Dissociation of emotional processes in response to visual and olfactory stimuli following frontotemporal damages

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Contemporary neuropsychological studies have stressed the widely distributed and multicomponential nature of human affective processes. Here, we examined facial electromyographic (EMG) (zygomaticus and corrugator muscle activity), autonomic (skin conductance and heart rate) and subjective measures of affective valence and arousal in patient TG, a 30 year-old man with left anterior mediotemporal and left orbitofrontal lesions resulting from a traumatic brain injury. Both TG and a normal control group were exposed to hedonically valenced visual and olfactory stimuli. Contrarily to control subjects, facial EMG and electrodermal activity in TG did not differentiate between pleasant, unpleasant and neutral pictures. In addition, the controls reacted spontaneously with larger corrugator EMG activity and higher skin conductance to unpleasant odors. By contrast, the subjective feeling states (pleasure and arousal ratings) remained preserved in TG. The covariation between facial and self-report measures of negative valence was also a function of the nature of the olfactory task in the patient only. Taken together, the data suggest a functional dissociation between brain substrates supporting generation of emotion and those supporting representation of emotion.

Introduction

A large body of research supports the view that the fundamental structure of emotion is mainly explained in terms of affective valence and arousal (Russell, 1980; Bradley, 1994). This dimensional conception of emotion is thought to reflect the evolutionary foundation of a basic motivational organization system underlying approach-withdrawal or appetitive-aversive behaviour (Lang *et al.*, 1998; Davidson and Irwin, 1999). Although the anatomical substrates of affective processes related to this superordinate division are not entirely elucidated, animal and human research has clearly implicated anterior mediotemporal lobe structures (e.g., amygdaloid complex) and the orbitofrontal cortex (OFC) as intimately connected regions of a distributed neural network playing a critical role in various aspects of approach- and withdrawal-related emotion and motivation (Damasio, 1994; Rolls, 2000; Lane and Nadel, 2000; Davidson, 2002). Accumulating evidence has established that these brain regions are involved in the processing of the reinforcing value of stimuli in relation to decision-making and goal-directed behaviors, in the encoding and consolidation of implicit or explicit learning of emotionally salient events, and in the evaluation of the affective significance of stimuli (e.g., Rolls, 2000; Adolphs and Damasio, 2001; Hamann, 2001; Davidson, 2002; Anderson *et al.*, 2003; Holland and Gallagher, 2004; Izquierdo and Muray, 2004).

While the current findings suggest that the amygdala and the OFC are part of an integrated neural system subserving critical functions in reinforcement mechanisms, decision-making, and affective memory, their role in various aspects of emotion (e.g., perception, appraisal, physiology, expression, and subjective experience) is not clearly understood in humans. Students of emotion provided evidence that affective valence and arousal are multicomponent processes, comprising expressive (i.e., facial and vocal expressions) and autonomic reactivity, and their subjective or experiential counterparts (Cacioppo *et al.*, 1992; Lang *et al.*, 1993; Soussignan, 2002). Autonomic responses and spontaneous facial actions constitute rapid changes in somatic and neurophysiological activity presumed to reflect emotional states, whereas the subjective experience of emotion is viewed as a mental representation of emotional states based on conscious awareness, recall of past affective experience, and language (Lane, 2000; Dolan, 2002). Such a distinction is well emphasized in current conceptualizations under the terms of emotion and feeling. For instance, according to Damasio (1995, 1998) emotion refers to “dispositional” responses to the perception of stimuli producing changes within the body itself (externalized aspects), whereas feeling designates a subject’s perception of bodily changes induced by responses or by mental states resulting from emotional state (internal experience).

Whether distinct, non-overlapping neural pathways are involved in physiological emotional responses and self-reported

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feeling states remains debated. On the one hand, in humans, the amygdala and the OFC exert modulating influences on autonomic responses probably through their projections to the hypothalamus and lower brainstem (Mangina and Beuzeron-Mangina, 1996; Williams *et al.*, 2001; Critchley, 2002), and subjective experience of emotion often engages neural structures not necessarily linked either to the OFC or amygdala (Lane, 2000). For instance, neuroimaging studies have shown that attention directed to one's own affective experience under various emotionally-laden conditions (films, recall, slides) increased activity preferentially within the anterior cingulate cortex, and the medial prefrontal cortex, but not in the amygdala or OFC (Georges *et al.*, 1995; Lane *et al.*, 1997; Lane *et al.*, 1998; Lane 2000). Furthermore, the amygdala recruitment in the conscious experience of emotion does not seem necessary because a lack of impairment of self-reported affective states was found in patients with unilateral or bilateral amygdala lesions (Adolphs *et al.*, 1997; Anderson and Phelps, 2002). On the other hand, functional neuroimaging studies have also shown that the activation of the amygdaloid complex or the OFC was associated with subjective ratings of emotionally valenced stimuli (Zald and Pardo, 1997) or with self-report of sadness during recall of emotionally-loaded situations (Pardo *et al.*, 1993). Finally, a number of studies demonstrated that neural structures hypothesized to be involved in the conscious experience of emotion (cingulate cortex, medial prefrontal cortex, insula, and somatosensory cortices) may be co-activated with the amygdala (Zald *et al.*, 1998; Liberzon *et al.*, 2000; Royet *et al.*, 2000) and/or the OFC (Schneider *et al.*, 1997; Paradiso *et al.*, 1999; Dougherty *et al.*, 1999; Damasio *et al.*, 2000).

Although functional neuroimaging techniques are powerful to illuminate the widely distributed nature of affective processes, they cannot directly specify the contribution of particular brain regions to specific emotional responses, and the associations detected between neural activity and subjective experience in a number of studies may reflect other aspects of emotional processing correlated with feeling states (e.g., physiological arousal, facial efference). A complimentary approach for exploring the contribution of specific neural structures to distinct emotional responses bears on the consequences of focal brain lesions. More specifically, patients with discrete brain damages afford the opportunity to investigate whether the areas identified by imaging are critical in the control or the modulation of multiple output components of emotion.

In the present study, we examined facial EMG, autonomic and self-reported verbal measures of affective valence and arousal in a male patient with left anterior temporal and left orbitofrontal damages while exposed to hedonically valenced visual and olfactory stimuli. We expected to evidence the following dissociation between these distinct components of emotion: the patient with frontotemporal damages should be more impaired in his facial and autonomic responses (measures of implicit processing) but less in his self-reported affective ratings (a measure of conscious experience), as would be consistent with the role of these brain regions in the mediation of automatic and unconscious bodily changes (Damasio, 1994). Facial EMG activity over the muscle regions responsible for frowning (*corrugator supercilii)* and smiling (*zygomaticus major*) was targeted because electrical activity from these muscles appeared to be a reliable correlate of the processing of the affective valence of the stimulus (Cacioppo *et al.*, 1992; Lang *et al.*, 1993) and may reflect automatically operating affect programs (Dimberg *et al.*, 2000). For instance, it was found that looking at or imagining pleasant scenes increased zygomatic activity, whereas viewing or recalling unpleasant scenes elevated corrugator activity (Schwartz *et al.,* 1980; Dimberg, 1990). Autonomic measures such as heart rate (HR) and skin conductance (SC) were recorded because they may index processes linked to orienting response (HR) or emotional arousal (SC) (Lang *et al.*, 1993) and reflect implicit processing (Kubota *et al.*, 2000; Öhman *et al.*, 2000).

A second purpose was to investigate whether affective reports, facial and autonomic responses to hedonically valenced stimuli depend on the sensory modality. Although neuroimaging studies have shown that both visual and olfactory stimuli can activate the amygdala and the OFC, the perception of odors is dominated by a hedonic dimension (Soussignan and Schaal, 1996; Royet *et al.*, 2000; Rouby and Bensafi, 2002) and may produce autonomic and expressive changes as early as the first days of life (Soussignan *et al.*, 1997). Anatomically, the primary olfactory cortex is continuous with the anterior portion of the amygdala and projects directly to the amygdala and posterior orbitofrontal cortex (Carmichael *et al.*, 1994; Zald and Pardo, 2000). In addition, functional brain imaging and lesion studies have consistently found that the exposure to odorants involved both the OFC and interconnected regions (anterior mediotemporal lobe and/or hypothalamus) (Eslinger *et al.*, 1982; Zatorre *et al.*, 1992; Zald and Pardo, 1997; 2000; Zatorre *et al.*, 2000; Royet *et al.*, 2000; 2001). For instance, regional cerebral blood flow(rCBF) recording during the presentation of emotionally valenced olfactory, visual, and auditory stimuli have shown increased rCBF in the left OFC for each sensory modality, whereas only odors induced rCBF increases in both the amygdala and the OFC (Royet *et al.,* 2000). Based on evidence cited above, we addressed the issue of whether psychophysiological and experiential correlates of affective processing would be more impaired for olfactory than visual stimuli in the patient with frontotemporal damages.

A final purpose of the study was to examine whether affective responsiveness following damages of frontotemporal structures is specifically related to the nature of the olfactory task. Because neural and autonomic responses to odors were found to be task-dependent (Royet *et al.*, 2001; Bensafi *et al.*, 2002a; Royet *et al.*, 1999, 2003), facial EMG and autonomic correlates of hedonic processing and arousal were compared during tasks of affective judgment (i.e., explicit task of affective processing) and of odor identification (i.e., implicit task of affective processing). We hypothesized that frontotemporal damages would produce a deficit in emotional physiological reactivity during the implicit task of affective processing of odors. This hypothesis is consistent with findings from functional imaging research which indicate that anterior mediotemporal structures and OFC can be activated by emotional stimuli even without awareness after parietal damage (Vuilleumier *et al*., 2002).

Patient report: Case TG

Medical history and personal information

TG is a 30-year-old, right-handed male. He was 19-years-old when he sustained a severe closed head injury during a car crash. Before, he was attempting a second year of superior degree and was socially integrated with a lot of friends and a girlfriend. Following the head trauma, he presented a nonreactive coma. He had an initial Glasgow Coma Scale of 9, and a mild right brachio-facial hemiparesia. At this time, a CT-scan was done, but did not reveal any hematoma. He was admitted to an intensive care unit because he needed assisted ventilation. The coma lasted about four days. After the comatose phase and during the following years, TG did not present any epileptic seizure. An EEG was done and indicated only small bursts of theta waves in the left frontotemporal lobe. His condition improved gradually so that he could be discharged from hospital after one month. TG was considered as cognitively not impaired, except for a mild anterograde amnesia, with a retrograde amnesia for a 3 month period. TG followed a mnemonic training and a physical therapy program during 6 months as an outpatient in a rehabilitation centre. He took up his everyday life apparently on a normal basis. However, the subsequent evolution was marked by many difficulties. TG left his girlfriend without clear motives. He tried to start again his studies, but gave up after 2 years of successive failing. His family reported that he was no longer able to organize conveniently his time to study or to develop learning strategies. All these facts constituted a clear change in TG's habits. During the 6 following years, TG returned to his parent's house. He manifested very little personal involvement in the search for new studies or for a job. TG's parents increased their commitment in this task. Finally, under the pressure of his parents, TG planned to open a small sandwich shop. Both these projects failed each time because he was not able to manage the required organizational tasks. For instance, he concentrated on the office furnishing while neglecting the legal paperwork. After these two failures, TG disappeared suddenly from his house during one year. His presence was occasionally mentioned in bars with suspect frequentations. He returned home twice, for brief periods and then disappeared again for one year. During this period he became homeless after having spent the totality of the compensation he had obtained for his trauma. Finally, his parents found him in a park and took him home. TG was neither able to explain his behavior during his wandering period, nor did he express any regret or remorse. Strictly coached by his family, TG was engaged in a sandwich shop managed by his cousin. He is reported to work well, but under strict supervision. Still, he disappeared again two or three times, but for very short periods. In February 2001, TG was addressed to our neurological department for an expert report at the request of his parents. At this examination, TG's parents reported that his behavior was still markedly impaired with a strong need for help from his family.

Neurological examination and neuropsychological assessment

A three-dimensional acquisition magnetic resonance imaging (MRI) was performed, including T1-weighted and T2-weighted sequences, fluid-attenuated inversion recovery (FLAIR) and T2 echo planar sequences. Figure 1 illustrates some examples of structural MRI scans in this patient. Axial FLAIR images through the frontal and temporal lobes indicated abnormal signal intensity in the left orbitofrontal cortex, in left anterior mediotemporal structures (anterior temporal pole, periamygdalar region), and in the left posterior insula. Most posterior regions of the temporal lobes appeared normal (e.g., hippocampus). It can be noted that there was no evidence of mass lesion and that the abnormal signals reflected mild aspects of sequelae of cerebral contusion (cortical

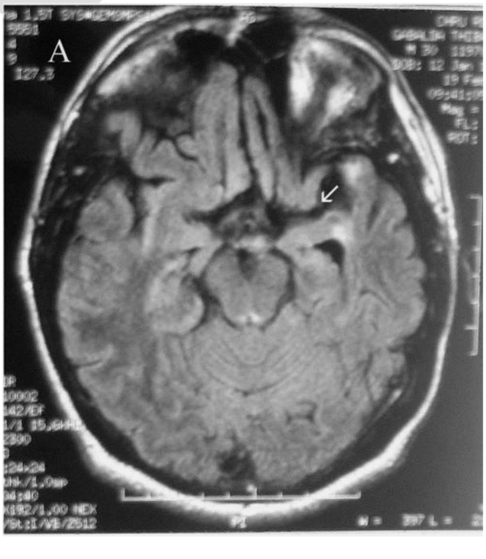

Fig. 1. Axial fluid-attenuated inversion recovery (FLAIR) images (A, B, C) through the frontal and temporal lobes of TG's brain. There is abnormal signal intensity in the left anteromedial temporal lobe (anterior temporal pole, periamygdalar region), in the left orbitofrontal cortex, and in the left posterior insula (see the arrows). A sagittal T1-weighted image (D) indicated a thinning of the anterior portion of the corpus callosum (see the arrow), but no damage in the anterior cingulate cortex and other frontal structures. Note that there was no evidence of mass lesion. The left hemisphere is depicted in the right side of each image.

Fig. 1. Continued.

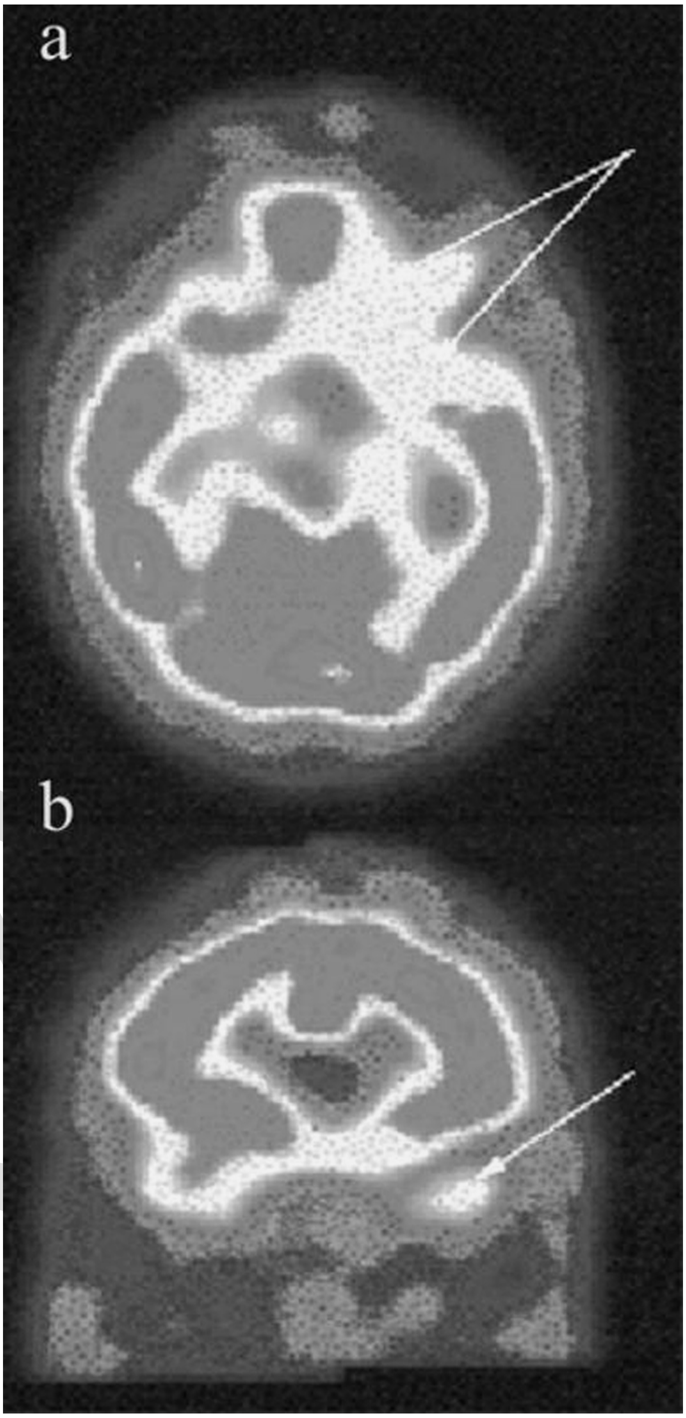

Fig. 2. SPECT images of TG‘s brain. Horizontal (a) and coronal (b) sections show respectively a blood flow reduction in the left orbitofrontal cortex and in the anterior part of the left temporal lobe involving the periamygdalar region.

deposits of hemosiderin and white matter T2 hyperintensities). A sagittal T1-weighted MRI also revealed a thinning of the anterior portion of the corpus callosum and a small lesion of the splenium. However, there is no evidence of damage in the anterior cingulate cortex and other frontal structures.

A single-photon emission computerized tomography (SPECT) scan was also performed indicating marked hypoperfusion in both the anterior part of the left anterior temporal region (periamygdalar portion) and the left orbitofrontal cortex (Figure 2).

The patient was assessed in our department 11 years after the injury. His cognitive performances are presented in Table 1. At this time, he was correctly oriented and presented a superior efficiency (GIQ: 120, shortened form of the Wechsler Adult Intelligence Scale-Revised, WAIS-R), without any significant dissociation between verbal (VIQ: 117) and performance IQ (PIQ: 120). Among the subtests used in the shortened form of the WAIS-R, only Digit Symbol subtest revealed abnormal slowing. His working and episodic memory performances were in the normal range, for both verbal (digit backward span; Rey Auditory Verbal Learning Test) and visual stimuli (localization backward span; Rey-Osterrieth Test). The examination of language did not demonstrate any naming, reading, writing, comprehension or fluency deficit (French version of the Boston Naming Test, Chapman-Cook Speed of Reading Test, Token test). His spontaneous expression was considered both formally and semantically rich. No sign of apraxia or visuo-spatial trouble was observed and the executive control was excellent, as assessed by the Trailmaking test, the Wisconsin Card Sorting Test, and the Stroop and Delis tests. In summary, TG seems to show a preservation of his whole cognitive functioning with performances often in the superior mean.

Method

Subjects

Patient TG's responses to a set of stimuli chosen for their arousing impact and their affective valence were compared to those of a normal control group. This latter group comprised 10 subjects matched to TG for gender and age (M = 26.4-years-old, SD = 4.87). Additional criteria for selection were: (a) full right handedness as defined by the Edinburgh Laterality Inventory (Oldfield, 1971); (b) 2 years college education; (c) absence of olfactory disturbances and respiratory allergies, and (d) absence of smoking habits. All the subjects participating in the study provided informed consent indicating their acceptance of the procedure.

Stimulus selection

The emotional material comprised visual and olfactory stimuli. First, 90 pictures were selected from the International Affective Picture System (IAPS) (Lang *et al.*, 2001). These pictures consisted of three 30-item sets of pleasant, neutral and unpleasant CD-ROM slides for which normative ratings on valence and arousal value were obtained from prior validation studies in male subjects. Unpleasant slides (valence: M = 2.46, SD = 0.96) included themes such as mutilated and dead bodies, skin disease, frightening animals, human violence, disgusting scenes, starving child, and so on. Neutral slides (valence: M = 4.97, SD = 0.21) showed items such as household objects, neutral faces, plants, and so on. Pleasant slides (valence: M = 7.37, SD = 0.42) showed human and animal babies, nature scenes, erotic females, sport events, social scenes, and so on.

Second, the odor stimuli were composed of pleasantly and unpleasantly valenced compounds (n=10 each) purchased from different aroma and chemical companies (Euracli, Chasse sur Rhône, and Sigma-Aldrich, Saint Quentin-Fallavier, France). Part of the pleasant and unpleasant stimuli was selected on the basis of previous studies on hedonic judgments of odorous stimuli (e.g., Royet *et al.*, 1999, 2001). The set of pleasant stimuli included odors of flower (rose, lavender, violet), fruits and comestible plants (banana, apple, coconut, vanilla, mint, anise, and caramel). Unpleasant stimuli consisted of pure chemical or mixtures evoking food, body and environmental odors. They included adoxal (rotten egg), butyric acid (cheesy), cod liver oil, triethylamine (fishy), synthetic sweat, skatole (faeces), castoreum (animal), pyridine (chemical industry), tetrahydrothiophene (THT: gas), and fuel oil. These odorants were diluted in mineral oil to produce 5 ml of solution (concentration: 1% v/v) that was absorbed on polypropylene placed in 50-ml brown glass bottles. The concentration of the compounds with high stimulative potency (THT, pyridine) was limited to 1‰. The neutral stimuli consisted of 10 50-ml bottles of the odorless solvent (mineral oil) absorbed on polypropylene.

Psychophysiological recording

Facial EMG activity and autonomic measures (heart rate, skin conductance) were recorded using a 4-channel Power Lab system (model 4SP, ADInstruments Pty Ltd), which was connected to a PC. The bioelectric signals were filtered and amplified before being fed into the analog input connector of the PowerLab unit, and were sampled at a rate of 40 points/s under the on-line control of an application program (Chart for Windows v 4.0.4).

Muscle activity was recorded over the left *corrugator supercilii* and *zygomaticus major* regions using miniature Ag/AgCl surface electrodes, filled with electrode paste and placed bipolarly following the guidelines proposed by Fridlund and Cacioppo (1986). Before the electrodes were attached, the target sites of the skin were cleaned with alcohol and slightly rubbed in order to reduce inter-electrode impedance. To minimize demand characteristics of the EMG experiments (Fridlund and Cacioppo, 1986), a cover story was given to the subjects by telling them that the facial electrodes were placed in order to record face temperature. The EMG signals were fed into electronic amplifiers and were band-pass filtered from 10 Hz to 250 Hz. The raw EMG was rectified and smoothed with a time constant set at 500 ms.

Skin conductance (SC) was transduced with Ag/AgCl electrodes filled with a conducting Biogel and attached with a Velcro strap on the volar surface of the distal phalanges of the second and third fingers of the nondominant (i.e., left) hand. A UFI Bioderm skin conductance coupler provided a constant 0.5 V current across the electrodes. Heart activity

Table 1. Results of TG's neuropsychological testing

Intellectual capacities		
WAIS-R Scores		
Full Scale Score	117	
Verbal Score	120	
Performance Score	117	
Memory		
Digit spans		
Forward	7	
Backward	6	
Localization spans		
Forward	7	
Backward	7	
Rey Auditory Verbal Learning Test		
Immediate Recalls	8-13-12-13-11/15	
Total	57/75	
Interference	5/15	
Retention after Interference	10/15	
Delayed Recall	11/15	
Recognition	12/15	
Rey-Osterrieth Test		
Immediate Recall	22/36	
Delayed Recall	22/36	
Orientation		
MEM-III (French version of the WMS-III)		
Information and Orientation Subtest	14/14	
Visuo-spatial tests		
Bells Test	35/35	
Copy of Rey Complex Figure	32/36	
Language		
Naming		
DO80 test (French version of the Boston Naming Test)	79/80	
Reading		
Words (Simple, Complex, Irregular)	16/16	
Non-Words	6/6	
Writing		
Words (Simple, Complex, Irregular)	16/16	
Non-Words	6/6	
Semantic Fluency (2 minutes each)	Words	
Animals	30	
Fruits	22	
Jobs	22	
Letter Fluency (2 minutes each)	Words	
P	22	
R	24	
V	22	
Comprehension	Score	
Chapman-Cook Speed of Reading Test	15 paragraphs	
Token Test	163/163	
Executive functioning		
Trailmaking Test	Time to Completion	Errors
Part A	26"	0
Part B	43"	0

Continued

Table 1. Continued

Intellectual capacities			
Stroop Color Word Test	Time to Completion	Errors	Self-corrected errors
Color	57"	0	0
Word	43"	0	0
Interference	107"	2	3
Wisconsin Card Sorting Test			
Categories	6 (74 cards)		
Total errors	1		
Perseverative errors	0		
Delis			
C1: Spontaneous Sorting			
Attempted sorts	21	21.25 (3.8)	
Percent of correct sorts	100%	85.24 (9.2)	
Percent of correct rules names	100%	77.84 (12.2)	
C1: Perseverations			
Sort perseverations	0	2.85 (1.75)	
Name perseverations	0	0.65 (1.1)	
C2: Structured Sorting			
Correct rule names	18	16.65 (4.3)	
Perseverations of rule names	1	0.65 (1.3)	
C3: Cued Sorting			
Percent of abstract cues	100%	92.29 (8.02)	
Percent of explicit cues	0%	6.04 (5.6)	
Perseveration	0	0.2 (0.5)	

was recorded with a pulse transducer using a piezoelectric device attached to the distal phalange of the fourth finger of the nondominant hand. A low-pass filtering of 50 Hz was used to eliminate high-frequency components. A computed input command allowed a threshold control to detect R wave pulses and to display on-line heart rate (HR) in beats per minute.

Procedure

The participants were tested individually. On arrival, they sat in a comfortable reclining chair in a small (3 x 1.5 m) cubicle. After attachment of physiological sensors, the subjects were asked to remain relaxed during the experimental sessions. In the first part of the session, they were instructed that pictures differing in emotional content would be displayed, and that each picture should be looked at during the entire time (6 s) it was presented on a monitor positioned 2 m in front of them. They were told that each visual stimulus would be signalled 6 seconds before its presentation by the word “slide” in the center of the screen. The duration of projection of the stimuli was controlled using the SuperLab software (Cedrus). The slides were presented on a 17 inch monitor in a landscape format with a high spatial resolution. The interstimulus interval was set at 26 s. Immediately after each slide presentation, the participants used 9-point Likert scales to rate their emotional experience. Self-reported affective valence ranged from extremely unpleasant feeling (1) to extremely pleasant feeling (9). Subjective emotional arousal was rated along a calm/arousal feeling dimension, ranging from extremely calm (1) to extremely excited (9). The presentation of the pictures was randomized across the same order for all the subjects. Prior to the onset of the experimental trials, four pictures served as practice stimuli.

In a second part of the session, subjects were presented birhinally olfactory stimuli from opaque glass bottles by an experimenter placed behind them. Bottles were presented for a duration of 6 s at a distance of about 1 cm from the nose, with an interstimulus interval greater than 1 min. The subjects were instructed to close their eyes during the smelling task and after the rating procedure. During the recording of facial EMG activity (indexing valence processing) and autonomic activity (indexing physiological arousal), the participants had to perform two tasks: a verbal identification of odors and a hedonic judgment (called thereafter implicit and explicit tasks of affective processing, respectively). For the implicit task, a forced choice paradigm with 5 alternatives was used, including the correct label, 3 verbal distractors, and a non-odor label. For the explicit task, the participants smelled the same olfactory stimuli (n = 30) and rated their feelings on a 9-point Likert scale ranging from extremely unpleasant (1) to extremely pleasant (9). The task presentation order was counterbalanced according to an ABBA design, with each condition including 15 olfactory stimuli contrasted in hedonic terms (5 pleasant, 5 neutral, and 5 unpleasant odors). At the end of the psychophysiological recording session, the subjects smelled again the 30 odorants in order to evaluate the intensity and arousal dimensions on 9-point scales raging from 1 (not at all intense or extremely relaxing) to 9 (extremely intense or extremely exciting). The intensity of a stimulus was defined as the degree of its "potency" regardless of its hedonic valence. Before testing, the subjects were trained to rate differences in subjective intensity perception between stimuli using two odorants of distinct intensity levels.

Physiological data reduction and analysis

EMG and HR data were averaged off-line for each of the 6 s periods immediately preceding (baseline period) and following (stimulus period) the stimulus onset. In accordance with standard statistical practice (Fridlund, 1991), mean EMG data were log transformed [$\log_{10}(\mathrm{EMG} + 1)$] to minimize skewness and heteroscedasticity. The EMG transformed baseline score (in log-μV) and the HR prestimulus levels (in bpm) were subtracted from the EMG transformed score and the HR value during stimulus presentation to extract mean changes for each physiological measure. Skin conductance response (SCR) was defined as changes in the amplitude with onset occurring 1–4 s after stimulus presentation. SCR change (in μSiemens) was calculated by subtracting the 2-s SC level immediately preceding stimulus onset from the largest value averaged in the 2-s window after stimulation[1].

For the control subjects, within-subjects comparisons of the facial, autonomic, and subjective rating data were performed using multivariate analysis of variance (MANOVA), as suggested by Jennings et al. (1987), the resulting Wilks' lambda statistics were referred to the F distribution. Bonferroni t tests were used for pairwise comparisons of means to control familywise error rate. These statistical analyses in a normative sample tested whether the distinct dependent variables discriminated between affectively valenced stimuli.

The comparison between TG and the normal subjects was investigated by calculating difference measures (pleasant – neutral, unpleasant – neutral) to control for the possible differential responsiveness to neutral stimuli between the patient and the normal subjects, and then by combining the data means of the trials for each subject in the control group to provide the reference data. Then, a one-sample-t-test was computed to see whether the patient's mean performance falls outside the reference distribution at $P < 0.05$.

Results

Facial muscle responses

A first question is whether the electrophysiological responses of facial muscles indexing the dimension of affective valence are reduced in a patient with damages of brain structures presumed to be involved in emotion. The facial-EMG means during the projection of slides for both the control subjects and TG are illustrated in Figure 3. The control subjects showed stronger reaction of the *corrugator supercilii* muscle region to unpleasant pictures (Figure 3a), compared to pleasant and neutral pictures [$F(2, 297) = 20.83$, $P < 0.0001$; Bonferroni tests, all $P < 0.0001$]. Furthermore, the controls exhibited on average higher EMG reactivity over the brow region than TG during projection of negative slides only, $t(29) = 5.44$, $P < 0.0001$. The zygomatic activity of controls also discriminated the affective valence of the pictures [$F(2, 238) = 4.81$, $P = 0.009$], particularly between pleasant and neutral conditions ($P = 0.02$), whereas for TG, zygomatic EMG activity did not vary as a function of picture valence, $t(29)$, all $P > 0.05$ (Fig. 3b). However, the control subjects did not reveal higher zygomatic responses over the cheek region during the presentation of pleasant slides compared to TG, $t(29) = 0.3$, $P > 0.05$.

For the olfactory experiment, in the control group, a two-way MANOVA was used with type of task (implicit vs. explicit affective processing) and odor valence (unpleasant, neutral, and pleasant) as repeated measures factors. Concerning *corrugator* activity, significant main effects were detected for the type of task, [$F(1, 99) = 3.86$, $P = 0.05$], and the valence of the odor, [$F(2, 98) = 28.47$, $P < 0.0001$]. Normal subjects exhibited greater *corrugator* activity during the explicit ($M = 0.06$, $SD = 0.09$) than during the implicit task of affective processing of odors ($M = 0.04$, $SD = 0.07$), [$F(1, 99 = 3.86$, $P = 0.05$]. They also showed stronger *corrugator* activity to unpleasant odors than to neutral or pleasant odors (Bonferroni tests, all $P < 0.0001$) (see Figure 4). Concerning zygomatic activity, control subjects exhibited a higher activity while smelling pleasant odors compared to neutral olfactory condition, however the effect was only marginally significant [$F(2, 82) = 2.70$, $P = 0.07$]. In contrast, TG's facial reactivity for both *corrugator* and *zygomaticus* muscles did not differentiate between the hedonically valenced odors (one-sample-t-tests, all $P > 0.05$). One-sample t-tests also indicated that the control group displayed higher EMG *corrugator* activity than did TG while smelling unpleasant odors during both the implicit and explicit tasks of affective processing [$t(9) = 2.25$ and 7.15, $P = 0.05$ and < 0.001, respectively], whereas no significant difference was detected for zygomatic activity between TG and the controls while smelling pleasant odors.

Autonomic tone

The autonomic measures were recorded to index both physiological arousal (SC) and attention (HR). We tested specifically whether emotional arousal is reduced in the patient.

Skin conductance

During the projection of slides, greater changes in SC were detected in controls while viewing unpleasant as compared to neutral pictures [$F(2, 259) = 4.11$, $P = 0.017$; Bonferroni test, $P = 0.02$]. TG also exhibited larger SC responses to unpleasant

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[1] Because of the presence of artefacts and equipment problems during the recording of zygomatic EMG muscle activity and electrodermal activity, data from one (for SC) or two (for zygomatic EMG) participants had to be excluded.

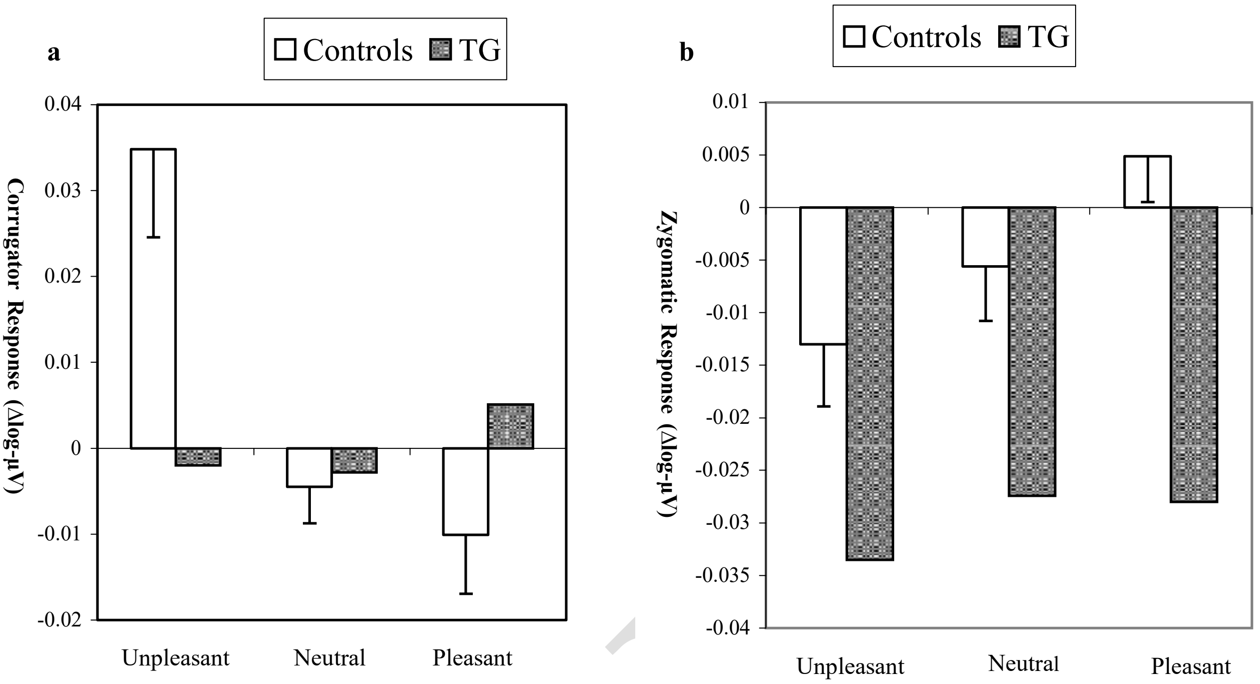

Fig. 3. Facial electromyographic (EMG) responses to pictures as a function of affective valence in controls and patient TG: (a) Mean responses of the *corrugator supercilii* muscle region; (b) Mean responses of the *zygomaticus major* muscle region. Error bars represent standard errors (SE).

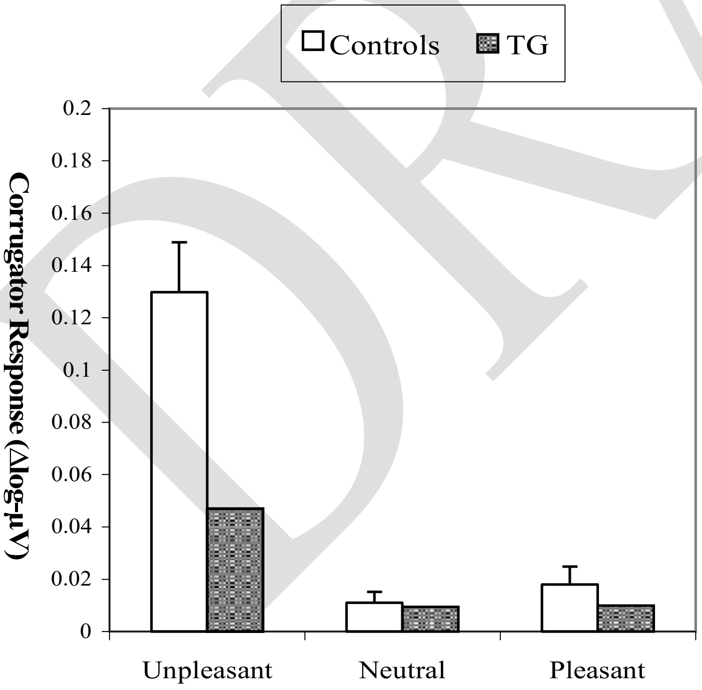

Figure 4. Mean responses of the *corrugator supercilii* muscle region to odors as a function of affective valence in controls and patient TG. Error bars represent SE.

relative to neutral pictures, however the difference failed to reach significance, $t(29) = 1.94$, $P = 0.06$. More interestingly, SC changes were larger in the controls than in TG, while viewing both unpleasant, $t(29) = 3.96$, $P < 0.0001$, and pleasant pictures, $t(29) = 2.26$, $P = 0.03$ (Figure 5a). The smelling of unpleasant odorants induced greater SC responses than did the pleasant or neutral olfactory stimuli in the controls ($F(2,82) = 9.29$, $P < 0.0001$; Bonferroni tests, all $P < 0.0001$) (see Figure 5b). Smelling unpleasant odorants also generated higher SC changes in the controls than in TG both during the implicit, $t(9) = 2.93$, $P = 0.02$, and explicit tasks of affective judgment, $t(9) = 8.17$, $P < 0.0001$.

Heart rate

During the projection of slides, the control subjects showed larger cardiac decelerative response to unpleasant pictures than to neutral or positive pictures, $F(2, 295) = 3.98$, $P = 0.02$ (see Figure 6), but HR did not change as a function of valence or type of task when they smelled the odors. No statistical difference was detected for HR data between TG and the control subjects (one-sample t-tests, all $P > 0.05$) for both the visual and olfactory stimuli.

Subjective experience

We examined the hypothesis of a dissociation between subjective experience of emotion (feeling) and emotional somatic and autonomic reactivity by testing whether the self-reported affective ratings (pleasure, arousal) are impaired in TG. Intensity ratings of odors were also assessed to verify

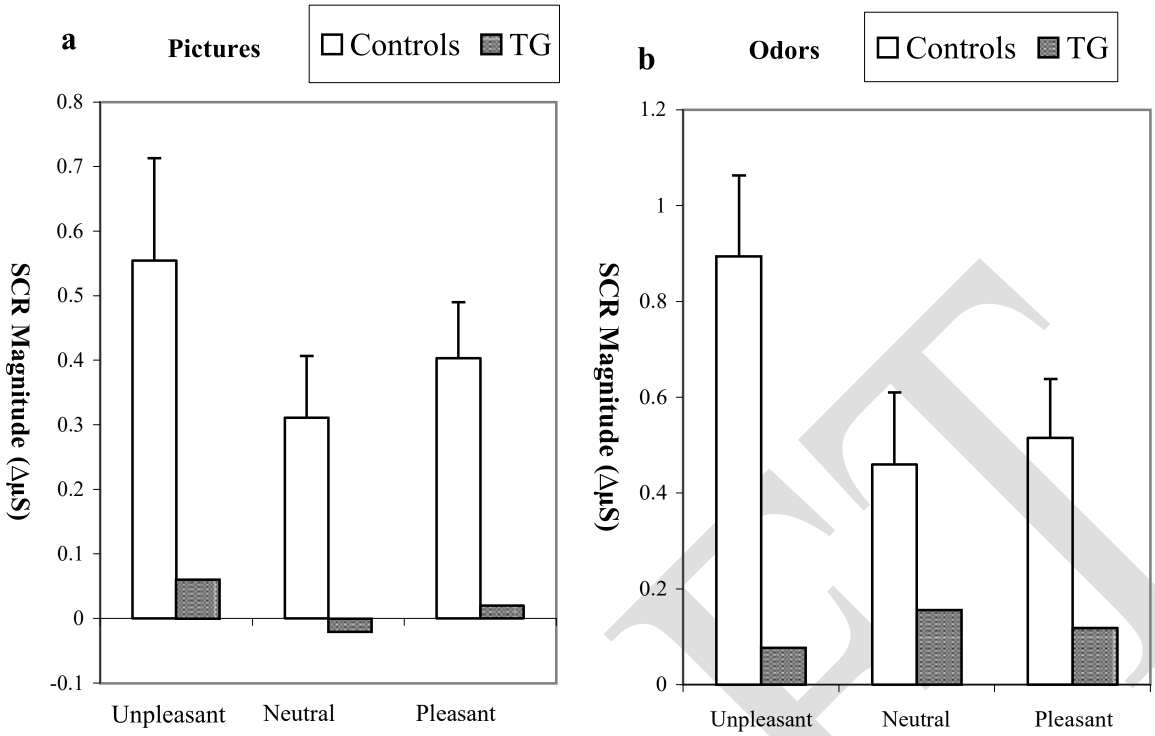

Fig. 5. Mean changes of skin conductance response to pictures (a) and odors (b) as a function of affective valence in controls and patient TG. Error bars represent SE.

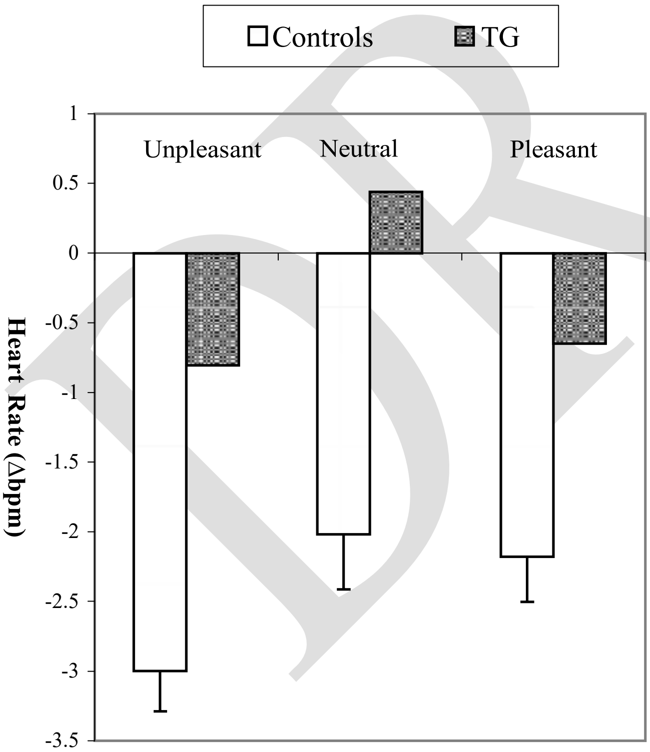

Fig. 6. Heart rate changes to pictures as a function of affective valence in controls and patient TG. Error bars represent SE.

that the perception of this chemical dimension was not affected in the patient and thus, was not a confounding variable contributing to the subjective experience of affect-related to olfaction.

Affective ratings

Both TG and the controls reported more pleasurable experience while viewing pleasant pictures, and more displeasure while viewing aversive pictures compared with the neutral condition (Figure 7a), [$F(2, 298) = 812.6$, $P < 0.0001$ and $t(29)$, all $P < 0.0001$, for controls and TG respectively]. More interestingly, no significant differences emerged between the controls and TG while viewing aversive pictures, $t(29) = 1.85$, $P > .05$. Furthermore, TG rated pleasant pictures as more pleasurable than did the controls, $t(29) = 2.27$, $P = 0.03$. All the subjects also rated the unpleasant pictures as more arousing than either neutral or pleasant pictures [$F(2, 298) = 210.03$, $P < 0.001$, and t(29), all $P < 0.0001$ for controls and TG respectively]. Finally, TG rated the pleasant [$t(29) = 4.48$, $P < 0.001$] and unpleasant [$t\ (29) = 2.4$, $P = 0.02$] pictures as more arousing than the normal subjects.

The affective ratings of both the control group and TG while smelling the odors also differed with respect to valence [controls: $F(2,98) = 196.68$, $P < 0.0001$; TG: $t(29)$, all $P < 0.05$]. As can be seen in Figure 7b, the controls reported more experience of displeasure in response to unpleasant odors, and more pleasure in response to pleasant odors, compared with the neutral condition (all $P < 0.0001$). For TG, unpleasant

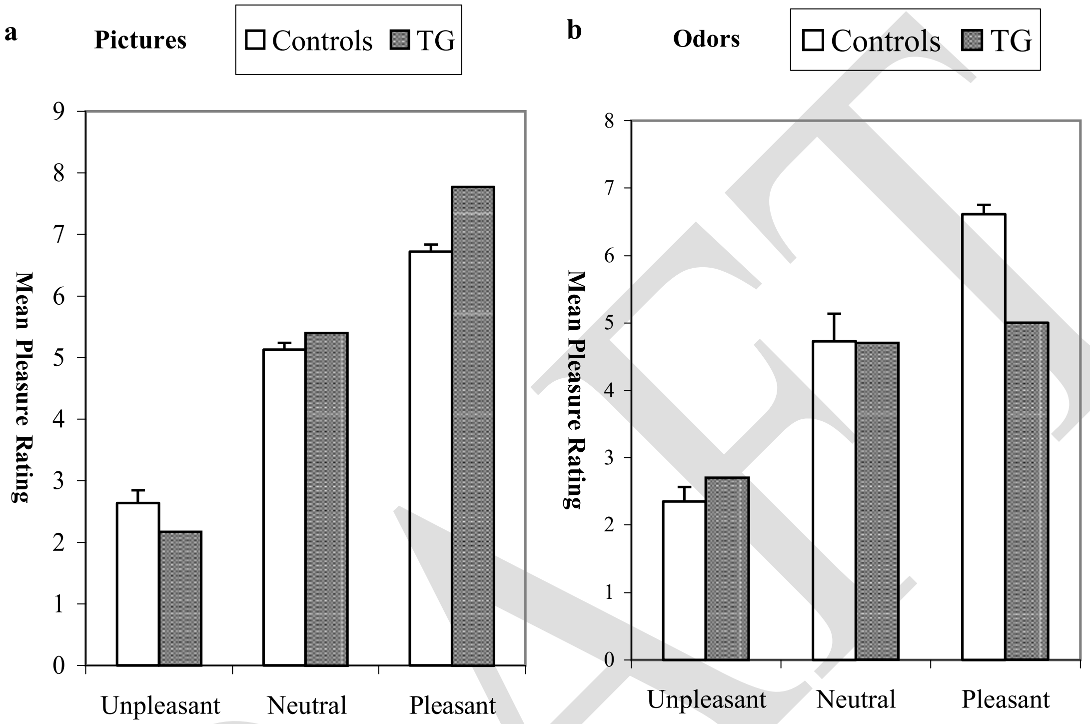

Fig. 7. Ratings of pleasure experience of pictures (a) and odors (b) as a function of affective valence in controls and patient TG. Error bars represent SE

odors were also experienced as more negative than the neutral olfactory condition (*P* < 0.05). However, TG's pleasure ratings did not differ from control subjects for both unpleasant [*t* (9) = 0.58, *P* > 0.05] and pleasant odors [*t*(9) = 2.01, *P* = 0.07]. Controls and TG rated unpleasant odors as more arousing than either pleasant (all *P* < 0.0001) or neutral odors (all *P* < 0.0001). However, TG's subjective arousal did not differ from the controls for both pleasant [*t*(9) = 0.92, *P* > 0.05] and unpleasant [t(9) = 1.62, *P*> 0.05] odors.

Intensity ratings

The rating of subjective intensity of olfactory stimuli also varied with affective valence for the controls [*F*(2, 98) = 648.38, *P* < 0.0001]. All the subjects rated unpleasant odors as more intense than pleasant odors (all *P* s < 0.0001), and pleasant odors as more intense than the neutral odors (all *P* s < 0.0001). However, no significant difference was detected between the controls and patient TG within either emotionally-valenced condition, *t*(9), all *P* > 0.05.

Covariation between subjective ratings and psychophysiological measures according to the olfactory task

For the control subjects, negative correlations were detected between *corrugator* EMG activity and pleasure ratings regardless of the nature of the olfactory task [explicit task: *r*(28) = -0.36, *P* = 0.05; implicit task: *r*(28) = -0.43, *P* < 0.05].

When intensity rating of odors was entered as a covariate, the negative correlations between *corrugator* EMG activity and pleasure ratings reached also significance (partial correlations, all $P < 0.05$). Skin conductance responses were also negatively correlated with pleasure ratings of odors [explicit task: r (28) = -0.45, $P < 0.05$; implicit task: r (28) = -0.36, P =0.05], and positively correlated with arousal during the explicit task of affective processing, r (28) = 0.39, P = 0.03. After controlling for intensity, the correlations between the SC responses and pleasure ratings remained significant (partial correlations, all $P < 0.05$).

For TG, the *corrugator* EMG activity during odor smelling was significantly related to pleasure ratings only during the explicit task of affective judgement (explicit task: r (28) = -0.59, P = 0.001; implicit task: r (28) = -0.31, P = 0.09). After controlling for intensity, the negative correlation between *corrugator* EMG activity and pleasure ratings during the implicit task of hedonic processing remained nonsignificant (explicit task: r = - 0.48, P = 0.007; implicit task: r = - 0.15, P = 0.44). Finally, SC responses exhibited by TG did not covary with affective or intensity ratings (all $P > 0.05$).

Identification of odors

To verify that the head injury in our patient did not reduce the keenness of smell, his ability to identify odors was assessed (olfactory identification performance is highly correlated with detection of odors, Cain, 1979). Patient TG and the controls provided accurate identification of verbal labels of odors more often than could be expected by chance (20%) during the task of forced-choice judgments. For TG, the level of accurate recognition reached 53.3% (16/30), whereas for the controls the percentage of accurate recognition of olfactory stimuli ranged from 53.3% to 76.66% (M = 64.66%). When only the pleasant and unpleasant stimuli were considered, the percentage of accurate recognition was 50% for TG, whereas for the controls the percentage varied between 50% and 70% (M = 62%). Chi-square tests comparing the individual correct responses of the controls with the accurate responses provided by TG revealed no significant difference between the latter and each subject of the control group (all $P > 0.05$). Thus, it can be concluded that the head trauma had not disturbed TG's ability to smell and identify odors.

Discussion

We undertook recording of multiple measures of emotion processes (facial muscles activity, indices of autonomic arousal, and self-reported subjective experience) to explore the proposed dissociation of these components in a patient revealing frontotemporal damages. Case TG provides evidence that damages altering the functioning of anterior temporal and orbitofrontal structures strongly affect facial EMG (corrugator activity being more reduced than zygomatic activity) and electrodermal responses to hedonically-valenced pictures or odors, whereas the subjective feeling states seem to be preserved[2]. The impairment in corrugator muscle region reactivity to unpleasant stimuli in TG suggests that the neural pathway involving the anterior temporal structures and/or the OFC likely plays a critical role in the processing of negative valence of stimuli. A similar alteration of facial EMG reactivity to negative pictures has been reported in a patient with a right orbitofrontal lesion (Angrilli *et al.*, 1999). Unlike control subjects, this patient did not show a high level of corrugator activity in response to either unpleasant pictures or unpleasant imagery scripts. In the case of olfaction, highly aversive odorant was found to produce strong rCBF increases in both amygdala and in the left OFC, whereas less aversive odorant produced rCBF in the OFC only (Zald and Pardo, 1997). Interestingly, a recent neuroimaging study, aimed at manipulating independently valence and intensity, demonstrated that orbitofrontal cortex activity was specifically related to the valence, but not the intensity of odors, whereas activity in the amygdala correlated with the intensity of odors, suggesting that the orbitofrontal cortex is the most promising candidate for exploring the neural basis of valence processing (Anderson *et al.*, 2003). These findings corroborate the relevance of our case study for studying the brain substrates of basic dimensions of the affective space. It is not clear, in the present study, why activity in the zygomatic region to pleasant pictures or pleasant odors did not differentiate between the brain-damaged patient and the control subjects. This result could be due to a selection of weakly evocative pleasant stimuli which only induced a slight increase of EMG activity over the cheek muscle region in our control subjects (see Cacioppo *et al.*, 1992). Furthermore, because zygomatic activity (smile muscle) reflects communicative intentions, future investigations need to consider the relevance of pleasant social stimuli in the processing of positive valence in our patient. As much as affective valence, physiological, but not subjective, correlates of arousal differentiated reliably between the brain-damaged patient and the control subjects. Electrodermal reactivity, as an index of sympathetic nervous system activation, was found to be higher in controls while being exposed to pleasant and unpleasant pictures or to unpleasant odors. By contrast, the self-reported scores of arousal discriminated the content of pictures and the quality of odors in both TG and the controls, suggesting that autonomic and experiential components of emotional arousal are likely mediated by distinct brain systems. Our finding of a lower electrodermal response to emotional stimulations confirms the critical role of the anterior temporal region (e.g., amygdala) and/or the orbitofrontal cortex in physiological arousal. Attenuation of skin conductance responses to unpleasant IAPS slides was found in patients with lesions of the amygdala or the orbitofrontal cortex (Angrilli *et al.*, 1999; Kubota *et al.*, 2000; Glascher and Adolphs, 2003). In humans, the direct electric stimulation of the amygdala increased skin conductance (Mangina and Beuzeron-Mangina, 1996), and the simultaneous recording of brain and electrodermal activity while subjects viewed aversive pictures indicated positive associations between amygdala activation and skin conductance responses suggesting a key role of this region in the modulation of autonomic arousal linked to perception (Liberzon *et al.*, 2000; Williams *et al.*, 2001). The slight heart rate deceleration in the controls and TG for pleasant and unpleasant pictures in our study can be interpreted as an indication of an orienting response (Graham and Clifton, 1966). However, the lack of significant difference between the patient and the control subjects suggest that cardiac responses in TG are consistent with non-altered attention to emotional pictures during the testing session.

Taken as a whole our findings support the view of a functional segregation between brain substrates supporting the neuromuscular, autonomic and experiential processing of affective valence and arousal effect of stimuli. The anterior temporal structures and the orbitofrontal cortex, probably functioning in tandem, mediate the elicitation of rapid somatic and autonomic changes to emotionally salient stimuli, while other brain regions, receiving inputs from the internal milieu, viscera and musculoskeletal structures (brainstem nuclei, anterior cingulate cortex, somatosensory cortices and insula) participate in the subjective experience of emotional states (Lane, 2000; Adolphs and Damasio, 2001; Dolan, 2002; Bechara and Naqvi, 2004). It can be noted that our

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[2] TG's average rating of the pleasant pictures, although higher than that reported by the control subjects, is very close to that provided by normal subjects in other studies (see stimuli selection section); thus it is reasonable to assume that TG's pleasure score is normally distributed.

patient had also minor damage in the left posterior insula, which does not appear to contribute strongly to emotional feelings. Accumulating evidence, based on functional magnetic resonance imaging (fMRI), pointed out that the anterior insular cortex, and predominantly the right portion, is involved in the conscious representation of visceral responses (i.e., interoceptive feelings) or in self-induced, and internally generated recalled emotion (Pardo *et al*., 1993; Lane *et al*., 1997; Damasio *et al*., 2000; Critchley *et al*., 2004; Craig, 2004). Other investigations further highlighted that emotional and feelings states are mediated by distinct brain regions. For instance, patients with unilateral or bilateral lesions of amygdala reported normal affective experiences in everyday life (Anderson and Phelps, 2002). Furthermore, fRMI experiments in patients with peripheral autonomic denervation suggested that the mental representation of bodily states of emotional arousal involved the anterior cingulate and/or insular-somatosensory cortices, but not the amygdala (Critchley, 2002; Critchley *et al*., 2002). Finally, subjects with alexithymia, which are impaired in their ability to explicitly recognize or experience emotions, but not in physiological arousal (Lane *et al*., 1997; Luminet *et al*., 2004), revealed differences in activity in the anterior cingular and mediofrontal cortices during emotional stimuli processing, but not in limbic structures (e.g., the amygdala, and the hypothalamus), or the orbitofrontal cortex (Berthoz *et al*., 2002).

The fact that a patient showing blunted facial and autonomic reactivity to emotional stimuli was able to report either similar (pleasantness ratings of unpleasant pictures and of odors) or higher (pleasantness ratings of pleasant pictures) subjective affective experience than normal subjects is not entirely consistent with a neo-Jamesian perspective of emotional consciousness (e.g., Damasio, 1995, 1998). According to this view, feelings are mental images arising from the representation of the changes that have just occurred in the body-proper and are being signalled to body-representing structures in the central nervous system (brainstem nuclei, somatosensory cortices, insula, cingulate cortex). Our results are rather consistent with emotion theories stating that feedback from the viscera (i.e., interoceptive cues) or facial expressions (i.e., proprioceptive/cutaneous cues from the striated muscles of the face) may contribute to the experience of emotion, but is not necessary to produce emotional experience (e.g., de Bonis, 1996; Keillor *et al*. 2002; Soussignan, 2004). It can be noted, however, that the findings of our study are in line with the elaborate "as-if-body-loop" mechanism proposed by Damasio (1995). Briefly, as a consequence of previous experience throughout ontogenesis, some brain regions (e.g., somatosensory structures/insular cortices) might have learnt to simulate an emotional body state and form representations of affective states, and later in life, might create a fainter image of an emotional state independently of actual body signalling. Although plausible, this hypothesis should be tested empirically in future studies using fMRI experiments in brain-damaged subjects displaying blunted emotional reactions.

An alternative interpretation of the observed dissociation between the physiological and experiential components of emotion processes have to be considered as well. Appraisal theorists claimed that emotional feelings result not only from the representation of current bodily states (i.e., bodily feelings or "feelings of"), but also from cognitive appraisals involving value judgments and semantic knowledge (i.e., "feelings about") (e.g., Averill, 1994). In this perspective, visual scenes and odors are semantically rich stimuli that contribute to emotional feelings with respect to standards or values allowing people to judge and experience them as being pleasant or unpleasant, even if they do not bodily react to them. For instance, although our patient displayed blunted bodily reactivity to unpleasant pictures, his conscious experience of unconscious emotional processing might be further related to the representation of the value of the stimuli rather than to the awareness of his bodily sensations.

A second purpose of the study was to examine whether affective reports and physiological responses to emotionally valenced stimuli are modality-specific. This purpose was guided by a previous neuroimaging study demonstrating that olfactory stimuli, as compared to other sensory stimuli, induced higher activation in both amygdala and orbitofrontal cortex (Royet *et al.* 2000). Furthermore, because of the extensive olfactory projections onto the anterior temporal regions and orbitofrontal cortex, and the greater potency of odors to evoke autonomic and subjective correlates of hedonic processing (Bensafi *et al.*, 2002b; Anderson *et al.*, 2003), a greater impairment of physiological responsiveness and verbal reports in our patient was expected for olfaction than vision. Our findings do not strongly support this hypothesis since facial and autonomic reactivity was similarly reduced to both pictures and odors, and TG's affective ratings of odors did not appear to be altered. However, it can be noted that we used a more limited number of odorant stimuli than pictures in our study, and given the wide variability of hedonic judgments for the pleasant dimension of odors reported in normative studies (Schaal *et al.*, 1997, 1998), further research is required to examine this issue with a larger sample of olfactory stimuli.

A final issue addressed in this study was the influence of the olfactory task on emotional processing, when the subjects were asked either to identify odors (implicit processing of affective valence) or to evaluate their hedonic valence (explicit processing of affective valence). Our results suggest that the pattern of psychophysiological activation depends in part on specific requirements of each task. More specifically, EMG reactivity of the *corrugator* to odors was higher in controls when they were instructed to process the hedonic meaning of the stimuli than when they were asked to identify them. This finding suggests that the explicit processing of affective stimuli by focusing attention on unpleasant features of odors increased facial muscle responsiveness in control subjects. This likely reflects the facilitating influence of top-down processes on facial efference. More interestingly, while *corrugator* activity, electrodermal activity and displeasure ratings were correlated in the controls regardless of the nature of the task, the facial and self-report measures of affective valence were related only during the hedonic judgement of unpleasant odors in TG (after controlling for intensity). That is, while unpleasant smells elicited negative facial responses for both implicit and explicit tasks in controls, TG did not appear to respond negatively while identifying unpleasant odors. This finding suggests that valence processing is not automatically activated when anterior temporal and orbitofrontal structures are damaged. In contrast, because feeling states seem to be preserved in TG, activity within structures presumed to support these feeling states (anterior cingulate, insula and somatosensory cortices) could be correlated with valence processing during the explicit task of affective judgement.

To our knowledge, this is the first study to examine facial, autonomic and subjective correlates of emotional processing to olfactory and visual stimuli in a patient with frontotemporal damages. In light of the present results and growing accumulative evidence, it appears that multiple components of emotion are probably mediated by distinct brain systems. More particularly, our findings provided evidence on the dissociability of the neural bases of subjective and physiological emotional responses. Thus, they suggest segregation between regions supporting generation of emotion and those supporting representation of emotion. Further experiments are required from both lesion and neuroimaging studies using implicit and explicit tasks with a number of psychophysiological and self-report measures in order to investigate the brain substrates mediating automatic processing and subjective awareness of affective valence and emotional arousal in humans.

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