Dissociating the Neural Correlates of Experiencing and Imagining Affective Touch

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This functional magnetic resonance imaging (fMRI) study examined experiencing and imagining gentle arm and palm touch to determine whether these processes activate overlapping or distinct brain regions. Although past research shows brain responses to experiencing and viewing touch, this study investigates neural processing of touch absent of visual stimulation. C-tactile (CT) nerves, present in hairy skin, respond specifically to caress-like touch. CT-targeted touch activates "social brain" regions including insula, right posterior superior temporal sulcus, amygdala, temporal poles, and orbitofrontal cortex (McGlone et al. 2012). We addressed whether activations reflect sensory input-driven mechanisms, cognitive-based mechanisms, or both. We identified a functional dissociation between insula regions. Posterior insula responded during experienced touch. Anterior insula responded during both experienced and imagined touch. To isolate stimulus-independent mechanisms recruited during physical experience of CT-targeted touch, we identified regions active to experiencing and imagining such touch. These included amygdala and temporal pole. We posit that the dissociation of insula function suggests posterior and anterior insula involvement in distinct yet interacting processes: coding physical stimulation and affective interpretation of touch. Regions active during experiencing and imagining CT-targeted touch are associated with social processes indicating that imagining touch conjures affective aspects of experiencing such touch.

Keywords: C-tactile, fMRI, insula, social brain, touch

Introduction

Microneurography studies indicate that C-tactile (CT) afferents, which are present only in hairy skin, respond to caress-like touch ranging from 1–10 cm/s (Nordin 1990; Vallbo et al. 1999). Neuroimaging studies have implicated "social brain" (Brothers 1990) regions in processing CT-targeted touch, including posterior superior temporal sulcus (STS), medial prefrontal cortex (mPFC), amygdala, posterior insula, and orbitofrontal cortex (OFC) (Olausson et al. 2002; Gordon et al. 2011; McGlone et al. 2012; Voos et al. 2012; Bennett et al. 2013), supporting the role of the skin as a social organ (Morrison et al. 2010). An unresolved question from this work is whether these activations reflect stimulus-dependent or stimulus-independent mechanisms. Is social brain activation in the context of CT-targeted touch elicited via sensory afferents carrying information from the peripheral nervous system, or is it elicited via a top-down mechanism of tactile appraisal?

Research has demonstrated overlapping brain mechanisms for viewing and imagining social stimuli, such as biological motion or faces, where imagining the stimuli activate the same brain regions as viewing, yet to a lesser magnitude (O'Craven and Kanwisher 2000; Grossman and Blake 2001). Both experiencing and viewing affective, caress-like, touch recruit similar neural mechanisms (Morrison et al. 2011), suggesting that some components involved in touch perception do not require physical sensation. However, it is unclear whether this phenomenon requires visual input in the absence of tactile stimulation. Stimulus-independent mechanisms have been identified in processing tactile sensory input. Affective experience associated with touch can be altered by using descriptive words (McCabe et al. 2008), or believing you are being touched by a man versus woman even when no change occurs (Gazzola et al. 2012). Research has shown somatosensory activation to imagining touch to the back of the hand (Yoo et al. 2003), however, no study to date has specifically examined CT-targeted touch, which is of particular interest given CT-afferents' sensitivity to and likely evolutionary role in processing slow, gentle, characteristically social touch (Morrison et al. 2010).

The insula seems to support both stimulus-dependent and stimulus-independent processing of touch. Research suggests that the posterior insula responds to tactile stimulation (Craig 2009) and is selective for CT-targeted touch (Björnsdotter et al. 2009), while the anterior insula is involved in subjective feeling states and affective learning (Singer et al. 2009). Independent of tactile stimulation, the anterior insula has been implicated in anticipating touch and coding its affective quality (Lovero et al. 2008). While the present study was designed to probe the neural correlates of stimulus-independent differentiation of CT-targeted touch with separate imagine and experience touch conditions, the design also enables a more thorough investigation of these proposed roles of the insula subregions independent of c-fiber innervation. The current study is poised to replicate and extend previous work differentiating the roles of anterior and posterior insula in integrating cognitive and perceptual processing of tactile stimulation.

We hypothesized that stimulus-independent cognitive mechanisms constitute some of the previous findings of unique brain responses to CT-targeted touch. We sought to characterize such stimulus-independent activations, which may be coding the affective aspects of gentle touch. To explore this possibility, we used functional magnetic resonance imaging (fMRI) to determine whether experiencing and imagining gentle touch to the arm and palm recruit overlapping or distinct brain responses. Including touch to the arm and palm permitted a comparison of brain responses to gentle touch in locations where CT-afferents are present and absent, respectively. Past research (Gordon et al. 2011; Voos et al. 2012) has demonstrated reproducibility in brain responses to comparisons of CT-targeted versus non-CT-targeted touch using manipulations of touch velocities (e.g., 8 cm/s vs. 32 cm/s) and body locations (e.g., arm vs. palm). The current study utilized a body location manipulation of CT stimulation (arm vs.

palm) as pilot trials deemed these types of touch to be easier to distinctly imagine than manipulations of velocity. Regarding our examination of subinsular roles in touch processing, we hypothesized that the posterior insula would be more involved in the processing of physical stimulation, whereas the anterior insula would be more involved in the coding of imagined touch.

Materials and Methods

Participants

Seventeen right-handed male adults participated in this study. Previous touch studies have used a combination of males and females (Yoo et al. 2003; Gordon et al. 2011; Morrison et al. 2011; Voos et al. 2012). Here, only male participants were used to minimize variability. We plan to specifically address the important issue of sex differences in social brain responses to touch in future research. Three participants were scanned but excluded for either head motion exceeding 3 mm or 3° from head position at first volume acquisition that could not be corrected, falling asleep in the scanner, or grasping the brush during palm trials. One participant's head shifted by >3 mm from his head position at initial volume acquisition. However, this head motion was isolated to the second half of the session, and thus only data from the first half of the experiment were analyzed for this participant. All participants were naïve to the experimental hypothesis. Ages ranged between 19 and 25 years (mean = 20.67; SD = 2.06). Informed written consent was obtained from each participant using a protocol approved by the Yale School of Medicine Human Investigations Committee. Each participant received $50 compensation for his participation.

Pre-Scan Practice and Ratings

Prior to entering the scanner, participants completed a practice trial for each condition in the study (Experience Arm, Experience Palm, Imagine Arm, and Imagine Palm). As in the fMRI session, participants wore a blindfold. During each trial within each condition, a tone (identical for all conditions) played (1 tone per second) for 6 s while the participant was instructed to either feel or imagine the sensation of touch to the arm or palm. For the experience conditions, back and forth brushing was administered with a 7 cm wide watercolor paintbrush in the proximo-distal orientation. While we recognize that a brush is not equivalent to actual human touch, it allows for a greater experimental control across all conditions. Based on previous studies using this method to investigate gentle touch (Löken et al. 2009; Gordon et al. 2011; Morrison et al. 2011; Voos et al. 2012; Bennett et al. 2013), we do not believe that using a brush compared with actual human touch fundamentally affects the results of the study. One experimenter (MVL) administered the brushing to all participants. Following each type of brushing experience (Arm and Palm), participants were asked to imagine the same type of touch during an identical 6-s tone. Imagine conditions followed Experience conditions so that participants could utilize their memory of the most recent touch. This could allow individuals to most accurately imagine the specific sensation. Participants rated the pleasantness for each type of touch using a Likert scale (1 = not pleasant at all, 2 = slightly pleasant, 3 = moderately pleasant, 4 = very pleasant, 5 = extremely pleasant).

Experimental Design

Prior to the fMRI scan, an area of 8 cm was measured and marked with a water-soluble marker on the right forearm (palm up), and an area of 4 cm was measured and marked on the right palm in order to delineate the brushing area in each condition. Brush strokes in both locations occurred at a rate of 8 cm/s, which is within the range of optimum velocities to target CT-afferents (Löken et al. 2009). Participants wore a blindfold over their eyes during the experiment to eliminate visual stimulation in all conditions. The entire experiment lasted 20.13 min, with an initial 6 s of rest, which was discarded from analysis.

During the scan, participants experienced and imagined gentle touch to the arm and palm in a block design procedure (Fig. 1). Experience blocks (Arm or Palm), were followed by Imagine blocks of the same kind of touch (Arm or Palm). The Experience trials included 6-s

periods of gentle brush strokes as described above. In each condition, a single trial lasted 6 s with a 12-s intertrial interval of rest. An auditory cue (1 tone per second) was used to distinguish between the active conditions (Experience or Imagine) and rest. The auditory cue (identical in Experience and Imagine conditions) was essential to indicate the active component of the Imagine conditions; participants were instructed to imagine the sensation of the touch (as opposed to the action of being touched) only during the tone. This instruction was aimed at reducing attention to the brush itself. Auditory cues have been utilized in prior imagery studies to signify active blocks in this way (O'Craven and Kanwisher 2000). Participants were questioned postscan about whether they were able to adhere to this and if their minds wandered during the task in order to monitor their attention during the scan. Each block included 8 trials of a given condition. There were 2 blocks of each condition. As illustrated in Figure 1, prior to each block, in an additional 6-s segment, participants heard verbal instructions for the upcoming block ("You are entering an Arm block. Focus on the touch," or "Now, imagine how that same touch feels when you hear the cue."). Each Imagine condition followed a block of experiencing that touch (i.e., Imagine Arm following Experience Arm) to encourage participants to imagine the specific feeling that they had just experienced, not any type of touch in general. A long rest period (12 s of rest plus 6 s of instruction for the next block) was utilized in order to avoid carry-over effects from the previous block. Arm and Palm blocks were counterbalanced such that 9 participants received Arm blocks first, and 8 participants received Palm blocks first.

Imaging Protocol

Data were collected using a Siemens 3-T Tim Trio scanner located in the Yale University Magnetic Resonance Research Center in New Haven, CT. An MPRAGE sequence was used to take high-resolution T_1-weighted anatomical images (time repetition [TR] = 1900 ms; time echo [TE] = 2.96 ms; field of view [FOV] = 256 mm; image matrix = 256 mm^2, voxel size = 1 × 1 × 1 mm, 160 slices). A single-shot, gradient-recalled echo planar pulse sequence sensitive to blood-oxygenation-level-dependent (BOLD) contrast was used to take whole-brain functional images (TR = 2000 ms; TE = 25 ms; flip angle = 60°; FOV = 220 mm; image matrix = 64 mm^2; voxel size = 3.4 × 3.4 × 4.0 mm, 34 slices). Three hundred and six successive brain volumes were acquired per run.

Postscan Ratings

Following the scan, participants rated the difficulty of imagining each type of touch using a Likert Scale (1 = not difficult at all, 2 = slightly difficult, 3 = moderately difficult, 4 = very difficult, 5 = extremely difficult). All participants reported moderate-to-no difficulty imagining touch.

fMRI Analysis

Data were processed using the BrainVoyager QX 2.0.8 software package (Brain Innovation, Maastricht, the Netherlands). Functional data were preprocessed using slice time correction (cubic spline interpolation), spatial smoothing [with a full-width at half-maximum (FWHM) 4-mm Gaussian kernel], 3-dimensional rigid-body motion correction (trilinear sinc interpolation), and temporal high-pass filtering (GLM Fourier basis, which was set using 2 cycles/time course). The functional datasets were coregistered to T_1-weighted anatomical images collected within the session. These were then normalized to Talairach space (Talairach and Tournoux 1988).

On a single-participant level, general linear model (GLM) based analyses were performed using task-related BOLD responses. Regressors for each of the 4 task conditions were identified as separate box-car functions, using a value of 1 during each condition and 0 for nonconditions. These were each convolved using a double-gamma hemodynamic response function (HRF). Regressors also included all 6 parameters of motion as predictors of no interest.

Whole-Brain Analyses

A group-level random-effects GLM analysis was run on all voxels within the Montreal Neurological Institute template brain, normalized
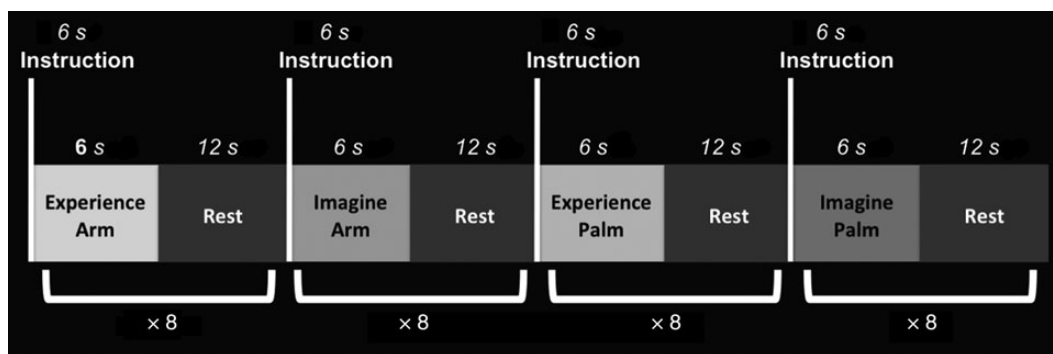
Figure 1. fMRI experimental design.

to Talairach space. This whole-brain mask consisted of 1 449 746 (1 mm³) voxels. All contrasts were assessed at $P < 0.05$ and corrected for multiple comparisons with a cluster threshold. Cluster thresholds were established via a Cluster-level Statistical Threshold Estimator plug-in (Forman et al. 1995; Xiong et al. 1995). Using 1000 iterations of a Monte Carlo simulation, the relative frequency of each cluster size was assessed. A corrected threshold was set at $\alpha < 0.05$ for each contrast. First, to identify a main effect of experiencing versus imagining touch, we examined the contrast Experience (Arm and Palm) > Imagine (Arm and Palm) ($k = 153$). The same contrast was also conducted within a structurally defined insula mask, in order to delineate specific regions of interest for subsequent analyses (see "ROI Analyses"). The limits of these left and right insula mask regions were the anterior, superior, and inferior peri-insular sulci (Deen et al. 2010).

In order to provide converging evidence for past research showing posterior insula involvement in processing CT-targeted touch specifically (e.g., Morrison et al. 2011), we also contrasted Experience Arm versus Experience Palm within the structural insula ROI. As an exploratory analysis, we conducted the same computation for Imagine Arm versus Imagine Palm.

To identify potential stimulus-independent mechanisms involved in the distinctive processing of CT-targeted touch at a whole-brain level, we first identified voxels where activation was modulated by experiencing CT versus non-CT touch (Experience Arm > Experience Palm). Within these voxels, we then identified voxels that were also differentially responsive to imagining CT versus non-CT touch (Imagine Arm > Imagine Palm).

Insula ROI Analysis

We conducted a bilateral insula region of interest (ROI) analysis utilizing functionally defined insula regions based on the contrast of Experience (Arm and Palm) versus Imagine (Arm and Palm), which revealed part of the anterior insula as more responsive to imagining touch and part of the posterior insula as more responsive to experiencing touch. The insula was of interest in the current study given its role in tactile processing (Craig 2009).

Due to the dissociation identified between the anterior and posterior regions, we investigated this difference further in post hoc analyses. Specifically, the results of the contrast of Experience versus Imagine demonstrated that anterior insula exhibited a selective response to imagining touch and posterior insula was selective for experiencing touch. However, we had not determined whether either of these regions exhibited a *specific* response to imagining or experiencing touch (i.e., whether either region was activated by one and *only* one touch condition when compared with baseline).

Within the functionally defined insula regions, we explored the differential response to imagining and experiencing touch, collapsing across CT and non-CT touch, by visualizing the time course of the hemodynamic response (from 2 volumes prestimulus onset to 9 volumes poststimulus onset) during each condition. Given the literature on the role of the posterior insula in processing tactile (e.g., stimulus-dependent, sensory) information and the role of the anterior insula in (cognitive-based) interpretation of the social and emotional

components of touch, we investigated not only distinct but also overlapping roles of anterior and posterior insula in processing touch. Toward this end, we determined at what volumes the anterior and posterior insula response to experiencing and imagining touch was significant by comparing % signal change at each volume to zero ($P < 0.05$).

Taking into account the biases introduced by the employed method of ROI definition (Kriegeskorte et al. 2009), we anticipated that the waveforms from the ROIs defined in the Experience versus Imagine contrast could follow 3 distinct patterns: 1) One condition (Experience or Imagine) would show a main effect versus baseline, while the other condition would show no main effect, suggesting that the insula activation was *specific* for that condition. 2) both conditions would show a main effect compared with baseline in the same direction, with the amplitude of one effect being stronger than the other, showing that the insula activation was *selective*, but not specific for one of the conditions, or 3) Both conditions would show strong effects versus baseline in opposite directions (one positive and one negative), suggesting that the insula activation was *selective* but not *specific* for one of the conditions. We utilized waveform analyses (instead of GLM analyses) to assess each condition independently because event-related averaging included a more clearly defined "baseline" than GLM analyses. We intentionally did not statistically compare waveforms from Experience and Imagine conditions to each other, as those results would reiterate the ROI definition criteria.

Results

Postscan Ratings

We examined whether CT-targeted touch was rated as more pleasant or difficult to imagine than non-CT-targeted touch. Paired-sample *t*-tests revealed Arm touch as being rated significantly more pleasant than Palm touch ($t_{(16)} = 2.75$, $P = 0.01$), replicating previous studies contrasting arm and palm touch (Gordon et al. 2011). Although in the current study, the surface area on arm and palm was not identical, a previous study controlling for surface area brushed found that slow, CT-targeted touch was rated as more pleasant than fast, non-CT-targeted touch (Voos et al. 2012). This finding suggests that the length of the area stimulated does not solely influence pleasantness. Although we had only limited access to the subjective experiences of the participants, we found that participants rated both types of touch as equally difficult to imagine ($t_{(16)} = -0.25$, $P = 0.81$), which indicates that differences in brain responses cannot be attributed to one imagination condition being more or less difficult than the other.

Whole-Brain Analysis

To identify distinct brain activations for experiencing and imagining touch, we examined the whole-brain response to

Experience (Arm and Palm) > Imagine (Arm and Palm) at a threshold of $P < 0.05$, $k = 153$. Regions that exhibited a greater response to Experience relative to Imagine included bilateral posterior insula and left postcentral gyrus. Regions that exhibited a greater response to Imagine relative to Experience included the bilateral anterior insula, bilateral postcentral gyrus, bilateral occipital cortex, and bilateral medial frontal gyrus (Fig. 2A, Table 1).

To identify potential stimulus-independent mechanisms involved in processing CT-targeted touch at a whole-brain level, we first found the brain response to Experience Arm > Experience Palm, $P < 0.05$, $k = 83$. Significant regions were then used as a mask within which we conducted a subsequent contrast of the nonoverlapping conditions Imagine Arm > Imagine Palm, $P < 0.05$, $k = 10$. We were interested in identifying regions that showed differential activation to CT versus non-CT touch during both experiencing and imagining tactile stimulation. This analysis revealed activation in the right amygdala, right anterior insula, left temporal pole, and bilateral middle temporal gyri (Table 2, Fig. 3).

Insula ROI Analysis

We conducted ROI analyses to investigate the bilateral insular response to CT-targeted versus non-CT-targeted touch for both the Experience and Imagine conditions, in order to attempt to replicate previous work showing posterior insula selectivity for experiencing CT-targeted touch (Morrison et al. 2011). We identified a region of the right middle and posterior insula that showed significant activation to Experience Arm > Experience Palm ($P < 0.05$, $k = 10$). We also identified a region of the right anterior insula that showed significant activation to Imagine Arm > Imagine Palm ($P < 0.05$, $k = 10$) (Table 3).

Within the anatomically defined bilateral insula mask defined independently by Deen et al. (2010), there were distinct anterior and posterior insula responses to experiencing and imagining touch (Fig. 2B, Table 4). Because of large contiguous regions of activation within the whole-brain mask, this approach allowed us to better describe insula activation distinctly from surrounding regions. As described above in the whole-brain analysis, we found activation in the bilateral posterior insula to Experience > Imagine and activation in the
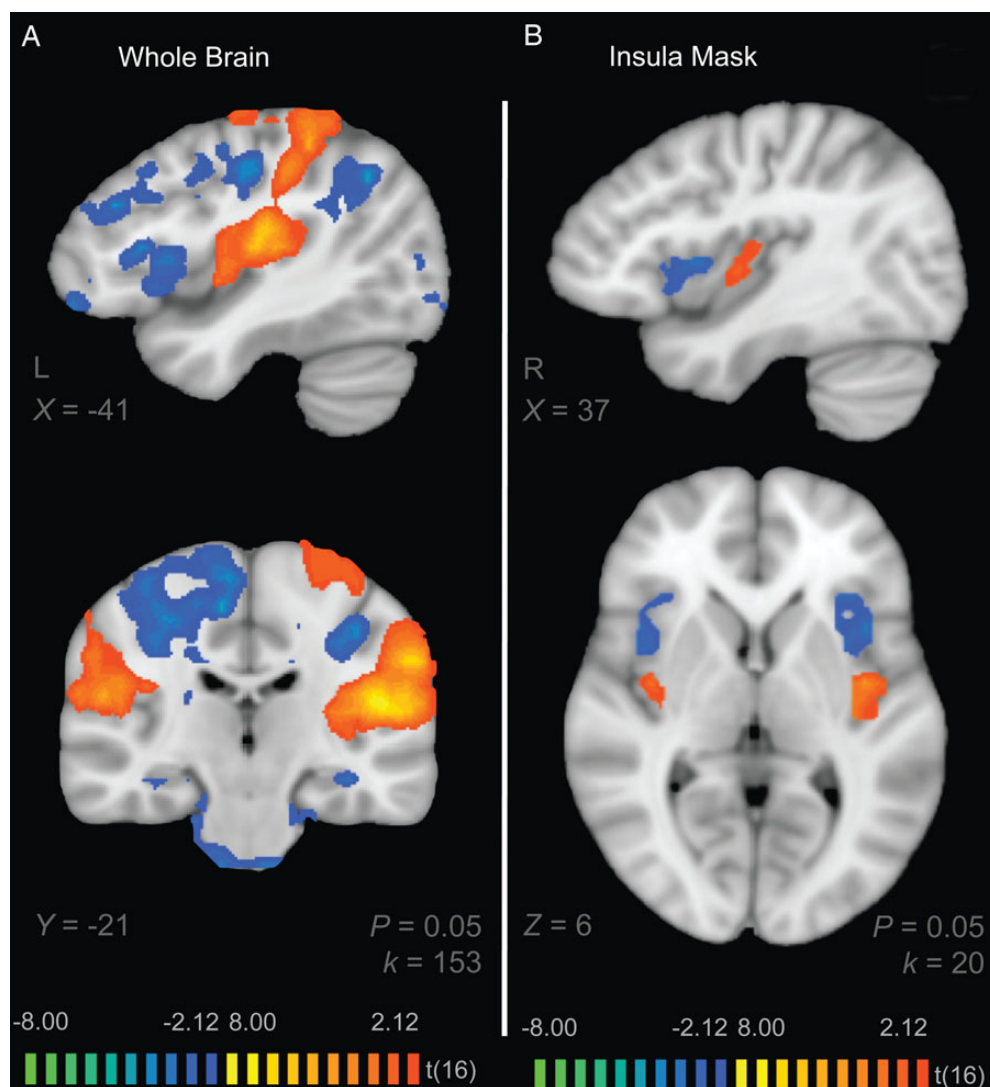
Figure 2. Experience > Imagine results at $P = 0.05$ at a whole-brain level ($k = 153$) (A), and using a bilateral insula mask ($k = 20$) (B).

bilateral anterior insula to Imagine > Experience. Interestingly, this pattern of activation held for CT-touch alone (i.e., Experience Arm > Imagine Arm; $P < 0.05$, $k = 10$) *and* for non-CT-touch alone (i.e., Experience Palm > Imagine Palm; $P < 0.05$, $k = 10$) with the exception of the expected right anterior insula activation for the Imagine Palm > Experience Palm contrast (see Supplementary Table 1).

To further examine both differential and overlapping activation in posterior and anterior regions to touch in general, collapsing across CT- and non-CT touch, we explored the time course of the hemodynamic response to the Experience and Imagine conditions within each of the 4 anatomically defined insula regions (left anterior, left posterior, right anterior, and right posterior). We sought to determine whether any of these insula subregion activations were specific (and not just selective) to imagining or experiencing touch (i.e., significantly activated to *only* one touch condition). For each of the 4 insular regions, we conducted 2-tailed one-sample *t*-tests for % signal change values in the Experience and Imagine conditions for each time point to determine when the % signal change significantly differed from zero.

Anterior Insula

We found that at 2 volumes (4 s) poststimulus onset, the left anterior insula response to experiencing touch was significantly greater than zero, and at 2 and 3 volumes poststimulus onset, the left anterior insula response to imagining touch was significantly greater than zero. At 2 and 3 volumes poststimulus onset, the right anterior insula response to both experiencing and imagining touch was significantly greater than zero (Table 5, Fig. 4*A*, *B*).
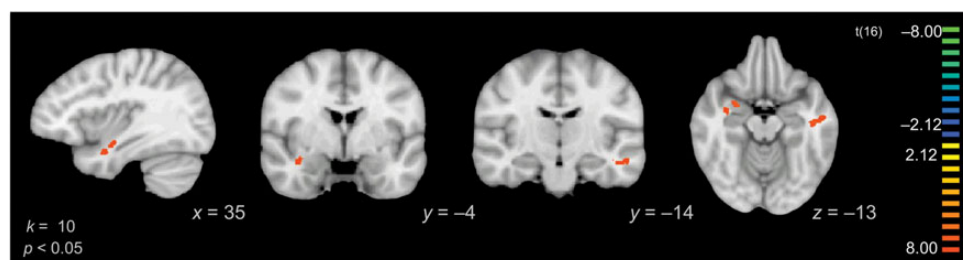
Posterior Insula

At 2, 3, and 4 volumes poststimulus onset, the left posterior insula response to experiencing touch was significantly greater than zero, and there were no volumes at which the left posterior insula response to imagining touch was significantly greater than zero. At 2 and 3 volumes poststimulus onset, the right posterior insula response to experiencing touch was significantly greater than zero, and there were no volumes at which the right posterior insula response to imagining touch was significantly greater than zero (Table 5, Fig. 4*C*, *D*).

Discussion

Past studies have demonstrated the phenomenon of sensation without stimulation both in the visual and tactile domains (O'Craven and Kanwisher 2000; Grossman and Blake 2001; Yoo et al. 2003). This is the first study, to our knowledge, to explore the brain mechanisms for imagining different types of touch subserved by distinct sensory nerve fibers. Here, we were particularly interested in CT-targeted touch, as CT-afferents' specific responsivity to caress-like touch implicates this system in social and emotional processes across the lifespan (Morrison et al. 2010). Further, several studies have found that important social brain regions exhibit a differential response to CT-targeted versus non-CT-targeted touch (Gordon et al. 2011; Morrison et al. 2011; Voos et al. 2012; Bennett et al. 2013). In this study, we examined brain responses to experienced and imagined gentle touch to the arm (CT-targeted) and palm (non-CT-targeted) in order to determine whether these processes recruit overlapping or distinct brain responses. We hypothesized that some aspects of brain mechanisms for processing touch may reflect stimulus-independent, cognitive-based, responses, which code for the affective response to touch.

A previous fMRI study by Morrison et al. (2011) demonstrated that the posterior insula is susceptible to top-down influences; this region activated both when participants were brushed at a CT-optimal velocity and when they watched someone else being brushed at the same velocity. The anterior insula, however,

Table 1
Contrast of Experience > Imagine within the whole-brain mask ($P = 0.05$, $k = 153$)

Region	Peak X	Peak Y	Peak Z	t	P	Number of voxels
Bilateral anterior insula, postcentral gyrus, Occipital, and medial frontal gyrus	−30	−49	25	−10.14	<0.01	261 663
R posterior insula	51	−19	19	6.14	<0.01	10 860
L posterior insula	−48	−19	16	9.25	<0.01	16 119
L postcentral gyrus	−60	−19	31	7.78	<0.01	25 080

Note: Coordinates represent the voxel of peak activation within each region, and reported statistics correspond to the peak voxel. Region extents are reported in structural voxels (1 mm^3). Coordinates are reported in Talairach space.

Table 2
Imagine Arm > Palm contrast within (Experience Arm > Palm) mask ($P = 0.05$, $k = 10$)

Region	Peak X	Peak Y	Peak Z	t	P	Number of voxels
R Middle temporal gyrus, R amygdala, and R anterior Insula	39	−2	−20	4.08	<0.001	700
L middle Temporal gyrus and L temporal Pole	−51	−10	−14	4.23	<0.001	312

Note: Coordinates represent the voxel of peak activation within each region, and reported statistics correspond to the peak voxel. Region extents are reported in structural voxels (1 mm^3). Coordinates are reported in Talairach space.

Figure 3. Imagine Arm > Palm contrast within Experience Arm > Palm mask ($P = 0.05$, $k = 10$).

Table 3

Experience Arm > Experience Palm and Imagine Arm > Imagine Palm within insula mask
($P < 0.05$, $k = 10$)

	Peak X	Peak Y	Peak Z	t	P	Number of voxels
Experience Arm > Experience Palm						
R posterior insula	33	−17	−2	4.29	<0.001	349
R middle insula	33	−5	−5	4.14	<0.001	541
Imagine Arm > Imagine Palm						
R anterior insula	42	11	−5	3.54	<0.01	352

Note: Coordinates represent the voxel of peak activation within each region, and reported statistics correspond to the peak voxel. Region extents are reported in structural voxels (1 mm^3). Coordinates are reported in Talairach space.

Table 4

Contrast of Experience > Imagine within the insula mask ($P = 0.05$, $k = 20$)

Region	Peak X	Peak Y	Peak Z	t	P	Number of voxels
R posterior insula	36	−7	4	4.26	<0.001	869
R anterior insula	30	23	0	−3.89	<0.01	1545
L anterior insula	−40	11	7	−4.17	<0.001	2466
L posterior insula	−35	−16	13	7.21	<0.0001	2470

Note: Coordinates represent the voxel of peak activation within each region, and reported statistics correspond to the peak voxel. Region extents are reported in structural voxels (1 mm^3). Coordinates are reported in Talairach space.

only responded when participants watched someone else being brushed at a CT-optimal velocity. This suggests a dissociation in insula subregion functions. We sought to determine whether this dissociation is a result of specifically viewing another being touched or whether, as we hypothesized, this reflects a more general, sensory-independent re-creation of the emotional or affective components of being touched. The current study demonstrated a greater response to experienced touch than to imagined touch in posterior insula (for both CT- and non-CT-targeted touch). This response elicited by tactile sensation is consistent with previous findings (Friedman et al. 1986; Coghill et al. 1994; Disbrow et al. 1998; Olausson et al. 2002). Additionally, we replicated previous studies (e.g., Olausson et al. 2002; Morrison et al. 2011) by showing that the Experience Arm > Experience Palm contrast (i.e., CT-targeted > non-CT-targeted touch) activates posterior insula. In contrast, the anterior insula showed a greater response during imagined touch, but also shows significant activation during experienced touch, which is consistent with the model of anterior insula involvement in subjective affective feelings and bodily states (Craig 2009; Singer et al. 2009).

The differential activation of anterior and posterior insula is concordant with previous findings of the posterior insula responding to tactile stimulation. The anterior insula has been

Table 5

Analysis of time points for each of 4 functionally defined insula regions for experience and imagine conditions

Region	Significant volumes (experience)[a]	Significant volumes (imagine)[a]
L anterior insula	Volume 2 ($t_{(16)} = 3.85$, $P = 0.001$)	Volume 2 ($t_{(16)} = 3.38$, $P = 0.004$), volume 3 ($t_{(16)} = 3.36$, $P = 0.004$)
R anterior insula	Volume 2 ($t_{(16)} = 6.29$, $P < 0.001$), volume 3 ($t_{(16)} = 4.59$, $P < 0.001$)	Volume 2 ($t_{(16)} = 4.26$, $P = 0.001$), volume 3 ($t_{(16)} = 3.59$, $P = 0.002$)
L posterior insula	Volume 2 ($t_{(16)} = 7.43$, $P < 0.001$), volume 3 ($t_{(16)} = 9.83$, $P < 0.001$), volume 4 ($t_{(16)} = 5.25$, $P < 0.001$)	No significant volumes
R posterior insula	Volume 2 ($t_{(16)} = 6.11$, $P < 0.001$), volume 3 ($t_{(16)} = 8.66$, $P < 0.001$)	No significant volumes

Note: Bonferroni corrected for multiple comparisons.
[a]Corrected for multiple comparisons using Bonferroni correction.
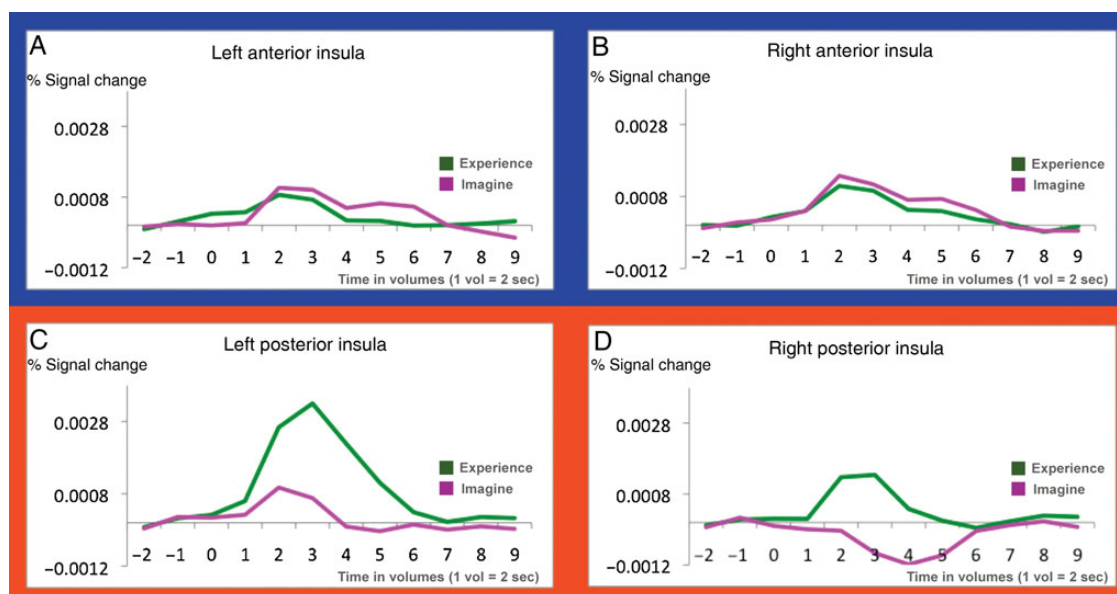
Figure 4. Event-related averaging of 4 functionally defined insula regions (as shown in Fig. 2), showing percent signal change over time in volumes. Significant time points show activation greater than zero. Left anterior insula: volume 2 is significant in the experience condition, and volumes 2 and 3 are significant in the imagine condition (A). Right anterior insula: volumes 2 and 3 are significant in the experience condition, and volumes 2 and 3 are significant in the imagine condition (B). Left posterior insula: volumes 2 and 3 are significant in the experience condition, and no volumes are significant in the imagine condition (C). Right posterior insula: volumes 2 and 3 are significant in the experience condition, and no volumes are significant in the imagine condition (D).

associated with primarily subjective body feelings (Lamm and Singer 2010). In particular, this has been studied extensively in neural responses to experiencing pain versus witnessing pain in others. Specifically, posterior insula activation is elicited by experiencing pain, yet anterior insula exhibits a response to participants experiencing pain or imagining pain in others (Jackson et al. 2006). The current findings extend this work to show anterior insula activation not from pain, but from pleasant tactile experience. Although several studies have alluded to the role of the anterior insula in processing the anticipation and affective nature of touch, the current study is the first to show a strong dissociation between posterior and anterior insula in the experience and imagination of touch. To further investigate the role of the insula in the Experience and Imagine conditions, we examined the time-course of the hemodynamic response within 4 functionally defined insula regions, taking care to account for the issue of nonindependence (Krieges-korte et al. 2009). We sought to determine to what extent experiencing and imagining touch recruited distinct or over-lapping regions of the insula. This analysis revealed that while the anterior insula is responsive to both experiencing and ima-gining touch, the posterior insula exhibits a specific response to tactile stimulation. Though the anterior insula region was defined as showing selectivity for imagining touch, this acti-vation was not specific, with significant responses to both the experience and imagination of touch.

To identify stimulus-independent mechanisms for proces-sing CT-targeted touch, we first located regions with a signifi-cantly greater response to experiencing CT-targeted versus non-CT-targeted touch. Within these circumscribed regions, we did a secondary analysis to identify voxels that also showed significantly greater activation to imagining CT-targeted touch versus non-CT-targeted touch. This 2-step analysis strategy allowed us to identify brain areas that show greater activation to imagining CT- versus non-CT-touch within regions also selective to experiencing CT-touch.

The 2-step analysis revealed the right amygdala, right anterior insula, left temporal pole, and bilateral middle tem-poral gyri as more active to experiencing and imagining CT versus non-CT touch. These social brain regions are known to be involved in the coding of social and emotional stimuli (Olson et al. 2007; Craig 2009; Adolphs 2010) and may reflect the emotional interpretation and valuation of CT-targeted touch in the current study. Importantly, 2 of these regions, the amygdala (Friedman et al. 1986; Augustine 1996) and temporal pole (Emmans et al. 1988; Augustine 1996), have structural connections to the insula, emphasizing the intimate relation-ship between a region that is known to process CT-targeted touch and 2 regions involved in broader social cognition.

In summary, the current study deepens our understanding of the brain mechanisms for processing touch. The results clarify the roles of the anterior and posterior insula. While the posterior insula showed activation only during the physical experience of touch, the anterior insula was responsive to both experienced and imagined touch, suggesting that this region plays a role in the interpretation of the affective meaning of the touch. Further, the novel study design in which participants experience and imagine CT-targeted and non-CT-targeted touch disambiguates past findings on neural correlates of pro-cessing CT-targeted touch by extracting stimulus-independent mechanisms. Several important social brain regions including the right amygdala, right anterior insula, left temporal pole,

and bilateral middle temporal gyri showed greater activation both when participants experienced and imagined CT-targeted versus non-CT-targeted touch. This is the first study to specifi-cally investigate whether brain responses to CT-targeted touch can be elicited in the absence of any sensory input (i.e., vision), thus identifying truly stimulus-independent brain mechanisms for processing gentle, caress-like touch. Our find-ings disambiguate brain activation resulting directly from acti-vating CT nerves from brain responses due to cognitive appraisal of the touch. The results of the current study support the hypothesis that brain mechanisms for processing touch include distinct yet interacting processes incorporating phys-ical tactile sensation and affect-related, stimulus-independent information.

These findings add to the growing literature related to the functional dissociation of the anterior and posterior insula. In-terestingly, a recent study found converging evidence for an anterior/posterior insula dissociation as early as the first 2 years of life (Alcauter et al. 2015). An important future direc-tion will be to downward extend the current study to younger age groups in order to understand how developments in cogni-tive and affective tactile processing may develop along with this early functional segregation.

Supplementary Material

Supplementary material can be found at: http://www.cercor.oxford journals.org/

Notes

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