Cerebral Bases of Emotion Regulation toward Odours: A First Approach

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Cerebral bases of emotion regulation toward odours: A first approach,
Behavioural Brain Research, volume 317, 2017, pages 37-45.
https://doi.org/10.1016/j.bbr.2016.09.027.

Cerebral bases of emotion regulation toward odours: A first approach

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A B S T R A C T

Emotion regulation is defined as an important mechanism for human adaptation. fMRI studies have recently highlighted its neural bases but most research uses visual stimulation to induce emotion, none of them using odorant stimulations. Nevertheless, olfaction is intimately linked to emotional pro-cesses, sharing some same neural bases and thus constitutes a valuable emotion-inducer in experimental conditions. The present study aims to determine the cerebral areas which might be involved in down-regulation, using pleasant and unpleasant odours as emotion-inducers. Eighteen subjects were scanned during 2 sequences of 12 stimulations, each with either a pleasant or an unpleasant odour. For one sequence, subjects were instructed to naturally experience their emotion induced by odour inhalation and for the other one, to decrease the intensity of their emotion. Consistent with previous work using emotion-inducers, emotion regulation resulted in higher activations of the dorsolateral prefrontal cortex and the anterior insula, but in lower activation of the amygdala. However, some areas (the posterior cerebellum and the orbitofrontal cortex) are less activated during regulation compared to maintain and thus appear to be specific to odorant stimulations. Finally the hedonic valence of the odour determines activations in different brain areas such as the supplementary motor area and the posterior cingulum. Thus, this study suggests abilities to regulate emotion in response to odours, involving brain areas usu-ally described in the literature for other emotional stimuli, but also specific areas depending partly of the hedonic valence of the odour.

1. Introduction

Airborne chemical stimuli constitute a continuous olfactory background in the everyday life environment. Our sense of olfaction is able to detect among these stimuli potential signals of interest and helps to cue an appropriate response. In particular, odours can colour perceptions about the world both positively or negatively through emotion processes and thus can modulate mood and behaviour [1,2]. This close relationship between olfaction and affective processing can be explained by the strong overlap between olfactory pathways and limbic brain structures. Projections from the olfactory bulb connect directly to the periamygdaloid region, subnuclei of the amygdala (corticomedial group) which form parts of the primary olfactory cortex [3,4]. Indeed, odours are able to more strongly modulate neuronal response within the amygdala than visual stimuli [5]. Other than the primary olfactory cortex, the

orbitofrontal cortex is well identified as part of the secondary olfactory cortex as well as a nexus for sensory integration, modulation of autonomic reactions and decision-making involving emotional components [6,7]. Other brain structures, described in cerebral imaging studies as being recruited by olfactory perception, are also involved in different emotion processing: particularly the hippocampal formation, the insula and the anterior cingulate cortex [8].

Emotions are necessary and helpful in numerous adaptive behaviours as they guide responses and decision-making processes. However, they can cause problematic situations when occurring, for example, at an inappropriate time or intensity level. Thus in these situations, emotion regulations can be of interest as a part of the emotional processes themselves. A growing literature has documented the abilities in emotion regulation in adults, children and the elderly as well as in patients suffering from mood disorders [9]. Typically, emotion regulation tends to decrease negative affect as well as increase or maintain positive affects [10]. Emotion regulation includes extrinsic and intrinsic processes implied in monitoring, evaluating and modifying emotions [11]. Automatic and voluntary emotion regulation can be distinguished. Voluntary emotion regulation is based on different cognitive strategies and the best-studied forms are attentional control and reappraisal [12], which are both supposed to depend greatly on individual resources in attention flexibility. More recently, cerebral imaging studies have shed light on the neural bases implied in these cognitive strategies, particularly distraction and reappraisal, and they point to a decreasing activity in limbic structures, particularly in the amygdala, and an increasing activity in the prefrontal cortex (PFC) during efficient emotion regulation [13–16]. Nonetheless, these studies focused mainly on cognitive reappraisal strategies, although the brain processes could be different for other strategies of emotion regulation [12,17–19].

Most studies on emotion regulation are based on visual stimuli (usually upsetting, disgusting or frightening pictures or films). To date, no study in cerebral imaging has investigated regulation abilities towards odour-generated emotion. Indeed, only one recent study [20] questioned the possibility of efficient emotion regulation with odours as stimuli. Subjects were instructed to use cognitive reappraisal strategies to enhance or down-regulate emotions generated by unpleasant odours. Self-evaluation of emotion was rated and the startle reflex was recorded. This study shows a delayed time course of emotion regulation towards odours compared to pictures and suggests that cognitive reappraisal of odour-evoked emotion may be limited when compared with that of picture-evoked emotion. Nevertheless, some abilities to modulate odour-generated emotions by cognitive processes have been demonstrated by de Araujo and his colleagues [21]: in their experiment, the subjects rated differently the pleasantness of a same odour (isovaleric acid combined with cheddar cheese flavour) according to the given semantic labels of “body odour” or “cheddar cheese”. Furthermore, these semantic labels also modulated the activations in some brain areas in response to this odour (i.e. anterior cingulate cortex, orbitofrontal cortex, amygdala). This study demonstrates the possibility of modulation of odour-generated emotion by cognitive (semantic) processes but does not respond to the question of voluntary emotion regulation in response to odours.

The present study aims to investigate by fRMI the brain areas which may be involved in the emotion regulation of pleasant and unpleasant odours. In this framework, we will firstly examine whole brain activations with odour stimulations contrasted with rest periods to ensure involvement of brain areas usually described in the literature in such experimental conditions. Secondly, we will examine the whole brain activations revealed by the contrast between regulated and non-regulated odour-induced emotions for both odorants. Thirdly, the analyses will focus on regions of interest (ROI) identified as important components of the secondary olfactory cortex to identify activations or modulations during the emotion regulation task.

2. Materials and methods

2.1. Participants

Participants were 24 right-handed students (9 females) at the University of Besançon (France). They were aged between 20 and 26 years and non-smokers. All participants were healthy, free of head colds or nasal allergies. They had no history of olfactory impairment and they were not under any regular medication (except for oral contraceptives for some of them). This study was reviewed and approved by the local ethics committee (Comité de Protection des Personnes Est II) and declared to the national authority (N° UF: 1013; DGS 2006/0494) in accordance with the Declaration of Helsinki on biomedical research. Participation required the completion of a written informed consent form and a medical examination prior to the fMRI session. All the subjects were scored for their olfactory sensitivity with the Sniffin' sticks test [22] to ensure that their sense of smell was appropriate for age. They obtained a mean score of 9.72 (sd = 0.60) for their olfactory threshold which is better than the norm [22].

2.2. Odorants and odour delivery

Two odours were used during the fMRI session. The first one (supplied by Across-Organics®), isoamyl acetate (IAA, banana-like odour) is usually considered to be pleasant [23] and the second one (Sigma-Aldrich®), thioglycolic acid (TA, rotten egg odour) is usually considered to be unpleasant [24].

These odours were delivered via a multi-channel custom-built olfactometer. This olfactometer was suitable for the fMRI environment and generated odours with a rapid and steady on-off time (for further details, see Andrieu et al., 2014 and Billot et al., 2011 [25,26]). A constant flow of odourless air ($1.4\,L\,min^{-1}$) was delivered to the subject through tubing with an output under the subject's nose (distance of 2 cm between output and the nostrils). The use of solenoid valves enabled odorant conditions to be switched with the air flow passing through bottles containing the odorants (1 mL), either IAA (50% diluted in diethyl phthalate: 171 ppm) or TA (4% diluted in diethyl phthalate: 2.8 ppm). These supra-threshold concentrations were chosen following preliminary tests on a panel of twenty undergraduate students (both males and females) to obtain approximately the same self-ratings of intensities. The measures of mean values on a Likert scale (from 0, low intensity to 9, high intensity) were 6.2 (sd = 1.96) for IAA and 5.7 (sd = 2.11) for TA. A Wilcoxon signed ranks test showed no difference between the intensity ratings of the two odorants ($W = 31.5$, $Z = 0{,}978$, $p = 0{,}328$). Although these odours are potentially olfactotrigeminal combinations, they were used with low concentrations and thus it can be assumed that the trigeminal component of the stimulation was weak. None of the subjects reported the typical feelings induced by trigeminal stimulations [27].

2.3. Experimental paradigm

2.3.1. Instructions to the subjects and training session

As odour-evoked emotion regulation is poorly documented, no particular cognitive strategy was prescribed to the subjects. They were only told that the aim of the study was to investigate the brain processes related to abilities to consciously decrease odour-triggered emotions. They were also told that they would have to smell a pleasant and an unpleasant odour. The labels of the odours were not mentioned as this can modulate the neural

olfactory processing [21]. Before the scan session, subjects were trained to decrease their emotions, inside the MRI scanner, with three stimulations of each odorant used. Each of the stimulations lasted twenty seconds and the subjects were instructed to try to decrease the intensity of the experienced emotion induced by the odours. After this training, they were asked to rate the pleasantness and unpleasantness of both odorants on two Likert scales (from 0, not pleasant/not unpleasant, to 9 very pleasant/very unpleasant) during a passive smelling phase. They were also asked about their strategy and instructed to keep the same one throughout the experiment. All the subjects reported that they understood the instructions and complied with them. Furthermore, they declared that they were able to down-regulate their emotions whatever the odour. Participants were also instructed to breathe normally and regularly (not to sniff during odour stimulation) and to keep their eyes closed during the scan session.

2.3.2. Experimental session

Participants were scanned during two sequences of 12 odorant stimulations each: 6 consecutive stimulations with IAA (pleasant) and 6 consecutive with TA (unpleasant). Between these two sequences, subjects were allowed a rest period of 1 min. For one sequence, subjects were instructed to maintain their emotion induced by odour inhalation (Maintain condition). For the other sequence, subjects were instructed to decrease the intensity of the emotion induced by odours (Decrease condition). These instructions were verbally given to the subjects through headphones at the beginning of each sequence. These two sequences, Maintain and Decrease, were counterbalanced from one subject to the other (Fig. 1A). Odour conditions (i.e. pleasant and unpleasant) were also counterbalanced between subjects. Each of the odorant stimulations lasted 20 s, alternated with 20 s of rest. Acoustic signals informed the subjects of the beginning and the end of the tasks for each stimulation (Fig. 1B). After scan sessions, participants were debriefed. They had to describe their strategy again and to rate, from 0 to 9, how successful their down-regulation of emotions was (0: low efficiency to 9: high efficiency).

2.4. fMRI data acquisition

Magnetic resonance images were collected on a 3-T scanner (G.E. Healthcare Signa, Milwaukee, WI, USA). First of all, a high-resolution T1-weighted (BRAVO FSPGR sequence) 3D anatomical scan with 134 slices, voxel size of 1×1 x 1 mm^3, 256×256 matrix and 256×256 mm^2 field of view (FOV) was recorded. Next, BOLD images were obtained covering the entire cerebrum and most of the cerebellum using an echo-planar imaging (EPI) sequence. Scan parameters included a 128×128 matrix, a repetition time (TR) of 2500 ms, an echo time (TE) of 35 ms and a FOV of 256 mm^2. Thirty-two 4-mm thick slices were acquired for each of the volumes. They were acquired in an oblique orientation 30° to the anterior commissure/posterior commissure line to minimise susceptibility artifacts in olfactory regions of the brain: ventral portions of the temporal and frontal lobes [28,29]. Functional scanning was always preceded by four dummy volumes to ensure tissue steady-state magnetisation. The total duration of the functional session was approximately 16 min. All the scans (2 per subject = 36) were inserted into the matrix design for statistical analysis.

2.5. Data analysis

2.5.1. Discarded participants

The aim was to create experimental groups according to strategy used to decrease emotions elicited by odorants. However, 22 subjects used the distraction (focusing their attention on something unrelated to the present stimuli) as an efficient regulation strategy and only two subjects used reappraisal (focusing their attention on re-interpretation of the stimuli). Among these 22 subjects, one subject was discarded because of a low score at the self-estimating task success scale (cut-off < 5), and three were discarded because of head movements. Thus, the subsequent analyses were performed on the 18 remaining subjects (7 females).

2.5.2. fMRI data

The block-design fMRI data were analysed with BrainVoyager QX™ 2.8 [30]. First of all, data were pre-processed, including head motion correction, temporal high-frequency filtering and spatial (FWHM = 8 mm) gaussian smoothing. Next, the functional data were spatially rescaled to a resolution of $3 \times 3 \times 3$ mm^3 using trilinear interpolation. Functional and anatomical images were normalized to Talairach space [31].

Following this pre-processing, a Random-effects General Linear Model-Based statistical analysis was performed [32]. Task regressors were defined as a boxcar function with 4 predictors of interest: Decrease-pleasant (Dp), Decrease-unpleasant (Du), Maintain-pleasant (Mp) and Maintain-unpleasant (Mu), and one predictor of no interest: rest. These boxcar functions were convolved with a double-gamma hemodynamic response function (HRF). To further account for head motion during scans, three rotations and three translations of head movement from each participant were included in each single-subject GLM-based analysis as predictors of no-interest.

Whole brain analyses were restricted to the only voxels located within the Montreal Neurological Institute (MNI) brain normalized to Talairach space. Results were assessed at an uncorrected statistical threshold of $p < 0.005$, corrected for multiple comparison with a cluster threshold calculated to correspond to $\alpha < 0.05$ via the BrainVoyager cluster-threshold estimator plugin performing 1000 iterations of a Monte-Carlo simulation [33,34]. We performed a 2 (TASK: Decrease and Maintain) x 2 (PLEASANTNESS: pleasant and unpleasant) analysis of variance (ANOVA) for repeated measures. In order to visualize whether brain regions were activated for unpleasant and pleasant odorants separately, *a posteriori* pairwise *t*-tests were used between several conditions: Decrease-pleasant *versus* Maintain-pleasant, Decrease-unpleasant *versus* Maintain-unpleasant and also (Decrease-pleasant + Decrease-unpleasant) *versus* (Maintain-pleasant + Maintain-unpleasant).

In the aim to perform more specific analyses, *a priori* regions of interest (ROIs) were delimited using a brain atlas [35]. ROIs were drawn for each subject in several regions known to play a key role in olfactory processing, namely the bilateral amygdala, piriform cortex, orbitofrontal cortex and anterior insula. These regions were combined into one mask, and we then performed the same 2×2 ANOVA for repeated measures, restricted to the only voxels located within this mask. Results were assessed at an uncorrected statistical threshold of $p < 0.05$ with a cluster threshold of 3 contiguous functional voxels. We used a more liberal cluster threshold as the ROIs already limited the number of statistical comparisons in the interaction analyses [36].

3. Results

3.1. Emotion regulation strategy and hedonic assessments of the odours

As mentioned above, 22 subjects spontaneously used distraction and 2 subjects used reappraisal as a regulation strategy. Considering the only 18 subjects taken into account for the fMRI analyses, the mean of their self-ratings of emotion regulation efficiency was 6.44 (sd = 0.98). Their ratings of the pleasantness/unpleasantness of the odours in a passive smelling phase during the training session

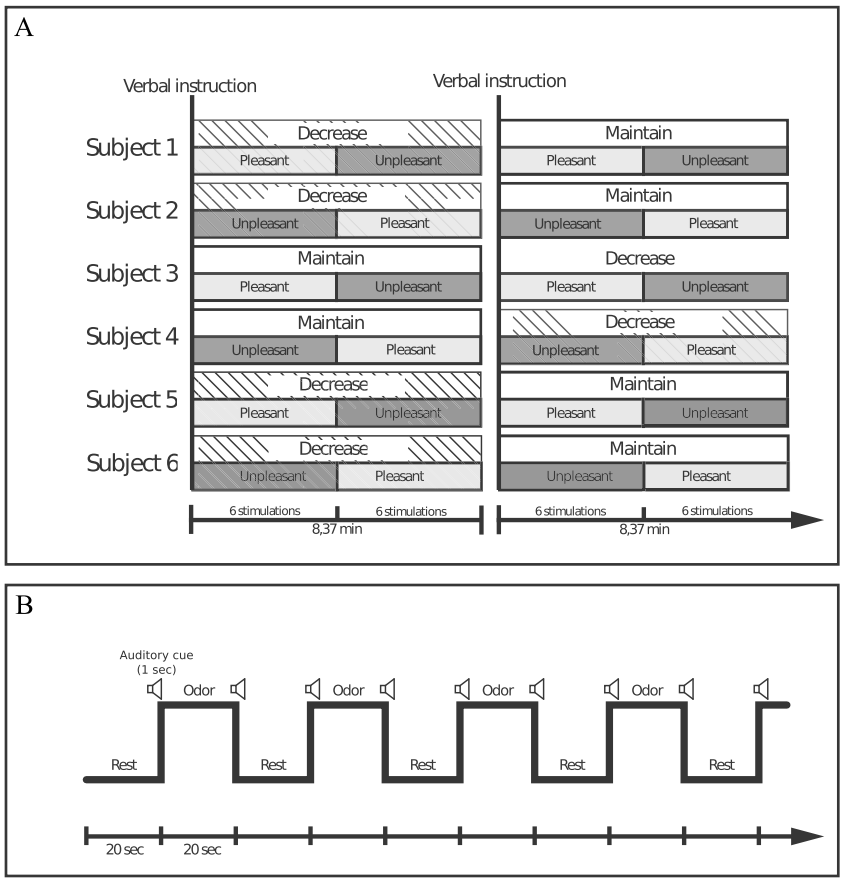

Fig. 1. Schematic view of the experimental design. (A) Experimental design during fMRI: the two sequences, "Maintain" and "Decrease" emotions, are counterbalanced from one subject to another as well as the order of the pleasant and unpleasant odorant stimulations. (B) Details of odorant stimulations during one sequence.

were, for IAA, mean values: 7.22 (sd = 1.40) for pleasantness and 1.17 (sd = 1.43) for unpleasantness. For TA, mean ratings were 0.89 (sd = 1.08) for pleasantness and 6.22 (sd = 1.63) for unpleasantness. In order to assess hedonic differences between odorants, Wilcoxon signed ranks tests were performed between IAA and TA (Statsoft – Statistica) for both pleasantness and unpleasantness ratings. There were highly significant differences between the two odorants for pleasantness ($W = 153, Z = 3.621, p = 0.0003$) and for unpleasantness ($W = 0, Z = 3.723, p = 0.0002$).

3.2. Whole brain analysis

The 2×2 ANOVA for repeated measures reveals a main effect of the factor TASK within clusters located in the left superior prefrontal cortex (PFC) and the left posterior cerebellum (Fig. 2A). Post-hoc paired *t*-test (Du + Dp) > (Mu + Mp) shows that the left PFC was more activated during Decrease than Maintain condition (whatever the pleasantness) whereas the left cerebellum was more activated during Maintain compared to Decrease condition (Fig. 3).

ANOVA also reveals a significant interaction between TASK and PLEASANTNESS within brain areas such as the bilateral posterior cingular cortex, the left superior temporal gyrus and the left supplementary motor area (SMA) (Fig. 2B). *A posteriori* paired *t*-test Du > Mu (Decrease *versus* Maintain for unpleasant odours only) shows that the bilateral posterior cingulate gyrus is more activated during decreasing than maintaining emotions induced by unpleasant odours, whereas the left temporal gyrus is less activated during Decrease than Maintain condition (Fig. 3). A second *a posteriori* *t*-test Dp > Mp (Decrease *versus* Maintain for pleasant odours only) reveals that the SMA is more activated during the Decrease task compared to the Maintain task (Fig. 3). Significant clusters are listed in Table 1.

Lastly, a paired *t*-test contrast Maintain > Rest shows activations within bilateral insular cortices and bilateral orbitofrontal cortices (Fig. 3).

3.3. ROI analysis

The 2×2 ANOVA for repeated measures restricted to ROIs (threshold at $p < 0.05$ uncorrected) points out an effect of factor TASK within the right anterior insula, right lateral orbitofrontal cortex (OFC) and left amygdala/piriform cortex. A posteriori paired *t*-test (Du + Dp) > (Mu + Mp) indicates that the right anterior insula was activated while participants decreased the intensity of their emotions, compared to the Maintain condition, whereas the right lateral OFC and the left amygdala/piriform area are more activated during the Maintain, compared to the Decrease condition (Fig. 4).

There is also a significant interaction between TASK and PLEASANTNESS in the bilateral anterior insula and the left anterior OFC. *A posteriori* paired *t*-test Dp > Mp and Du > Mu reveals that the right anterior insula was more activated during the Decrease task, especially for pleasant odours, than in the Maintain task. The t-map (Fig. 4) also points out that the left anterior OFC was less activated during the Decrease task compared to the Maintain task, only for pleasant odours. Significant clusters are listed in Table 1.

4. Discussion

The aim of this study was to highlight neural substrates of emotion regulation towards odorant stimulations. The perceptual

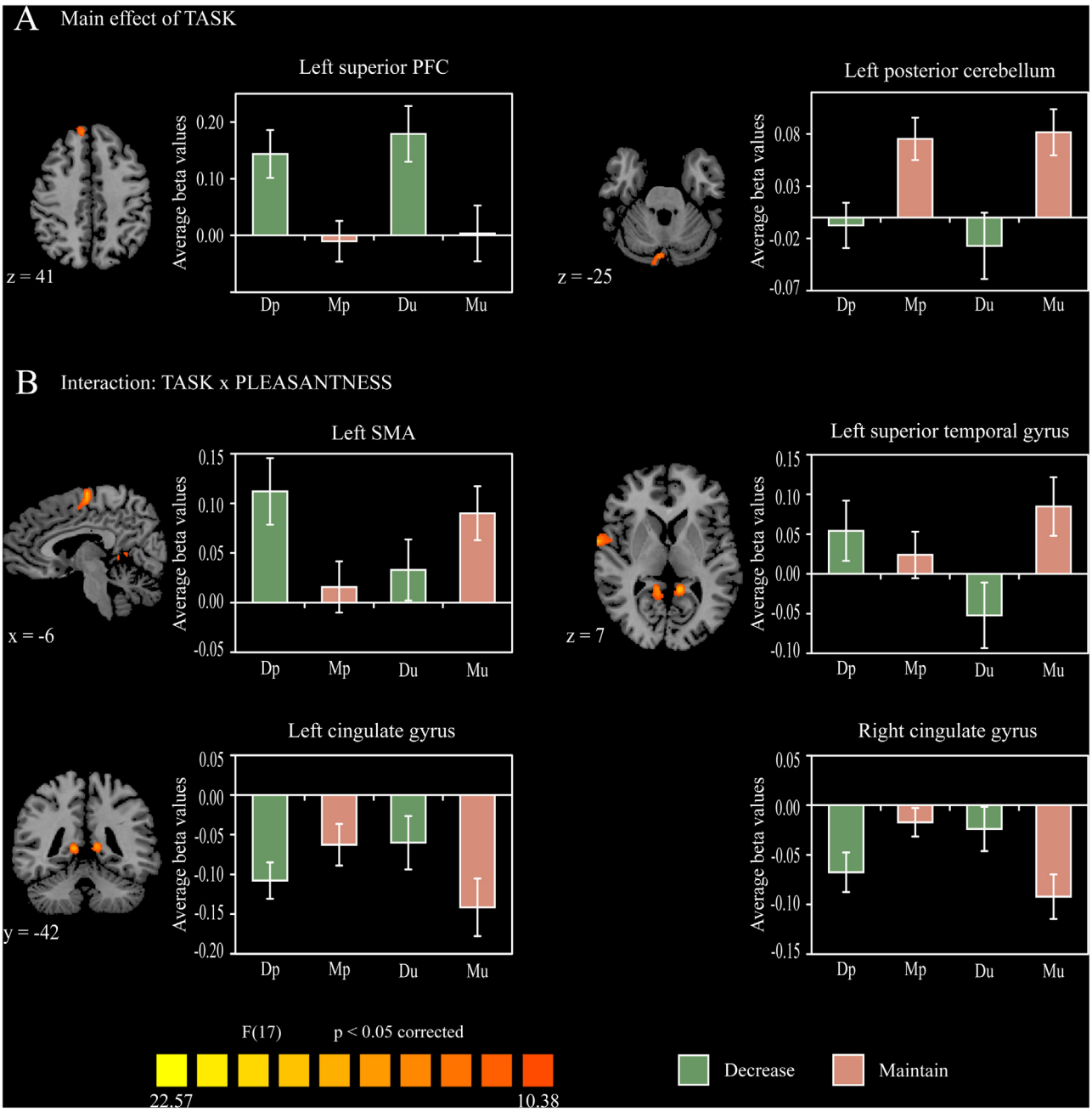

Fig. 2. Whole brain analysis of variance. The colour scale illustrates F values reflecting the degree of activation. Only voxels with a p value less than 0.05 (corrected) are displayed. x, y and z represent the Talairach coordinates. Brain is displayed in neurological convention (left hemisphere is on the left). Histograms illustrate averaged beta values across all subjects and all clusters for the four conditions. Dp: Decrease pleasant, Mp: Maintain pleasant, Du: Decrease unpleasant, Mu: Maintain unpleasant. Error bars show the standard errors of the mean. (A) Main effect of factor TASK shows the areas involved in down-regulation, whatever the odour (pleasant or unpleasant). (B) Interaction between TASK and PLEASANTNESS shows areas involved in down-regulation for specific odour (pleasant or unpleasant).

processing of emotions and odours is dominated by its hedonic feature (pleasantness/unpleasantness) but odours as emotion-inducers have been rarely used in the literature on emotion regulation. Ratings of pleasantness by participants clearly shows that the two odours have opposite hedonic features.

The present experiment is the first attempt to our knowledge to describe the neural networks involved with olfactory cues. First of all, the results obtained in the present experimental conditions show a strong preference for distraction when participants had to decrease emotions induced by odorants. In their study, Adolph and Pause (2012) [20] showed that subjects had a mild preference for self-focused reappraisal compared to situation-focused reappraisal, but participants had to use a reappraisal strategy. On the contrary, in the present study, they were free to use any strategy. Distraction was not shown as more efficient than reappraisal in other experimental conditions [37]. However, it could appear to be more efficient in everyday life experiences [38] and is less costly in cognitive resources, which can explain the choice of our subjects. Further studies would be of interest to investigate the preferential strategies, and their efficiencies, in down- or up-regulation spontaneously used by subjects in response to odours compared to visual cues, for example. It cannot be excluded that distraction could be a more efficient strategy when olfactory cues are concerned due to their specific cerebral pathways.

Considering the imaging data, a contrast compared the passive smelling of odours (Maintain condition) to the Rest condition, with-

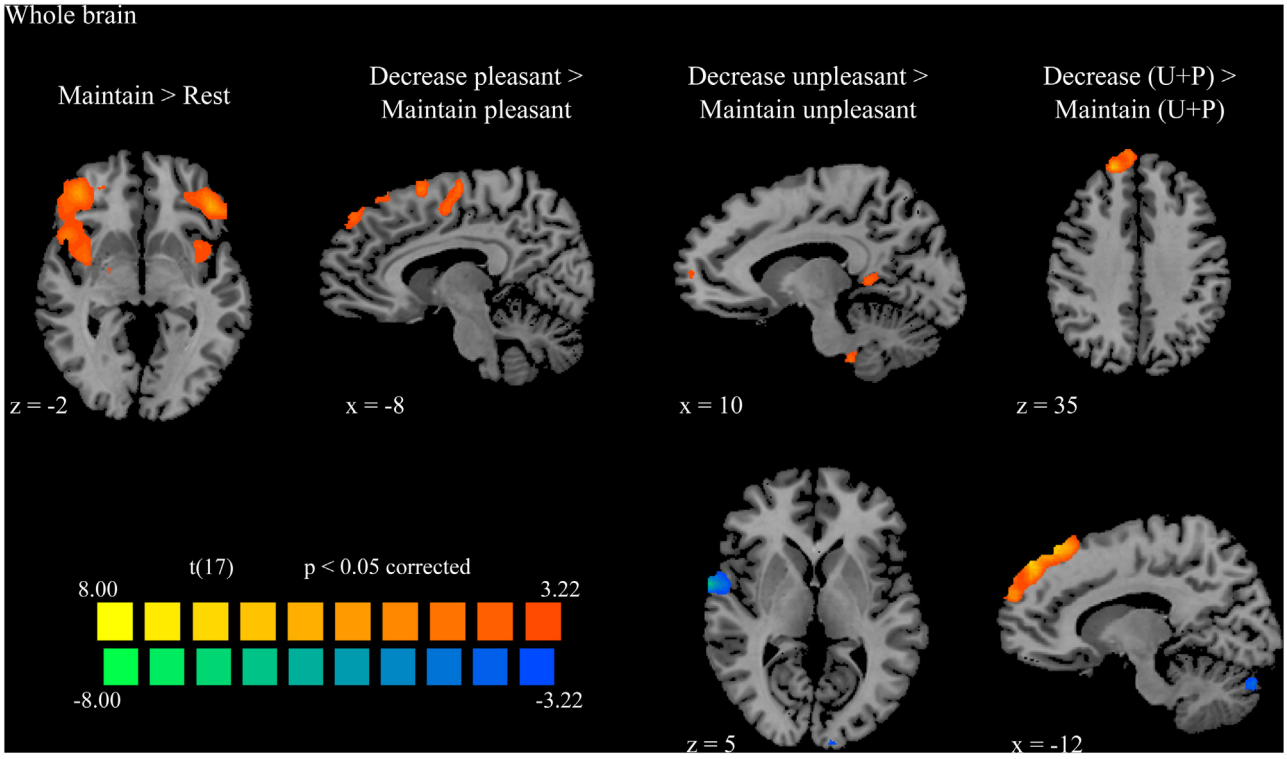

Fig. 3. Whole brain *a priori* paired *t*-tests. Four contrasts are depicted: Maintain > Rest (areas activated during an odorant stimulation), Decrease pleasant > Maintain pleasant (areas involved in down-regulation for only pleasant odours), Decrease unpleasant > Maintain unpleasant (areas involved in down-regulation for only unpleasant odours) and Decrease (unpleasant + pleasant) > Maintain (unpleasant + pleasant) (areas involved in down-regulation for pleasant and unpleasant odours collapsed). The colour scale illustrates t values, reflecting the degree of activation. Only voxels with a p value less than 0.05 (corrected) are displayed. x and z represent the Talairach coordinates. Brain is displayed in neurological convention (left hemisphere is on the left).

Table 1
Significant clusters of whole brain and ROI ANOVA.
R: right hemisphere; L: left hemisphere; x,y,z: Talairach coordinates; F: F-value of the voxel peak; p: significance of the voxel peak; K: size of the clusters in number of connected voxels of 3 × 3 × 3 mm3. SMA: Supplementary Motor Area; OFC: Orbitofrontal Cortex.

Brain regions		Tal. Coords				Voxel peak	
		x	y	z	K	F	p
Whole brain ANOVA ($p \leq 0.05$ corrected)							
Main effect of factor TASK							
L	Superior Frontal Gyrus	−9	47	43	20	15.5207	0.0010
L	Pyramis (Cerebellum)	−3	−74	−23	22	20.4803	0.0003
Interaction: TASK × PLEASANTNESS							
L	SMA	−6	−13	64	28	26.4015	0.0001
L	Superior temporal gyrus	−63	−1	7	43	23.6041	0.0001
R	Posterior cingulate gyrus	9	−46	7	30	25.5132	0.0001
L	Posterior cingulate gyrus	−12	−43	4	26	28.8169	0.0001
ROI ANOVA ($p \leq 0.05$)							
Main effect of factor TASK							
R	Anterior insula	42	8	20	24	13.6046	0.0018
R	Anterior insula	45	21	10	36	10.4459	0.0049
R	Anterior insula	36	8	1	7	6.3987	0.0216
R	Lateral OFC	45	38	−1	4	5.8057	0.0276
L	Amygdala/Piriform	−24	6	−17	29	7.3027	0.0151
Interaction: TASK × PLEASANTNESS							
R	Anterior insula	42	14	−5	158	14.276	0.0015
L	Anterior insula	−54	1	4	93	10.4697	0.0049
L	Anterior OFC	−24	38	−1	8	8.7358	0.0089

out odour. We observe in this situation bilateral activations in the OFC and insular cortex. These areas are typically described as parts of the secondary olfactory cortex. Both areas are also involved in the integrative processes of emotion [8].

When participants have to down-regulate their emotions compared to the Maintain task, the most significant findings were the increased BOLD signal in the dorsolateral prefrontal cortex (dlPFC) and the decreased BOLD signal in the posterior cerebellar regions. Thus the present data indicate that the superior part of the dlPFC is actively involved in cerebral mechanisms of emotion regulation towards odours. In the growing literature of fMRI studies, the PFC is systematically identified as playing a key role in emotion regulation

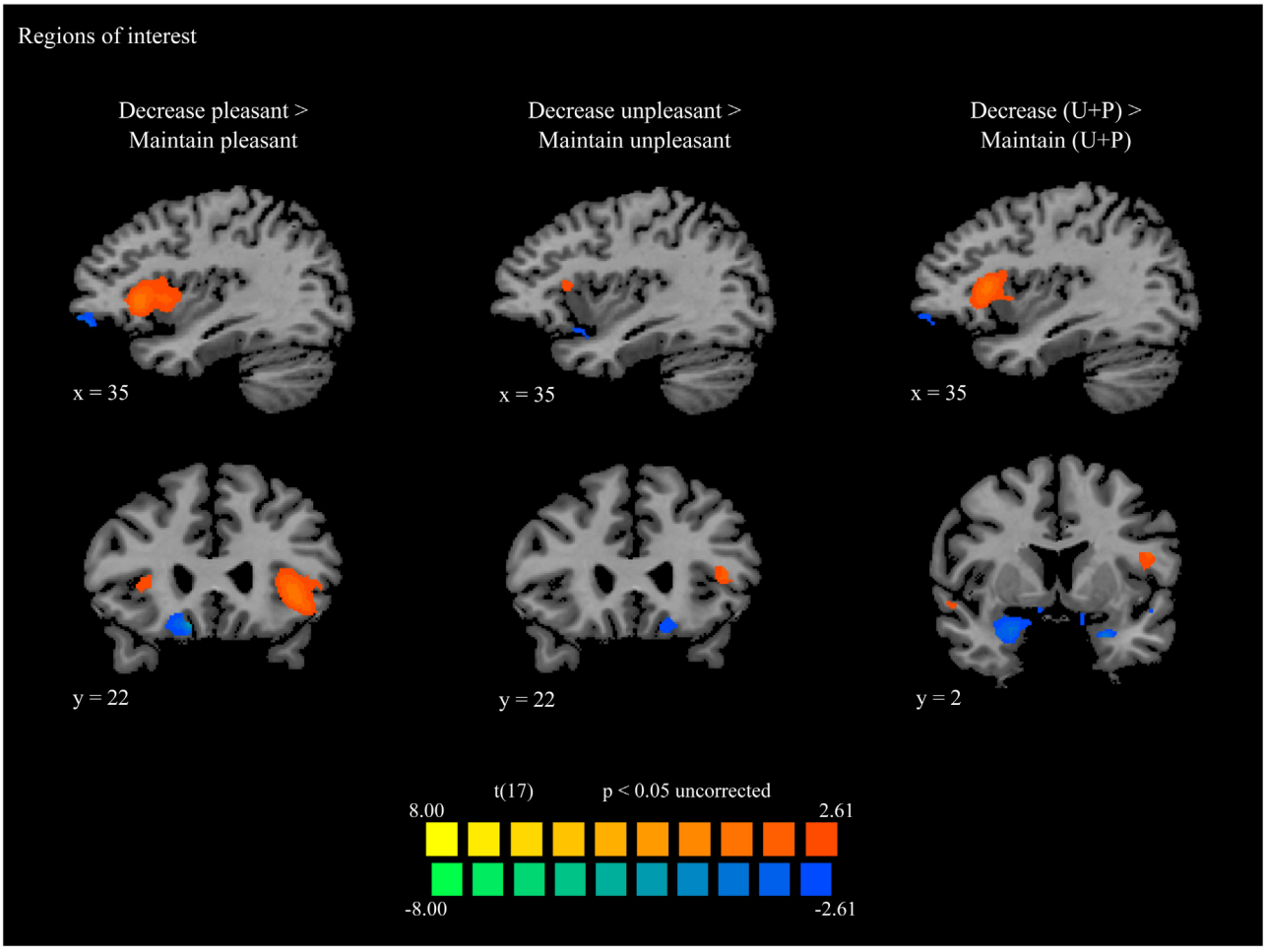

Fig. 4. Region of interest *a priori* paired *t*-tests. Three contrasts are depicted: Decrease pleasant > Maintain pleasant (areas involved in down-regulation for only pleasant odours), Decrease unpleasant > Maintain unpleasant (areas involved in down-regulation for only unpleasant odours) and Decrease (unpleasant + pleasant) > Maintain (unpleasant + pleasant) (areas involved in down-regulation for pleasant and unpleasant odours collapsed). The colour scale illustrates t values, reflecting the degree of activation. Only voxels with a p value under 0.05 are displayed. x and y represent the Talairach coordinates. Brain is displayed in neurological convention (left hemisphere is on the left).

processes. Moreover, it appears to be especially involved in voluntary control of attention [39]. More generally, the Brodmann area 8 does not seem to be specifically activated by a particular strategy. Indeed, activations in this region were observed in previous works studying reappraisal [16,40], suppression [17] and attentional deployment [41,42]. In our study, participants were free to use any strategy but most of them used attentional deployment. The dlPFC appears to be strongly implicated in cognitive control of attention, especially in situations of cognitive conflict [43–45]

According to these studies, the dlPFC is "warned" when a cognitive conflict is detected. Its role is to transfer the treatment of information in other regions more relevant to reach the goals of individuals. Moreover, lateral parts of the PFC appear to sort and select stimuli, and bring them to focus their attention according to the relevance for the goal of individuals [19,46]. However, the dlPFC does not seem to only play this role for cognitive stimuli, but also for emotional ones, according to many authors [19,40,46]. Thus, our data suggest that the predominant role of the dlPFC usually described in the literature on emotion regulation is also present when odours are the emotion-inducers.

The fact that cerebellum is less activated during emotion regulation than during the Maintain condition deserves special attention. The cerebellum was not taken into account in the recent meta-analyses on cerebral imaging of emotion regulation [47,48]. Indeed, it can be supposed that it is just not considered in most of the studies on emotion regulation which focused on the cerebral networks. Cerebellar activations in response to odours have been reported in several imaging studies, with unpleasant or pleasant odorants [26,49–51], and these activations are proportional to odour concentration [52]. As sniff volume is inversely proportional to odour concentration, the hypothesis [29] is the involvement of the cerebellum in a rapid feedback for regulation of the sniff volume, more activated when the sniff volume has to be controlled (decreased in the case of a high concentration). In the present study, the cerebellum is deactivated when the odour-induced emotion has to be decreased, underlying a poor automatic feedback control in this situation following this previous hypothesis. Thus a voluntary regulation of odorant-induced emotion would shunt out this automatic pathway of control of perception. Alternatively, other roles of the cerebellum in processes of emotion and/or cognitive processes such as attention have also been mentioned [53–55] and could explain our results.

We observe that specific cortical areas are activated according to the regulation task but differentially due to the valence of the odorant. Particularly, when the odour is unpleasant and during the regulation task, the posterior cingulate cortex (CC) is more activated than during the Maintain condition. No activation of this sub-region is mentioned in the recent meta-analyses on cerebral imaging of emotion regulation [47,48]. However, activations of this sub-region have been reported in cerebral imaging of olfaction,

especially in the case of odorants with a trigeminal component [56] which stimulate not only the olfactory system (cranial nerves I), but also the trigeminal system (cranial nerves V). It can be assumed that the odours used in the present experiments both have a trigeminal component but perhaps more important for the TA. The CC involvement is usually interpreted in terms of activation of a part of a network in response to nociceptive stimulation and it has been suggested that sub-regions of the CC have a role in avoidance behaviour in response to trigeminal stimulations [57]. This avoidance behaviour, in the present experiment, could participate in the regulation processes. Thus, the CC could be a part of the cerebral network implied in emotion regulation but specifically in response to unpleasant odours with a trigeminal component. The superior temporal gyrus was less activated in the same contrast. This area is not consistently mentioned in the literature on emotion regulation but its activation has been mentioned when contrasting an evocative, emotionally potent odour with a control odour [58].

When a pleasant odour is used, the activation of the SMA can be noted during down-regulation compared to the Maintain condition. On the contrary to the posterior CC, the SMA is a well identified component of the neural networks described in emotion regulation, mentioned by both Frank et al. (2014) and Kohn et al. (2014) [47,48]. Moreover, its activation would be more important with distraction than with reappraisal in a down-regulation task [19]. Its activation is interpreted as reflecting cognitive aspects of the regulatory task, which would be thus shared by down-regulation in response to odours as well as in response to other types of emotion-inducers at least when the odour is pleasant.

The ROI analysis points out some areas also concerned by the regulation task. Thus the activation of the right anterior insula is increased during down-regulation compared to the Maintain condition. This cannot be considered as specific to the regulation of an odour-induced emotion. Similar activation is noted by Winecoff et al. (2011) [16] with visual-induced emotions. Co-activations of the insula with others brain areas is also mentioned by Kohn et al. (2014) [48] during down-regulation. Giuliani et al. (2011) [59] have pointed out that the anterior insula is concerned by expressive suppression as a strategy for emotion regulation. Moreover, odorant-induced insular activation is commonly reported in neuroimaging studies of olfaction, interpreted as related to the integration of olfactory information and perhaps in its hedonic assessment [60,61]. This involvement in hedonic assessment could explain the differential activation according to the pleasantness of odours. Not surprising, the activation of the amygdala decreased during the down-regulation task, in the same way as with other emotion-inducers [47]. The activation of the lateral OFC also decreased during the regulation task. The OFC is an important component of the second olfactory cortex as an integration centre of odour perception. Some brain imaging studies of emotion regulation described activations of the OFC during cognitive reappraisal but not during distraction or expressive suppression [17,41]. In the present study, the activation of the lateral OFC during the Maintain condition could correspond to its contribution in selective attention towards the olfactory stimuli by inhibiting interference [62] and this selective attention to the odour could be removed with distraction. When the pleasantness of the odour is considered (i.e. pleasant or unpleasant), post-hoc analysis reveals a decreasing activation for pleasant odours during the regulation task in the anterior OFC. It can be explained by the fact that the anterior part of the OFC appears more concerned by higher levels of processing of information, including subjective pleasantness and unpleasantness ratings [63] Nonetheless, results of the ROI analysis should be considered very cautiously because of the low statistical threshold (0.05). Further studies are necessary to confirm or rule out the hypothesis of an activation of the anterior insula and a modulation of the amygdala and OFC in the down-regulation of odour-triggered emotions.

To summarize, the present study was a first attempt to identify some brain areas which could be specifically or not concerned by emotion regulation with odour-inducers. Due to the strategy spontaneously used by the participants, our results are restricted to distraction as a strategy for regulation. However, this spontaneous choice questions the efficiency of cognitive reappraisal in the context of odour-induced emotion and it would be necessary to take into account this question for further investigation setting cognitive reappraisal to subjects in response to odours. The results from our experimental paradigm showed that some brain areas, such as the dlPFC, the anterior insula, the amygdala, appear recruited in the same way as with other emotion-inducers, such as visual stimuli. However, other brain regions, such as the posterior CC, could be specific to emotion regulation in response to odours, or to some types of odours with a trigeminal component, which is the case for most odorants [64]. At least, specific parts of networks (posterior CC, SMA) could be concerned depending on the pleasantness of the odorant stimulation. Thus, the understanding of the emotion regulation networks towards odours needs different studies investigating the implied processes, and their efficiencies, according to the acute characteristics of odorants used.

Declaration of interest

No competing interests exist.

Acknowledgments

This study was supported by a grant from the “Agence Nationale de la Recherche” ANR 11 EMCO 003 002 STREEM project “Stratégies de Régulation Emotionnelle”. We are also grateful to Nathalie Islam-Frénoy for her language assistance in the manuscript and we thank all the healthy volunteers for participating in the study.

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