

## **The perception of affective touch in Anorexia Nervosa**

Laura Crucianelli<sup>a</sup>, MSc, Valentina Cardi<sup>b</sup>, PhD, Janet Treasure<sup>b</sup>, PhD, MD, Prof, Paul M. Jenkinson<sup>a</sup>, PhD and Aikaterini Fotopoulou<sup>c\*</sup>, PhD

*<sup>a</sup>School of Life and Medical Sciences, University of Hertfordshire, UK*

*<sup>b</sup>Section of Eating Disorders, Institute of Psychiatry, King's College London, UK*

*<sup>c</sup>Division of Psychology and Language Sciences, University College London, UK*

\*Corresponding author:

Aikaterini (Katerina) Fotopoulou,

Research Department of Clinical, Educational and Health Psychology

University College London

1-9 Torrington Place

London WC1E 7HB, UK

Tel: (+44) 020 7679 3079

e-mail: [a.fotopoulou@ucl.ac.uk](mailto:a.fotopoulou@ucl.ac.uk)

## **Abstract**

Anorexia nervosa (AN) is a disorder characterized by restricted eating, fears of gaining weight, and body image distortions. The etiology remains unknown; however impairments in social cognition and reward circuits contribute to the onset and maintenance of the disorder. One possibility is that AN is associated with reduced perceived pleasantness during social interactions. We therefore examined the perception of interpersonal, ‘affective touch’ and its social modulation in AN. We measured the perceived pleasantness of light, dynamic stroking touches applied to the forearm of 25 AN patients and 30 healthy controls using C Tactile (CT) afferents-optimal (3cm/s) and non-optimal (18cm/s) velocities, while simultaneously displaying images of faces showing rejecting, neutral and accepting expressions. CT-optimal touch, but not CT non-optimal touch, elicited significantly lower pleasantness ratings in AN patients compared with healthy controls. Pleasantness ratings were modulated by facial expressions in both groups in a similar fashion; namely, presenting socially accepting faces increased the perception of touch pleasantness more than neutral and rejecting faces. Our findings suggest that individuals with AN have a disordered, CT-based affective touch system. This impairment may be linked to their weakened interoceptive perception and distorted body representation.

**AN** = anorexia nervosa; **HC** = healthy controls

**Key words:** body representation; CT system; interoception; interpersonal touch; facial expressions; social modulation

## 1. Introduction

Anorexia nervosa (AN) is a psychiatric disorder characterized by: (a) the persistent restriction of energy intake leading to significantly low body weight relatively to health norms, (b) fear of gaining weight and related behaviors, and (c) a disturbance in body weight or shape perception, including unawareness of such perceptual disturbances (DSM-V, 2013). In addition, patients with AN may show other deficits, such as hyperactivity (Kron et al., 1978), repetitive and stereotypic behaviors (Anderluh et al., 2003, Cassin and von Ranson, 2005), disturbances in mood (Blinder et al., 2006) as well as social cognition and attachment difficulties (see Zucker et al., 2014; Caglar-Nazali et al., 2014 for systematic reviews).

The etiology of AN remains unknown. One proposal is that decreased serotonin neurotransmission as a consequence of malnutrition is thought to play a role in the hyperactivity, depression and behavioral impulsivity observed in this population (Haleem, 2012; Kaye et al., 2009). Another line of research including animal models and human neuroimaging studies suggests that a dysfunctional dopamine-based reward system is associated with the disorder (Avena and Bocarsly, 2012; Kaye et al., 2013). It is unclear whether these abnormalities are the cause or the result of chronic dysfunctions in eating behavior; nevertheless, AN patients show low novelty seeking and seem to be more anhedonic than those with bulimia nervosa (Davis and Woodside, 2002) and other eating disorders (Tchanturia et al., 2012). Some researchers propose that restricting food intake and exercising have become aberrantly rewarding in AN patients, in a fashion similar to the pathological processes seen in addiction (Scheurink et al., 2010). Other theorists claim that AN is associated with a reduced experience of pleasure associated with food (food anhedonia) and a hyporesponsive striatal dopamine system (Zink and Weinberger, 2010). In the present paper, we focus mainly on the latter aspects of the disorder.

More generally, it has been proposed that impaired social cognition and interpersonal relating play a key role in the onset and maintenance of anorexia nervosa (Zucker et al., 2007; Castro et al., 2010; Arcelus et al., 2013). Individuals with AN are typically reserved, have limited social networks, and self-report poorer quality and quantity of relationships (Tchanturia et al., 2013; Tiller et al., 1997). Furthermore, experimental studies have shown that patients with AN have impairments in emotion recognition, as well as cognitive and affective ‘theory of mind’ (i.e. inferring other people’s mental states; see Zucker et al., 2013; Caglar-Nazali et al., 2014, for reviews). For example, people with AN may show attentional biases when processing social stimuli, paying more attention to angry, negative (Harrison et al., 2010), or ‘rejecting’ human faces (Cardi et al., 2012). Moreover, some of these attentional biases are correlated with early adverse social experiences (e.g. early separation from parents, unwanted sexual experiences) (Cardi et al., 2012).

Despite the above evidence and theories, few studies have attempted to understand the possible relationship between social cognition and reward abnormalities in AN. One possibility is that some of the social difficulties patients with AN show may be associated with the lack of pleasant feelings coming from social interactions; a disturbance termed social anhedonia (Tchanturia et al., 2012). To examine this further, we focused on the perception of interpersonal, ‘affective touch’ and its social modulation. Affective touch is associated with a distinct class of slow-conducting, unmyelinated tactile C (CT) afferents, present only in the hairy skin of mammals and responding specifically to gentle stroking delivered at slow speeds (between 1-10 cm/s) (Löken et al., 2009). Microneurography studies in humans have found that CT firing rates are correlated with subjective pleasantness ratings (Löken et al., 2009). Moreover, neuroimaging evidence suggests that CT afferents take a distinct ascending pathway from the periphery to the

posterior insular cortex (Morrison et al., 2011; Olausson et al., 2002). This pathway is thought to serve the convergence of interoceptive signals from the body, i.e. signals that monitor the homeostatic state of the organism (Craig, 2009). Further re-mappings of such signals in anterior cortical areas are thought to allow integration of such signals with other information about the body, as well as with other cognitive and social factors, ultimately serving body awareness and its modulation by dispositional and contextual factors (Craig, 2009; Critchley et al., 2004).

Given the aforementioned role of the anterior insula in bodily self-awareness, and the altered neural activity in this area in individuals with AN as shown by a functional neuroimaging study (Kerr et al., 2015), it has been argued that this population might suffer from a physiologically distorted sense of self (Pollatos et al., 2008; Kaye et al., 2009).

Interoceptive perception in individuals with AN has been associated with altered activity in the insular cortex (Strigo et al., 2013; Wagner et al., 2008; Vocks et al., 2011; Kerr et al., 2015). Indeed many of the symptoms observed in AN could be related to deficits in interoceptive perception, such as altered subjective responses to food (Bruch, 1962), pain and heart beat awareness (Raymond et al. 1999; Pollatos et al., 2008; Strigo et al., 2013). There is also a more general, increasing interest in somatosensory disturbances in AN, and their potential role in body image distortions (Zucker et al., 2013; Keizer et al., 2011). Keizer et al. (2014) reported that patients with AN do not differ from healthy controls in the amount of pleasantness they report from interpersonal, ‘neutral’ touch, delivered as part of a body perception task (Keizer et al., 2014). However, in order to specifically assess the perception of CT-based, ‘affective touch’ in patients with AN, the perceived pleasantness of gentle, dynamic touch applied at CT-optimal versus non-optimal speeds must be tested, as in the present study.

Given the aforementioned social difficulties in AN, studying the CT afferent system in AN is important, not only because affective touch is a distinct interoceptive modality, but also because the CT afferent system is considered specialized for detecting the velocities of interpersonal touch that may have social relevance (Olausson et al., 2008), and for promoting social bonding and affiliation between individuals (Morrison et al., 2010). Indeed, more recent neuroimaging studies (e.g. Gordon et al., 2011; Voos et al., 2013), have shown that in addition to the insular cortex, the processing of affective, CT-based touch involves several key nodes of a neural network previously implicated in social perception and social cognition (for reviews see Gallagher and Firth, 2003; Koster-Hale and Saxe, 2013). These regions involve the posterior superior temporal sulcus (pSTS), medial prefrontal cortex (mPFC), the orbitofrontal cortex (OFC) and the amygdala (Gordon et al., 2011; Voos et al., 2013). Thus, it would be of interest to investigate how this socio-affective modality can be influenced by both bottom-up factors (sensory properties of the tactile stimulation) and top-down factors (concomitant manipulations of social context) in individuals with AN.

Accordingly, in this study we aimed to examine 1) whether the perception of affective touch (as operationalized by responses to a pleasantness rating scale) is reduced in patients with AN compared to healthy controls, 2) whether this effect could be linked to the CT fibers system, and 3) whether the perception of tactile stimulation is differentially affected in AN and healthy controls by the concomitant presentation of emotional facial expressions. We predicted that the perception of touch pleasantness would be reduced in people with AN, given their general anhedonia. However, we expected this effect to be specific to the CT afferent system, in the sense that it would be driven by the perception of tactile stimulation at CT-optimal speeds. Furthermore, we predicted that simultaneously presenting socially accepting vs. neutral faces

would increase the perception of touch pleasantness, while rejecting vs. neutral faces should have the opposite results. Finally, we expected this effect to be stronger in patients with AN compared to controls, given the selective biases of the former towards rejecting faces (Cardi et al., 2012).

## **2. Methods**

### *2.1. Participants*

Twenty-five female participants with AN were recruited from clinics associated with the Maudsley NHS Trust in London over a one year period. All patients met the Diagnostic and Statistical Manual of Mental Disorders, 4<sup>th</sup> Edition (DSM-IV) criteria for AN, as assessed using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID). Thirty, gender and age matched healthy controls (HC) were also recruited from University College London. Exclusion criteria for both groups included being left handed, any skin condition (e.g. psoriasis, eczema, etc.) and any substance abuse (i.e. drug and alcohol). Exclusion criteria specific for the HC group included a known history of any other axis I clinical disorder, a body mass index (BMI) out of the normal range (18.5 – 25) and any indications on psychometric assessments of clinical depression, or anxiety disorders. A total of one AN and five HC participants were later excluded from the data analysis; one AN patient and one HC did not comply with the experimenter instructions, two HC had a body mass index below the normal range, and two HC showed a depression score outside the normal range as assessed using the Depression Anxiety Stress Scale (DASS, Lovibond and Lovibond, 1995; a 21-item, three-scale self-reported measure of depression, anxiety and stress. where higher scores are related to a higher level of depression, anxiety and stress).

### *2.2. Design and data analysis*

We used a 2 (Group: AN vs. HC) x 2 (Stroking Velocity: slow vs. fast) x 3 (Facial Expression: accepting vs. rejecting vs. neutral) mixed factorial design, with repeated measures on the latter two factors. The dependent variable was the perceived pleasantness of touch, measured using a pleasantness rating scale ranging from 0 (not at all pleasant) to 100 (extremely pleasant), presented visually, to which participants responded verbally by choosing a number between the two specified anchors.

Statistical analyses were conducted with SPSS version 21.0. The data were tested for normality by means of the Shapiro-Wilk test and found to be non-normal ( $p < .05$ ). Subsequent Log, Square Root and Reciprocal transformations did not correct for the normality violations, therefore appropriate non-parametric tests were used to analyze the data (described below). Bonferroni-corrected planned contrasts ( $\alpha = 0.025$ ) were used to follow up significant interactions between group and the two within-subject factors. Thus, to assess whether reduced pleasantness in AN relates specifically to impairment in the CT afferents system we compared between groups the responses to CT optimal speeds, and separately the non-optimal speeds. To assess whether affective touch perception is modulated by social feedback we contrasted the perception of accepting vs. neutral faces between groups, and the perception of rejecting vs. neutral faces between groups. Given the directional nature of these predictions we used one-tailed tests for all analyses.

We also controlled whether differences in somatic and psychological characteristics of our two samples could influence the perception of pleasantness. Therefore, we ran non-parametric correlational analysis to investigate possible association of pleasantness ratings with BMI, mood ratings (DASS 21) and duration of illness.

### *2.3. Stimuli and apparatus*

Participants sat at a table in front of a 15-inch laptop computer screen positioned ~60 cm from their eyes. The visual stimuli were 45 gray-scale photos (8cm x 13cm) of young female (age matched with our sample) faces displaying accepting/smiling (n=15), rejecting/critical (n=15) or neutral (n=15) expressions (Dandeneau and Baldwin, 2004; Cardi et al., 2012). Pre-testing conducted before the first use of the stimuli confirmed that the faces showing a smile were judged as more accepting than a neutral point on a 7-point scale. Using the same rating scale, participants judged the frowning faces as being significantly more rejecting (Dandeneau and Baldwin, 2004). Photos of age-matched females have been chosen based on evidence supporting the importance of peer influence in this clinical sample (Quiles Marcos et al., 2013; Keel and Forney, 2013). Stimuli were presented for 3 seconds on a black background in a random order using Microsoft PowerPoint 2010 (Microsoft Corporation). A blank (black) screen was displayed for 3 seconds between each face (i.e. inter-stimulus-interval = 3 seconds).

Simultaneous tactile stimulation of the left forearm (i.e. stroking) was administered during the 3 seconds when each face was presented, using a soft cosmetic make-up brush (Natural hair Blush Brush, N°7, The Boots Company) at two different velocities: one CT-optimal (3 cm/s) and one not CT-optimal (18 cm/s), for a total of 45 trials including 3 buffer trials. Each speed was paired with seven faces of each of the categories in random order. Three buffer trials were delivered in these velocities at random pairings for familiarization purposes. Previous research showed that stroking movements at 3 cm/s velocity are optimal for CT afferent activation, while touch faster than 10 cm/s (e.g. 18 cm/s) and slower touch (below 1 cm/s) are not related to CT activity (31). To avoid visual feedback of the tactile stimuli, participants were asked to place their left arm inside a white plastic box (25 x 40 x 25 cm), open on two, opposite sides to allow the experimenter to deliver the touch (Figure 1).

#### *2.4. Procedure*

Institutional ethical approval was obtained and all subjects gave written informed consent. The study was carried out in accordance with the provisions of the Helsinki Declaration of 1975, as revised in 2008.

Prior to the main experimental phase, participants were familiarized with the experimental procedure and the rating scale. Participants placed their left hand with the palm facing down on a table and two adjacent stroking areas, each measuring 9cm long  $\times$  4cm wide were identified and marked with a washable marker on the hairy skin of participants' left forearm (wrist crease to elbow, McGlone et al., 2012). Stimulation was alternated between these two areas to minimize habituation (Crucianelli et al., 2013), and because CT fibers are easily fatigued (Vallbo et al., 1999). Additionally, delivering the touch inside the delineated rectangular spaces allowed the experimenter to be constant not only in space, but also in force/pressure by controlling the lateral spreading of the brush bristles. Subsequently, participants were instructed to place their left arm inside the box and to watch the computer screen showing the pictures, while simultaneously receiving the tactile stimulation delivered at one of the two velocities (i.e. fast, slow) as described above. The experimenter was trained to deliver the touch at the exact speed by counting the number of strokes within the tactile stimulation window of 3 seconds (i.e. 1 stroke, 3-seconds-long for the 3 cm/s velocity and 6 strokes, each 0.5-seconds-long for the 18 cm/s velocity). The order of conditions was randomized across participants.

After each trial participants used the rating scale ranging from 0 (not at all pleasant) to 100 (extremely pleasant) to judge the tactile sensation.

### **3. Results**

### 3.1. Demographics and mood

Demographic and clinical measures are summarized in Table 1. As expected the BMI was significantly higher in the HC group compared to the AN group. In addition, the DASS-21 questionnaire indicated significantly greater depression, anxiety and stress in AN patients compared to HCs, in line with previous research (15). No significant differences in age were found.

**Table 1.** Summary of demographic and clinical measures.

<i>Demographic / Clinical measures</i>	<i>Anorexia Nervosa (n=20)<sup>a</sup></i>	<i>Healthy Controls (n=25)</i>	<i>Z</i>	<i>P</i>
Age	24 (12.75)	26 (7.25)	-0.32	0.75
BMI	14.38 (1.68)	21.03(3.04)	- 6.041	<0.001***
Years of illness	9.50(21.50)	NA		
Depression (DASS 21)	12.00 (10)	3.00 (5.25)***	-4.71	< 0.001***
Anxiety (DASS 21)	8.00 (7.75)	3.00 (4.50)***	-4.26	< 0.001***
Stress (DASS 21)	15.00 (6)	6.00 (6.50)***	-4.68	< 0.001***

*Values provided are medians and interquartile ranges (in parentheses) for both Anorexia Nervosa (AN) and Healthy Control (HC) groups.*

*\*\* p <.05 difference between AN and HC groups*

*\*\*\* p <.001 difference between AN and HC groups*

*<sup>a</sup>Demographic data were not available for four AN patients due to an administrative error*

### 3.2. Pleasantness ratings

#### 3.2.1. Main effects

A Mann-Whitney *U* Test revealed a main effect of Group on pleasantness ratings, with HCs rating touch as significantly more pleasant overall compared to patients with AN (see Table

1). A Wilcoxon signed rank test also showed a main effect of Stroking Velocity ( $Z = -4.30, p < 0.001$ ), with slow touch (median = 57.50, Interquartile Range, IQR = 26.22) producing significantly higher pleasantness ratings compared to fast touch (median = 44.73, IQR = 24.78). Finally, a Friedman's ANOVA revealed a main effect of Facial Expression ( $\chi^2(2) = 16.52, p < 0.001$ ; median accepting = 57.00, IQR = 15.38; median rejecting = 46.75, IQR = 19.69; median neutral = 50.00, IQR = 22.23). Bonferroni-corrected post hoc analyses ( $\alpha = 0.017$ ) revealed that touch was rated as significantly more pleasant when it was delivered simultaneously with accepting faces compared to neutral faces ( $Z = -3.32, p = 0.001$ ) and rejecting faces ( $Z = -4.65, p < 0.001$ ). No significant differences were found between rejecting and neutral faces ( $Z = -2.08, p = 0.037$ ).

### 3.2.2. *Two-ways effect*

We analyzed the interaction between Group and Stroking Velocity by calculating the difference between fast and slow stroking in each group separately, and comparing these differential scores between groups using a Mann-Whitney *U* Test. This analysis revealed a significant interaction ( $Z = -1.78, p = 0.038$ ). Subsequent Bonferroni-corrected planned contrasts ( $\alpha = 0.025$ ; see section 2.2. above) using Mann-Whitney *U* tests showed a significant difference between the groups in the slow ( $Z = -1.99, p = 0.023$ ; median AN = 50.33, IQR = 37.40; median HC = 59.57, IQR = 59.57) but not the fast condition ( $Z = -1.03, p = 0.16$ ; median AN = 35.20, IQR = 29.78; median HC = 47.00, IQR = 16.32; see Table 2).

The interaction between Group and Facial Expression, Velocity and facial Expressions, and Group, Stroking Velocity and Facial Expressions were similarly analysed by calculating and comparing relevant difference scores, revealing no additional, significant interactions (all  $ps > 0.10$ ).

**Table 2.** Summary of experimental measures. Ratings of pleasantness of slow and fast touch reported during vision of Accepting, Neutral and Rejecting facial expressions. The Total rating refers to the rating of pleasantness regardless of facial expressions and it has been obtained by averaging the pleasantness scores obtained during the Accepting, Neutral and Rejecting conditions.

Velocity of touch	Facial Expression	Group		Z	p
		Anorexia Nervosa	Healthy Controls		
Slow touch	Accepting	51.59 (22.74)	63.09 (11.05)	-1.49	0.14
	Neutral	46.68 (21.86)	59.95 (13.16)	-1.93	0.053
	Rejecting	44.51 (21.26)	57.88 (17.27)	-2.29	0.021
	Total	47.62(21.45)	60.31(12.85)	-1.99	0.023*
Fast touch	Accepting	43.98 (19.53)	47.28 (16.89)	-0.88	0.38
	Neutral	39.17 (18.93)	44.78 (17.06)	-1.15	0.26
	Rejecting	36.85 (20.94)	43.08 (17.75)	-1.20	0.23
	Total	40.00(19.12)	45.05(16.91)	-1.03	0.16

For illustration purposes only, values provided are means and standard deviations for both anorexia nervosa (AN) and healthy controls (HC) groups. The analyses were conducted using non-parametric tests; medians and interquartile ranges of significant analysis are reported in subsection 3.2.2.

\* Significant difference between AN and HC groups, based on Bonferroni corrected analysis.

### 3.2.3. Correlations

Spearman's correlations were run to investigate whether the aforementioned experimental effects on pleasantness ratings were associated with the groups' ratings on mood questionnaires (DASS 21), BMI, and duration of illness. Neither the total DASS score nor the depression, anxiety and stress subscales correlated with (i) pleasantness scores in each group, nor (ii) the difference between slow and fast touch in each group (all  $r$  between -0.34 and -0.08; all  $p$  between 0.14 and 0.71). No correlations were found between the BMI and the pleasantness scores in each group, nor the difference between slow and fast touch in each group (all  $r$  between -0.32 and 0.21; all  $p$  between 0.13 and 0.36). Finally, no relationship was found between the duration of illness (in subjects with AN) and pleasantness scores during slow touch, nor the difference between slow and fast touch (all  $r$  between -0.27 and -0.06; all  $p$  between 0.28 and 0.81).

#### 4. Discussion

The aim of the present study was to investigate (1) whether the perception of affective touch would be reduced in AN compared to healthy controls; (2) whether the bodily pleasure reduction would relate specifically to the CT-afferent system, and (3) whether these effects would be modulated by social stimuli differentially between the two groups. The results confirmed our first prediction, showing that individuals with AN perceived affective touch as less pleasant compared to healthy controls. Furthermore, this difference between groups was specific to CT-optimal (i.e. slow) stroking velocities; although patients with AN rated CT-optimal touch as more pleasant than non-CT optimal touch, there was no significant difference between groups when touch was delivered at a non-CT optimal speed (i.e. a fast velocity). These findings confirm our second prediction, suggesting that the reduced pleasantness of interpersonal touch may at least in part relate to a dysfunctional CT afferent system. However, contrary to our third prediction, the perception of affective touch was not differently affected by social stimuli in healthy controls and AN patients. The simultaneous display of accepting faces enhanced the perceived pleasantness of touch, irrespective of group, while there were no statistically significant differences between rejecting and neutral faces.

It has long been established that individuals with AN show reduced subjective perception of pleasure (anhedonia) and several interoceptive deficits, possibly related to abnormalities in various dopamine-based brain systems (see Kaye et al., 2013, for a recent review). Our findings suggest that patients with AN show anhedonia also in the perception of tactile stimuli, replicating previous findings (Keizer et al., 2014). However, our study is the first to demonstrate that this reduction in tactile pleasure in individuals with AN could relate, at least in part, to a dysfunctional CT afferent system. Moreover, this ‘bottom-up’ explanation of the observed tactile

anhedonia is supported by the secondary finding that ‘top-down’ socio-affective modulation of tactile stimuli (i.e. synchronous viewing of human faces) did not seem to affect the perception of tactile pleasure differently between the groups. This suggests that tactile perception in people with AN can be positively influenced by top-down, cognitive mechanisms of social feedback, which do not differ from those of healthy controls. Lastly, ratings of tactile pleasantness did not correlate with depressive symptoms in either group, providing further support for a potential abnormality that is specific to CT-based, tactile perception rather than generally related to the observed anhedonia.

A possible alternative explanation for our finding might be that the observed reduction in pleasantness perception reflects an attempt to control (i.e. reduce) anxiogenic experiences. Research in AN has shown that there is a high prevalence of anxiety, and increased activation of cognitive control as an attempt to counteract the reduced limbic function (i.e. more strategic choices can compensate for the impaired ability to perceive interoceptive information; Connan et al., 2003). Thus, the reduced bodily pleasantness that we observed could be an attempt to cognitively control for an “unwanted” arousing experience (i.e. pleasant interpersonal touch). However, this explanation would need to be investigated in further studies, as we did not find any correlation between anxiety and pleasantness ratings in individuals with AN or healthy controls in the present study.

The finding that individuals with AN have a disordered, CT-based affective touch system may have implications for their distorted body representation. Affective touch has been shown to contribute uniquely to the multisensory integration processes that underlie the subjective sense of body ownership (Crucianelli et al., 2013; van Stralen et al., 2014; see also Lloyd et al., 2013 for top-down contributions to such effects). Moreover patients with AN have been found to be more

susceptible to the influence of visual, exteroceptive signals about the body rather than proprioceptive information (Eshkevari et al., 2012; Keizer et al., 2014). Individuals with strong interoceptive signals seem to possess a body representation that is more resilient to visual changes (Tsakiris et al., 2011) and vice versa (Mosley et al., 2008, but see Rohde et al., 2013). Our findings raise the possibility that an enhanced susceptibility to visual signals about the body, and related body distortions in AN, may in part be linked to their weakened interoceptive perception. However, these conclusions remain tentative, serving as hypotheses for future studies.

Furthermore, given the social aspects of CT-based touch, our findings suggest future avenues for the investigation of a potential link between tactile anhedonia, social anhedonia, and other social disturbances observed in individuals with AN. As our study focused on adults with AN, we cannot know the developmental time course of the CT-afferent system in this population, nor can we know whether this sensory disturbance is secondary to other pathological factors in AN, such as a primary disturbance in appetite and motivational systems. Recent studies have formulated similar hypotheses for the role of an abnormal CT afferent system in autistic spectrum disorders, in both healthy population (Voos et al., 2013) and in individuals with autistic spectrum disorders (Casio et al., 2008; 2012). Thus, our results justify further investigations of the developmental time course of disturbances in the CT-afferent system, and its implication for social relating and cognition in individuals with AN.

The unique role played by the CT afferent system in social interaction is supported and further specified in recent studies. Croy and colleagues (2015) showed that slow, CT optimal touch seems to be the spontaneously preferred one in human social interaction, specifically when stroking partners and babies, compared to the situation in which participants were asked to stroke

a rubber arm (Croy et al., 2015). Furthermore, the activation of the CT afferent system seems to be maximized at human skin-like temperature, rather than at cooler or warmer temperatures (Ackerley et al., 2014). Additionally, the affective but also motivational role of the CTs system is supported by a recent study showing that participants constantly rated others' skin as being softer than their own, giving rise to the so-called social softness illusion (Gentsh, Panagiotopolou and Fotopoulou, 2015). Taken together this evidence is in line with our findings. However in our study the touch was always delivered by a stranger/experimenter and the social modulation has been investigated by mean of pictures showing different facial expression (offline social interaction). Therefore, we suggest that the results of our study could be extended and further clarified by investigating affective touch and the potential modulation of facial expressions in an experimental setting involving participants' loved ones and online social interaction (see Krahé et al., 2013; Krahé et al., 2015 for a similar approach in the domain of pain).

#### *4.1. Limitations and future directions*

Future studies need to replicate the present findings, ideally with a larger sample of individuals, including both males and females, different types of eating disorders, weight-restored participants, medicated and non-medicated individuals, and possibly also testing tactile perception on body parts that do not contain CT-afferents, such as the glabrous skin of the palm (Olausson et al., 2002). In addition, neural and physiological responses to affective versus neutral touch could provide additional specificity regarding the involvement of the CT-afferent system in the observed tactile anhedonia. It is possible that the social modulation task used in this study had a limited effect in AN because of their more general social cognition difficulties and their specific face recognition and attentional biases (see section 1). However, we feel this interpretation is unlikely, given the fact that AN patients were influenced by the current social

stimuli in the same way as healthy controls, and also contrary to their own attentional biases in previous studies (Cardi et al., 2012). However, future studies could control for gaze and attention on such tasks, and social cognition difficulties could be tested in the same sample to determine the precise relation between the CT afferent system and social cognition.

Furthermore, future studies could explore other facets of rewarding tactile perception, such as its anticipation and desirability, which were not explored in the current study. In addition, given that the majority of our sample were outpatients at the time of the research, we do not have reliable, nor comprehensive information on medication that may have affected their symptoms, and particularly reward circuits. Only sixteen patients self-reported being on medication and only a small proportion of those were able to specify the type of medication. However, these included Selective Serotonin Reuptake Inhibitors (SSRIs) that have been shown to reduce the processing of both rewarding and aversive stimuli (e.g. McCabe et al., 2010). Future studies should therefore examine the effect of SSRIs and other medications on affective touch perception, although our results were selective in the sense that positive social stimuli (i.e. accepting\smiling faces) had a comparable ‘top-down’ effect of increasing the perceived pleasantness of the touch in healthy controls and anorexia nervosa participants, and tactile pleasantness ratings did not correlate with other psychometric measures of mood. Lastly, it would be of interest to test the role of affective touch in multisensory integration paradigms targeting the formation of body representations in AN, in both developmental and cross-section studies.

In conclusion, our findings suggest a disturbance of the CT-afferent system in AN, and open novel avenues for integrative research on some of the core facets of AN, such as reward processing, somatosensory perception and social cognition.

**Conflict of interest**

None.

**Acknowledgments**

The work was supported by: a 'European Research Council Starting Investigator Award' [ERC-2012-STG GA313755] (to AK); a Neuropsychanalysis Foundation grant (to PMJ) and a University of Hertfordshire studentship (to LC). We thank Giulia Botteon, Daniela D'Imperio and Charlotte Rhind for their assistance with data collection. The authors acknowledge S. Dandeneau for the experimental materials used in our social manipulation, namely the rejecting, neutral and accepting faces.

**Author contributions**

L. Crucianelli, A. Fotopoulou and P. M. Jenkinson contributed to the concept and design of the study. Testing and data collection were performed by L. Crucianelli and V. Cardi. L. Crucianelli performed the data analysis and interpretation under the supervision of A. Fotopoulou and P. M. Jenkinson. L. Crucianelli drafted the manuscript, with input from Drs. Fotopoulou and Jenkinson. Professor Treasure and Dr. Cardi provided critical comments. All authors approved the final version of the manuscript for submission.

## References

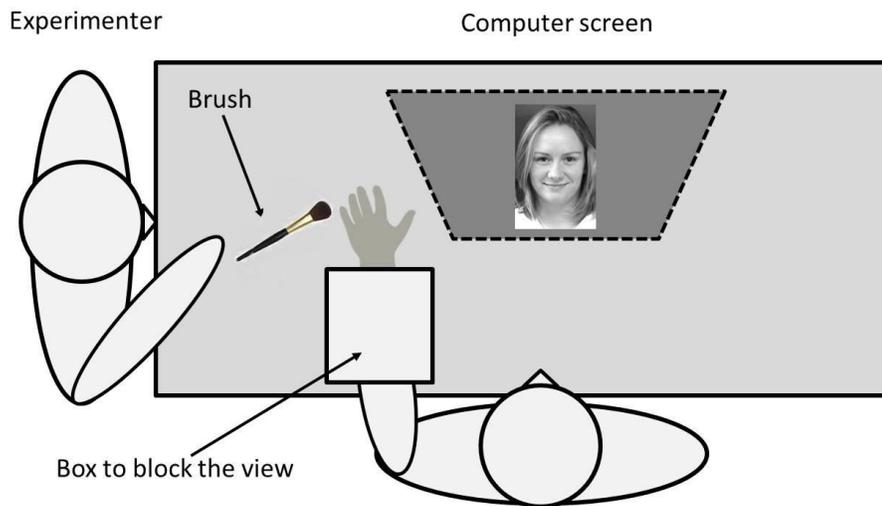
- Ackerley, R., Backlund Wasling, H., Liljencrantz, J., Olausson, H., Johnson, R. D., Wessberg, J., 2014. Human C-Tactile Afferents Are Tuned to the Temperature of a Skin-Strokeing Caress. *J. Neurosci.* 34(8), 2879-2883. doi: 10.1523/JNEUROSCI.2847-13.2014
- American Psychiatric Association, 2013. *Diagnostic and Statistical Manual of Mental Disorders*, 5<sup>th</sup> ed., Washington, DC: American Psychiatric Press.
- Anderluh, M.B., Tchanturia, K., Rabe-Hesketh, S., Treasure, J., 2003. Childhood obsessive-compulsive personality traits in adult women with eating disorders: Defining a broader eating disorder phenotype. *Am. J. Psych.* 160, 242–247. <http://dx.doi.org/10.1176/appi.ajp.160.2.242>
- Arcelus, J., Haslam, M., Farrow, C., Meyer, C., 2013. The role of interpersonal functioning in the maintenance of eating psychopathology: A systematic review and testable model. *Clin. Psychol. Rev.* 33, 156–167. <http://dx.doi:10.1016/j.cpr.2012.10.009>
- Avena, N.M., Bocarsly, M.E., 2012. Dysregulation of brain reward systems in eating disorders: Neurochemical information from animal models of binge eating, bulimia nervosa, and anorexia nervosa. *Neuropharmacology.* 63, 87-96. <http://dx.doi:10.1016/j.neuropharm.2011.11.010>
- Blinder, B.J., Cumella, E.J., Sanathara, V.A., 2006. Psychiatric comorbidities of female inpatients with eating disorders. *Psychosom. Med.* 68, 454–462. <http://dx.doi:10.1097/01.psy.0000221254.77675.f5>
- Bruch, H., 1962. Perceptual and conceptual disturbances in anorexia nervosa. *Psychosom. Med.* 24, 187–194.
- Caglar-Nazali, H.P., Corfield, F., Cardi, V., Ambwani, S., Leppanen, J., Olabintan, O., Deriziotis, S., Hadjimichalis, A., Scognamiglio, P., Eshkevari, E., Micali, N., Treasure, J., 2014. A systematic review and meta-analysis of “Systems for Social Processes” in eating disorders. *Neurosci. Biobehav. Rev.* 42, 55–92. <http://dx.doi:10.1016/j.neubiorev.2013.12.002>
- Cardi, V., di Matteo, R., Corfield, F., Treasure, J., 2012. Social reward and rejection sensitivity in eating disorders: An investigation of attentional bias and early experiences. *World J. Biol. Psychiatry.* 1–12. doi: 10.3109/15622975.2012.665479
- Cascio, C., McGlone, F., Folger, S., Tannan, V., Baranek, G., Pelphrey, K., Essick, G., 2008. Tactile perception in adults with autism: A multidimensional psychophysical study. *J. Autism Dev. Disord.* 38, 127–137. <http://dx.doi:10.1007/s10803-007-0370-8>
- Cascio, C.J., Moana-Filho, J., Guest, S., Nebel, M.B., Weisner, J., Baranek, G.T., Essick, G.K., 2012. Perceptual and Neural Response to Affective Tactile Texture Stimulation in Adults with Autism Spectrum Disorders. *Autism Res.* 5, 231–244. <http://dx.doi:10.1002/aur.1224>
- Cassin, S.E., von Ranson, K.M., 2005. Personality and eating disorders: a decade in review. *Clin. Psychol. Rev.* 25, 895-916. <http://dx.doi:10.1016/j.cpr.2005.04.012>

- Castro, L., Davies, H., Hale, L., Surguladze, S., Tchanturia, K., 2010. Facial affect recognition in anorexia nervosa: is obsessiveness a missing piece of the puzzle? *Aust. N. Z. J. Psychiatry.* 44, 1118-1125. <http://dx.doi: 10.3109/00048674.2010.524625>
- Connan, F., Campbell, I., Katzman, M., Lightman, S., Treasure, J.A., 2003. Neurodevelopmental model for anorexia nervosa. *Physiol. Behav.* 79, 13–24. doi:10.1016/S0031-9384(03)00101-X
- Craig, A.D., 2009. How do you feel-now? The anterior insula and human awareness. *Nat. Rev. Neurosci.* 10, 59-70. <http://dx.doi: 10.1038/nrn2555>
- Critchley, H.D., Wiens, S., Rotshtein, P., Öhman, A., Dolan, R.D., 2004. Neural systems supporting interoceptive awareness. *Nat. Neurosci.* 7, 189-195. doi:10.1038/nrn1176
- Croy, I., Luong, A., Tricoli, C., Hofmann, E., Olausson, H., Sailer, U., 2015. Interpersonal stroking touch is targeted to C tactile afferent activation. *Behav. Brain Res.* 297, 37-40. doi:10.1016/j.bbr.2015.09.038
- Crucianelli, L., Metcalf, N.K., Fotopoulou, A., Jenkinson, P.M., 2013. Bodily pleasure matters: velocity of touch modulates body ownership during the rubber hand illusion. *Front. Psychol.* 4 (703). <http://dx.doi:10.3389/fpsyg.2013.00703>
- Davis, C., Woodside, D.B., 2002. Sensitivity to the Rewarding Effects of Food and Exercise in the Eating Disorders. *Compr. Psychiatry.* 43, 189-194. <http://dx.doi:10.1053/comp.2002.32356>
- Dandeneau, S.P., Baldwin, M.W., 2004. The inhibition of socially rejecting information among people with high versus low self-esteem: The role of attentional bias and the effects of bias reduction training. *J. Soc. Clin. Psychol.* 23, 584 – 602. <http://dx.doi: 10.1521/jscp.23.4.584.40306>
- Eshkevari, E., Rieger, E., Longo, M., Haggard, P., Treasure, J., 2012. Increased plasticity of the bodily self in eating disorders. *Psychol. Med.* 42, 819–828. <http://dx.doi.org/10.1017/S0033291711002091>
- Gallagher, H.L., Firth, C.D., 2003. Functional imaging of ‘theory of mind’. *Trends Cogn. Sci.* 7 (2). [http://dx.doi:10.1016/S1364-6613\(02\)00025-6](http://dx.doi:10.1016/S1364-6613(02)00025-6)
- Gentsh, A., Panagiotopolou, E., Fotopoulou, A., 2015. Active Interpersonal Touch Gives Rise to the Social Softness Illusion. *Curr. Bio.* 25(18), 2392-2397. doi:10.1016/j.cub.2015.07.049
- Gordon, I., Martin, C., Feldman, R., Leckman, J.F., 2011. Oxytocin and social motivation. *Develop. Cogn. Neurosci.* 1, 471–493. <http://dx.doi:10.1016/j.dcn.2011.07.007>
- Haleem, D.J., 2012. Serotonin neurotransmission in anorexia nervosa. *Behav. Pharmacol.* 23 (5), 478-495. doi: 10.1097/FBP.0b013e328357440d
- Harrison, A., Tchanturia, K., Treasure, J., 2010. Attentional bias, emotion recognition, and emotion regulation in anorexia: state or trait? *Biol. Psychiatry.* 68, 755 – 761. <http://dx.doi:10.1016/j.biopsych.2010.04.037>
- Kaye, W.H., Fudge, J.L., Paulus, M., 2009. New insights into symptoms and neurocircuit function of anorexia nervosa. *Nat. Rev. Neurosci.* 10, 573–584. <http://dx.doi:10.1038/nrn2682>

- Kaye, W.H., Wierenga, C.E., Bailer, U.F., Simmons, A.N., Bischoff-Grethe, A., 2013. Nothing tastes as good as skinny feels: The neurobiology of anorexia nervosa. *Trends Neurosci.* 36, 110–120. <http://dx.doi:10.1016/j.tins.2013.01.003>
- Keel, P. K., Forney, K. J., 2013. Psychosocial risk factors for eating disorders. *Int. J. Eat. Disord.* 46, 433–439. doi: 10.1002/eat.22094
- Keizer, A., Smeets, M.A.M., Dijkerman, H.C., van den Hout, M., Klugkist, I., van Elburg, A., Postma, A., 2011. Tactile body image disturbance in anorexia nervosa. *Psychiatry Res.* 190, 115–120. <http://dx.doi:10.1016/j.psychres.2011.04.031>
- Keizer, A., Smeets, M.A.M., Postma, A., van Elburg, A., Dijkerman, H.C., 2014. Does the experience of ownership over a rubber hand change body size perception in anorexia nervosa patients? *Neuropsychologia.* 62, 26–37. <http://dx.doi:10.1016/j.neuropsychologia.2014.07.003>
- Kerr, K.L., Moseman, S.E., Avery, J.A., Bodurka, J., Zucker, N.L. Simmons, W.K., 2015. Altered insula activity during visceral interoception in weight-restored patients with Anorexia Nervosa. *Neuropsychopharmacology* (2015). doi:10.1038/npp.2015.174
- Koster-Hale, J., Saxe, R., 2013. Theory of Mind: A Neural Prediction Problem. *Neuron.* 79, 836–848. <http://dx.doi:10.1016/j.neuron.2013.08.020>
- Krahé, C., Springer, A., Weinman, J.A., Fotopoulou, A., 2013. The social modulation of pain: others as predictive signals of salience – a systematic review. *Front Hum Neurosci.* 7 (386). doi: 10.3389/fnhum.2013.00386
- Krahé, C., Paloyelis, Y., Condon, H., Jenkinson, P. M., Williams, S. C. R., Fotopoulou, A., 2015. Attachment style moderates partner presence effects on pain: A laser-evoked potentials study. *Soc. Cogn. Affect. Neurosci.* 10, 1030-1037. doi: 10.1093/scan/nsu156
- Kron, L., Katz, J.L., Gorzynski, G., Weiner, H., 1978. Hyperactivity in anorexia nervosa. *Compr. Psychiatry.* 19, 433-440. [http://dx.doi:10.1016/0010-440X\(78\)90072-X](http://dx.doi:10.1016/0010-440X(78)90072-X)
- Lloyd, D.M., Gillis, V., Lewis, E., Farrell, M.J., Morrison, I., 2013. Pleasant touch moderates the subjective but not objective aspects of body perception. *Front. Behav. Neurosci.* 7, 207. <http://dx.doi:10.3389/fnbeh.2013.00207>
- Löken, L.S., Wessberg, J., Morrison, I., McGlone, F., Olausson, H., 2009. Coding of pleasant touch by unmyelinated afferents in human. *Nat. Neurosci.* 12, 547-548. <http://dx.doi:10.1038/nn.2312>
- Lovibond, P.F., Lovibond, S.H., 1995. The structure of negative emotional states: Comparison of the depression anxiety stress scales (DASS) with the Beck Depression and Anxiety Inventories. *Behav. Res. Ther.* 33, 335–343. [http://dx.doi:10.1016/0005-7967\(94\)00075-U](http://dx.doi:10.1016/0005-7967(94)00075-U)
- McCabe, C., Mishor, Z., Cowen, P.J., Harmer, C.J., 2010. Diminished neural processing of aversive and rewarding stimuli during selective serotonin reuptake inhibitor treatment. *Biol. Psych.* 67:439-445. doi:10.1016/j.biopsych.2009.11.001
- McGlone, F., Olausson, H., Boyle, J.A., Jones-Gotman, M., Dancer, C., Guest, S., Essick, G., 2012. Touching and feeling: Differences in pleasant touch processing between glabrous

- and hairy skin in humans. *Eur. J. Neurosci.* 35, 1782-1788. <http://dx.doi:10.1111/j.1460-9568.2012.08092.x>
- Morrison, I., Löken, L., Olausson, H., 2010. The skin as a social organ. *Exp. Brain Res.* 204, 305–314. <http://dx.doi:10.1007/s00221-009-2007-y>
- Morrison, I., Björnsdotter, M., Olausson, H., 2011. Vicarious responses to social touch in posterior insular cortex are tuned to pleasant caressing speeds. *J. Neurosci.* 31, 9554-9562. <http://dx.doi:10.1523/JNEUROSCI.0397-11.2011>
- Moseley, G.L., Olthof, N., Venema, A., Don, S., Wijers, M., Gallace, A., Spence, C., 2008. Psychologically induced cooling of a specific body part caused by the illusory ownership of an artificial counterpart. *Proc. Natl. Acad. Sci. U S A.* 105, 13169–13173. <http://dx.doi:10.1073/pnas.0803768105>
- Olausson, H., Lamarre, Y., Backlund, H., Morin, C., Wallin, B.G., Starck, G., Ekholm, S., Strigo, I., Worsley, K., Vallbo, Å.B., Bushnell, M.C., 2002. Unmyelinated tactile afferents signal touch and project to insular cortex. *Nat. Neurosci.* 5, 900-904. <http://dx.doi:10.1038/nn896>
- Olausson, H.W., Cole, J., Vallbo, Å., McGlone, F., Elam, M., Krämer, H.H., Rylander, K., Wessberg, J., Bushnell, M.C., 2008. Unmyelinated tactile afferents have opposite effects on insular and somatosensory cortical processing. *Neurosci. Lett.* 436, 128–132. <http://dx.doi:10.1016/j.neulet.2008.03.015>
- Pollatos, O., Kurz, A.L., Albrecht, J., Schreder, T., Kleemann, A.M., Schöpf, V., Kopietz, R., Wiesmann, M., Schandry, R., 2008. Reduced perception of bodily signals in anorexia nervosa. *Eat. Behav.* 9, 381–388. <http://dx.doi:10.1016/j.eatbeh.2008.02.001>
- Quiles Marcos, Y., Quiles Sebastián, M.J., Pamies Aubalat, L., Botella Ausina, J., Treasure, J., 2013. Peer and family influence in eating disorders: a meta-analysis. *Eur. Psychiatry* 28(4), 199–206. [doi:10.1016/j.eurpsy.2012.03.005](http://dx.doi:10.1016/j.eurpsy.2012.03.005)
- Raymond, N.C., Faris, P.L., Thuras, P.D., Eiken, B., Howard, L., Hofbauer, R.D., Eckert, E.D., 1999. Elevated pain threshold in anorexia nervosa subjects. *Biol. Psychiatry.* 45, 1389–1392. [http://dx.doi:10.1016/S0006-3223\(98\)00177-2](http://dx.doi:10.1016/S0006-3223(98)00177-2)
- Rohde, M., Wold, A., Karnath, H.-O., Ernst, M.O., 2013. Human Touch: Skin Temperature during the Rubber Hand Illusion in Manual and Automated Stroking Procedures. *PLoS ONE.* 8 (11). DOI: 10.1371/journal.pone.0080688
- Scheurink, J.W., Boersma, G.J., Nergårdh, R., Södersten, P., 2010. Neurobiology of hyperactivity and reward: Agreeable restlessness in Anorexia Nervosa. *Physiol. Behav.* 100, 490–495. <http://dx.doi:10.1016/j.physbeh.2010.03.016>
- Strigo, I.A., Matthews, S.C., Simmons, A.N., Oberndorfer, T., Klabunde, M., Reinhardt, L.E., Kaye, W.H., 2013. Altered insula activation during pain anticipation in individuals recovered from anorexia nervosa: Evidence of interoceptive dysregulation. *Int. J. Eat. Disord.* 46, 23–33. <http://dx.doi:10.1002/eat.22045>

- Tchanturia, K., Davies, H., Harrison, A., Fox, J.R.E., Treasure, J., Schmidt, U., 2012. Altered social hedonic processing in eating disorders. *Int. J. Eat. Disord.* 45, 962–969. <http://dx.doi:10.1002/eat.22032>
- Tchanturia, K., Smith, E., Weineck, F., Fidanboylu, E., Kern, N., Treasure, J., Baron Cohen, S., 2013. Exploring autistic traits in anorexia: a clinical study. *Mol. Autism.* 4 (44). doi: 10.1186/2040-2392-4-44
- Tiller, J. M., Sloane, G., Schmidt, U., Troop, N., Power, M., Treasure, J. L., 1997. Social support in patients with anorexia nervosa and bulimia nervosa. *Int. J. Eat. Disord.* 21, 31–38. [http://dx.doi:10.1002/\(SICI\)1098-108X\(199701\)21:1<31::AID-EAT4>3.0.CO;2-4](http://dx.doi:10.1002/(SICI)1098-108X(199701)21:1<31::AID-EAT4>3.0.CO;2-4)
- Tsakiris, M., Tajadura-Jiménez, A., Costantini, M., 2011. Just a heartbeat away from one's body: interoceptive sensitivity predicts malleability of body-representations. *Proceedings Biological Sciences / The Royal Society.* 278, 2470–2476. <http://dx.doi:10.1111/j.1469-8986.2012.01468.x>
- Vallbo, Å.B., Olausson, H., Wessberg, J., 1999. Unmyelinated afferents constitute a second system coding tactile stimuli of the human hairy skin. *J. Neurophysiol.* 81, 2753-2763.
- Van Stralen, H.E., van Zandvoort, M.J.E., Hoppenbrouwers, S.S., Vissers, L.M.G., Kappelle, L.J., Dijkerman, H.C., 2014. Affective touch modulates the rubber hand illusion. *Cognition.* 131, 147–158. <http://dx.doi:10.1016/j.cognition.2013.11.020>
- Vocks, S., Herpertz, S., Rosenberger, C., Senf, W., Gizewski, E.R., 2011. Effects of gustatory stimulation on brain activity during hunger and satiety in females with restricting-type anorexia nervosa: An fMRI study. *J. Psychiatr. Res.* 45, 395–403. <http://dx.doi:10.1016/j.jpsychires.2010.07.012>
- Voos, A.C., Pelphrey, K., Kaiser, M.D., 2013. Autistic traits are associated with diminished neural response to affective touch. *Soc. Cogn. Affect. Neurosci.* 8, 378–386. <http://dx.doi:10.1093/scan/nss009>
- Wagner, A., Aizenstein, H., Mazurkewicz, L., Fudge, J., Frank, G.K., Putnam, K., Bailer, U.F., Fisher, L., Kaye, W.H., 2008. Altered insula response to taste stimuli in individuals recovered from restricting-type anorexia nervosa. *Neuropsychopharmacology.* 33, 513–523. <http://dx.doi:10.1038/sj.npp.1301443>
- Zink, C.F., Weinberger, D.R., 2010. Cracking the moody brain: the rewards of self starvation. *Nat. Med.* 16, 1382–1383. <http://dx.doi:10.1038/nm1210-1382>
- Zucker, N.L., Losh, M., Bulik, C.M., LaBar, K.S., Piven, J., Pelphrey, K.A., 2007. Anorexia nervosa and autism spectrum disorders: Guided investigation of social cognitive endophenotypes. *Psychol. Bull.* 133, 976-1006. <http://dx.doi.org/10.1037/0033-2909.133.6.976>
- Zucker, N.L., Merwin, R.M., Bulik, C.M., Moskovich, A., Wildes, J.E., Groh, J., 2013. Subjective experience of sensation in anorexia nervosa. *Behav. Res. Ther.* 51, 256–265. <http://dx.doi:10.1016/j.brat.2013.01.010>



**Figure 1.** *Experimental set-up. Participants were asked to sit in front of a computer screen with their left arm rested on the table. The experimenter was sitting on the left hand side of the table, delivering the touch with a soft brush. A plastic box was used to block the visual feedback of the touch.*