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Neuroimaging evidence for the emotional potency of odor-evoked memory

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Abstract

To assess past behavioral reports of the emotional distinctiveness of odor-evoked memories, functional magnetic resonance imaging (fMRI) was used to compare regions of activation during recall triggered by olfactory and visual cues that were connected to a personally meaningful memory and a comparable control cue presented in olfactory and visual form. Five healthy right-handed females experienced both behavioral and fMRI memory testing. fMRI analyses indicated significantly greater activation in the amygdala and hippocampal regions during recall to the personally significant odor than any other cue, and behavioral responses confirmed that emotional responses were greatest to the personally meaningful odor. These findings provide convincing neurobiological evidence that the subjective experience of the emotional potency of odor-evoked memory is correlated with specific activation in the amygdala during recall and offers new insights into the affective organization of memory.

Keywords: Olfaction; Emotion; Memory; fMRI

1. Introduction

In *Swann's Way* (Proust, 1919), the smell of a madeleine biscuit dipped in linden tea triggers intense joy and memory of the author's childhood. This experience, now referred to as the "Proust phenomenon," is the basis for the hypothesis that odor-evoked memories are more emotional than memories elicited by other sensory stimuli. To date, there is good behavioral support for this proposition. In a number of cross-modal laboratory and autobiographical studies of episodic memory comparing olfactory, visual, verbal, tactile and auditory variants of the same cues Herz and colleagues have consistently shown that when a cue is presented in its olfactory form, memories are more emotional as indicated by self-report and physiological responses, such as heightened heart-rate, than memories evoked by the same cue presented in other sensory formats (Herz, 1998; Herz & Cupchik, 1992, 1995; Herz & Schooler, 2002). Researchers have also compared odors with other sensory stimuli to examine differences in autobiographical memories and observed that odor-cued memories were rated as more pleasant and thought of less often than memories elicited by visual or verbal variants of the same items (Rubin, Groth, & Goldsmith, 1984). Chu and Downes (2002) also noted that compared to verbal odor labels, odors themselves were especially potent reminders of autobiographical experiences. These findings strongly argue that odors are more emotional and evocative memory cues than other sensory stimuli.

The olfactory system is unique among the senses in projecting directly to the amygdala (Aggleton & Mishkin, 1986; Cahill, Babinsky, Markowitsch, & McGaugh, 1995; Cahill & McGaugh, 1998). It is well established that an intact amygdala is critical for the expression and experience of emotion (Aggleton & Mishkin, 1986; LeDoux, 2000) and substantial evidence suggests that the amygdala is necessary for human emotional memory (Aggleton & Mishkin, 1986; Cahill et al., 2001; Cahill & McGaugh, 1998; LeDoux, 2000) and emotional perception and cognition (Dolan, 2002). Thus, neuroanatomical connections support the emotional salience of odor-evoked recall. However, no direct neurobiological evidence to date has shown that a special relationship exists between olfaction and emotion during memory.

Over the past decade, neuroimaging techniques have been applied to study human olfaction (Zatorre, Jones Gotman, Evans, & Meyer, 1992). Functional magnetic resonance imagining (fMRI) in particular has elucidated a number of important features of olfactory processing in both healthy

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subjects as well as patient populations (Levy, Henkin, Hutter, Lin, & Schellinger, 1998; Sobel, Prabhakaran, Desmond et al., 1998; Williams et al., 1997; Yousem et al., 1999, 1997). In general, odor perception elicits activation in the piriform, entorhinal and orbitofrontal cortex, amygdala and hippocampus. The thalamus, caudate nucleus and insula are also involved (Poellinger et al., 2001).

Considering the distinguishing behavioral and neuroanatomical features of olfaction and emotional-memory, we hypothesized that the amygdala should be especially activated during meaningful episodic memories elicited by odors in contrast to other sensory cue-types. Neuroimaging techniques, such as fMRI, are ideally suited to assess whether there are neurological differences between the experience of significant personal memories elicited by odors in comparison to memories elicited by the same cues mediated by other senses, such as vision. The goal of this study was thus to conduct a cross-modal autobiographical memory study using fMRI and to test hypothesis that the emotional potency of odor-evoked memory is correlated with specific neurobiological activation in the amygdala.

2. Materials and methods

2.1. Participants

Five normal right-handed female subjects were chosen from 12 volunteers on the basis of a pre-test interview (age range 21–25; mean = 22). One to two months prior to the scanning procedures, potential participants were telephoned and asked to identify a perfume whose sight and scent elicited a specific, pleasant, personal memory associated to a person, place or event. Individuals were asked to give a brief description of their memory and to rate how emotional they felt about it (1 = not at all emotional; 9 = extremely emotional) and how pleasant the memory was to them (1 = extremely negative; 9 = extremely positive). Criteria for participant selection was recalling a positive, personal memory in which both the smell and sight of a perfume figured. For example, participant 1 stated that her memory was:

> A trip to Paris when I was in 4th grade and me sitting and watching my mother while she was getting ready to go out and the Opium perfume that she used which was on her vanity.

The mean emotional intensity of selected participants' memories was 6.40, with a mean of 7.60 for positive emotional valence. Informed consent, approved by both the Institutional Review Boards of Brown University and Memorial Hospital of Rhode Island, was obtained from all participants. All participants had a self-reported normal sense of smell and were free from respiratory infections and allergies, in good neurological and medical health, and met all MRI screening criteria; none were regular smokers and none were pregnant.

2.2. Test stimuli

Each participant's perfume stimulus, as reported in the pre-test interview, was purchased and prepared for olfactory delivery at 100% concentration and absorbed into diethyl phthalate (DEP) pellets. These items are referred to as the experimental stimuli and were: Royal Secret; Lilac Perfume Oil from the Body Shop; Opium for Women; White Musk from the Body Shop; Juniper Breeze from Bath and Body Works. The control stimulus was a generic unmarketed perfume presented in both its olfactory and visual form, and was the same for all participants (obtained from Haarmann & Reimer, Inc.). Pre-testing established that the control odor and various experimental odors were equivalent in perceived intensity. During functional scanning, odor stimuli were presented via an olfactometer that was developed for this research. Visual stimuli were presented as color photographs of the experimental and control fragrance bottles projected onto a LCD screen in front of the subject (viewed by an angled mirror) that was linked to a computer and manually operated through slide-show software.

2.3. Olfactometer

The olfactometer consists of five identical channels adjusted to deliver a constant flow rate of 2 l/min of odorized air from a diaphragm compressor (Precision Medical Inc., Easy Air, PM15P). The flow from any one or more channels is selectable by the experimenter with a designated switch. These switches activate 12 V dc solenoid valves that are installed in each of the delivery tubes. All tubing is 0.309 cm i.d. × 0.635 cm o.d. and all interconnecting fittings are Teflon. One DEP odor saturated pellet was placed in a Teflon T-fitting for installation in one of the delivery tubes. A check valve was installed in the output side of the T-fittings to prevent back flow and mixing of odors within the system. One output tube was designated for the control odor and one tube for the experimental odor, which was changed for each subject. The output end of each tube was adjusted for each subject so that it was at a distance of 5 cm from the subject's nose. During fMRI testing, the olfactometer was manually operated from within the technician's booth, with the tubing extending through a porthole connecting to the MRI room. A constant air flow of 265.2 m^3/min was generated from a fan positioned one foot behind the participant's head for the entire time that participants were in the scanner.

2.4. Behavioral procedures during scanning

During functional scanning, participants were presented with four sensory stimuli: experimental odor (EO), experimental visual (EV), control odor (CO), control visual (CV), in three blocks of 16 trials. Sensory stimuli were presented on half of the trials, while the first trial of every block and between each stimulus trial was an air-only trial. Each sensory stimulus was presented twice per block and the order

of stimulus presentation was randomly determined across blocks and subjects. During the olfactory and visual trials, participants were asked to consider whether the stimulus evoked a memory, and if it did to remain thinking about one (same) memory while the stimulus was present. During the visual trials no odor stimuli were present and during the olfactory trials there was no visual stimulation. During the air-only trials participants were asked to clear their mind as much as possible. Every trial lasted for 30 s. There was a 2 min intertrial interval between blocks during which no scanning occurred.

2.5. Behavioral procedures post-scanning

After the scanning procedure, participants were escorted to an adjacent room and presented with their four sensory stimuli one at a time. To evaluate the EO and CO, the participant sniffed a T-fitting containing the appropriate DEP pellet. To evaluate the visual stimuli, the EV and CV were presented as 20.32 cm × 25.4 cm color photographs. Participants were first asked to verify that the stimulus now presented was the same as they had experienced in the scanner. They were then asked what they had been thinking about when presented with the stimulus, and to rate on a 1–9 Likert scale how emotional they felt during stimulus presentation (1 = not at all emotional, 9 = extremely emotional). Subjects were also asked if they were reminded of the same memory or association each time the stimulus was presented throughout the scanning procedure. Participants were then asked to evaluate how much they liked the stimulus (1–9 Likert scale). For EV and EO presentations, subjects were further questioned as to whether what they reported thinking about during scanning was the same memory they had described during the pre-test interview.

2.6. MR imaging

A 1.5 Tesla Siemens Medical Systems Symphony MR system with Quantum gradients was used to scan the participants. A circularly polarized quadrature head coil was used to receive the radio frequency pulses. Mild cushioning minimized head movements. The entire experiment consisted of the acquisition of a single high-resolution T1-weighted anatomical scan and several hundred T2∗-weighted echo planar images (EPI) tuned to the intrinsic blood oxygenation level dependent (BOLD) contrast mechanism (Kwong et al., 1992; Ogawa et al., 1992). The high-resolution, three-dimensional anatomical data set was acquired into 160 slices with 1 mm × 1 mm × 1 mm resolution (Siemens MPRAGE sequence, TR = 1900 ms, TI = 1100, TE = 4.1 ms, 256×256 matrix, 256 mm field of view (FOV), 1 mm slice thickness). EPI images were acquired in a transverse plane and consisted of 25 slices sampled approximately from the inferior extent of the temporal lobes to the superior extent of the corpus callosum in order to acquire images of orbitofrontal cortex and amygdala. Each slice was 3 mm thick with FOV of 192 mm and an image matrix of 64 × 64. The EPI sequence used a TR = 2 s and a TE = 38 ms.

2.7. Methods for MRI data analyses

The MR images were transferred to Silicon Graphics workstations and manipulated and analyzed using Analysis of Functional NeuroImages (AFNI), (Cox, 1996; Cox & Hyde, 1997); 720 EPI volumes were acquired during the experiment in three “measurements” (blocks) of 240 volumes, each lasting 8 min. The first two volumes in each measurement were discarded due to T1 saturation effects, leaving a total of 714 EPI volumes that were analyzed for brain activation. Each participant’s MPRAGE and EPI image series were co-registered using the positioning coordinates from the scanner system. The MPRAGE was normalized to the standardized space of Talairach and Tournoux (Talairach & Tournoux, 1988) using tools provided in AFNI. Following motion correction, the EPI image set was also transformed to standardized space by adopting the landmarks defined in the MPRAGE and then analyzed for functional activation.

2.7.1. Motion correction

Each participant’s EPI images were co-registered to the first EPI volume in the experiment using a six-parameter rigid body transformation (Cox & Jesmanowicz, 1999) to correct for head movements. After the co-registered EPI images were normalized to Talairach space (Talairach & Tournoux, 1988), the data set was resampled to an isotropic resolution of 3 mm. This normalized and resampled EPI data set was then smoothed using an isotropic 6 mm Gaussian kernel. The normalized, resampled, and smoothed EPI data set was analyzed as described below to obtain functional brain activation maps.

2.7.2. Deconvolution of hemodynamic response and activation calculation

Deconvolutions were performed separately on each participant’s EPI data on a voxel-by-voxel basis to estimate the hemodynamic response during each of the four behavioral tasks. We used deconvolution to estimate independent averages and linear drifts of the EPI signal during each of the three measurements as well as the hemodynamic response functions for the five behavioral tasks. Deconvolution was used to model the hemodynamic response at successive points following the beginning of a behavioral block, in this case from 2 to 15 TRs after the beginning of a task block (EC, CV, etc.). The motion correction parameters were also modeled to remove residual effects of head movement. Deconvolution yielded 14 fit coefficients (1 at each TR) for each of the five behavioral tasks. These raw fit coefficients were taken as the functional image intensity. The fit coefficients were then averaged to arrive at an activation value for each condition.

The activation values were analyzed using the general linear model to create statistical parametric maps (SPMs) of

activation which were thresholded to a corrected P-value <0.05. To create the SPMs we employed two-factor analysis of variance (ANOVA) using behavioral condition as a fixed effect and participant as a random effect. Several contrasts were included in the ANOVA to determine activation specific to the various behavioral conditions. These included EO versus EV, EO versus CO, EV versus CV, CO versus CV, and EO versus EV + CO + CV. The SPMs were initially thresholded to eliminate voxels that did not surpass a significance level of $P < 0.005$. Monte Carlo simulations indicated that a cluster size of 22 or more voxels would reduce false positives to a corrected level of $P < 0.05$, a correction for multiple comparisons.

A mask from which non-brain voxels were eliminated was created for each subject. This mask served two purposes. First, the mask allowed us to establish the appropriate cluster size to correct for multiple comparisons as described above. Second, the mask was used to eliminate from analysis any voxels from which weak signal was obtained. Masks were created for each subject individually and combined as follows. In the first step an individual mask is created using the Talairach normalized reference EPI volume from the motion correction step. For this volume, an initial clipping level is set to the signal value above which 65% of all positive voxels in the volume lie. Then the clip level is iterated upward until it reaches a point where the median of all voxel values larger than the clip level is twice the clip level. All voxels below this value are set to zero and then only the largest set of connected surviving voxels is kept. In AFNI this is accomplished with the program 3dAutomask. In the second step, the masks from each individual are combined into a single volume such that only voxels that survive the masking procedure in each and every participant are kept. This masking procedure allows us to eliminate from analyses brain regions that could be affected by weak signal including inferior temporal regions, medial and orbital frontal cortex, and lateral inferior cerebellum. Thus, we can reduce the potentially unreliable contributions of voxels in these regions but still keep neighboring voxels from which sufficient signal strength is obtained. We also employ the mask as the volume upon which Monte Carlo simulations base the determination of the appropriate cluster size to correct for multiple comparisons.

Due to the specific nature of our research question and our a priori hypothesis, that a salient memory cue in olfactory form would evoke the most emotional recollection, we conducted a contrast between EO and EV using a small volume correction. We performed a region of interest (ROI) analysis using the reduced volume that included the amygdala, hippocampus, and parahippocampal gyrus, and compared left and right hemisphere activation levels in a spherical region centered on the center of mass of the cluster identified in EO versus EV contrast. The determination of the ROI was based upon the Talairach atlas labels implemented in AFNI (Lancaster et al., 2000). The small volume correction resulted in a cluster size threshold of 11 voxels, rather than the 22 required when considering the entire brain. For comparing left and right hemisphere activation, we calculated the average activation level across a spherical region (12 mm radius) centered on the center of mass of the medial temporal lobe cluster of activation in the EO versus EV contrast and contained within the ROI and its right hemisphere homologue. The average activation level served as the dependent variable in a linear regression analysis, with participant, condition, and hemisphere as independent variables.

3. Results

3.1. MRI data

Fig. 1 displays the medial temporal lobe cluster of positive activation for the contrast between EO and EV + CO + CV. As can be seen, significantly greater activation occurred in the amygdala for EO compared to the other cue types. Four clusters were more active for the condition EV + CO + CV (Table 1: left lingual gyrus, left fusiform gyrus, and two clusters in the left middle occipital gyrus). Table 1 displays additional clusters of activation that were present. Fig. 2 shows the contrast in activation between EO and CO. Significant positive activation with EO appeared in the posterior parahippocampal gyrus and the anterior parahippocampal gyrus/amygdala as well as the thalamus and anterior cerebellum.

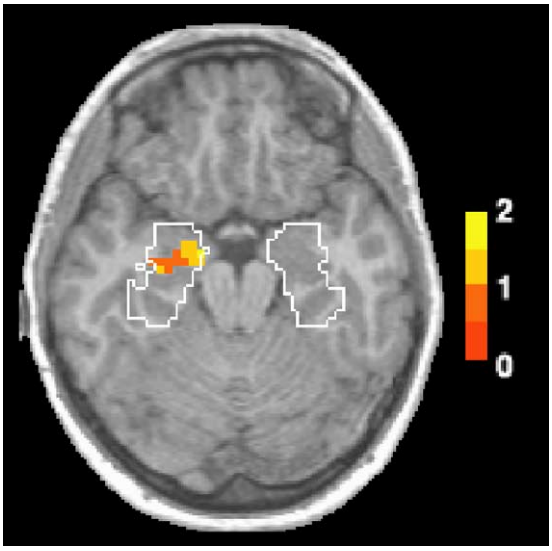

Fig. 1. Activation for experimental odor in the amygdala. The positive activation difference for the comparison EO vs. EV + CO + CV is shown in color on the left side of the brain with the scale bar to the right in arbitrary MR units. The slice shown is at $Z = -16$ mm inferior to anterior commissure (AC). The maximum intensity difference of 1.65 (MR units) appeared at 14, 8, −16, relative to the AC, corresponding to left hemisphere Broadmann's areas 28 and 34. The white outline denotes the ROI on the left, including the hippocampus, amygdala, and parahippocampal gyrus, used for tests of lateralization. The equivalent right ROI has been omitted for viewing purposes.

Table 1
Location and size of active clusters

Contrast	Location (BA)	Size (μl)	Coordinates (mm from AC)			Maximum intensity difference (MR units)	Significance (*P*-value)
			X (+L)	*Y* (+P)	*Z* (+S)		
EO vs. EV + CO + CV	L. lingual gyrus (18)	2403	8	86	−10	−3.44	0.0031
	L. fusiform gyrus (19)	1323	32	62	−10	−2.05	0.0013
	L. lingual gyrus (19)	891	29	77	−10	−3.86	0.0043
	L middle occipital gyrus (18, 19)	891	35	89	12	−2.2	0.0005
	L. parahippocampal gyrus/ amygdala/hippocampus (34, 28)	648	14	8	−16	1.65	0.00001
EO vs. EV	L. lingual gyrus (18,19)	6507	32	74	−7	−5.57	0.0039
	L. lingual gyrus (17)	2349	5	89	−4	−4.48	0.0009
	R. middle occipital gyrus (18,19)	648	-29	89	6	−2.73	0.0006
	L. parahippocampal gyrus/ amygdala/hippocampus* (34)	324	14	11	−16	1.5124	0.0006
EO vs. CO	L. Parahippocampal Gyrus (35)	891	17	35	−10	2.17	0.0005
	L thalamus	764	2	8	−4	2.73	0.0002
	L. middle temporal gyrus (21)	783	50	14	−10	1.33	0.0006
	L. cerebellum	702	5	44	−1	2.58	0.00008
	R. superior temporal gyrus (38)	621	−41	−14	−22	1.89	0.0040
	L. parahippocampal gyrus/ amygdala/uncus (34)	621	26	8	−19	1.34	0.0005
CO vs. CV	R. lingual gyrus (18)	1134	−11	89	−16	−5.68	0.0031

For each contrast, the table reports the anatomical region underlying the location of maximum intensity difference of each cluster as well as the cluster size in microliters (1 voxel = 27 μl). Additional regions underlying the cluster are reported for the medial temporal lobe. The reported Broadmann's area (BA) underlies the maximum intensity difference or is a BA in close proximity to the maximum difference. *X* coordinates are positive to the left of the anterior commissure (AC), *Y* coordinates are positive posterior to AC, *Z* coordinates are positive superior to AC. The symbol (∗) indicates that this cluster was identified as significant through a small volume correction considering only the amygdala, hippocampus, and parahippocampal gyrus, region of interest as shown in white outlines of Fig. 1. The center of max. *X* of this cluster is 22, 9, −16.

The a priori hypothesis concerning amygdala activation, addressed by the contrast between EO and EV using a small volume correction, indicated a cluster of 12 voxels in the amygdala and parahippocampal gyrus (Tables 1 and 2, Fig. 3) which overlapped the cluster shown in Fig. 1. No significant activation differences appeared in the contrast between EV versus CV. One concern regarding these results is that five participants may be too few to obtain a reliable measure of activation. However, the individual subject data, plotted in Fig. 3 and shown in Table 2 indicate consistently higher activation of the left amygdala for the EO. In only one participant did any condition exceed the EO activation and that was the AIR condition for participant 4. The air condition represents a task-less control condition and such conditions have been shown to be a poor basis for comparison with experimental manipulations (Stark & Squire, 2001).

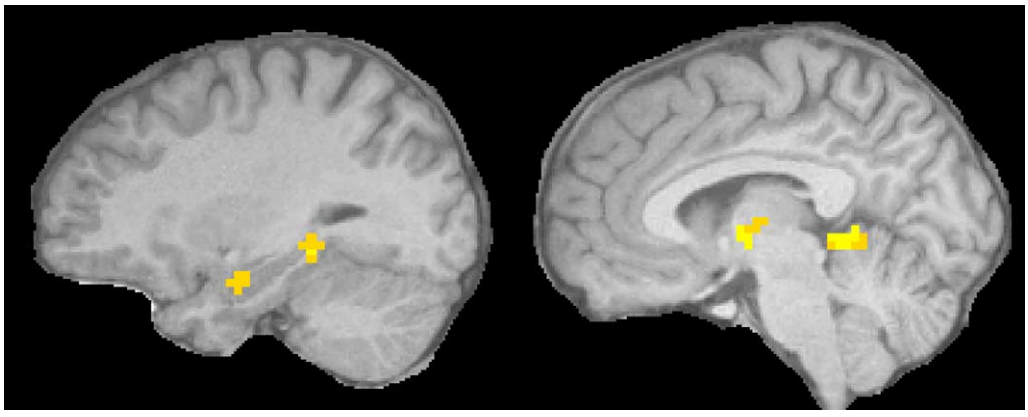

Fig. 2. Activation for experimental odor vs. control odor. In the left panel, the positive activation difference is evident in the posterior parahippocampal gyrus and the anterior parahippocampal gyrus/amygdala. Left slice is shown at 25 mm to the left of AC. Scale as in Fig. 1. In the right panel, the positive activation difference is evident in the thalamus and the anterior cerebellum. Right slice is shown 4 mm to the left of AC.

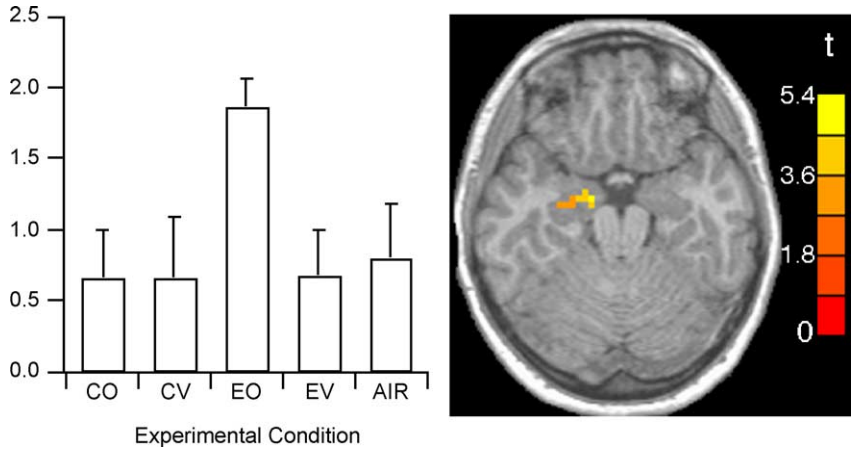

Fig. 3. Activation in amygdala ROI. The left panel displays the magnitude of brain activation for each of the behavioral conditions as an average across the cluster of activation shown in the right panel. The error bars are standard error of the mean across subjects. The right panel displays the cluster of activation identified in the contrast between experimental odor (EO) and experimental visual (EV) conditions using the small volume correction (Region of Interest shown in Fig. 1). The cluster's location of maximum intensity difference is shown in Table 1.

This minor discrepancy notwithstanding, even participant 4 showed complete consistency between the other experimental manipulations and the EO condition. Thus, significantly greater activity in the amygdala to the EO is a reliable effect.

Tests of lateralization showed no hemispheric differences. Although we observed significant medial temporal lobe activation only in the left hemisphere (Figs. 1 and 3), statistical tests of lateralization revealed no significant differences. The linear regression, which accounted for 83% of the variance in activation values within the ROI (see Fig. 1), did not reveal significant hemispheric differences overall ($F(1, 4) = 2.38$, $P > 0.13$) or for the EO condition ($F(1) = 1.36$, $P > 0.25$), nor was there a significant interaction between condition and hemisphere ($F(4) = 0.12$, $P > 0.97$). We note that five participants may be too few to achieve sufficient statistical power.

3.2. Behavioral data

Responses to the post-scanning interview questions revealed the following. First, all participants reported that all stimuli were the same as they had experienced during scanning and that the memories they had described in the pre-test interview were the same as they had experienced in the scanner to the EO and EV. All participants also reported that every time their experimental stimuli were presented they thought about the same memory, but for the control stimuli more inconsistent responses were obtained. Some participants reported that the CO reminded them of something or someone but others had no specific associations. The CV tended to elicit few specific associations and the same associations were not always evoked by the control stimuli for a given subject. To evaluate the emotionality of the memory/associations that were elicited by the stimuli, ANOVA was performed on the post-scan rating scale data. ANOVA and Newman–Keuls post hoc comparisons ($P < 0.05$) confirmed that EO elicited the most emotional memories, $F(3,16) = 9.73$, $P < 0.01$. Mean emotional memory ratings to the four stimuli were as follows: EO = 7.00(±0.42), EV = 4.40(±0.74), CO = 4.40(±1.16), CV = 1.40(±0.25). ANOVA performed on the rating scale data for stimulus liking also revealed that EO received the most positive response, $F(3,16) = 16.35$, $P < 0.01$. Means were: EO = 8.00(±0.32), EV = 5.20(±0.49), CO = 3.20(±0.58), and CV = 4.40(±0.63). Ratings of CO versus CV and EV versus CV did not differ statistically (Newman–Keuls, $P < 0.05$).

Table 2
Individual activation levels for cluster shown in Fig. 3

Condition	Participant				
	1	2	3	4	5
CO	0.045	0.478	0.064	1.588	1.137
CV	0.189	0.655	−0.417	1.685	1.231
EO	1.709	1.706	1.361	2.125	2.406
EV	0.141	0.846	0.230	1.693	0.495
AIR	0.346	0.577	0.330	2.169	0.583

The reported activation is the average for each of the five behavioral conditions over the entire cluster identified in Fig. 3.

4. Discussion

The present neuroimaging data provide convincing neurobiological evidence that the subjective experience of the emotional potency of odor-evoked memory is correlated with specific activation in the amygdala during recall. Although not originally predicted, significantly greater activation in the parahippocampal gyrus was also obtained with EO and is consistent with the neuronal interactions between the amygdala and hippocampus and the fact that

the hippocampus is involved in long-term declarative memory (Eichenbaum, 2001). The experimental odor cues also elicited greater activation in the amygdala–hippocampal complex than a comparable but non-personally meaningful control odor. Thus, despite the fact that odors generally elicit activation in limbic structures, the present finding was due to the emotionality of memory and not an olfactory artifact. As expected, visual cues elicited greater activation in occipital areas, thus validating our methods and analyses. Behavioral experimentation on the Proust phenomenon has shown that the subjective experience of a memory triggered by the olfactory form of a specific cue is more emotional than when memory is elicited by alternate sensory variants of the same item (Herz, 1996, 1998; Herz & Schooler, 2002), and this was also confirmed here.

In addition to producing greater activation in limbic structures, EO also elicited more activation in the anterior cerebellum than CO. Sobel et al. (1998) demonstrated that sniffing, in contrast to passive smelling, elicits activation in the anterior cerebellum. In considering our data, a possible explanation is that when participants were exposed to their experimental odor, they sniffed more strongly than when exposed to the control odor. More active smelling during exposure to EO could be due to participants recognizing an odor that was meaningful to them.

Our data also suggest left hemisphere dominance during episodic odor-evoked recall. However, a statistical analysis of voxel activation did not reach significance most likely due to insufficient power from our relatively small sample size. A comment on our small sample size is here due. The enrollment of participants in this study was limited by the number of available young women who could recollect a positive emotional memory to both the sight and smell of a specific perfume and who met all of the stringent health and fMRI criteria. For example, in addition to volunteers who did not meet the experimental criteria, several potential participants were excluded at the time of testing because it was discovered that they had at one time welded without eye protection, or had tattooed makeup. Given the difficulty in recruiting suitable participants, we examined the data after five had completed testing and considered the findings to be strong and interesting enough to publish.

Sample size notwithstanding, the laterality observation is provocative and might be explained by various coincident independent or interactive factors. One possibility is that left dominance reflects female processing of emotional memories (Cahill et al., 2001; Canli, Desmond, Zhao, & Gabrieli, 2002). Alternatively or additionally, left dominance may be due to perceiving emotionally intense odors, as Zald and Pardo found a left hemisphere bias during exposure to a highly aversive odor but not during exposure to more mildly noxious scents (Zald and Pardo, 1997). Questions pertaining to gender and stimulus hedonic intensity need to be addressed in future research. It would also be important to compare odors that trigger episodic memories of a positive versus negative valence so as to assess the hypothesis that there are hemispheric biases for positive (left) and negative (right) emotional experiences (Davidson, 1992).

It is unlikely that the present activation differences can be explained by differences in stimulus hedonic evaluations. Even though there were differences in liking ratings (i.e., pleasantness) between stimuli, particularly between CO and EO, a previous fMRI study comparing perception of vanillin and propionic acid, odors with opposing valence, revealed no differences in regions of activation (Sobel et al., 1998). A methodological issue may also explain the rating scale responses. As a function of the post-scan evaluation procedures and scaling techniques, the stimuli were evaluated relative to each other, and as such pleasantness values do not reflect absolute perceptual responses (Bartoshuk, 2000). In other words, a perfume rated as unpleasant relative to another perfume is surely not as unpleasant as a sulfide mixture, though depending on the sample set in which they are each assessed these two stimuli may be given the same numeric rating. More importantly, recent work by Anderson et al. (2003) suggest that the amygdala is responsive to the hedonic intensity of olfactory stimuli independent of valence. That is, equivalently unpleasant and pleasant odors will show comparable amygdala activation if they are of equal emotional intensity. Anderson's data strengthen our observation that EO, as the most emotionally stimulus, elicited the most amygdala activation.

Our results provide strong support for the hypothesis that odor memory cues elicit greater activation in the neural substrates of emotion than visual cues and non-meaningful odors. These findings are consistent with behavioral research and the unique neuroanatomical connection that exists between the olfactory system and the amygdala–hippocampal complex. However, there is a potential confound to the conclusions drawn from our findings. It may be that the sight of a perfume bottle is not as salient or as significant a feature of a memory experience as the odor of that perfume is. Ideally, a comparison between an equivalently salient visual stimulus with the perfume odor would, if the same results were obtained, make a more convincing case that odors truly elicit more emotional memories than other memory cues. However, there are several problems of finding equitable visual cues and they provide their own confounds. This being the case, we decided to equate sensory cues as my laboratory has done previously and use the approach of comparing the visual and olfactory representation of the same stimulus. We were further encouraged to do so as all participants stated that they were aware of seeing the perfume bottle in their memory. Nonetheless, the conclusions drawn from our data should be treated as preliminary and as such provide the basis from which to conduct more definitive research on the potentially unique emotional potency of odor-evoked memories.

In sum, the present findings offer new insights concerning the perceptual and affective components of memory. The results also suggest that olfaction is an excellent model for studying many questions germane to the field of affective

neuroscience (Dolan, 2002). Finally, for anyone who has ever experienced the Proust phenomenon, our results offer an illustration of how the brain responds to odor memory cues to elicit this special, emotional experience.

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