NeuroImage 139 (2016) 360–367

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Temporal dynamics of brain activation during 40 minutes of pleasant touch

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ARTICLE INFO

Article history:
Received 29 January 2016
Revised 16 May 2016
Accepted 17 June 2016
Available online 20 June 2016

Keywords:
Touch
Reward
Stroking
Inferior frontal gyrus
Putamen
Secondary somatosensory cortex

ABSTRACT

Introduction: Touch is important for individuals' subjective well-being, is typically rewarding, and is one of few sensory stimuli which are experienced as pleasant for a rather long time. This study tracked brain activation during slow stroking stimulation of the arm that was applied continuously for 40 min - a much longer time than what previous studies have investigated.
Methods: 25 subjects were stroked for 40 min with a soft brush while they were scanned with functional Magnetic Resonance Imaging, and rated the perceived pleasantness of the brush stroking. Two resting baselines were included. Whole brain-based analyses investigated the neural response to long-lasting stroking.
Results: Stroking was perceived as pleasant throughout scanning and activated areas that were previously found to be involved in the processing of pleasant touch. Activation in primary somatosensory cortex (S1) and S2, subdivision OP1, decreased over time, whereas activation in orbito-frontal gyrus (OFC) and putamen strongly increased until reaching a plateau after approximately 20 min. Similarly, functional connectivity of posterior insula with middle cingulate and striatal regions increased over time.
Discussion: Long-lasting stroking was processed in similar areas as shorter-lasting stroking. The decreased activation in somatosensory cortices over time may represent stimulus habituation, whereas increased activation in OFC and putamen may relate to the stimulation's subjective reward value. This involvement of reward-related brain circuits can facilitate maintenance of long-lasting social touch interactions.

Introduction

Affective touch plays an important role in individuals' subjective well-being and is assumed to form the basis for affiliate behavior and social bonding (McGlone et al., 2014; Morrison et al., 2010). People touch and stroke each other frequently and by that express affection, security and positive attention (for overview, see Gallace and Spence, 2010). Affective touch varies from short tapping or touching the hand, as is common for contact between strangers, to stroking and massaging that endures for minutes and hours. Such long-lasting touch spontaneously happens between intimate partners, family members, and in parent-child interactions (Suvilehto et al., 2015) and often signals deep emotion and affection. Indeed, pleasant touch seems to be one of few sensory stimuli which is experienced as pleasant for a rather long time (Triscoli et al., 2014). However, although many studies (Francis et al., 1999; Rolls et al., 2003; Rolls, 2010), identified the neural correlates of short-lasting pleasant touch, there has never been any attempt of investigating brain activation during prolonged touch.

The importance of pleasant touch is underlined by the finding that such stimulation is transmitted by a separate sensory system of low-threshold mechanoreceptive tactile C-afferents (CT-afferents). These CT-afferents innervate all hairy parts of human skin and exhibit the highest firing frequency when the skin is gently stroked at speeds corresponding to a caress. Furthermore, the firing rate of CTs highly correlates with subjective ratings of pleasantness of stroking (Ackerley et al., 2014; Löken et al., 2009). CT afferents project to the posterior insula (Morrison et al., 2011a; Olausson et al., 2002), as shown by results from fMRI investigations of brain areas activated by slow touch in patients lacking Aβ afferents. Whereas slow stroking activated somatosensory areas and insular cortex in healthy subjects; only the

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http://dx.doi.org/10.1016/j.neuroimage.2016.06.031

posterior insula was activated in subjects lacking Aβ afferents (Olausson et al., 2008; Olausson et al., 2002).

In addition to the insula, slow stroking commonly activates orbitofrontal cortex (OFC) (Lamm et al., 2015a; Mc Glone et al., 2012; Morrison et al., 2011a; Olausson et al., 2002; Rolls et al., 2003). Even more, activation in the orbitofrontal cortex correlates with the subjective pleasantness of touch (as reviewed by Rolls and Grabenhorst, 2008). Since the OFC is activated by a large number of rewarding and punishing stimuli such as taste (Kringelbach et al., 2003; Veldhuizen et al., 2010), odors (e.g., Rolls et al., 2010), money (e.g., O'Doherty et al., 2001) and erotic stimuli (e.g., Sescousse et al., 2010), it appears to generally track rewards regardless of modality.

A further region coding for the hedonic aspect of touch is the ventral striatum (May et al., 2014). Previous work showed a correlation between activation in the ventral striatum and pleasantness ratings when participants were touched on their forearm with a "rich" vs "thin" body cream (McCabe et al., 2008). In addition to these regions, the posterior superior temporal sulcus (Bennett et al., 2013; Voos et al., 2013), the medial prefrontal cortex (Gordon et al., 2013; Voos et al., 2013), and the pregenual anterior cingulate cortex (Lindgren et al., 2012) have been implicated in processing slow pleasant touch.

To the best of our knowledge, neural processing of pleasant touch has only been examined on time scales shorter than several minutes (Morrison et al., 2011a; Olausson et al., 2002; Rolls et al., 2003). However, the willingness of people to pay for longer-lasting touch in the form of massage, the intimate quality of long-term stroking and the long duration of experienced pleasantness suggests that long-lasting stroking has rewarding effects in humans which may evolve over time. Alongside a rich literature about short-lasting pleasant touch, the present study is the first to investigate which brain regions code hedonic experience during long-lasting pleasant touch.

To this end, brain activation and subjective evaluation of continuous touch were monitored over an extended period of time (around 40 min). Tactile stimulation was performed with the slow stroking velocity of 3 cm/s. This velocity is typically experienced as most pleasant and is the optimal speed to elicit CT-fibres discharge (Ackerley et al., 2014; Löken et al., 2009). BOLD changes over time were monitored in the whole brain and related to subjective ratings of pleasantness. In addition, changes of connectivity during long-term stroking were explored.

Methods

Participants

25 healthy subjects (15 women), right-handed, with normal or corrected-to-normal vision by contact lenses, aged between 19 and 38 years (Mean age = 23; SD = 3.85) were recruited locally. The majority of the participants were students.

All subjects gave written informed consent and received financial compensation of 200 SEK/h (~25 dollars) for participation in the study.

The study was performed in agreement with the Declaration of Helsinki and has been approved by the regional medical research ethics committee.

Experimental setting and procedure

Acquisition parameters for fMRI

Images were acquired with a 3-Tesla PHILIPS Achieva scanner fitted with a 32 channel head coil. Changes in blood oxygen level dependence (BOLD) were obtained from T2*-weighted scans using a gradient-echo single shot EPI sequence (repetition time: 3000 ms; echo time: 35 ms). Volumes were acquired in 40 transverse ascending slices without gap with an in-plane resolution of 2.8 mm and a reconstructed voxel size of 2.50 × 2.55 × 2.80 mm. Field of view was 20 × 24 cm, matrix size 144 × 144 and flip angle 90°. Two dummy volumes were acquired at the beginning of the first block to reduce possible saturation effects. An anatomical T1 volume with slice thickness 0.9 mm (170 slices) and in-plane resolution of 0.94 × 0.94 mm (matrix size 256 × 256) was additionally acquired for anatomical mapping of activation.

Setup

Participants lay in the scanner with their left arm comfortably stabilized with medical cushions. To minimize head movements participants' heads were stabilized with foam padding and adhesive tape.

Altogether, subjects were scanned during 18 blocks of two minutes duration each. During all these blocks, the computer screen in front of the subjects was black. 37 volumes were acquired during each block (666 volumes in total). The first and the last of these blocks constituted a baseline, during which the subjects were instructed to lie still and "do nothing". The remaining 16 blocks in-between represented the active tactile stimulation condition. The subjects' left dorsal forearm was stroked with a custom-built MR-compatible robotic device which delivers highly replicable force (linear tactile stimulator, LTS; Dancer Design; St Helen's, UK, driven by LabVIEW software (National Instruments; Austin, TX)) (see Fig. 1). The subjects were informed that they would be brushed by a robot both in the consent-form and the verbal instruction given before the experiment, and they saw the machine already when entering the scanner room. A 60 mm wide flat water-colour brush made of fine, smooth goat's hair was attached to the robot. Continuous back-and-forth brush strokes on the participant's left dorsal forearm were given at a predefined force of 0.4 N ± 0.05 and a velocity of 3 cm/s. The brush traversed a distance on the skin of ~10 cm for each direction.

Stroking was performed continuously and without interruption during the whole session for an average duration of 39 min (range 38–40 min). In our previous study on long-lasting touch (Triscoli et al., 2014), brushing was applied for 50 min and was paused during the time the subjects gave their rating. In the present study, we did not want to keep the subjects in the scanner for too long and therefore reduced brushing time for 40 min. At the same time, we were interested in the decrease in ratings. Therefore, we decided to speed up the "satiation process" by brushing continuously. After every 2 min, fMRI acquisition stopped and participants rated the sensation on a subsequently presented visual analogue scale (VAS) using a response box attached to the subject's left leg. The visual analogue scale was presented on a computer-controlled screen which the subjects could see via a mirror on the head coil. Participants were asked to answer the question: "How pleasant was the brushing?" on a scale with the endpoints "not at all pleasant" (−10) and "very pleasant" (+10). After the subjects had given their rating the VAS disappeared, and fMRI measurement started again for another 2-min interval (see Fig. 2). This was repeated for 16 blocks in total. The average time in-between blocks was 15 s (range 7–19 s). Prior to the experiment, subjects were trained to use the button press for VAS rating.

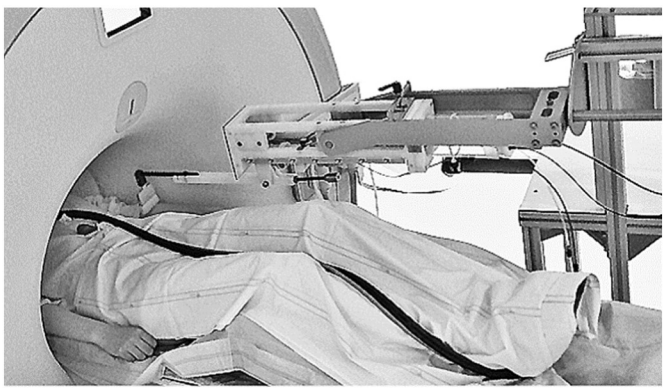

Fig. 1. Linear tactile stimulator for high-precision brush stroking of the left forearm.

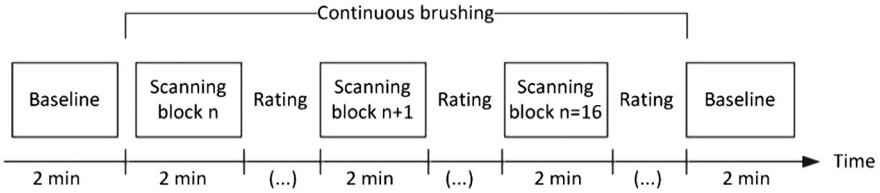

Fig. 2. Time-line of events during experimental session.

Questionnaires

All participants were asked to fill in the "Subjective Measure of Positive Affect and Negative Affect Scale" (PANAS) (Watson et al., 1988) prior to the experiment. Three additional questionnaires on trait measures were given to 21 of the participants after the experiment; the "Behavioural Inhibition and Activation Systems Scale" (BIS/BAS; Carver and White, 1994), the "Temporal Experience of Pleasure Scale" (TEPS; Gard, 2006), and the "Need for Touch Scale" (Peck and Childers, 2003).

Statistical analyses

Touch ratings and questionnaire data

Ratings and questionnaires data were analysed using SPSS Statistics version 21 (IBM; Chicago, USA). The ratings of touch pleasantness per block were subject-wise submitted to a linear regression analysis where the number of blocks served as predictor. Two one-sample *t*-tests were performed in order to determine whether stroking was perceived as significantly pleasant in block 1 and block 16 of the experiment. Moreover, a paired samples *t*-test was run in order to assess whether the pleasantness ratings statistically differed between the first and the last stroking block. Additionally, the standard deviation of the individual ratings in blocks 1–8 was compared with that during blocks 9–16 by means of a paired samples *t*-test. The mean pleasantness ratings were correlated with the mean scores of each questionnaire scale (Spearman's correlations).

fMRI analysis

Data were analysed using the SPM 8 software package (Statistical Parametric Mapping; Welcome Department of Imaging Neuroscience, in the Institute of Neurology at University College London [UCL], UK) implemented in Matlab (Matlab 6.5 R3, The MathsWorks Inc., Natick, MA). Data was preprocessed with motion correction using a 4th degree B-spline algorithm, filtered temporally with a high pass filter cut-off at 200 s, and normalized using segmentation procedure and smoothing of functional data with a Gaussian kernel of $6 \times 6 \times 6$ FWHM.

First, a whole-group comparison between the first and last baseline was calculated. Potential scanner drift containing variations of signal amplitude with every volume was corrected by use of the global mean (for the first baseline and participant) as covariate in the analysis. No significant differences were observed between the first and the last baseline (FWE < 0.05). Accordingly, for all following subject-wise first level analyses, each of the 16 stroking blocks was compared to the first baseline, resulting in 16 contrast files per subject. Six directions of movement parameters were included as regressors subject-wise. The resulting contrast files were submitted to a full factorial second level analysis with stroking blocks (16) as within-subject factor. The overall effect of stroking (collapsed over all 16 blocks) was examined and a conjunction analysis over all blocks was performed in order to map activation present in every single block. Additionally, activations observed in the first and last block were compared to each other, using *t*-tests.

To investigate the relation between neural reward response and pleasantness ratings, a further analysis was conducted. In this global mean-corrected full factorial design, the ratings were subject- and block-wise entered as a parametric covariate. The reason for performing this analysis separately for the first 8 trials and the last 8 trials was that the subjective ratings followed different patterns in the first than the second half of the experiment.

All analyses were performed voxel-wise with FWE-correction at $p < 0.05$. A minimum cluster size (k) of ten voxels was applied to the FWE $p < 0.05$ corrected images in order to limit the amount of data presented. Labels for the activated regions were obtained from the Anatomy toolbox (Eickhoff et al., 2005) and from the WFU Pick Atlas software package v2.5. Locations are reported in MNI space.

Functional connectivity

As posterior insula is the main target of CT afferents, networks of connectivity were explored for this region. To this end, a sphere of 4 mm around the coordinates of the contralateral posterior insula activation peak (obtained from the touch vs baseline contrast) was created using the WFU Pick Atlas software package v2.5 (Maldjian et al., 2004; Maldjian et al., 2003). Functional connectivity (FC) was computed over each block as linear regression between this insular seed and the rest of the brain with the conn-toolbox that performs voxel-seed correlations by estimating temporal correlation maps (Whitfield-Gabrieli and Nieto-Castanon, 2012). Single-subject contrast maps were calculated for each block (N = 16) and further analysed using SPM 8.

Group analysis was performed in a full factorial analysis with the within-subjects factor block (16 levels). As no significant impact of time (blocks) was observed on head motion ($p = 0.12$), frame-wise displacement was not included as nuisance factor. Functional connectivity of the posterior insula seed in the first and the last stroking block was separately assessed. Subsequent t-contrasts between the first and the last stroking block were masked inclusively ($p < 0.05$) by activation obtained in the first block. Similar contrasts between the last and the first block were masked inclusively by activation obtained in the last block ($p < 0.05$). This masking procedure restricts our results and ensures that differences between conditions/blocks A and B are only reported if the coupling reaches a statistical threshold in condition A. The final statistical map of this explorative analysis was created using a threshold of $p < 0.001$, uncorrected. FWE corrected results are reported in addition.

Results

Pleasantness ratings

Stroking was perceived as significantly pleasant at the beginning of the experiment ($t = 5.51$, $p < 0.001$) and remained pleasant throughout scanning. However, there was a decrease of pleasantness over time ($t(396) = -5.35$, SE = 0.04, R = 0.26, Beta = −0.26, B = −0.22, $p < 0.001$). This means that for every further block, there was a decrease of 0.3 rating points. R-square was 0.07, which implies that 7% of the variation in the ratings was explained by block number. Accordingly, the pleasantness ratings for the first stroking block (M = 3.61, SD = 3.27) were significantly higher than for the last stroking block (M = 0.34, SD = 4.39) ($t = 2.84$, $p = 0.009$). In the last block, the stimulation was rated to be neutral ($t = 0.38$, $p = 0.705$), but not unpleasant (see Fig. 3). Overall, there appears to be a steady decrease of the ratings in the first half of the experiment (blocks 1–8), and a plateau in the second half of the experiment (blocks 9–16). The standard deviation of the

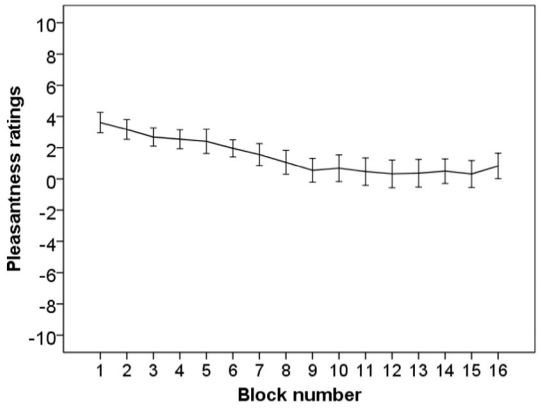

Fig. 3. Mean pleasantness ratings (N = 25) over stroking blocks (with standard error).

individual ratings was larger during the first half (mean SD = 0.93) than during the second half (mean SD = 0.47) of the experiment ($t(24) = 2.74$, $p = 0.011$).

A significant positive correlation was found between the pleasantness ratings and the TEPS Consummatory Scale ($r(24) = 0.45$, $p = 0.029$), indicating that subjects who typically experience more rewarding feelings in response to pleasant stimuli enjoyed the stroking more. None of the other scales correlated with the ratings.

fMRI results

Pleasant touch activated tactile and reward areas

The overall activations touch vs baseline in the whole brain showed a strong response to pleasant tactile stimulation in five activation clusters (see Table 1). Cluster 1 was a large response cluster, encompassing 28,236 voxels, which contained 59% of the contralateral (right) OP1, 88% OP3, 40% OP4, all of them subdivisions of S2 (Eickhoff et al., 2007), 5% Brodmann area 1, 3% Brodmann area 2, 13% Brodmann area 3b, all of them subdivisions of S1 (Eickhoff et al., 2010) as well as 75% posterior insula. The cluster further expanded anteriorly to the right inferior frontal gyrus, caudate, putamen, and bilaterally to the OFC. Cluster two encompassed mainly the ipsilateral (left) S2, S1, as well as ipsilateral posterior insula. Cluster three contained the left inferior, middle and superior temporal gyrus. Further smaller activation clusters are reported in Table 1. Conjunction analysis revealed that contra- and ipsilateral activations of S2 and S1 as well as bilateral OFC activation were present during the whole course of the experiment (compare Inline Supplementary Table S1).

Inline Supplementary Table S1 can be found online at http://dx.doi.org/10.1016/j.neuroimage.2016.06.031.

Development of response to pleasant touch over time

The comparison of first and last block revealed that activation in the right middle and superior occipital cortex including cuneus, in the precuneus and bilaterally in the S2, subdivision OP1, decreased over time. At the same time, activation in the right OFC, putamen, S2, subdivision OP3 and in the right middle temporal gyrus increased up to about half of the experimental session (approximately 20 min), and reached a plateau afterwards (Table 2 and Fig. 4).

Activation related to touch pleasantness

Entering the pleasantness ratings as covariate in the analysis, no significant results survived FWE-correction. Using a lower threshold of $p < 0.001$ (uncorrected) to explore potential trends, rating-related activation emerged. In the first half of the experiment, ratings were correlated to activation in S1, bordering Brodmann area 4a (k = 12, t = 3.8, MNI: −38/−24/65) and to the middle frontal cortex (k = 44, t = 4.1, MNI: −32/16/49), however both activations did not hold for FWE correction. In the second half of the experiment, pleasantness ratings were not only correlated to activation in S1 (k = 139, t = 4.2, MNI: −46/−14/29) and orbitofrontal regions (k = 27, $p_{FWE\text{-}corr} = 0.01$, t =

Table 1
Overall activations[a] touch versus baseline in the whole brain. For comprehensive overview, only local maxima are reported in the table. Note that clusters are very large and encompass more areas than reported (see Results section).

Cluster #	Area[b] local maxima	Cluster size	T-score	x	y	z
1	R insula	28,236	12.61	34	12	−9
	R inferior frontal gyrus (IFG), pars triangularis		12.18	42	36	−1
	R IFG, pars triangularis		11.96	40	40	−1
	R rolandic operculum		11.78	52	−2	13
	R IFG, pars orbitalis		11.49	26	28	−11
	R IFG, pars opercularis		11.41	44	16	5
	R IFG, pars orbitalis		10.74	26	36	−7
	R precentral gyrus		10.49	56	6	25
	L supramarginal gyrus		8.98	−46	−28	25
	L IFG, pars opercularis		8.65	−60	10	19
	L precentral gyrus		8.50	−60	4	23
	L precentral gyrus		8.43	−58	6	25
	L superior temporal gyrus		8.26	−54	−28	19
	L rolandic operculum		8.13	−44	−18	19
	L rolandic operculum		7.86	−46	−16	21
	L postcentral gyrus		7.65	−50	−14	21
	L supramarginal gyrus		7.60	−56	−30	25
	L rolandic operculum		7.29	−44	−6	13
3	L inferior temporal gyrus	1240	8.43	−48	−40	−15
	L inferior temporal gyrus		8.43	−50	−46	−7
	L inferior temporal gyrus		8.02	−42	−38	−15
	L middle temporal gyrus		7.82	−64	−28	5
	L superior temporal gyrus		7.25	−56	−44	13
	L middle temporal gyrus		7.13	−54	−42	11
	L middle temporal gyrus		6.78	−56	−26	−1
	L middle temporal gyrus		6.75	−54	−56	15
	L superior temporal gyrus		6.63	−60	−46	15
4	L precentral gyrus	363	6.62	−46	−2	47
	L precentral gyrus		6.41	−24	−16	65
	L precentral gyrus		6.28	−34	−10	55
	L precentral gyrus		6.26	−36	−10	59
	L precentral gyrus		6.10	−26	−14	53
	L precentral gyrus		6.08	−30	−14	51
	L middle frontal gyrus		5.65	−34	6	55
	L middle frontal gyrus		5.50	−32	4	57
5	R postcentral gyrus	209	6.74	32	−42	67
	R superior parietal lobule		6.41	20	−44	71
	R postcentral gyrus		6.24	16	−42	73
	R inferior parietal lobule		5.78	32	−40	53
	R postcentral gyrus		5.58	12	−36	75
	R postcentral gyrus		5.55	34	−42	61
	R postcentral gyrus		4.97	18	−32	73
6	L middle temporal gyrus	59	5.94	−60	−14	−5
	L middle temporal gyrus		5.74	−60	−12	−11
	L middle temporal gyrus		5.47	−56	−2	−15
7	L middle frontal gyrus	41	5.49	−30	10	39
	N/A		5.34	−26	6	37
	N/A		5.06	−22	4	37
8	L superior frontal gyrus	39	5.61	−14	34	49
	L superior frontal gyrus		5.43	−18	36	47
9	N/A	37	6.05	−16	−2	47
10	L middle occipital gyrus	35	5.79	−32	−74	−1
	L inferior occipital gyrus		5.25	−32	−72	−7
11	R postcentral gyrus, area 3b	33	6.09	42	−20	47
	R postcentral gyrus, area 3b		5.64	44	−20	51
	R precentral gyrus, area 3b		5.62	44	−18	43
12	N/A	33	5.55	−12	−22	27
13	L insula lobe	26	5.48	−38	10	−7
14	L middle temporal gyrus	25	5.35	−50	0	−25
15	L caudate nucleus	19	5.54	−12	2	23
16	N/A	15	5.64	−18	24	−7
17	L precentral gyrus	13	5.62	−36	−8	39
18	L paracentral lobule	11	5.40	−6	−22	67

[a] Activations reported are significant at FWE < 0.05, with a cluster size of k > 10 contiguous voxels. All coordinates are in MNI space.
[b] R, right hemisphere; L, left hemisphere.

Table 2
Activation[a] comparison of first versus last stroking block and vice versa in the whole brain.

Comparison	Area[b]	Cluster size	T-score	*x*	*y*	*z*
First versus last brushing block	R middle occipital gyrus	223	5.94	30	−76	33
	R superior occipital gyrus		5.61	20	−80	33
	R cuneus		5.60	18	−68	33
	L superior temporal gyrus (OP1)	88	7.06	−44	−28	9
	R superior temporal gyrus (OP1)	71	5.98	48	−24	11
	R precuneus	17	5.41	2	−48	59
Last versus first brushing block	R inferior frontal gyrus (p. orbitalis)	772	6.59	38	34	−7
	R putamen	114	7.03	32	14	−5
	R rolandic operculum (OP3)	79	5.07	44	−10	21
	R middle temporal gyrus	14	5.29	46	6	−25

[a] Activations reported are significant at FWE < 0.05, with a cluster size of k > 10 contiguous voxels. All coordinates are in MNI space.
[b] R, right hemisphere; L, left hemisphere.

5.4, MNI: −14/62/−5), but interestingly, also to activation in putamen (k = 7, t = 3.6, *p* = −22/8/7) and superior temporal gyrus (k = 23, t = 3.9, MNI: −30/−40/65; k = 4, t = 3.4, MNI: 56/−6/3). Besides the orbitofrontal activation, none of those activations did hold for FWE correction. None of the latter rating-activation associations were present in the first half of the experiment.

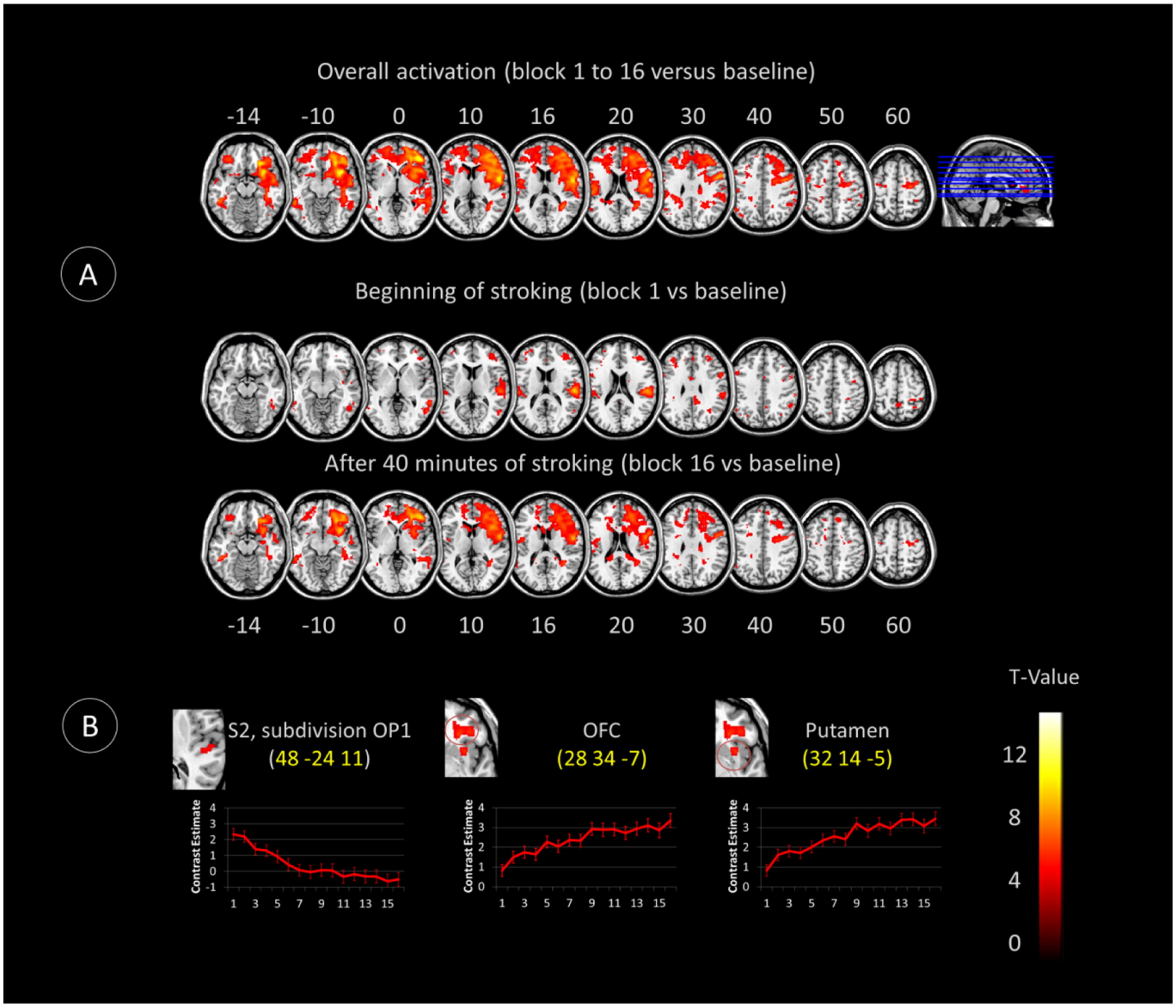

Fig. 4. Overall activation in blocks 1–16 vs baseline as well as significant activation in the first stroking block vs baseline and in the last stroking block vs baseline (upper panel). Line graphs (lower panel) show change of activation in areas involved in the processing of tactile information across blocks. Data are extracted from the peak voxels of the respective areas in the first vs last or last vs first stroking block contrast. Data is thresholded at FWE < 0.05 and presented on a T1-weighted template provided by MRIcron.

Functional connectivity of posterior insula

In the beginning of the experiment, the posterior insula was coupled with the anterior cingulate cortex (k = 644, t = 4.9, MNI: −10/34/23; k = 208, t = 4.1, MNI: −10/2/29), amygdala (k = 112, t = 4.4, MNI: 23/−1/−24) and hippocampal and parahippocampal regions (k = 136, t = 4.4, MNI: −25/−17/−20) (see Fig. 5).

At the end of the experiment, the posterior insula was connected to the middle cingulate region (k = 312, t = 4.7, MNI: 22/−36/23) and interestingly, to striatal regions in putamen (k = 372, t = 4.1, MNI: −23/−3/−8) and caudate (k = 464, t = 4.5, MNI: −16/−34/23) However, except for being coupled to S2, none of the other connections were significant after FWE correction (Table 3). Compared to the first block, connectivity from posterior insula to striatal areas (more specifically, the globus pallidus) increased significantly in the last block (k = 192, t = 4.2, MNI: 22/−12/−3) (see Fig. 5).

Furthermore, the seed in the posterior insula was significantly coupled with ipsi- and contralateral somatosensory areas at the beginning and at the end of stroking (Table 3).

Discussion

Pleasantness ratings decreased in the course of stroking, and even after about 40 min the stroking was not perceived as unpleasant. This striking stability of touch pleasantness corroborates our previous findings (Triscoli et al., 2014). Throughout the entire stroking period, areas involved in tactile sensory processing such as S2, S1 and posterior insula were activated, as well as areas of the common reward network such as OFC, caudate and putamen. Except for caudate and putamen, all of these regions have been previously found to be activated during pleasant touch (Ackerley et al., 2012; Francis et al., 1999; Gordon et al., 2013; Lamm et al., 2015b; Morrison et al., 2011a; Olausson et al., 2002; Perini et al., 2015; Rolls et al., 2003; Wei and Bao, 2013). We suggest that shorter intervals of stimulus presentation prevented the detection of striatal activation in previous studies.

The temporal dynamics during long lasting pleasant touch revealed the expected decrease of activation in S1 and S2, most likely reflecting habituation. However, no such decrease was observed in the posterior insula. Pleasant touch perception involves different pathways; the peripherally activated A-beta fibres are encoded in S1 and S2 while C-tactile fibres target the posterior insula (Olausson et al., 2002). The observed decrease of neural activation in somatosensory processing areas such as the precuneus and S2, subdivision OP1, may reflect habituation and lead to a reduced percept of the stimulus. The reduction of initially high pleasantness ratings to a more neutral range may indicate reduced detectability of the stimulus.

Parallel to the decrease and subsequent stabilization of pleasantness ratings, activation of putamen and OFC built up considerably in the first half of the experiment and reached a plateau after about 20 min of stroking. After this time, inter-individual pleasantness ratings are substantially related to OFC activation and – although not holding for FWE correction – to activation of putamen and superior temporal sulcus. Such a coherence between pleasantness ratings and OFC activation has been reported before in an experiment using short-lasting pleasant touch stimulation (Rolls and Grabenhorst, 2008).

The opposite trends of activation in somatosensory and reward-related areas could be interpreted as a shift from processing the stimulation's discriminative or sensory aspects to its more affective aspects at about half of the experimental session. The posterior insula is a region specifically involved in the processing of affective touch (McGlone et al., 2012; Morrison et al., 2011b; Olausson et al., 2002). The connectivity analysis suggested that both at the beginning and the end of the stroking posterior insula activation was strongly coupled to activation of somatosensory regions processing the discriminative aspects of touch, such as S1 and S2. Only at the end of the experiment, coupling to striatal areas such as putamen and caudate was observed, and coupling to striatal areas built significantly up over time. We assume that prolonged posterior insula activation facilitates recruitment of areas implicated in the processing of reward, which could be one of the neural mechanisms underpinning the rewarding experience of long term stroking important for maintaining social bonds. However, one has to bear in mind the insufficient control of type 1 error for this explanatory analysis. Further limiting the interpretation of our results, no control condition of 40 min of rest or different sensory input was applied in our study. Our results are relatively distinct; a potentially habituation based decrease of activation was found in somatosensory areas and increase of activation in reward-related areas. However, based on our data we do not know to which degree this pattern of activation is specific for pleasant-touch stimulation.

The puzzling decoupling between explicit ratings and implicit neural processes warrants explanation. We observed a decrease of pleasantness ratings in the first half of the experiment and an increase of OFC activation at the same time. This opposite pattern is counterintuitive as the OFC known to be a critical structure for encoding reward value (e.g. Levy and Glimcher, 2012; O'Doherty, 2004). In a study about food satiety, OFC activation decreased in parallel with satiety (Kringelbach et al., 2003). However, it is important to keep in mind that “touch satiety” never occurred in the present experiment: the stimulation never became unpleasant. The role of OFC not only involves representation of specific outcomes (Schoenbaum et al., 2011), but also tracking of changes in reward preferences over time (for a review, see Ostlund and Balleine, 2007). Thus, OFC is typically activated when there is a

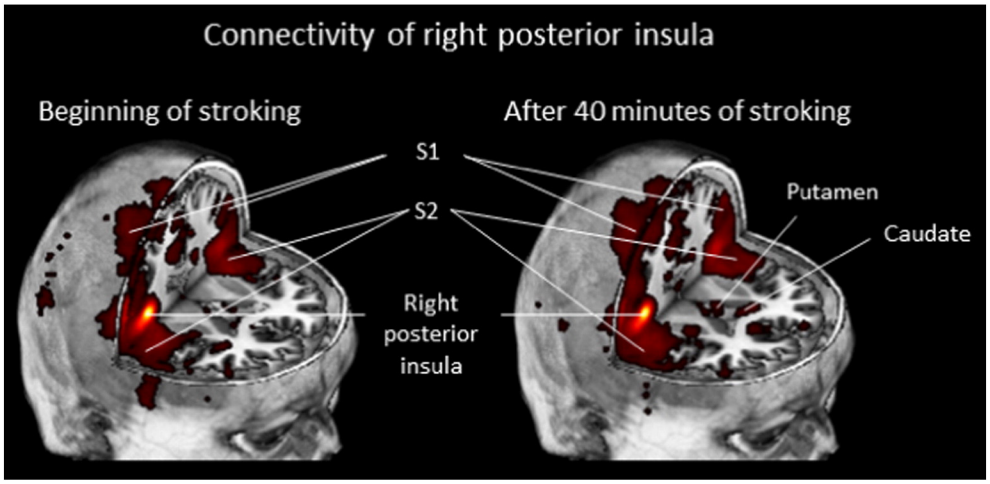

Fig. 5. Functional connectivity of posterior insula at the beginning and at the end of the stroking.

Table 3
Functional connectivity[a] of posterior insula in the first and in the last stroking block.

	Area[b]	Cluster size	T-score	p(FWE-corr)	x	y	z
First block	L postcentral gyrus	1088	5.52	n.s.	−20	−44	67
	R precentral gyrus	120	4.99	n.s	10	4	27
	L anterior cingulate cortex	644	4.90	n.s	−10	34	23
		208	4.14	n.s	−10	2	29
	R rolandic operculum	47,191	41.12	<0.001	40	−20	17
	L rolandic operculum	29,254	10.11	<0.001	−48	−22	13
	R inferior temporal gyrus	600	5.32	n.s	57	−11	−34
	R inferior occipital gyrus	230	4.79	n.s	24	−103	−11
	L middle occipital gyrus	114	4.59	n.s	−48	−82	17
	L hippocampus	136	4.42	n.s	−25	−17	−20
	R amygdala	112	4.35	n.s	23	−1	−24
	R precuneus	128	4.24	n.s	10	−54	19
	R fusiform gyrus	208	3.72	n.s	41	−17	−30
Last block	L postcentral gyrus	280	5.32	n.s	−28	−32	53
	R precentral gyrus	712	4.90	n.s	60	4	27
	R anterior cingulate cortex	440	4.76	n.s	5	37	2
	R inferior frontal gyrus	296	4.58	n.s	31	33	−8
	L inferior frontal gyrus	192	4.25	n.s	−33	31	−8
	L putamen	372	4.10	n.s	−23	−3	−8
	L caudate	464	4.53	n.s	−16	−34	23
	R rolandic operculum	66,471	42.99	<0.001	40	−18	19
	L rolandic operculum	29,857	12.15	<0.001	−48	−22	13
	L temporal pole	864	5.38	n.s	−41	9	−16
	R middle cingulate cortex	312	4.71	n.s	22	−36	23
	L parahippocampal	392	4.52	n.s	−27	−21	−20
	R parahippocampal	168	3.97	n.s	25	−17	−32

[a] Activations reported are significant at $p < 0.001$, with a cluster size of $k > 10$ contiguous voxels. All coordinates are in MNI space.
[b] R, right hemisphere; L, left hemisphere.

shift in stimulus-reward associations, i.e. when a previously rewarded stimulus is no longer rewarded, and a previously non-rewarded stimulus is suddenly rewarded (Ghahremani et al., 2010; O'Doherty et al., 2003). The increase of OFC activation in the first half of the present experiment fits to the updating of changed reward contingencies: the more the ratings changed, the more updating was required.

In the second half of the experiment, however, OFC activation correlated positively with the ratings. The different relationship between OFC activation and ratings in the first and second half of the experiment may be due to the fact that subjective pleasantness was evaluated by a single-item question which possibly comprises more than just pleasantness. For instance, at the beginning the ratings may represent the comprehensive assessment of intensity, novelty and pleasantness. Aspects of intensity and novelty may fade out over time which may cause stabilization of ratings after about 20 min. In the second half of the experiment, ratings stabilized and pleasantness ratings co-varied with OFC activation. Future studies should collect different types of implicit rating data and psychophysiological data to capture the psychological and physiological responses more exhaustively.

Summarizing, long-lasting slow touch is not only experienced as pleasant over a short time, as already shown by previous research (e.g. Field, 2010; Gordon et al., 2013; Morrison et al., 2011a, Morrison et al., 2011b), but also over the course of 40 min or longer (Triscoli et al., 2014). Brain regions typically involved in reward processing, such as putamen and OFC showed an increasing activation pattern over time which may monitor the amount of updating of the on-going stimulation's reward value, which in our experiment never fell below the neutral level. This may contribute to the maintenance of long-lasting tactile interactions between humans.

Competing financial interests

The authors declare no competing financial interests that might be interpreted as influencing the research and, APA ethical standards were followed in the conduction of the study.

Acknowledgements

This study was supported by the Swedish Research Council (grant number 2011-1529) and by a grant of the Marcus och Amalia Wallenbergs Minnesfond to IC (MAW 2014.000).

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