), as well as to rate their abdomen and hands on the same scale. Body, hand, and abdomen satisfaction ratings were each significantly higher in the CON group than in the AN group (body: t(14) = 8.1, p < 0.0001; hand: t(13) = 2.7, p < 0.05; abdomen: t(13) = 6.9, p < 0.0001; one control data point was missing for hand and abdomen and one AN response was re-coded<sup>4</sup>; see Figure 4.0). The difference between hand satisfaction and abdomen satisfaction was much greater in the AN group than in the CON group (t(13) = 5.1, p < 0.001), demonstrating more dysphoria for the abdomen than for the hand in the AN group.

Insert Figure 4.0 about here

## Magnetoencephalography Recordings

Data collection was performed identically to that described in Chapter 2. The only difference was that the body parts tapped were the hand (neutral-feeling) and abdomen (aversive-feeling; see Figure 4.1). On some participants, the foot was also tapped as an additional control condition (not analyzed in the current work). Participants' eyes were closed during every block.

<sup>&</sup>lt;sup>4</sup> One AN participant rated her body and hand a "1" on the 1-10 scale and her abdomen a "-10." She refused to relocate her responses to the 1-10 range, so we recoded her responses as 5, 5, and 1 to reflect the relative difference between her ratings of these body parts.

Insert Figure 4.1 about here

## **Data Analysis**

Data analysis for this study was identical to that conducted in Chapter 2 except that we were able to include only 145 (+/- 5) events per block due to increased noise and time constraints during these sessions. For several AN participants (one hand block, three abdomen blocks) only 129-139 events were available. One AN participant had only one hand block and another AN participant had only one abdomen block. Sample sensory evoked fields (SEFs) in sensor space (after filtering and trial rejection) from 1 AN participant and 1 CON participant are provided in Figure 4.2.

Insert Figure 4.2 about here

# Results

We found a significant 4-way interaction between group, body site (abdomen versus hand), time (40-140ms), and region of interest (eight ROIs), F(7, 866) = 3.92, p < 0.001, as well as 3-way interactions between group, time, and body site (F(1, 14) = 11.7, p < 0.001) and group, body site, and ROI (F(7, 98) = 2.01, p = 0.05), but not group, time, and ROI (F(7, 98) = 0.27, p = 0.96). There was no main effect of group (F(1, 14) = 0.39, p = 0.54) and no interaction between group and ROI (F(7, 98) = 1.23, p = 0.29), group and body site (abdomen versus hand; F(1, 14) = 2.43, p = 0.14), or group and time (F(1, 14) = 3.39, p = 0.09). The groups did not statistically differ in early (24-40ms) S1 activation levels (F(1, 14) = 0.10, p = 0.76). See Figure 4.3 for average group contrasts in the abdomen condition and Figure 4.4 and Figure 4.5 for dSPM timecourses for AN and CON abdomen and hand.

# Abdomen

A 3-way interaction between group, time, and ROI for the abdomen condition alone was statistically significant, (F(7, 482) = 4.15, p < 0.001). The 2-way interactions between group and ROI and group and time were not statistically significant (F(7, 98) = 0.60, p = 0.76; F(1, 14) = 1.19, p = 0.29). To investigate the interactions between group and time (40-140ms) in individual ROIs, we computed eight rmANOVAs (group × time). An interaction of group × time for the abdomen was statistically significant in two of the eight ROIs below or near the Bonferroni-corrected p-value of 0.006: S1 F(1, 62) = 11.29, p = 0.001), and the intraparietal sulcus F(1, 62) = 7.47, p = 0.008). When the hand condition was included as a covariate, the effects remained the same, except the superior parietal lobe was an additional ROI that was marginally significant at the uncorrected p value: F(1, 64.5) = 3.91, p = 0.052). The differences in activation across time appeared to reflect peaking in the middle of the waveform and then dropping, resulting in less change over time. While not statistically significant, every brain area studied showed a trend towards higher activation in the AN group (see Figure 4.4).

#### Hand

A 3-way interaction between group, time, and ROI was not significant for the hand condition (F(7, 482) = 1.49, p = 0.17) but an interaction of group by time was significant (F(71, 14) = 6.57, p = 0.02). In the hand condition, every ROI except the medial temporal lobe showed interactions between group and time below p = 0.05, though only the superior parietal lobe, anterior insula, and supramarginal gyrus were significant at the corrected p value of 0.008. Using the abdomen data as a covariate, the same results were obtained, except that the posterior insula was not significant and S1 and the intraparietal sulcus were additionally significant at the corrected p value of 0.008. Insert Figure 4.3 about here Insert Figure 4.4 about here Insert Figure 4.5 about here

Monte Carlo *p*-values below 0.05 were found in contiguous clusters of 3 or more only in the intraparietal sulcus: six contiguous timepoints showed significant differences between AN and CON in the 56-76ms time window. Simulation showed that a cluster this size would be expected with a *p* value of 0.056, suggesting a marginally significant finding. Activity in this time window showed a trend towards correlating positively with BMI within both groups (AN: Pearson's r(6) = 0.52, p = 0.19; CON: r(6) = 0.52, p = 0.39), but negatively when collapsed across groups (Pearson's r(14) = -0.25, p = 0.39).

# Discussion

In the current study we find significant differences in somatosensory-evoked field (SEF) response to tapping of the left hand and left abdomen between female participants with a current diagnosis of anorexia nervosa (AN group) and healthy female control participants (CON group). Specifically, we find an overall interaction between group, time, ROI, and body site, suggesting different spatiotemporal patterns of sensory processing for the hand versus abdomen in women with and without AN. We also found a significant group  $\times$  ROI  $\times$  time interval interaction in the abdomen condition alone, suggesting differences in integration of sensation from a body part that feels dysphoric to AN individuals. Finally, we identify differences in the timing of response between groups in the hand condition, irrespective of ROI.

In the abdomen (dysphoric for AN) condition, with or without the hand condition activation as a covariate, different temporal patterns of activation were seen between patients and healthy controls in S1 and in the intraparietal sulcus, with greater SEF activation in the middle and late portion of the waveform relative to the earlier portion in the AN group. In the hand condition, interactions between group and time were observed at the corrected threshold in the superior parietal lobe, anterior insula, and supramarginal gyrus, as well as in S1 and the intraparietal sulcus when the abdomen data were utilized as a covariate.

## **Integration of Sensation from the Abdomen**

In the current study we observe greater activity in S1 in the middle of the SEF waveform in the AN group than in the CON group. Could individuals with AN have a generally heightened sensitivity to sensation? Indeed, individuals with AN have been found to have heightened sensory sensitivity in psychophysical studies (e.g. Zucker et al., 2013), and Zucker et al. found heightened sensory sensitivity to be associated with body image disturbance. A heightened sensory response could also reflect a nonpathological process, such as heightened sensitivity of the skin due to low BMI (obese individuals have been found to show higher sensory thresholds, e.g. Price et al., 2013). However, the abdomen condition showed greater increase relative to hand condition in AN even when controlling for the hand SEF, suggesting that the increase in activation in SEF over time in AN patients is not a general exaggeration of sensory integration processes in AN, but is associated with body parts involving greater body distortion and dysphoria.

It is interesting to note that we do not observe under-representation of the abdomen in AN, in spite of a number of reports of reduced parietal lobe activation and insular activation in AN (e.g. Grunwald et al., 2001; Komatsu et al., 2010; Kaye et al., 2009). In contrast, we observed similar levels of activation between AN and CON, but heightened peaks in the middle

of the timecourse in S1 and the intraparietal sulcus (IPS). This may indicate heightened functional representation of the abdomen in the brain in individuals with AN. Increases in activity over time in S1 may indicate back-modulation of S1 by other ROIs like S2 that have been shown to bias S1 activation (e.g. Mountcastle & Powell, 1959; Schaefer et al., 2006). Heightened activation around the midpoint of the sensory response (e.g. 70ms) in the IPS may give individuals with AN a sense of distorted, increased body size given the putative role of the superior parietal regions in the feeling of "over-presence" in Xenomelia.

Monte Carlo *p*-values showed significant differences between AN and CON only in the intraparietal sulcus, in the 56-76ms time window. Interestingly, IPS activation in this time window was positively correlated with BMI in each group separately. Yet the AN group, which had a much *lower* BMI than the CON group, showed *higher* activity in the INS. This suggests that low BMI cannot be the explanation for increased IPS activation in the AN group, as in general, an increase in BMI was associated with an increase in IPS activation (at least within each group). The heightened activation in IPS is thus more likely to reflect some kind of distortion or amplification of the sensory signal from the abdomen in AN- perhaps related to the IPS activation observed during the "shrinking waist illusion" by Ehrsson et al. (2005). This response may reflect active distortion of the incoming sensory data.

We did not observe differences between groups for sensation from the abdomen in the amygdala or insula. Heightened activation of the medial temporal lobe over time was expected in AN based on greater anxiety and alarm about sensation from the body (heightened amygdala activation is seen with body image distortion in anorexia; e.g. Seeger et al., 2002). Greater increases in anterior insula activation over time were also expected based on feelings of disgust towards the body (e.g. Craig et al., 2009). Indeed, we did observe a trend towards greater activation in the anterior insula over time (p = 0.11), suggesting that individuals with AN may integrate sensation from the abdomen more than CON individuals and may also have a

heightened disgust response. Kaye et al. (2009) postulate dysfunction of the insula in relation to integration of bodily needs and desires, which would in turn affect behavioral motivation assessments in the anterior cingulate cortex leading to food restriction. Indeed, the differences in anterior insula activation over time in the current study suggest that with more participants, we might observe dysfunctional levels of sensory integration in the insula, perhaps reflecting amplification of the sensory signal. Nunn et al. (2008) also hypothesize insular dysfunction as a unifying neural basis for anorexia. However, the authors do not describe what type of dysfunction they expect or how it corresponds to the behaviors and perceptions seen in ill patients.

# Integration of Sensation from the Hand

The differences in timing of activation observed across ROIs in the hand condition between AN and CON participants suggest diminished response to sensation from the hand in the AN group. This is surprising given reports of heightened sensory sensitivity in AN (e.g. Zucker et al., 2013) and at odds with the increased activation over time in the abdomen condition. One possible explanation for the diminished hand response is that individuals with AN have an expansion in representation of the abdomen and a decrease in cortical representation of the hand. Another possibility is that the AN participants were actually focusing spatially on the abdomen during the hand tapping, due either to baseline pathological differences in attention to dysphoric body parts, or due to anticipation of the next block of tapping (of the abdomen). The reduced response in the hand condition suggests that the heightened sensory response to the abdomen in AN is specific to a dysphoric-feeling body part and not a general increase in sensory sensitivity.

# Attention

It is possible that differences in the spatiotemporal dynamics of the SEF for the abdomen may reflect general amplification or distortion of sensory processing for the abdomen based on an attentional biasing signal, perhaps due to heightened salience and self-relevance of sensory information from a body part with strong relevance to self-image in AN. Individuals with AN tend to attribute more significance to sensation from their bodies, and may pay more attention to it. This may be driven by sensory differences or by higher-level cognitive-emotional interpretations of sensation as originating from a disliked body part. Heightened attention can indeed increase sensory evoked response in S1 and S2 (e.g. Noppeney et al., 1999; Fujiwara et al., 2002). This explanation is not entirely distinct from the explanation of magnified body representation: a greater focus on sensation from the abdomen may magnify sensory processing of sensation from this body part, which could in turn increase its functional representation in the brain. Heightened processing of sensation, however, conflicts with reports of reduced interoceptive sensitivity in AN (e.g. Pollatos 2008). While we did not observe differences in parietal activation overall in the current study, it is possible that patients have reduced resting state activity in the parietal lobes, but heightened response to somatosensation. Tsakiris et al. (2011) report that individuals with diminished interoceptive sensitivity experience stronger body ownership in the multisensory rubber hand illusion. People with anorexia may thus have impoverished determination of body boundaries from internal cues, and magnified sensory processing of external cues, leading to significant distortion in body perception.

Differences between SEF in the current study and the study presented in Chapter 2 may be instructive about the differences in bodily dysphoria between transsexuality (TR) and AN. TR individuals show reduced integration of sensation from the chest, yet AN individuals show heightened response to sensation from the abdomen. Thus while TR individuals may feel reduced ownership of their incongruent-feeling body parts, individuals with AN may feel that these body parts are *too* connected to their self, and thus heavily influence self-concept. This argues against attention or emotion as providing a common explanation for both sets of findings, though it remains possible that the AN differences are due to heightened attention, while the TR findings are due to a direction of attention *away* from the sensation. This explanation, however, begs the question of why anorectic individuals would attend more to sensation from a body part that feels highly dysphoric and causes increased anxiety. If attention is the true explanation for the current findings, it is likely a pathological form of sensory attention that the patient does not volitionally choose. The significant difference in SEF before 100ms and across hundreds of taps suggest a form of heightened sensory response that is sustained and does not significantly habituate, suggesting automatic direction of attention to sensation from the abdomen– or amplification of sensory processing due to distortions in body representation.

## **Limitations and Future Directions**

One potential confound in the current study is variability in the rate of manual tapping. As in Chapter 2, however, we checked tapping rates and did not find significant differences between groups. On average, participants were tapped every 1.19s (SD 0.24) on the hand and every 1.16s (SD 0.31) on the abdomen; average ISI across blocks for each participant did not differ significantly between groups (Hands: t(14) = 0.13, p = 0.90; Abdomen: t(14) = 1.55, p = 0.14; abdomen AN mean = 1.12, abdomen CON mean = 1.20). Other limitations described in Chapter 2 also apply to the current study: a general limitation of MEG in localizing non-sulcal sources, and a small sample size with too low power for a full-brain analysis or analysis comparing averaged time windows. The current analysis can describe only linear effects in the data, which is not an ideal model for waveform data. In addition, all participants who enrolled in the current study were cissexual females; it would be helpful to study males with AN to see whether the differences generalize to both sexes or whether effects of sex or gender moderate the role of sensory abnormalities in AN. Finally, the AN participants in the current study differed

from the CON individuals not only in their diagnosis of AN but also in diagnosis of mood and anxiety disorders and use of psychoactive medications such as SSRIs. It is possible that some of the differences observed in the current study are caused by differences in psychopathology other than AN, or use of psychoactive medications. However, the SEF differences between groups were quite different for the abdomen versus the hand, suggesting that the differences observed in sensory process had more to due with representation of each body part or attention to them than with overall differences in sensory processing.

We studied sensory stimulation of the left side of the body because it is processed primarily in the right hemisphere, which is specialized for representation of one's own body. While explicit differences in body image for the right and left sides of the body have not been reported in AN to our knowledge, studies of implicit body image have found increased distortion for the left side of the body: Nico et al. (2010) found distortion for spatial body boundary only on the left side of the body (similar to patients with right parietal lobe damage) and Mussap & Salton (2006) report a correlation between the rubber hand illusion (RHI) and eating disorder behaviors only for the RHI administered to the left hand. While the authors do not provide an explanation for this lateralized effect, it likely relates to the representation of the left body boundary in the right-hemisphere. It would be interesting to conduct further work on differences between sensation on the left and right sides of the body in AN to see whether differences in activation of brain regions like the amygdala would be seen for sensation from the left side of the body than for sensation from the right side of the body.

In addition, to further explore whether the differences observed in the current study might be due to heightened attention and emotional processing, it would be interesting to test whether differences would persist if patients were given competing task demands that removed their focus from bodily sensation. Similarly, it would be interesting to test whether sensory processing below the threshold for conscious perception would show a similar difference between anorexia and healthy controls. These conditions would allow us to determine the role of attention and conscious awareness in the heightened SEFs observed in the current study. Finally, it would be interesting to directly test the role of top-down emotional and cognitive influences on sensory processing by manipulating the patient's mood or higher-level body image (e.g. across separate scan sessions, by telling the patient they had lost or gained weight since the previous session).



**Figure 4.0: Body satisfaction ratings for overall body, hand, and abdomen.** AN participants were significantly less satisfied with their body, hand, and abdomen than CON participants. They were also significantly more dissatisfied with their abdomen than with their hands, relative to the CON participants.



**Figure 4.1: Illustration of MEG somatosensory stimulation paradigm.** White rectangles show placement of reflective tape where the participant was tapped.







Figure 4.3: Mean dSPM values for the abdomen condition for the AN versus CON groups at (A) 40ms; (B) 72ms in CIS group; (C) 140ms. Units of activation amplitude are arbitrary. Yellow: AN > CON; Blue: CON > AN





Figure 4.4: Averaged dSPM timecourses for the abdomen condition for each ROI.







Figure 4.5: Averaged dSPM timecourses for the hand condition for each ROI.



Supramarginal gyrus





Posterior insula





Figure 4.5: continued.

Table 4.0: Characteristics of participants with an orexia (N = 8) and healthy controls (N = 8).

Characteristic	Mean (SD)
Participants with anorexia (8)	
Age	23.4 (6.4)
BMI	16.9 (1.4) **
Body satisfaction	3.8 (1.3) **
Hand satisfaction	7.1 (1.3) *
Abdomen satisfaction	2.4 (1.6) **
Average duration of illness (years)	4.3 (4.4)
Control participants (8)	
Age	25.5 (7.9)
BMI	20.9 (1.8) **
Body satisfaction	8.0 (0.8) **
Hand satisfaction	8.9 (1.2) *
Abdomen satisfaction	7.7 (1.4) **

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# CHAPTER 5

Allocentric Body-Viewing: Effects on Body Size Estimation and Body Satisfaction in Patients with Eating Disorders

## Abstract

Despite the centrality of body image distortion to the clinical presentation of eating disorders, little psychophysical work has been conducted to identify which aspects of body representation are distorted, or whether these distortions can be modified through sensory feedback. Recent studies have documented distortions in anorexia nervosa in both visual and tactile body size estimation. Further, these distortions have been shown to correlate with severity of body dissatisfaction (Keizer et al., 2011), between individuals. To date, no studies have explored *within*-subject associations. We aimed to investigate whether shifts in body satisfaction within an individual are accompanied by shifts in visual and tactile body representation.

In addition, we aimed to ascertain whether allocentric viewing strategies could change body satisfaction ratings. Mirror visual feedback for phantom limb pain and illusions like the rubber hand illusion demonstrate how body image and body schema can be modified through sensory feedback. Simple body exposure for patients with eating disorders can be helpful, but it is constrained by egocentric pathways for body processing in the brain and associations that join familiar views of the body to somatosensory representations, memories, and emotions. We tested whether patients with eating disorders could obtain improvements in body image by viewing their body in ways that engaged allocentric modes of body processing. To do this we manipulated both familiarity of mirror visual feedback (front reflection versus side or back reflection) and identity (self versus other: mask, or another person's head). We hypothesized that body image ratings would improve in the allocentric conditions and would be paralleled by decreases in visual and tactile estimates of body size. We found a main effect of the identity manipulation but not of the familiarity manipulation, suggesting that allocentric visual feedback can modify body image. We also found that within-subject increases in body satisfaction ratings decreased both visual and tactile estimates of abdomen size, suggesting that visual feedback quickly modulates multisensory representations of the body.

# Introduction

A core feature of anorexia is disturbed body image: an individual with anorexia perceives him- or herself to be fat, despite external feedback to the contrary. Why can't an individual with normal visual acuity look in a mirror and see that she is not as large as she feels? Why is veridical sensory feedback of little use to a distorted body image? Traditionally, body image distortion in anorexia has been viewed as a cognitive-emotional distortion. Cognitive and emotional ("attitudinal") factors may influence sensory body representation, and distorted body representation may influence cognitive and emotional beliefs and attitudes about the body. Conversely, induction of negative mood can cause increased distortion in body size perception (Taylor et al., 1992). However, the causal connections between cognitive distortions (thinking "I am fat"), emotional factors (feeling anxious and depressed), and sensory processing and neural body representation in eating disorders are not clear.

Increasingly, studies have documented distortions in body representation at a sensory level. People with anorexia appear to have intact sensory functioning: Goldzak-Kunik et al. (2012) found little to no difference from healthy controls in taste, odor, shape and size of objects, kinesthesia, body size, or auditory and visual processing. Yet despite an absence of abnormalities in basic sensation, visual body size overestimation is found in many (though not all) studies of AN (Cornelissen et al., 2013). Research suggests that one component of body size overestimation is perceptual and another component is attitudinal (Cash & Deagle, 1997). Some of the perceptual component may be due to a general, nonpathological effect of low body mass index (BMI), leading individuals to estimate their own body to be more like the average body they see in the world, despite being comparatively smaller (Cornelissen et al., 2013). Even at an implicit level, however, AN patients show an enlarged implicit body schema when judging what size of aperture they can fit through (Guardia et al., 2010) and show misjudgment of their body boundary (though only on the left side) when judging whether a light aimed near their body will contact their body or not (Nico et al., 2010).

Body image and body schema are profoundly multisensory. Mohr et al. (2010) suggest that body size overestimation in women may relate to difficulty retrieving multimodal body schema in the precuneous and posterior parietal cortex. Distortions in body representation in AN may even extend beyond the visual domain and into the tactile domain. Keizer et al. (2011), for example, found disturbances in patients with anorexia not only in visual body size estimation, but also in tactile body size estimation. Interestingly, both of these measures correlated with severity of body dissatisfaction. Individuals with eating disorders are also found to have heightened global sensory sensitivity (Zucker et al., 2013) but impoverished interoceptive sensitivity (e.g. Pollatos 2008).

Knowing what we know at present about distortion in body representation in AN and its relationship to body satisfaction, could we modulate body satisfaction in AN through visual feedback? Crossmodal effects play a strong role in body representation; in the rubber hand illusion, for example, synchronized illusory sensory feedback shifts one's perception of body position and body ownership (Botvinick & Cohen, 1998). Utilizing the same principle of visual capture of sensation and motion, mirror visual feedback therapy (MVFT) is used to reduce pain in phantom pain and chronic pain conditions, and assist in post-stroke motor rehabilitation (Ramachandran & Altschuler, 2009). A visual superimposition (in a mirror) of a person's healthy limb onto their unhealthy or missing limb often creates a robust motor and sensory experience of the damaged or phantom limb, reducing its perceived pain (even weeks after treatment; Chan et al., 2007). Visual feedback thus has a striking effect on multimodal body representation.

Indeed, body exposure therapy, in which the patient focuses visually on parts of his or her body for extended periods of time, has had some success in providing persons with anorexia with insight into their condition and decreasing negative body-related emotions and cognitions (e.g. Rushford & Ostermeyer 1997; Vocks et al., 2007). Yet body exposure therapy is limited by the fact that visual feedback about one's own body appears to be processed differently in the brain in AN. Sachdev et al. (2008) show abnormal processing of self-images in anorexia using fMRI, such that self-image processing lacked activation of attentional networks and the insula that are seen in healthy participants. Similarly, Blechert et al. (2010) demonstrated attentional bias for self-photos in anorexia. In addition to processing egocentric visual images differently than allocentric ones (e.g. Saxe et al., 2006), we also have strong multisensory connections between familiar (typically egocentric) views of the body (usually the front of the body) and our somatosensory and visceral experience of the body. These crossmodal influences likely distort visual feedback, lessening its ability to correct body image. Could patients with eating disorders be forced to view their body in a way that disconnected from these egocentric modes of processing- and the sensations and emotions associated with them- and engage in third person, allocentric modes of body viewing? If so, what effect would this have on body image?

We hypothesized that viewing the body from the allocentric (external) position could bypass distorted egocentric body processing and rehabilitate patients' views of their bodies. One way to view the body from an allocentric viewpoint is to view it in two mirrors facing each other at an angle (such as in a dressing room), and view the reflection of your reflection. This allows visual access to the body from behind and to the side– angles most people rarely see– and seems to create some dissociation from the viewed body (e.g. Altschuler & Ramachandran 2007). Another allocentric viewing strategy is to view your body while wearing a mask or otherwise visually substituting another person's face for your own. While little experimental work has been conducted on masks, several studies have found that wearing a mask causes a shift away from selfidentification and towards the identity represented by the mask, especially while attending to the mask (such as by looking in a mirror, e.g. Cooper 1999). We also hypothesized that at the withinsubject level, changes in body satisfaction based on the mirror visual feedback would be accompanied by changes in sensory representation of the body measurable by estimates of visual and tactile body size.

In the current study participants engaged in body-viewing activities designed to shift their processing of body image and body schema into an allocentric framework. Participants thus viewed their body from the front and then from the side and back in a double-reflection (familiarity manipulation). They also viewed their reflection while wearing a full-head mask or while viewing their body in a mirror with the experimenter's head replaced on top of their body (identity manipulation). We measured body satisfaction ratings as well as visual and tactile estimations of body size. We hypothesized that (1) body image ratings would improve in the allocentric viewing conditions and (2) changes in body image ratings within subjects would be paralleled by changes in sensory body representation, as measured by decreased visual and tactile body size estimates.

# Methods

This study was conducted in accordance with approval from the University of California, San Diego Human Research Protections Program. Participants aged 13 and older with current or past eating disorders and current body image dissatisfaction were recruited through email announcements distributed to local eating disorder clinicians and treatment centers. Eight females with current or past anorexia nervosa participated in the current study. Participants' mean age was 26.3 (SD 15.7, range = 17-63). All participants were in the healthy or underweight BMI categories.

Participants were asked to rate their overall body satisfaction on a 1-10 scale (1 = extremely dissatisfied; 10 = extremely satisfied). They then participated in a series of 35-second mirror viewing exercises in which they were instructed to view their body in a mirror. After each mirror view participants rated their overall body satisfaction again. They then provided a visual

estimate of the width of their waist using a string (a measure of explicit visual body image), and estimated the distance (perceived tactilely with eyes closed) between two points of a compass that was pressed onto their right forearm and then right abdomen (a measure of implicit sensory body representation). Participants were told that the two points would vary in distance but in reality the compass was always set to 4cm. Clinical assessment tools (not reported in the current paper) were administered before the study, between conditions, and at the end of the study.

Participants completed mirror-viewing exercises in the following order of angles (see Figures 5.0 and 5.1 for illustrations):

A: Mirror, front view (familiar)

B: Mirror double-reflection, side view (less familiar)

C: Mirror double-reflection, back view (less familiar)

The order of identity conditions for every participant was as follows:

1: Regular identity: views A, B, C

2: Full head mask: views A, B, C

3: Head swap: view A only. Participant saw her body reflected in the mirror with the experimenter's head above the mirror aligned with the participant's body (matching scarves were used to better blend the head with the body).

Insert Figure 5.0 about here Insert Figure 5.1 about here

**Data Analysis** 

First we tested the effect of the angle manipulation (views A, B, and C) and the identity manipulation (conditions 1, 2, and 3) on body satisfaction ratings, waist estimates, and tactile body size in three separate 2-factor repeated measures ANOVAs (data from Participant 6 was re-coded<sup>5</sup>). Contrasts were conducted comparing the levels of each factor for any statistically significant factors.

Second, repeated measures linear regressions were conducted to examine the effect of body satisfaction ratings on waist estimates and on abdomen tactile estimates (arm estimates were collected as a control site for abdomen estimates in the event of significant effects related to the abdomen estimates). For these measures, Participant 6 was excluded<sup>6</sup>.

# Results

## Effects of Allocentric Viewing on Body Satisfaction and Body Size Estimates:

We found a main effect of the identity manipulation (F(2, 44) = 3.37, p = 0.04), such that the mirror and the head swap manipulations provided higher body satisfaction ratings than the regular mirror view (LS means contrast: mask versus mirror: F(1, 44) = 5.69, p = 0.02; head swap versus mirror: F(1, 44) = 2.97, p = 0.09). We did not find a main effect of viewing angle (F(2, 44) = 0.74, p = 0.49). An effect of identity was also found on visual estimates of waist size (F(2, 43) = 3.63, p = 0.04), but no effect of angle was found (F(2, 43.01) = 0.46, p = 0.63). No effects

<sup>&</sup>lt;sup>5</sup> Data from Participant 6 were re-coded because she interpreted the body satisfaction scale in terms of "extremely satisfied = appearing healthy" and "extremely dissatisfied = appearing unhealthy (thin)," in contrast to the other participants, who indicated rating higher satisfaction with their body when it appeared smaller or thinner. This participant had had recurrent episodes of anorexia nervosa and was concerned about her health. She expressed conflicting desires to be healthy and to be thin.

<sup>&</sup>lt;sup>6</sup> Data from this participant were excluded in these analyses because body size estimates were difficult to interpret in light of the way this participant interpreted the Body Satisfaction Rating scale.

of either identity or angle were found on tactile abdomen estimates (F(2, 43.01) = 0.44, p = 0.64; F(2, 43.01) = 1.09, p = 0.35; see Figure 5.2).



#### Effects of Body Satisfaction Ratings on Visual Waist Estimate and Tactile Estimates:

Body satisfaction significantly predicted visual waist estimates (b = -1.79; F(1, 45.58) = 14.7, p < 0.001) and also (marginally) tactile estimates for the abdomen (b = -0.28; F(1, 43.79) = 4.03, p = 0.051).

# Discussion

A mirror allows real-time visual feedback about the size and shape of the body, but typically engages self-related modes of processing. In the current study we asked whether visual feedback therapies could be modified to create allocentric body processing in individuals with past or present eating disorders (and current body dysphoria). We also asked whether withinsubject increases in body satisfaction would be associated with decreases in visual and tactile estimates of body size.

We tested the effect of two allocentric mirror-viewing strategies, identity manipulation and familiarity manipulation, on body satisfaction ratings and visual and tactile estimates of waist size. Allocentric viewing indeed affected body image ratings: we found that identity manipulation (mask and head swap) increased participants' ratings of body satisfaction. No effect of viewing angle (familiarity manipulation) was found. In addition, we found that withinsubject increases in body satisfaction (due in part to the allocentric viewing manipulations) were associated with decreases in estimates of both visual and tactile waist/abdomen size. This suggests that changes in visual processing of one's body rapidly alter both visual and somatosensory maps of the body, implying changes to both body image (representation of visual body form) and body schema (implicit representation of the size and position of the body).

Previous literature on body image distortion has focused on static measurements of body dissatisfaction and estimated size. Our results suggest that these measures are not static at all, and can be shifted strongly by visual feedback from an allocentric point of view. From a clinical standpoint, this is useful knowledge for the evaluation and treatment of patients with body image distortion. From a basic research standpoint, these results point to strong coupling between higher-level and lower-level representations of the body in the brain. Body image distortion appears to occur at both explicit and implicit levels in both the visual and tactile domains, and visual feedback appears capable of altering both higher-level body image (body satisfaction) and lower-level sensory representations (visual and tactile spatial estimates of body size). The effect of the identity manipulation suggests that egocentric visual processing pathways contribute strongly to body distortion at both the visual and somatosensory level. This finding is consistent with studies finding small beneficial effects of body viewing on body image satisfaction and sensations of fatness (e.g. Rushford & Ostermeyer 1997; Vocks et al., 2007). Indeed, in their study of visual body exposure, Rushford & Ostermeyer- without any discussion about their theoretical motivation- mention telling patients to "view the figure on the screen as someone she might see standing on a beach" in order to "strengthen objectivity," suggesting they also found allocentric strategies useful.

It is unknown whether the effects found in the current study are due to pathological processes related to body image distortion in eating disorders, or normal modes of processing egocentric and allocentric information about the body. Certainly, body representation is plastic and all manner of multisensory effects have been reported to affect it. Still, patients with eating disorders may have differences in their body representation and the plasticity of this

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representation. Individuals with AN show decreased rCBF in the right parietal lobe that is restored after recovery (Komatsu et al., 2010). There is also some evidence that for a decreased effect of vision on somatosensation in AN (e.g. Case et al., 2012, as presented in Chapter 3), and decreased connectivity in ventral visual areas but increased connectivity on somatosensory areas in resting state fMRI (Favaro et al., 2012). On the other hand, Eshkevari et al. (2012) found that patients with AN appear to have a more malleable body representation as evidenced by *increased* strength of the rubber hand illusion (RHI), a crossmodal illusion. Viewing the body has also been found to distort (increase) tactile size perception (Longo & Sadibolova 2013), so egocentric body-viewing may also distort tactile representations of the body.

The effect of somatosensation and visceral sensation on body image and body schema has been studied in less detail than the effect of visual feedback. Inaccurate interoceptive feedback may play a role in the distortion of visual body representation. Tsakiris et al. (2011) report that people with low interoceptive sensitivity experienced a stronger rubber hand illusion (RHI), and individuals with anorexia exhibit poor interoceptive sensitivity (e.g. Pollatos et al., 2008). This suggests that individuals with eating disorders may have more plasticity in their body representation- and might be more sensitive to exteroceptive feedback such as mirror therapy. Indeed, Ainley et al. (2012) found that healthy individuals with low baseline interoceptive sensitivity show significant improvement in interoceptive sensitivity while looking in a mirror. It is also interesting to consider that under local anesthesia, with somatosensory feedback from a body part removed, surgical patients often experience phantom enlargement of the anesthetized body part (e.g. Gandevia & Phegan, 1999). Thus it is possible that reduced interoceptive sensitivity in individuals with AN contributes to their experience of body size distortion, and that visual feedback, particularly less-distorted allocentric feedback, can anchor and correct somatosensory representation of the body. It is possible that a similar process occurs in eating disorders where the patient 1) receives impoverished and distorted interoceptive feedback, 2) associates this sensation of largeness with his or her visual body form, 3) begins to dislike the visual image of his or her body, and 4) begins to experience emotional and sensory distortion of visual feedback for egocentric visual feedback of his or her body. Thus visual, sensory, and emotional feedback come to be mutually distorted and mutually self-reinforcing.

#### **Limitations and Future Directions**

One limitation of the current study is the heterogeneity of the participant sample with regard to eating disorder status (how recently the participant met criteria for anorexia nervosa, and whether the participant additionally had a current or past diagnoses of bulimia nervosa) and current BMI. Another limitation is the fixed order of viewing exercises. This was done out of concern that effects from the allocentric views might affect subsequent ratings of normal body views. However, it is possible that participants' adaptation to their body in the mirror over the course of the session contributed to the effects obtained in the allocentric viewing conditions. We do not believe this was the case because a number of the participants also received several other experimental views after the mask and head swap, and these views often caused body satisfaction ratings to drop down again. These views were not included in the current analyses because they were administered inconsistently and only to some of the participants due to time limitations. Second, the personage of the mask- Hillary Clinton- presents a significant limitation to the study. Clinton is a well-known public figure who elicits positive affective reactions in many individuals and negative reactions in others. The full-head mask was also slightly bigger than participants' own heads, which could partially account for improvements in body image, as the larger head would make the participant's body appear smaller in proportion. These limitations of emotional response and head-to-body ration were less present in the head swap condition, however, which

achieved a similar magnitude of improvement in body satisfaction. Another potential confound to the results occurs in the familiarity (angle) manipulation: in the side and back views, the reflection of the body in the mirror is smaller and appears further away. Effects of familiarity (angle) were not found in the current study, however. Finally, the current study is limited by the small sample size, which may preclude detection of smaller effects of the various manipulations or correlations between them.

Future work should be conducted to determine what types of patients might benefit most from allocentric mirror viewing in terms of eating disorder diagnosis, current BMI, current level of body image distortion, current mirror-viewing habits, and other clinical and demographic factors. In addition, it will be important to determine how long body representation can be affected by mirror viewing and what duration and schedule of viewing creates the most enduring change in body representation.

### **Clinical Utility**

Even after successful treatment, many patients with eating disorders experience strong distortions in body image (Lautenbacher et al., 1997). Indeed, Freeman et al. (1985) report that in women recovered from bulimia, body image dissatisfaction at the end of treatment was the strongest predictor of relapse. Allocentric body viewing may have therapeutic value in the treatment of body image distortion and body dissatisfaction. Remarks made by participants in the follow-up interviews after the completion of the study session are of interest because some participants reported experiences not fully captured in the quantitative dependent measures. For example, one participant reported that her body satisfaction upon first viewing herself with a mask rose to about an 8 (of 10), but slowly dropped back down as she viewed herself longer in the mirror and she began to feel her identity attach back to the reflection. She attributed the rise in body satisfaction to a temporary sensation that she was looking at another woman, not herself,

and thought that woman had a "nice body". As her visual reflection re-captured her identity, distortion set back in. She rated the insight gleaned from this moment of allocentric viewing as highly valuable. This type of insight suggests strong therapeutic potential for allocentric mirror viewing.



А

В

С

**Figure 5.0: Familiarity manipulation.** Participants viewed their body for 35-second duration of time from the A) front, B) side in double-reflection, and C) back in back double-reflection.



A



В

**Figure 5.1: Identity manipulation.** Participants viewed their reflection first without a mask, then with a mask (A). Finally, they viewed their body in the mirror from the front, aligned with the head of the experimenter ("head swap"; B).



A



Figure 5.2: Effects of Familiarity and Identity manipulations. Effect of manipulations on (A) Body Satisfaction Ratings, (B) Visual Waist Estimates, and (C) Tactile Abdomen Estimates. Error bars show SEM.

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# CONCLUSION

The studies presented in this dissertation aim to uncover the role of implicit, sensory body representation in the construction of bodily identity and body image. The studies focus on two populations neglected by cognitive neuroscientists until relatively recently: presurgical female-to-male (FTM) transsexual individuals, who perceive the female sex of their body to be incongruous with their male gender identity, and patients with anorexia nervosa (AN), a psychological disorder involving severe body image distortion and caloric restriction. While these conditions are quite distinct, they share a core phenomenon of discrepancy between how the body is (body sex and body size) and how it feels it *ought* to be (desired body sex and body size). In anorexia nervosa body image distortion also occurs. AN patients are inaccurate in their estimates of their own size, and also desire a size that is unhealthy. In transsexuality the incongruity of body sex and body image is typically distressing to the individual but is largely resolved once hormonal and surgical procedures are successfully completed. The studies undertaken in this dissertation are not meant in any way to suggest that neural body representation in transsexual individuals is wrong or should be changed. Rather, anorexia and transsexuality are used as models in which to study how sensory information is processed from body parts that feel "wrong" or incongruous with identity, allowing us to learn about the relationship between sensory processing and feelings of bodily congruence. Hopefully, knowledge gleaned from research in this area can be applied to improve treatments for body image distortion and dysphoria in eating disorders.

The study described in Chapter 1 examines autonomic nervous system response to sensory input from an incongruous-feeling body part. We demonstrate that presurgical FTM individuals showed a heightened galvanic skin response to poking on the left breast relative to cissexual controls. This suggests that aversion to gender-incongruent body parts extends to the level of automatic sensory processing. FTM body dysphoria is not merely an abstract cognitiveemotional attitude towards the body; it has a rapid physiological correlate (increased skin conductance response) indicating an alarm response to incoming sensory input from the incongruous-feeling body part. This alarm signal may be caused by differences in neural representation of the chest in FTM individuals.

Indeed, writings by transgender individuals (e.g. Prosser 1998) and reports of phantom breasts and genitals in transsexual individuals (e.g. Ramachandran 2008) suggest that presurgical FTM individuals may have neural body maps corresponding to male anatomy. The study described in Chapter 2 investigates sensory representation of body parts that feel incongruous or congruous with gender in presurgical FTM individuals and cissexual female individuals. Specifically, we demonstrate differences in sensory evoked fields (SEFs) between FTM and CIS individuals in response to tapping of the left breast versus left hand. The breast SEFs show less increase over time in S2 and greater increase over time in FTM individuals than in CIS individuals, suggesting reduced integration of sensation and heightened emotional response from the breast in individuals who experience this body part as incongruent with their gender. This suggests that the body sex dysphoria experienced by transsexual individuals may be tied to differences in neural representation of the sexed body. These differences may arise early in development, before socialization and acculturation exert high-order influences on gender identity, or may reflect functional plasticity in the sensory system in response to long-standing abstract dissatisfaction with the sex of the body. Further research might be able to differentiate between these alternatives by testing individuals when they first begin to question their gender, and again when they are fully identified as transsexual, to see whether differences from CIS individuals in low-level body representation are present at similar or different magnitudes at these time-points.

Like transsexual individuals, people with anorexia experience clinically significant levels of body dysphoria. Unlike those with transsexuality, however, people with anorexia also experience significant body distortion: the perception that their body is much larger than it actually is. Relatively little is known about the neural mechanisms underlying this body image distortion. Recent studies have demonstrated significant distortion in implicit body representation in AN, including enlarged tactile and motor (body schema) representations of the body, as well as distorted visual estimates of body size (e.g. Keizer et al., 2011). Yet individuals with AN perceive others relatively normally (e.g. Sachdev et al., 2008), suggesting self-specific distortions in body size perception. This led us to ask whether people with AN are able to use available sensory feedback to update their perception of size: a deficit in visual and tactile integration could explain why veridical visual feedback, such as looking in a mirror, does not correct a distorted multisensory body representation.

In Chapter 3 we thus investigate the size-weight illusion (SWI), an illusion that arises when two objects of equal weight but different sizes are held, one in each hand. Typical individuals experience a strong and robust illusion that the smaller object feels much heavier than the larger object because of an expectation that weight scales with size. We found that individuals with AN exhibited a markedly reduced SWI relative to controls even though their ability to discriminate weight was unaffected. Because the SWI is strongly modulated by visual appearance, we believe our finding reflects decreased integration of visual, tactile, and proprioceptive information in anorexia. This finding may explain the fact that visual perception of the body in a mirror does little to correct an AN patient's distorted body image. Patients with AN may be less able to correct body image distortion because conflicting information between different sensory modalities is ignored or discarded. We speculate that methods to correct visuotactile-proprioceptive integration may help rehabilitate patients' judgments of size and weight regarding their own bodies. This finding is interesting in light of the increase in rubber hand illusion reported in AN patients (Eshkevari et al., 2012), which would suggested increased visuotactile-proprioceptive integration in patients. However, these tasks differ in many ways; integration may be enhanced when visual and somatosensory cues are aligned, for example, but

diminished more than in controls when the cues conflict, as in the SWI.

Chapter 4 discusses SEFs in response to tapping of a body part that feels dysphoric (abdomen) or neutral (hand) in individuals with anorexia, compared to healthy control participants. The SEFs show different patterns over time in S1 and the intraparietal sulcus in the right hemisphere between AN and CON individuals. These findings suggest that dysphoria related to the body in anorexia is reflected in differences in early somatosensory representation of the body– specifically, a heightened integration of the sensory stimulus in the mid or late part of the sensory response. This finding may also indicate increased general salience of, and attention to, sensory stimuli and increased identification of the body with self.

Across the magnetoencephalography studies described in Chapters 2 and 4, we observed differences in sensory body representation in transsexuality and in anorexia, with some general differences and some differences specific to the dysphoric-feeling body part. Transsexual FTM individuals generally exhibited lower activation of body representation areas in the later relative to earlier part of the 40-140ms time window than cissexual controls, while AN patients generally showed *greater* mid or late relative to earlier timecourse activation than healthy controls. This provides an interesting contrast between two types of body dysphoria: dysphoria for a body part that feels incongruent with gender, or dysphoria for a body part that feels too big. In both cases the body part that feels dysphoric activates the medial temporal lobe (presumably the amygdala) more than in controls, suggesting that while both types of dysphoria show an alarm or anxiety response, the neural mechanisms underlying each type of dysphoria are different. In FTM individuals the breast appears to integrate less than normal, and the contrast between underintegration and normal S1 response may reflect under-representation in parietal body representation areas and set off an alarm response, similar to in Xenomelia (e.g. McGeoch et al., 2011). In AN individuals, on the other hand, the heightened sensory response to the abdomen may reflect identification with the body part but clash with body templates that are of normal size or smaller than normal. An alternative explanation is that TR individuals have developed the ability over time to pay less attention to sensory feedback but body parts they dislike, and AN individuals to pay more attention. This begs the question of why they do this, however, and we believe the differences in SEF responses reflect early and automatic functioning of the extended body representation network in its current state, demonstrating differences in functional representation that underlie feelings of dysphoria.

In Chapter 5 we present preliminary research on the use of mirror visual feedback therapy for anorexia nervosa, and on the correlation between within-subject changes in body satisfaction and patients' visual and tactile estimates of their body size. We find that allocentric views of the body (specifically, a full head mask or head swap illusion) increase body satisfaction ratings, and that within-subject increases in body satisfaction ratings are associated with decreases in visual and tactile estimates of the size of the abdomen or waist. Given the difficulty correcting body image distortion, we believe that allocentric viewing strategies provide a novel potential therapeutic method for proving a patient with visual feedback about their body that is less distorted by neural pathways that process information about one's own body. In addition, we show that changes in body image have psychophysical correlates in sensory body perception in both the visual and tactile domains. This exploratory research suggests previously unrecognized level of coupling between higher-level body image, visual feedback, and tactile representation of the body, in the absence of any induction of illusion. Body image and sensory body representation should be viewed as intertwined systems, and this view may inform the treatment of body image distortion.

In conclusion, we demonstrate, in two distinct populations, low-level sensory and physiological correlates of higher-level (explicit) reports of dysphoria for particular body parts. Because both transsexuality and anorexia are rare, it is difficult to conduct studies of these individuals prior to onset of body dysphoria. Future work should attempt to do this in order to begin to tease apart the causal interactions between cognitive-emotional body image dissatisfaction and low-level distortions or differences in body representation. It may be that lowlevel differences precede conscious dissatisfaction with the body, or it may be that low-level differences follow changes in thought, emotion, and identity. Clearly, however, the two are coupled. Together these studies inform our understanding of the involvement of lower-level sensory processing and sensory integration in feelings of incongruity and dysphoria for body sex and body size, and of the coupling of sensory and cognitive processes in body representation at large.

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