

The neural correlates of maternal and romantic love

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Romantic and maternal love are highly rewarding experiences. Both are linked to the perpetuation of the species and therefore have a closely linked biological function of crucial evolutionary importance. Yet almost nothing is known about their neural correlates in the human. We therefore used fMRI to measure brain activity in mothers while they viewed pictures of their own and of acquainted children, and of their best friend and of acquainted adults as additional controls. The activity specific to maternal attachment was compared to that associated to romantic love described in our earlier study and to the distribution of attachment-mediating neurohormones established by other studies. Both types of attachment activated regions specific to each, as well as overlapping regions in the brain's reward system that coincide with areas rich in oxytocin and vasopressin receptors. Both deactivated a common set of regions associated with negative emotions, social judgment and 'mentalizing', that is, the assessment of other people's intentions and emotions. We conclude that human attachment employs a push–pull mechanism that overcomes social distance by deactivating networks used for critical social assessment and negative emotions, while it bonds individuals through the involvement of the reward circuitry, explaining the power of love to motivate and exhilarate.

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The tender intimacy and selflessness of a mother's love for her infant occupies a unique and exalted position in human conduct. Like romantic love, to which it is closely linked, it provides one of the most powerful motivations for human action, and has been celebrated throughout the ages—in literature, art and music—as one of the most beautiful and inspiring manifestations of human behavior. It has also been the subject of many psychological studies that have searched into the long-lasting and pervasive influence of this love (or its absence) on the development and future mental constitution of a child (Alexander, 1992; Benoit and Parker, 1994; Cassidy and Shaver, 1999; Fisher, 1998; Harlow, 1958; Hatfield and Rapson, 1993). Yet little is known of brain areas and pathways

that correlate with this extraordinary affective state in the human. In pursuing our studies of the neurological foundations of love (Bartels and Zeki, 2000), we therefore thought it worthwhile to turn our attention next to maternal love. Maternal and romantic love share a common and crucial evolutionary purpose, namely the maintenance and perpetuation of the species. Both ensure the formation of firm bonds between individuals, by making this behavior a rewarding experience. They therefore share a similar evolutionary origin and serve a similar biological function. It is likely that they also share at least a core of common neural mechanisms. Neuro-endocrine, cellular and behavioral studies of various mammalian species ranging from rodents to primates show that the neurohormones vasopressin and oxytocin are involved in the formation and maintenance of attachment between individuals, and suggest a tight coupling between attachment processes and the neural systems for reward (Carter, 1998; Insel and Young, 2001; Kendrick, 2000; Pedersen and Prange, 1979). This is confirmed by lesion, gene expression and behavioral studies in mammals (Numan and Sheehan, 1997). Interestingly, the same neurohormones are involved in the attachment between mother and child (in both directions) and in the long-term pair bonding between adults, although each neurohormone may have distinct binding sites and may be gender-specific (Curtis and Wang, 2003; Insel and Young, 2001; Kendrick, 2000). Such similarities, as well as the obvious differences between the two kinds of love, lead one to expect a neural architecture that differs between the two modes of love in some respects and yet is identical in others.

To preserve continuity, we pursued our current study in the same way as our previous one (Bartels and Zeki, 2000), namely by measuring brain activity in volunteers who viewed pictures of their infants, and compared this to activity evoked by viewing pictures of other infants with whom they were acquainted for the same period. In addition, we compared this activity to that when our volunteers viewed their best friend and an adult acquaintance to further control for familiarity and friendly feelings. Such an approach, we hoped, would reveal what the two types of attachment have in common in neural terms. In addition, it promised to tell us whether we could associate functional brain activity related to attachment with cortical and subcortical sites in the human brain that contain a high density of the neurohormones oxytocin and vasopressin (Loup et al., 1991). We were also curious to learn how the activity obtained here would compare to previous neuroimaging studies on emotions, especially those related to different aspects of reward (Aharon et al., 2001; Breiter and Rosen, 1999; Breiter et al., 1997; Elliott et al., 2003; Kelley and Berridge, 2002; Knutson et al., 2001; White, 1989)

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including those involved in sexual arousal (Arnou et al., 2002; Beauregard et al., 2001; Karama et al., 2002; Rauch et al., 1999; Stoleru et al., 1999). Equally interesting would be a comparison of deactivated regions with those associated with negative emotions (Beauregard et al., 1998; Davidson et al., 2002; George et al., 1996; Liotti et al., 2000).

Methods

The general procedures and methods of display, scanning and analysis were very similar to our previous study on romantic love (Bartels and Zeki, 2000), thus ensuring as much consistency as possible for data comparison.

Volunteers and stimuli

Twenty mothers (two left-handed; mean age: 34.0 years; range: 27–49), all of whom reported a normal medical and psychological history, were recruited via posters in nurseries in the London area. Each gave informed consent and filled in short questionnaires about themselves and their emotional relation to those whose photographs they were asked to provide with the opportunity to make additional comments. Each provided photographs of their own child (cO, age: 9 months–6 years, mean: 24.4 ± 15.7 SD months, median = 20 months), of another child of the same age (cA) with whom they had been acquainted for about the same length of time, of their best friend [aF; all female, age: 36.4 ± 9.5 years, known for 15.9 ± 10.1 years (median: 13 years)], and of another person they were acquainted with [aA; all but one female, age: 36.1 ± 9.1 years, known for 6.9 ± 7.7 years (median: 5 years)]. Nine mothers provided two photographs of each person, the remaining provided one. The photographs were prepared in passport format with the faces appearing against a neutral gray background. During the scan, photos of these socially and emotionally defined persons were displayed along with a gray baseline. The sequence also contained photos that are of less relevance for the current report; these included the volunteers' partners, a disliked person, an unknown child and adult; however, we concentrate in this report only on findings relevant to maternal attachment. Photos were displayed by computer via backprojection onto a translucent screen of 1024×768 pixels resolution subtending $24 \times 18^\circ$ visual angle, with the face occupying about $8 \times 12^\circ$. They were presented in a sequence of pseudorandom permutations that was counterbalanced across subjects. The sequence was designed so that each person was equally often preceded by each of the remaining persons, to

minimize carry-on effects from one condition to the next. Each person was presented six times for 15 s. Like in our previous study on romantic love (Bartels and Zeki, 2000), the volunteers were instructed to simply view the pictures and to relax. Since subjects reported after the scan (see below) that their emotions were less intense during the last cycle of photopresentations, the last repeat was omitted from analysis.

fMRI scanning

Subjects were scanned in a 2T Siemens Vision scanner (Erlangen, Germany), using a T2* weighted echo planar imaging (EPI) sequence that maximizes blood oxygen level dependent (BOLD) signal. Whole brains were acquired with 48 slices (1.8-mm thick, 1.2-mm gap) of 64×64 pixels, leading to a resolution of $3 \times 3 \times 3$ mm. Echo time (TE) was 40 ms. The repetition time (TR) was 3.694 s (for technical reasons, subjects 1–3 had a TR of 4.553 s) and scanning sessions lasted 14 min. After the functional session, a T1 weighted high-resolution structural scan was obtained to detect potential abnormalities (none was detected).

Data analysis and statistical tests

Subjects were analyzed separately using SPM99 (www.fil.ion.ucl.ac.uk/spm) (Friston et al., 1995). Images were (i) spatially realigned to compensate for head-movements; (ii) 'time-sliced' using sinc-interpolation to compensate for the time-lag between subsequent slices, leading to images obtained at a single time-point; (iii) spatially normalized to SPM's EPI template that resembles the 305-average brain from the Montreal Neurological Institute; (iv) spatially smoothed using a Gaussian filter of 10-mm full width at half height to reduce spatial noise and to compensate for anatomical differences among the subjects in view of the random-effects population analysis. A multiple regression was performed on each brain separately, using SPM99. Each of the persons shown in the stimuli and the rest condition were modeled using a separate regressor [box car, convolved by the hemodynamic response function (HRF)]. Additional regressors were included to model the six head-movement parameters obtained during the realignment (translation and rotation in 3D) and the overall baseline. Before regression, the functional data were temporally convolved with the HRF to minimize nonfunctional high-frequency noise and high-pass filtered with a cutoff period of 320 s to reduce slow drifts of the signal. A random effects analysis was then performed, in which the difference images from all subjects for a given contrast were submitted to a one-sample *t*

Table 1
Post-scan assessment of emotions felt for persons viewed during the scan

	cO	cA	cU	aF	aA	aU
Friendship	6.2 ± 3.1	4.7 ± 2.9	2.6 ± 2.5	7.9 ± 1.8	3.9 ± 1.8	1.5 ± 1.2
Love	8.3 ± 1.3	4.1 ± 2.5	2.3 ± 2.7	6.1 ± 2.3	2.1 ± 1.4	1.1 ± 0.3
Dislike/contempt	1 ± 0	1.5 ± 1.2	1 ± 0	1.1 ± 0.3	1.8 ± 1.7	1 ± 0
Indifference	1.2 ± 0.8	2.6 ± 2.6	4.9 ± 3.6	1.3 ± 0.8	3.3 ± 2.3	5.5 ± 3.9
Wanting to protect	7.7 ± 2.2	5.4 ± 1.6	3.1 ± 2.6	4.5 ± 3.1	1.7 ± 1.3	1.3 ± 1.1
Admiration/respect	6.4 ± 3.3	3.1 ± 2.1	1.6 ± 1.2	6.3 ± 2.7	3.2 ± 1.9	1.7 ± 1.7
Arousal/eroticism	1.6 ± 1.9	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0
Tender/sentimental feelings	8.7 ± 0.6	5.1 ± 2.1	2.8 ± 2.3	6.5 ± 2.5	2.4 ± 1.9	1.5 ± 1.2

Mean \pm SD across all 19 mothers.

1 = none; 5 = medium; 9 = intense. cO: own child; cA: child acquaintance; cU: unknown child; aF: (adult) best friend; aA: (adult) acquaintance; aU: (adult) unknown person.

test. This is a population test where the significance values assigned to each voxel indicate the likelihood of its being activated in the whole population from which the sample (our 19 subjects) has been drawn (Friston et al., 1999). In our case, the population is that representing mothers of young children in this study, or people in deep love in the previous study (Bartels and Zeki, 2000). In an additional analysis, the difference images of the 17 volunteers from our previous study on romantic love (contrast: loved partner vs. three friends) were compared to the difference images of the 19 mothers (contrast: own child vs. acquainted child) in a two-sample *t* test, allowing a statistical comparison of these two populations. In a further analysis, we reanalyzed our previous study on romantic love considering the 11 female volunteers separately from the 6

males. This allowed us to make female-only comparisons of maternal and romantic love, to confirm that the differential involvement of regions in maternal and romantic attachment is not due to gender differences. The population comparison was also repeated using only female volunteers from both studies. Regions reported here reached a threshold of $P < 0.001$ ($Z > 3.61$) uncorrected with an extent threshold of six voxels unless stated otherwise. Regions hypothesized to be active, based on the activity obtained in our previous study on romantic love (Bartels and Zeki, 2000), or based on their high density of oxytocin or vasopressin receptors [e.g., substantia nigra (SN)] (Loup et al., 1991), or on their critical involvement in maternal behavior (e.g., periaqueductal gray, PAG) (Miranda-Paiva et al., 2003) were tested for activity

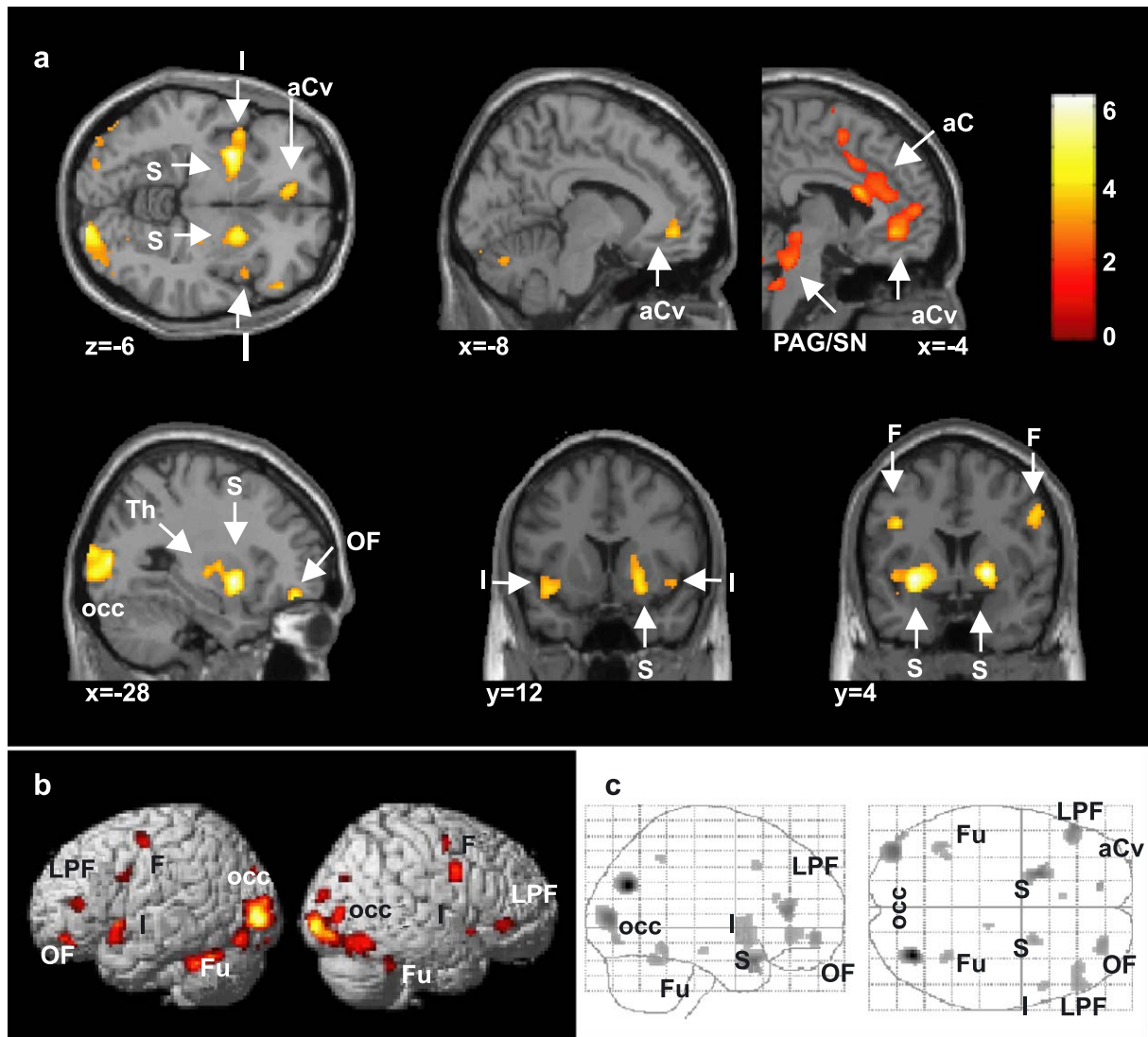


Fig. 1. Activations with maternal love. (a,b) Activations revealed when mothers viewed their own child versus an age and familiarity matched acquainted child (contrast: cO vs. cA), superimposed on a template structural brain. For illustration, sections and rendered brains are thresholded at $P < 0.005$, uncorrected, with an extent threshold of 6 voxels ($Z = 2.88$, random effects, $n = 19$), the back-set section at $P < 0.05$ to show the extent of activity in the aC (overlapping with romantic love activity). Note that all labeled regions reached a threshold of at least $P < 0.001$ (uncorrected) or $P < 0.05$ (corrected) (see Table 2). (c) Control for emotional valence: the same results were obtained with the contrast [(cO vs. cA) vs. (aF vs. aA)], that is, when activity related to adult friendship was subtracted from maternal love. Shown are glass-brain views ($P < 0.001$, uncorrected) to provide an overview of this contrast in the whole brain. Abbreviations: aC = anterior cingulate cortex; aCv = ventral aC; C = caudate nucleus; F = frontal eye fields; Fu = fusiform cortex; I = insula; LPF = (ventral) lateral prefrontal cortex; occ = occipital cortex; OF = orbito-frontal cortex; Tha = thalamus; S = striatum (consisting of putamen, caudate nucleus, globus pallidus); PAG = periaqueductal (central) gray; SN = substantia nigra. Color scale: Z-values, applies to sections only. Sections: transverse: bottom = right, coronal: right = right.

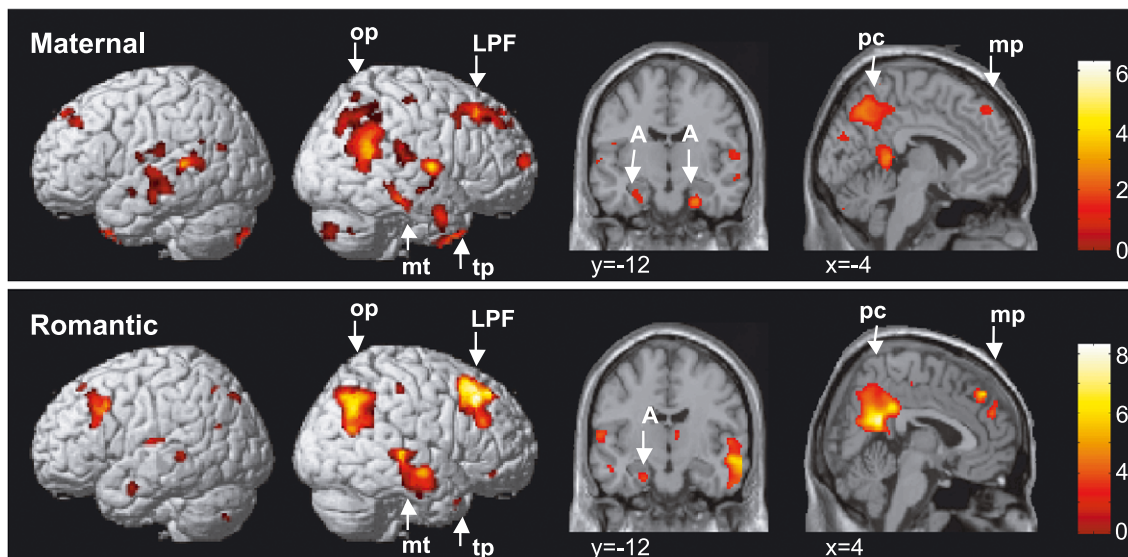


Fig. 2. Deactivated regions with maternal and romantic love. The sections and rendered views show regions whose activity was suppressed with maternal love (cO vs. cA) (top). These regions were the same as those that were deactivated with romantic love (viewing loved partner vs. friends) in our previous study (bottom). All labeled regions reached significance at $P < 0.05$, corrected for small volume (for illustration, following thresholds were used—top: $P < 0.05$, uncorrected; bottom: $P < 0.001$, uncorrected). Abbreviations: A = amygdaloid cortex, pc = posterior cingulate cortex, mp = mesial prefrontal/paracingulate gyrus; mt = middle temporal cortex; op = occipitoparietal junction; tp = temporal pole.

using a small volume correction (SVC) for false discovery rate (FDR) (Genovese et al., 2002) with a threshold of $P < 0.05$ (corrected). The small volume consisted of a sphere of 10-mm

radius, centered on the most significant voxel of the clusters activated in our previous study (Bartels and Zeki, 2000), or centered on the midpoint of an anatomically defined structure in

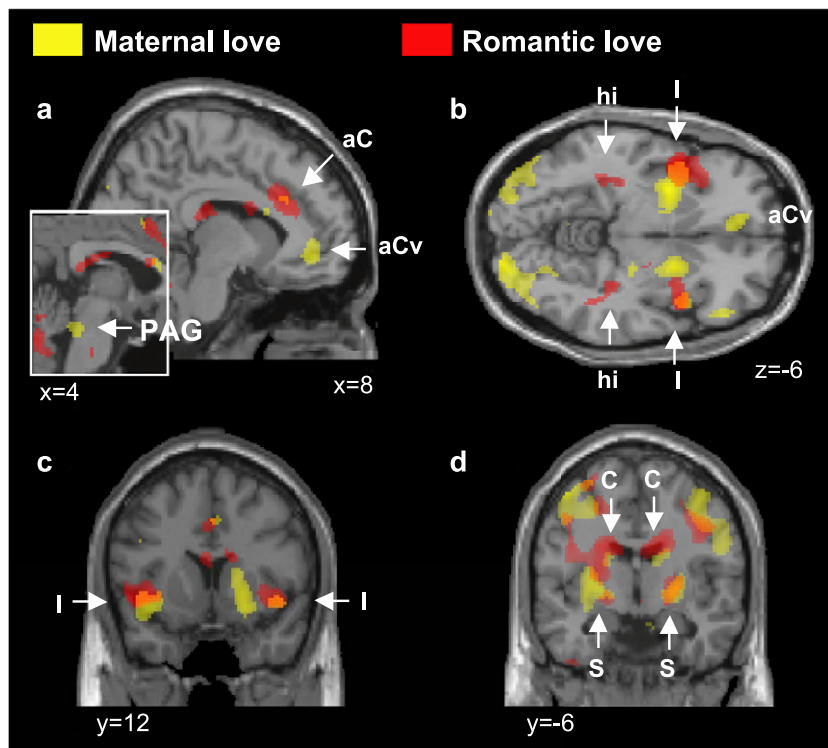


Fig. 3. Overlap between activity of maternal love and romantic love. Activity obtained in this study (contrast: cO vs. cA) was colored in yellow and overlaid on sections through a template brain, along with activity obtained in our previous study on romantic love (contrast: 'loved partner vs. friends') colored in red. Note that all regions displayed here for romantic love also reached significance when only female or only male subjects were included ($P < 0.001$, see Methods and text). The activation of aCv with maternal love overlapped with activation of the same region in female subjects only in romantic love ($P < 0.005$). For illustration, a–c were thresholded at $P < 0.01$, and d with $P < 0.05$, to reveal overlapping activity in the caudate nucleus. hi = hippocampus. See Fig. 1 for additional abbreviations.

the case of the substantia nigra (SN) and the periaqueductal gray (PAG). For completeness, Table 2 reports bilateral activities even if activity was significant only in one hemisphere.

Post-scan questionnaire

After the scan, each mother completed a post-scan questionnaire in which she rated the intensity of eight different feelings she felt during the scan for each of the people viewed, on a scale from 1 to 9 (1 = no feeling, 5 = medium, 9 = very intense). The results are listed in Table 1. The mothers were also asked to report any other associations or emotions that they had while viewing each of the persons. No consistent pattern emerged other than the expected one. One mother reported strong associations to a recent argument with her husband, which also affected the emotions she felt while viewing her child. She was therefore excluded from the study, leading to a total of 19 individuals included in the analysis.

Results

The design of this experiment, like our previous one (Bartels and Zeki, 2000), allowed us to determine the activation related to maternal love while at the same time controlling for the effects of familiarity, friendly feelings and visual input. The activity observed depended therefore primarily on attachment-specific emotions that our volunteers experienced during the presentation of the photographs. These were assessed in a post-scan questionnaire (see Methods and Table 1) and corresponded to those expected by the social and emotional context of the people viewed.

Activations with maternal love

Fig. 1 shows activity obtained when mothers viewed their own child compared to that when they viewed an age-matched child whom they were well acquainted with. Contrasts with a less stringent control of the unknown child (cU) led to the same results with slightly elevated significance (not shown). All activated regions were bilateral, as in our previous study, and achieved a similar significance [random effects analysis, $n = 19$, $P < 0.001$ ($Z > 3.61$), uncorrected], and regions hypothesized to be active reached $P < 0.05$, corrected for a small volume (Methods and Table 2). Activations are listed together with their significance values and Talairach coordinates in Table 2.

In the cortex, activity was found in the medial insula and in the cingulate gyrus dorsal and ventral of the genu (BA 24), all overlapping with activity observed with romantic love (activity ventral of the genu was present in romantic love only in females). Activity specific to this study included regions in the lateral orbito-frontal cortex and in the lateral prefrontal cortex (LPF). We also noticed activity in regions that are only indirectly associated with higher cognitive or emotive processing (see Discussion): a region near to the frontal eye fields, the occipital cortex (near visual area V3) and the lateral fusiform cortex.

Subcortical activity was also bilateral and overlapped with that found with romantic love in the striatum (putamen and the globus pallidus, and the head of the caudate nucleus at lower thresholds of $P < 0.05$) and with thresholds of $P < 0.05$ in the substantia nigra and in subthalamic regions. Additionally, activity was found in the postero-ventral part of the thalamus and in a region overlapping the periaqueductal (central) gray (PAG) of the midbrain, none of which

were active with romantic love. The activity in the midbrain also overlapped with the reticular formation, the locus ceruleus and raphe nucleus. It is likely to originate from activity in PAG as this region has not only a high concentration of oxytocin receptors (as does locus ceruleus), but it is also known to be involved in maternal

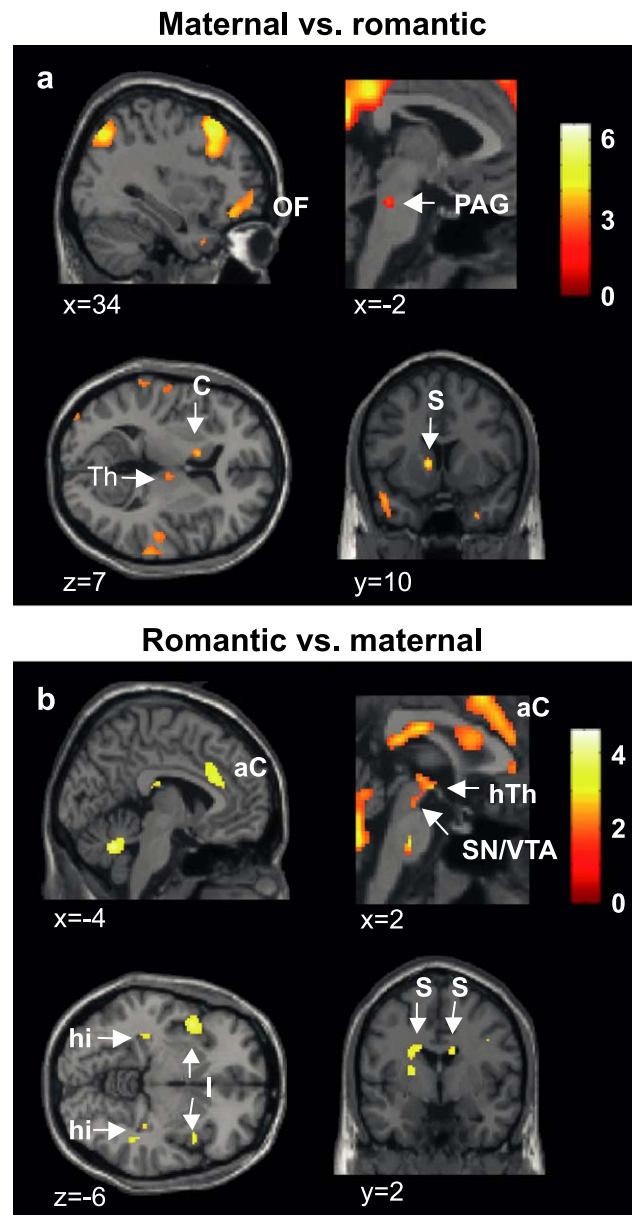


Fig. 4. Population comparison (two-sample t test) between activity obtained with romantic love and maternal love ($n = 17$ and $n = 19$, respectively). (a) Contrast maternal vs. romantic. Note that regions other than the labeled ones have to do with greater deactivation obtained in romantic love, and are of less interest here. (b) Contrast romantic vs. maternal: although most regions apparent here (apart from hippocampus) were also active with maternal love, they appear significant here because romantic love produced results of higher significance than maternal love. Same results were achieved when only female subjects ($n = 11$) were included from the romantic love study. Thresholds for illustration: $P < 0.005$, magnifications at $P < 0.05$ (uncorrected). HTh = hypothalamus; VTA = ventral tegmental area. See Fig. 1 for additional abbreviations.

behavior (Jenkins et al., 1984; Lonstein and Stern, 1998; Miranda-Paiva et al., 2003).

To determine whether the activity detected here could be confounded by some more general feelings of friendship, or

possibly by an enhanced arousal evoked by the stronger emotional valence of viewing one's own child, we calculated the contrast ([cO vs. cA] vs. [aF vs. aA]). This subtracts activity related to friendship (aF vs. aA) from that related to maternal attachment (cO vs. cA).

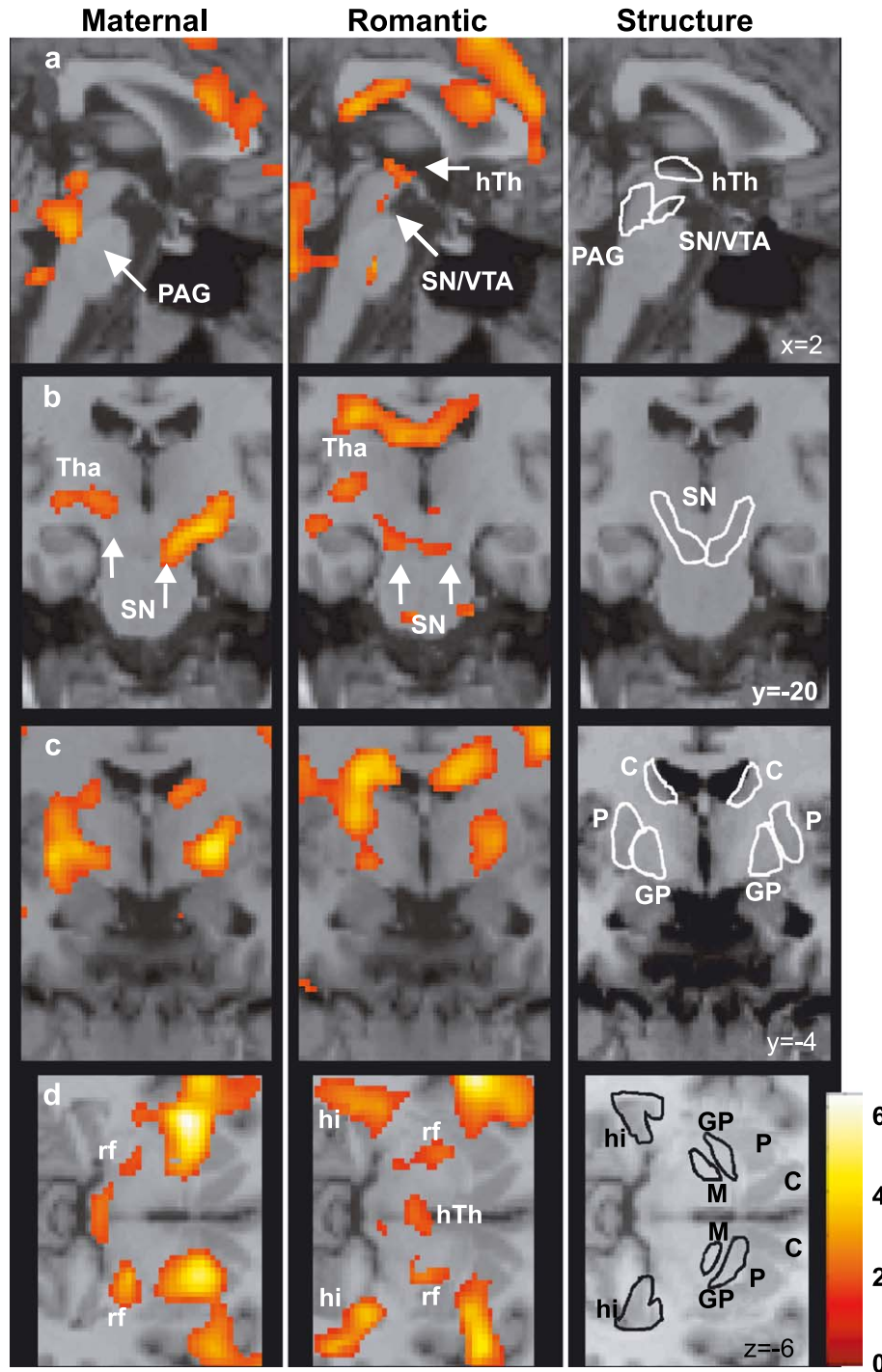


Fig. 5. Regions that contain a high density of receptors for oxytocin and vasopressin and their overlap with activity related to maternal and romantic love. All labeled regions contain a high density of these attachment related neurohormones in the human (Loup et al., 1991). Abbreviations: C = caudate nucleus; GP = globus pallidus; hi = hippocampus; hTh = hypothalamus; P = putamen; PAG = periaqueductal (central) gray; M = nucleus of Meynert; rf = retrorubal fields/intralaminar/subthalamic nuclei; SN = substantia nigra; Tha = lateral thalamus; VTA = ventral tegmental area. For illustration, the extent of activity is shown at thresholds of $P < 0.05$, uncorrected. Sections have the same orientation as in previous figures. (a): sagittal, (b,c): coronal, (d): transverse.

The same activity as in cO vs. cA emerged (Fig. 1c). To see whether friendship is neurally related to love, we calculated the main effect of friendship (aF vs. aA), which revealed no significant activity ($P < 0.001$, uncorrected). The latter two results lead us to conclude that the activity described above is specific to maternal love.

Deactivations with love

Deactivations are also of interest here since emotions are likely to be the product of both increases and decreases of activity in specialized regions. Although weaker, the pattern of deactivations was remarkably similar to that observed with romantic love. The typical pattern was bilateral and affected the right hemisphere substantially more; it was focused on the middle prefrontal cortex (BA 9, 46, 10), the parieto-occipital junction/superior temporal sulcus (BA 39, 40), the medial prefrontal/paracingulate cortex (BA 9/32) and the temporal poles. It also involved the posterior cingulate gyrus (BA 29, 30), the medial cuneus (BA 7, 31) and the amygdaloid region (Fig. 2).

Comparison of maternal love and romantic love

The similarity of the present results compared to those obtained in our previous study on romantic love is striking (Bartels and Zeki, 2000); several regions overlap precisely, while others are specific to each form of attachment. A color-coded overlay of the activity associated with maternal and romantic love is shown in Fig. 3. Overlapping regions include those in the striatum (putamen, globus pallidus, caudate nucleus), the middle insula and the dorsal part of the anterior cingulate cortex. A gender-separated analysis of the romantic love data revealed that all of the above regions were active in both genders, reaching significance ($P < 0.001$) when only male or only female subjects were included. Romantic love activated specifically the dentate gyrus/hippocampus and the hypothalamus (the latter with $P < 0.005$; avg. coords.: $-3, -12, -14$ in gender-separated analyses), which were not active with maternal love (at $P < 0.1$). Both these regions were active in separate analyses using only male or female subjects, thus allowing us to rule out gender-specific effects and confirming that these regions were specifically active in romantic but not maternal attachment. The ventral tegmental area (VTA) was active with romantic love. Its more posterior part was likely to be involved in maternal love as well, which is difficult to tell due to overlap with activity in the substantia nigra (SN). Activity in the dorsal part of the anterior cingulate cortex was considerably more prominent in romantic love than with maternal love. The ventral part of the anterior cingulate cortex that was activated with maternal love also reached significance of $P < 0.005$ in the female-only analysis of the romantic love study, while it was not activated in males (at $P < 0.1$). Activity entirely specific to maternal love included the lateral orbito-frontal cortex, and, subcortically, the periaqueductal gray (PAG), both of which were not active with romantic love (overall or gender-specific analyses at $P < 0.1$).

The same differences were revealed when the two data sets were submitted to a statistical population test (see Fig. 4 and Methods), which revealed significant results despite the relatively small samples for this two-sample t test [$P < 0.001$, uncorrected, $n = 19$ (mothers) and $n = 17$ (romantic) or $n = 11$ (females romantic), respectively]. This comparison also revealed all the areas that we described in our previous study on romantic love since the results obtained for romantic love were generally more significant

Table 2
Activations and deactivations with maternal love

	Left				Right			
	x	y	z	Z	x	y	z	Z
<i>Activations (Brodmann area)</i>								
Middle insula (14)*	-42	8	-4	3.97	46	12	-6	3.22
Anterior cingulate dorsal (24)*	-10	26	30	2.85	10	34	18	2.35
Anterior cingulate ventral (24)	-8	44	-6	3.89	10	44	-6	1.87
Caudate nucleus (dorsal head)*	-22	2	16	2.37	14	-2	18	2.67
Putamen (medial)/globus pall.*	-30	2	-4	6.16	22	4	0	6.29
Subthalamic nucleus	-28	-14	2	3.60	20	-18	-10	4.25
Lateral thalamus	-18	-18	0	2.59	28	-20	-2	3.02
Periaqueductal gray (PAG)*					2	-32	-24	3.36
Substantia nigra (SN)*					14	-22	-14	3.73
Lateral prefrontal cortex (46/45)	-52	36	12	4.03	54	38	-2	4.66
Lateral orbitofrontal cortex	-28	46	-14	4.65	26	54	-14	2.74
Frontal eye fields (6)	-40	4	30	4.29	54	2	36	3.92
Lateral fusiform gyrus	-38	-58	-24	4.69	28	-48	-22	5.33
Occipital cortex	-30	-90	2	5.04	18	-98	-6	5.20
Dorsal occ. cortex (V3A)	-16	-88	34	3.49	30	-74	30	3.47
<i>Deactivations</i>								
Prefrontal cortex								
Mes. sup. front gyrus (32/9)*	-4	44	46	2.29				
Lateral prefront (9/46)*	-30	40	42	2.59	30	28	50	2.96
Ventro-lateral prefront (10)					34	44	42	2.51
					26	64	12	2.76
Parietal cortex								
Lateral parietal (7)					46	-74	36	2.90
Parieto/occ. junction (39/40)*	-40	-52	26	2.91	46	-46	30	3.48
	-58	-40	10	3.15	42	-54	6	3.22
Temporal cortex								
Medial temporal (21)*	-50	-26	-6	2.40	66	-32	-16	2.41
Medial STS	-50	-22	18	2.04	44	-20	16	4.06
Medial STG	-62	-18	2	2.31	60	-6	8	3.21
Inferior temporal lobe	-38	-24	-26	2.92	56	-24	-22	2.61
Temporal pole*	-40	16	-42	2.59	42	14	-46	3.16
Posterior cingulate cortex								
Retrosplenium (26/29/30)*	-6	-46	6	3.15	10	-44	8	5.86
POS (31/7)*	-22	-60	16	2.51	22	-60	26	4.71
Medial precuneus (7)*					0	-74	46	3.84
Amygdaloid region*	-28	-14	-20	2.16	22	-6	-34	3.80

* Significant at $P < 0.05$ in at least one hemisphere, corrected for small volume (Methods).

(both activations and deactivations). The latter might be so, first, because volunteers for the romantic study had been selected for being in a very intense state of love, which was not guaranteed for our mothers, and, secondly, because the mothers felt very positively toward the acquainted children as well (see Table 1).

Neurohormone binding sites and love

We specifically examined regions in the human brain known to contain high densities of receptors for the attachment-mediating neurohormones oxytocin and vasopressin (Loup et al., 1991). Fig. 5 shows activity that was specific to maternal and romantic love in relation to sites with a high density of oxytocin or vasopressin receptors. Activity related to both forms of attachment overlapped with receptor-rich sites in the substantia nigra, the globus pallidus, the nucleus of Meynert (substantia innominata/substriatal grey) and structures that are too small to assign reliably with fMRI, including subthalamic nuclei, the bed nucleus of the stria terminalis (BNST) and the ventral tegmental area (VTA), while the amygdala was deactivated. Romantic love activated the hilum of the dentate gyrus/hippocampus and the hypothalamus, and maternal love the periaqueductal gray (PAG). Together, this comprises almost all of the regions critical for these attachment-mediating neuropeptides in the human brain, the major exceptions being the septal nucleus and the preoptic region, which were not detected in either study (Jenkins et al., 1984; Loup et al., 1991).

Discussion

This study complements our earlier one and shows that (i) romantic and maternal love both involve a unique and overlapping set of areas, as well as areas that are specific to each; (ii) the activated regions belong to the reward system and are also known to contain a high density of receptors for oxytocin and vasopressin, suggesting that the neurohormonal control of these strong forms of attachment observed in animals also applies to the human; (iii) both forms of attachment suppressed activity in regions associated with negative emotions, as well as regions associated with ‘mentalizing’ and social judgment. This suggests that strong emotional ties to another person inhibit not only negative emotions but also affect the network involved in making social judgments about that person. Overall, the results lead us to conclude that attachment processes employ a push–pull mechanism that activates a specific pathway of the reward system of the brain. At the same time, circuits that are responsible for critical social assessment and for negative emotions are deactivated.

Attachment and reward

Both studies on maternal and romantic attachment revealed activity that was not only overlapping to a large extent with each other, but also with the reward circuitry of the human brain. The latter is increasingly seen in a more encompassing behavioral context (White, 2002), recognizing that regions in addition to the core regions [SN, nucleus accumbens, sublentiform extended amygdala (SLEA)] such as the striatum (classically associated to motor functions) and other regions receiving projections from the core regions (see below) play a direct role in human reward (Kelley and Berridge, 2002; White, 1989). For simplicity, we use the term ‘reward’ here to refer to a complex circuitry and its diverse

functions, which also include novelty and salience. The striatum (caudate nucleus, putamen, globus pallidus) contains cells that respond to food and drink reward and it is activated by monetary reward stimuli (Elliott et al., 2003; Knutson et al., 2001; Schultz, 2000), by cocaine (Breiter and Rosen, 1999; Breiter et al., 1997), and sexual arousal in human and monkey (Arnow et al., 2002; Ferris et al., 2001; Karama et al., 2002; Rauch et al., 1999; Stoleru et al., 1999). The hypothalamic activation specific to romantic love could reflect the component of erotic arousal inherent to this sentiment (Arnow et al., 2002; Ferris et al., 2001; Karama et al., 2002). All regions commonly activated here have been involved in reward, although with less spatial specificity, for example, after acute administration of euphoria-inducing drugs such as cocaine (Breiter and Rosen, 1999; Breiter et al., 1997; Schlaepfer et al., 1998). We therefore believe that the particular subregions in the reward structures activated here reveal a general, modality-independent network that is specialized to mediate attachment. They should appear again if one were to repeat our study using auditory or olfactory stimuli instead of visual ones. Indeed, a recent study on mothers’ responses to infant cries activated some of the regions active here (e.g., substantia nigra, striatum, anterior cingulate), but also revealed activity in regions that we found to be deactivated (e.g., mesial prefrontal cortex) (Lorberbaum et al., 2002). However, that study used nonpersonalized stimuli [cries of children unknown to the mothers, compared to nonhuman controls (white noise)] and the stimuli elicited emotions in addition to maternal instincts, namely of anxiety and sadness in response to the child-cries, and annoyance to sound-bursts (Lorberbaum et al., 2002), therefore making it difficult to interpret.

Attachment and oxytocin

The neurohormones oxytocin and vasopressin have been shown to be crucially involved in both maternal attachment and adult pair-bonding in animals (Insel and Young, 2001; Kendrick, 2000; Pedersen, 1997), and may even play a more general role in mediating social memory and learning (Ferguson et al., 2000). Our results show that most regions charted by autoradiography to contain receptors for these neuropeptides in the human brain are activated by both maternal and romantic love (Jenkins et al., 1984; Loup et al., 1991).

The specific activation of a region overlapping with periaqueductal (central) gray matter (PAG) with maternal but not romantic love recalls this region’s important role in rats, where maternal behavior can be inhibited when this region is pharmacologically or physically targeted (Lonstein and Stern, 1998; Miranda-Paiva et al., 2003). Our results therefore constitute the first evidence that PAG may be specifically involved in human maternal (and not pair-bonding) behavior. PAG receives direct connections from the limbic areas (including those activated here), and contains a high density of vasopressin and oxytocin receptors (Jenkins et al., 1984). It is also known to be involved in endogenous pain suppression during experience of intense emotional experiences such as childbirth, and recent evidence demonstrates that this is facilitated through oxytocinergic action (Lund et al., 2002). PAG has direct connections with the orbitofrontal cortex (Cavada et al., 2000), which perhaps accounts for the equally specific activation of the latter with maternal love. The lateral orbitofrontal cortex is activated with pleasant visual, tactile and olfactory stimuli, with its response depending on pleasantness rather than intensity of stimulation (Francis et al., 1999; Kawabata and Zeki, 2004; Rolls et al.,

2003). Here, its activity is likely to reflect one aspect of the pleasant emotions associated with motherly love.

The activation of the VTA with romantic and probably also maternal love corresponds to this region's important role in rats, where at least maternal behavior can both be facilitated or disrupted by the presence or absence of oxytocin in it (Pedersen et al., 1994). Although closely related, the nine-amino-acid peptides oxytocin and vasopressin have different distributions of binding sites in the brain and their function concerning maternal behavior or pair-bonding can be differentiated (Winslow et al., 1993). The specific activation of the dentate gyrus/hippocampus with romantic love and its specificity for vasopressin constitutes the first evidence for similar functional/neurohormonal associations in the human (Loup et al., 1991).

The anterior cingulate cortex and its distinct roles in emotive processing

The anterior cingulate (aC) cortex has many subdivisions, many of which seem to be involved in different aspects of social or emotive processing (Devinsky et al., 1995). It should be noted that reference to activity in the 'anterior cingulate' has led to much confusion in the past, as it has been used to refer to functionally and anatomically entirely distinct subdivisions, in some studies even two separate Brodmann areas (24 and 32). Many of these subdivisions are spatially sufficiently separated to be distinguished with fMRI. Our activation there might pinpoint the location within the aC that has led to the disturbance of maternal behavior in animals when it was lesioned (Devinsky et al., 1995). The subgenual region of the aC is near (though not overlapping) an area activated by studies on sadness and anxiety (Liotti et al., 2000), suggesting a potential link to the mother's feelings of empathy and urge to care for her infant. By contrast, the dorsally located region was preferentially active with romantic love (weaker with maternal love) and lies ventral (though not overlapping) to one of the 'theory of mind' regions (Gallagher and Frith, 2003) and anterior (and not overlapping) to a region involved in the experience of social exclusion (Eisenberger et al., 2003). Overlapping activity is found in studies involving pleasant experiences, for example, pleasant touch (Rolls et al., 2003), potentially reflecting not the 'pleasantness' but the volunteer's knowledge of the positive intention behind it (Frith and Frith, 1999). Our results on human maternal and romantic attachment, in combination with previous studies, thus highlight the subdivision of the anterior cingulate cortex into regions of distinct involvement in social and emotive processing.

The medial insula

The insula has several subdivisions, some of which are concerned with visceral sensations and thought to mediate the 'gut feelings' of emotive states (Damasio, 1999). A recent study revealed a pathway for 'limbic touch' that bypasses somatosensory cortices and activates directly the middle insula, evoking pleasant feelings of touch and regulating 'emotional, hormonal and affiliative responses to caress-like, skin-to-skin contact between individuals' (Olausson et al., 2002). The activity obtained in that study overlaps precisely with that obtained here with both maternal and romantic love and may well reflect this sensory-emotive component that is common to and crucial for such caring relationships (Harlow, 1958). By contrast, the anterior part of the insula (not activated here) contains a distinct functional subdivision, and is

consistently activated by negative stimuli (Augustine, 1996; Buchel et al., 1998; Coghill et al., 1994; Garcia-Larrea et al., 1999; Kosslyn et al., 1996; Phillips et al., 1997).

Processing of faces

The activity in the face-selective lateral fusiform gyrus (FG) observed with maternal love could be explained by both, (i) increased attention to faces (George et al., 1999; Kanwisher et al., 1997; O'Craven et al., 1999; Wojciulik et al., 1998), and, more importantly, (ii) emotional valence leading to elevated activity in the FG (Pessoa et al., 2002). However, activity in the FG persisted even when we controlled for emotional valence, and romantic love did not produce activity in any visual area (even at $P < 0.1$). Furthermore, both attention to faces and their emotional valence additionally activate the superior temporal sulcus (STS) (Chao et al., 1999; George et al., 1999; Kanwisher et al., 1997; O'Craven et al., 1999; Pessoa et al., 2002; Wojciulik et al., 1998), while this region was suppressed here. Therefore, a mechanism that is specific to maternal attachment may account for the activity observed here in the FG. We speculate that the rapid rates with which the facial features of babies and young children change and the importance of reading children's facial expressions require a constant updating of the face-recognition machinery, leading to heightened activity in the FG (Gauthier et al., 1999).

Deactivation of the social judgment network

Both maternal and romantic love elicited an entirely overlapping set of deactivations, which can be subdivided into two sets of areas. Regions of the first set (middle prefrontal, inferior parietal and middle temporal cortices mainly in the right hemisphere, as well as the posterior cingulate cortex) play predominantly a role in cognition (attention, short- and long-term memory) but have also been shown to be involved in (often negative) emotions (Beauregard et al., 1998; Cabeza and Nyberg, 2000; Maddock, 1999). Lesions therein lead to impaired emotional judgment of mostly negative emotions (Adolphs et al., 2000) and artificial deactivation of the lateral prefrontal cortex leads to reduced depression (Menkes et al., 1999). However, the variable involvement of these areas in both positive and negative emotions (Beauregard et al., 1998; George et al., 1995; Kimbrell et al., 1999; Lane et al., 1997b; Mayberg et al., 1999) has led to the suggestions that activity in these regions may (i) be modulated through obligatory projections from limbic/paralimbic regions, potentially explaining facilitatory or inhibitory effects of mood on cognitive processing (in this case the latter) (Liotti et al., 2000; Mayberg et al., 1999) and (ii) reflect their supportive role for emotion-related imagery or recall (Cabeza and Nyberg, 2000; Fletcher et al., 1995; Maddock, 1999).

The second set of areas deactivated here (amygdala, temporal poles, parietotemporal junction and mesial prefrontal cortex) has consistently been associated to negative emotions and to social, moral and 'theory of mind' tasks. The amygdala is reliably activated in neuroimaging studies involving negative emotions, aggression and fear (Aggleton, 2000; Breiter et al., 1996; Morris et al., 1996), and lesion studies show its involvement in social and emotional judgment (Adolphs et al., 1998). The mesial prefrontal cortex, the parietotemporal junction and the temporal poles constitute a network of areas invariably active with 'mentalizing' or 'theory of mind', that is, the ability to determine other people's emotions and intentions (Brunet et al., 2000; Castelli et al., 2000; Frith and Frith,

1999; Gallagher and Frith, 2003). The same areas are also active in the assessment of social trustworthiness (Winston et al., 2002), of facial expressions (Critchley et al., 2000), in moral judgment (Greene and Haidt, 2002; Moll et al., 2002) and during attention to one's own emotions (Gusnard et al., 2001; Lane et al., 1997a).

In summary, our findings show that both romantic and maternal love activate specific regions in the reward system and lead to suppression of activity in the neural machineries associated with the critical social assessment of other people and with negative emotions. Since surprisingly little is known about social processing in the human brain, we should emphasize that the following interpretations are of a rather tentative nature. There is no doubt that future studies will address these points more explicitly. Nevertheless, a potential model may be that once one is closely familiar with a person (in a positive or negative way), the need to assess the social validity of that person is reduced. This correlates with a reduction of activity in the systems necessary for doing so; these findings therefore bring us closer to explaining in neurological terms why 'love makes blind'. The neural mechanisms suppressed here might be the same that, when active, are responsible for maintaining an emotional barrier towards less familiar people, corresponding to the avoidance behavior observed both in rats and in voles against pups or potential partners, which is reversed by administration of oxytocin (Insel and Young, 2001; Pedersen, 1997; Pedersen et al., 1982; Winslow et al., 1993). Our findings of consistently activated and deactivated regions with attachment may be indicative a fine balance between activity states of these regions that needs to be maintained to ensure a healthy social interaction. This may be important for the understanding of the severe psychological and clinical consequences that ensue when elements of this circuitry are interrupted, through inheritance, lesion or upbringing (Alexander, 1992; Benoit and Parker, 1994; Cassidy and Shaver, 1999; Suomi et al., 1975). The link of activated brain sites to the well-studied neurohormones oxytocin and vasopressin and their binding sites offers a surprisingly straightforward way for pharmacological intervention that could be used both to induce and maybe more importantly to suppress feelings of attachment, as it has been successfully done in animals (Ferguson et al., 2000; Insel and Young, 2001; Winslow et al., 1993).

On the whole, our results suggest a push–pull mechanism of attachment, that on one hand deactivates areas mediating negative emotions, avoidance behavior and social assessment, and on the other triggers mechanisms involved in reward.

These results have thus brought us a little, but not much, closer to understanding the neural basis of one of the most formidable instruments of evolution, which makes the procreation of the species and its maintenance a deeply rewarding and pleasurable experience, and thereby ensures its survival and perpetuation.

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