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Perfumers' expertise induces structural reorganization in olfactory brain regions

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ABSTRACT

The human brain's ability to adapt to environmental changes is obvious in specific sensory domains of experts, and olfaction is one of the least investigated senses. As we have previously demonstrated that olfactory expertise is related to functional brain modifications, we investigated here whether olfactory expertise is also coupled with structural changes. We used voxel-based morphometry to compare the gray-matter volume in student and professional perfumers, as well as untrained control subjects, and accounted for all methodological improvements that have been recently developed to limit possible errors associated with image processing. In all perfumers, we detected an increase in gray-matter volume in the bilateral gyrus rectus/medial orbital gyrus (GR/MOG), an orbitofrontal area that surrounds the olfactory sulcus. In addition, gray-matter volume in the anterior PC and left GR/MOG was positively correlated with experience in professional perfumers. We concluded that the acute olfactory knowledge acquired through extensive olfactory training leads to the structural reorganization of olfactory brain areas.

Introduction

Numerous studies in humans have indicated that functional and anatomical modifications occur in the brain because of learning and training. In experts with enhanced visual, auditory or motor skills, such as musicians and athletes, greater performance is associated with functional (Cross et al., 2006; Lotze and Halsband, 2006; Ross et al., 2003) and structural (Bermudez and Zatorre, 2005; Draganski et al., 2004; Gaser and Schlaug, 2003a,b; Kleber et al., 2010; Maguire et al., 2000; Sluming et al., 2002) brain changes in modality-specific brain areas, which supports the view that brain reorganization is associated with expertise.

What about olfactory expertise? Could the brain reorganization observed with expertise in other modalities be generalized to olfaction? This question has been addressed only once before (Plailly et al., 2012), probably because human olfactory abilities are less essential for survival than other senses and are more poorly developed compared to those of other mammals, and because olfactory experts, such as perfumers, are rare. While exploring brain processes that are related to odor mental imagery, we observed an expertise-dependent functional reorganization in olfactory and memory-related brain areas, such as the primary olfactory (piriform) cortex (PC) and the hippocampus. This effect was concomitant to enhanced behavioral performances with expertise. To the best of our knowledge, brain structural reorganization in olfactory expert has never been investigated. However, focusing on alterations of olfactory processes, several studies have shown gray matter (GM) atrophy in olfactory-related areas in patients suffering from anosmia, or hyposmia because of peripheral dysfunction (Abolmaali et al., 2002; Bitter et al., 2010a,b; Collet et al., 2009; Haehner et al., 2008; Mueller et al., 2005; Rombaux et al., 2006, 2009a,b) or neurological disease (Ibarretxe-Bilbao et al., 2010; Rupp et al., 2005; Wattendorf et al., 2009). Whether subjects with olfactory expertise present modifications of GM volume in olfactory areas is an open question.

Computational morphometry tools allow for investigation of structural brain changes related to development, learning, expertise and pathology (for a review, Mietchen and Gaser, 2009). The voxel-based morphometry (VBM) technique is broadly used and remains an active field of methodological research (Ashburner and Friston, 2000). Several pitfalls in image preprocessing, including inter-individual misregistration and errors in the segmentation procedure (Bookstein, 2001), skull-stripping and bias correction (Acosta-Cabronero et al., 2008), and bias induced by improper templates and priors, are the subjects of vigorous debate in the neuroimaging community. However, methodological improvements have recently been developed that may limit

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possible errors (Ashburner, 2007; Klein et al., 2010). First, the segmentation algorithm can include bias correction, and can now model not only brain tissues but also non-brain tissues. This allows removing potential contamination from soft tissues outside the brain, large vessels and skull. Second, a study-specific template can be created. Third, algorithms for diffeomorphic image registration with a high number of degrees of freedom can be employed to obtain accurate registration of each individual brain with a given template. In particular, the algorithm for "Diffeomorphic Anatomical Registration using Exponentiated Lie algebra" better known under the DARTEL acronym (Ashburner, 2007) is considered as being among the best algorithms available (Klein et al., 2010). Fourth, the segmentation and the spatial registration procedure can be combined in a unified approach to improve preprocessing steps (Ashburner and Friston, 2005). A recent VBM test–retest study showed that when using all above-mentioned improvements as implemented in Statistical Parametric Mapping 8 (SPM8) using DARTEL, this permits to avoid obtaining most of the false positives (Focke et al., 2011). Fifth, voxels which feature low effect-size and very low variance can be artifactually significant (Bookstein, 2001). In order to reduce false positives, the newest SPM8 release (v.4010, April 04, 2011) includes a scheme to force such voxels to have low significance in VBM statistical analysis.

In the current study, we used structural magnetic resonance imaging (MRI) and the VBM pipeline with DARTEL (Ashburner, 2007) in (SPM8) software. We scanned 14 perfumers renowned for creating perfumes, 13 students from an international school of perfumery and 21 control subjects. We took advantage of variability in length of expertise in professional perfumers to identify structural brain reorganization that is associated with experience under the hypothesis that intensive olfactory training may lead to increased GM volumes in olfactory- and memory-related areas.

Materials and methods

Subjects

Forty-eight healthy right-handed subjects participated in our study. The perfumers' group included 13 young experts (YE; 3 men; mean age, 23 years; range, 21–26 years) who were students at an international school of perfumery (Institut Supérieur International de la Parfumerie, de la Cosmétique et de l'Aromatique, Versailles, France), and 14 older experts (OE; 10 men; mean age, 42 years; range, 29–59 years) who were professionals known for creating perfumes. While the YE had been trained for 2 years at most as part of their education, all OE had 5–35 years of career-relevant business experience. The control group was composed of 21 untrained subjects, including 8 young controls (YC; 2 men; mean age, 25 years; range, 24–28 years) and 13 older controls (OC; 6 men; mean age, 40 years; range, 30–55 years). Subjects from both groups were matched in age ($F_{(1,47)} = 0.10$, $p = 0.712$) and gender ($\chi^2 = 0.34$, $p = 0.560$).

The exclusion criteria were rhinal disorders (e.g., a history of nasal-sinus surgery), pregnancy, ferrous implants (e.g., pacemakers and cochlear implants), claustrophobia, or any neurological disease. This study was conducted according to French regulations on biomedical experiments using healthy volunteers and according to the principles outlined in the Declaration of Helsinki. All subjects gave written informed consent, as required by the local Institutional Review Board.

Structural data acquisition

All structural images were acquired on a Philips NT 1.5-Tesla MRI scanner (Philips Medical Systems, Best, Netherlands) with a birdcage head coil. The high-resolution anatomical images of the olfactory experts were acquired during an fMRI study that investigated the neural substrates of olfactory mental imagery (Plailly et al., 2012) and on controls during a visual retinotopy protocol that was conducted in the same scanner, with the same sequence and during the same period of time as the scanning of the olfactory experts (Warnking et al., 2002). A high-resolution (1 mm^3) structural image was acquired with the same sequence for all subjects using a 3-dimensional, T1-weighted gradient echo sequence [repetition time = 23.7 ms, echo time = 6.9 ms, flip angle = 28°, number of accumulations = 2]. This acquisition sequence type has been shown to be particularly efficient when studying the inner part of the cortex (Tardif et al., 2009).

Structural data preprocessing

We processed and analyzed the structural data using a VBM approach and SPM8 software (www.fil.ion.ucl.ac.uk/spm/software/spm8/) with default parameters.

For the first step, each individual image was segmented using the 'New Segment' tool provided with the DARTEL toolbox (Ashburner and Friston, 2005). This procedure performs segmentation and spatial normalization in a unified generative model based on a mixture of Gaussians with spatial priors and bias correction. In addition, the algorithm includes non-brain tissues (dura, scalp and large vessels), which ensures that the calculation of GM images is uncontaminated by either the skull or large veins. This approach permits to skip the bias correction and skull-stripping procedure, which improves VBM preprocessing (Acosta-Cabronero et al., 2008). It is important to note that this segmentation procedure considers the olfactory bulbs as non-brain tissue and that those structures were thus absent from segmented individual images.

In a second step, a study-specific template was calculated from all subjects' GM and white matter (WM) images using the DARTEL framework (Ashburner, 2007). This diffeomorphic registration algorithm iteratively estimates the non-linear deformations that best align the GM and WM images together, which provides a common study-specific template and deformation field that parameterizes the deformations for each subject's image.

In a third step, to spatially normalize the images to the Montreal Neurological Institute (MNI) standard brain, we calculated the affine registration that realigned our study-specific template generated using DARTEL with the GM tissue probability map in the MNI space. For each subject, we applied a combination of the deformation field and affine registration to the GM and structural images of each individual. The spatially normalized GM segmented images were further modulated with the Jacobian of the deformation field to adjust for the resulting volume changes (Good et al., 2001) and derive GM volume-related images. The realigned structural images of all subjects were averaged for display purposes.

In a fourth step, to improve the sensitivity of the analysis to regional differences at a small spatial scale (required by small structures, such as the PC), we smoothed the GM volume images using a small isotropic Gaussian kernel with a 6-mm full width at half maximum. This kernel width ensures that any non-normality in the error term is sufficiently attenuated in balanced designs to render the tests valid (Salmond et al., 2002).

Olfactory-related regions of interest

Statistical analyses were performed on brain areas known to play a role in olfactory and memory processing. As no probabilistic maps have been proposed for the olfactory areas, anatomical volume of interests (VOIs) in the PC, amygdala, hippocampus, insula and thalamus were drawn from the study-specific template realigned to the MNI using MRIcron (www.mccauslandcenter.sc.edu/mricro/mricron/) and human brain atlases (Duvernoy, 1999; Mai et al., 2008). The VOIs were drawn from coronal slices for the PC (from y = 12.5 anterior to −2.7 posterior to the anterior commissure), amygdala (from y = 0 to −13.3), insula (from y = −22 to 36), and thalamus (from y = 8 to 29.2), and from sagittal slices for the hippocampus (from x = −24 to −38 on the left, and