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The Faces in Radiological Images: Fusiform Face Area Supports Radiological Expertise

Merim Bilalić[1,2], Thomas Grottenthaler[1], Thomas Nägele[1], and Tobias Lindig[1]

[1]Department of Neuroradiology, University of Tübingen, Tübingen 72070, Germany and [2]Department of Cognitive Psychology, Alpen-Adria University Klagenfurt, Klagenfurt 9020, Austria

Address correspondence to Merim Bilalić, Department of Neuroradiology, University of Tübingen, Hoppe-Seyler-Str. 3, 72076 Tübingen, Germany. Email: merim.bilalic@aau.at

Abstract

The fusiform face area (FFA) has often been used as an example of a brain module that was developed through evolution to serve a specific purpose—face processing. Many believe, however, that FFA is responsible for holistic processing associated with any kind of expertise. The expertise view has been tested with various stimuli, with mixed results. One of the main stumbling blocks in the FFA controversy has been the fact that the stimuli used have been similar to faces. Here, we circumvent the problem by using radiological images, X-rays, which bear no resemblance to faces. We demonstrate that FFA can distinguish between X-rays and other stimuli by employing multivariate pattern analysis. The sensitivity to X-rays was significantly better in experienced radiologists than that in medical students with limited radiological experience. For the radiologists, it was also possible to use the patterns of FFA activations obtained on faces to differentiate X-ray stimuli from other stimuli. The overlap in the FFA activation is not based on visual similarity of faces and X-rays but rather on the processes necessary for expertise with both kinds of stimulus. Our results support the expertise view that FFA's main function is related to holistic processing.

Key words: expertise, face recognition, fusiform face area, multivariate pattern analysis, radiology

Introduction

One of the most controversial views in philosophy is that the mind is composed of innate modules with clearly specified functions (Fodor 1983). A prime example of such modules in the human brain would be the fusiform face area (FFA; Kanwisher et al. 1997). According to the face specificity view (Kanwisher and Yovel 2006), the processing of faces is of such evolutionary importance that the brain has responded to these demands by evolving a module for faces. Faces, however, happen to be not only one of the most important stimuli but also one of the most frequently encountered. Many argue that FFA is actually an area that enables differentiation between exemplars within the same category, regardless of the kind of stimulus (Gauthier et al. 1999). In other words, expertise within a domain should modulate activation patterns in FFA. Here, we provide evidence for this expertise view by demonstrating that the FFA in experienced radiologists is more sensitive to radiological images than that in inexperienced medical students.

The expertise view has been investigated by comparing FFA's activation in experts and novices in response to stimuli relating to their domain of specialization (Gauthier et al. 1999, 2000; Grill-Spector et al. 2004; Rhodes et al. 2004; Xu 2005; Yue et al. 2006; Brants et al. 2011; James and James 2013). In some of the studies, experts had higher activation levels within FFA but other studies could not identify the expertise modulation in FFA. The situation is further complicated due to the similarity of the stimuli used in the studies to actual faces (e.g. cars, birds, greebles, Pokémon characters). The expertise modulation found in FFA in a small number of studies could therefore be a consequence of visual similarity with faces and not expertise-related processes (Kanwisher and Yovel 2006; Op de Beeck et al. 2006).

Even the few studies that employed stimuli which do not share any similarities with faces, such as chess positions and radiological images (X-rays), could not resolve the issue (Harley et al. 2009; Bilalić et al. 2011; Krawczyk et al. 2011; Boggan et al. 2012; Bartlett et al. 2013; Righi et al. 2013). Our group (Bilalić

et al. 2011), as well as Righi et al. (2013), demonstrated the expertise effect in FFA with chess positions. However, Bartlett and colleagues (2011; 2013) could not find any differences in the FFA activation between expert and novice chess players with chess positions. The expertise modulation of FFA was not found with radiological images either—experienced radiologists and medical students had similar activation levels in FFA when diagnosing suspicious nodules in X-rays (Harley et al. 2009). Harley and colleagues, however, related FFA to radiological expertise through positive association between the performance in identifying pathological nodules and activation within FFA.

Here, we continue with the stream of research that circumvents the problem of using stimuli similar to faces by using thorax X-rays that do not share any obvious features with faces. We employ the expertise approach of comparing differently skilled groups (Bilalić et al. 2010, 2012) while they observe stimuli from their domain of specialization (X-rays) and outside their domain (rooms and tools). We do, however, use a more sensitive approach than the classical univariate analysis used in the previous studies on the FFA controversy. Full activation patterns in FFA as they are used in the multivariate pattern analysis (MVPA) are more likely to capture expertise differences than the commonly used average values across the whole FFA area. If FFAs were an expertise-related module responsible for processing stimuli holistically, we would expect MVPA to differentiate better between X-ray stimuli and other neutral stimuli (e.g. rooms and tools) among radiologists than among medical students.

Our other goal is to identify the neural basis behind the radiological expertise. For this reason, we do not solely focus on the FFA but instead employ the searchlight technique (Haynes and Rees 2006; Kriegeskorte et al. 2006) in MVPA analyses on the whole brain to identify other regions related to radiological expertise.

Materials and Method

Participants

There were 16 radiologists (6 female, M age ± SD age = 35.2 ± 4.3) and 15 medical students (6 female, M age ± SD age = 28.1 ± 4.9). Besides the basic medical education, radiologists had a further specialization degree in radiology (at least 5 additional years) and have had examined over 10 000 X-rays on average based on their official records. Medical students were in their last year of studies and had taken basic courses involving X-rays. All participants were right-handed, and a written informed consent was obtained in line with the study protocol as approved by the Ethics Committee of Tübingen University.

Tasks, Stimuli, and Apparatus

The participants' task was to indicate if the current stimulus was the same as the previous one (1-back task). There were 5 classes of stimuli: face (stimuli from Leube et al. 2001), room (taken from the Internet), tool (Brodeur et al. 2010), upright X-ray and inverted X-ray (Shiraishi et al. 2000). All stimuli had the same dimension—400 × 400 pixels. The stimuli were projected onto a screen above the heads of the participants via a video projector in the adjacent room. Participants saw the stimuli through a mirror mounted on the head coil. The physical dimensions of the stimulus were 336 × 336 mm. The setup resulted in a visual field of 14.8° for the whole stimulus.

We followed the advice of Coutanche and Thompson-Schill (2012) (see also, Mumford et al. 2012) and improved the power

behind the MVPA analysis by presenting stimuli in many short blocks. There were 10 runs, each featuring 5 different blocks, 1 for each of the 5 stimulus categories. Blocks lasted for 12 s and contained 6 stimuli that were presented for 1.75 s, each followed by a stimulus mask (made of randomly arranged small parts of the same stimulus) for 0.25 s. The run started with a baseline (gray screen with a cross in the middle) lasting 12 s and finished with the same baseline lasting 18 s. The order of the runs, as well as that of blocks within a run, was counterbalanced separately for each participant. In a single block, there were on average 2 direct repetitions requiring a response from participants. The stimuli for repetitions within a block were chosen randomly for each participant. The blocks were chosen as the basic units for fMRI and MVPA analyses.

Localizer Experiment

All participants were initially presented with a localizer run that featured the following stimulus categories: face, room, tool, and upright X-ray. The stimuli were different, but the dimensions of the stimuli were the same as in the experiment. They were presented in a single run that featured 8 blocks of each condition. The design and task were otherwise the same, except that there were fewer repetitions in the localizer run (a single repetition within a block).

Imaging Data Acquisition

We acquired fMRI data using a 3T scanner (Siemens Trio) with a 12-channel head coil at the fMRI center in Tübingen, Germany. We covered the whole brain using a standard echo-planar-imaging sequence with the following parameters: reaction time [RT] = 2.5 s; FOV = 192 × 192; ET = 35 ms; matrix size = 64 × 64, 36 slices with thickness of 3.2 + 0.8 mm gap resulting in voxels with the resolution of 3 × 3 × 4 mm³. Anatomical images covering whole brain with 176 sagittal slices were obtained after the functional runs using an MP-RAGE sequence with a voxel resolution of 1 × 1 × 1 mm³ (TR = 2.3 s, TI = 1.1 s, TE = 2.92 ms).

Functional MRI Data Analysis

The preprocessing was done with SPM8 and involved spatial realignment to the mean image including unwarping and co-registration of the anatomical image to the mean EPI. We did not perform segmentation, normalization or spatial smoothing procedures because we wanted to use original unstandardized data for the MVPA and univariate analysis. We modeled the blocks explicitly for the duration, whereas the baseline was modeled implicitly in a general linear model (hemodynamic activation modeling relying on a canonical response function, AR(1) and a 128-Hz high-pass filter). We also added 6 movement parameters in the GLM to account for the variance introduced through head motion.

Univariate Analysis

For all univariate analyses of the fMRI data, we used the Statistical Parametric Mapping software package (SPM8; Wellcome Department of Imaging Neuroscience, London, UK; http://www.fil.ion.ucl.ac.uk/spm). Modeling of the time series of hemodynamic activation relied on a canonical response function. Autocorrelation of the data was corrected using a first-order autoregressive model. A high-pass filter with a cut-off of 128 Hz was applied to eliminate low-frequency noise components. The ROI analysis was performed on the mean percentage signal change extracted

from all the voxels within the selected region using Marsbar SPM Toolbox. The results were presented in Supplementary Material.

Multivariate Pattern Analysis

We performed the MVPA analyses using the Decoding Toolbox (Görgen et al. 2012). The toolbox uses support-vector-machine (SVM) method of MVPA to see whether the ROIs (see below) differentiate between different stimulus categories among radiologists and medical students. Our comparisons were binary SVM classifications and centered on the comparisons between X-rays on the one hand, and the rooms and tools as controls on the other (see Fig. 1A). We also compared faces with rooms and tool, as well as with upright and inverted X-rays. For all 4 classifications, a linear SVM with standard cost parameter, $c = 1$, as implemented in the LIBSVM 3.0 library (Chang and Lin 2011) was used. The classification was based on the β values previously obtained by the GLM and all voxels with an ROI. We employed a leave-one-trial-out method (e.g. Sterzer et al. 2008) where the data set was divided into: 1) a training set of N pattern vectors (vector length = number of voxels) and 2) a test set of 2 pattern vectors, 1 from each stimulus type. We then scaled the β in all training sets (0–1) as well as well as in test sets to ensure that we do not duplicate the univariate analysis. The SVM classifier was iteratively trained on the training data sets (N) and then tested on an independent test data set. These training and testing procedures were repeated 100 times. The percentage of successful categorization of tests items based on the previous independent training data was obtained for each comparison and for each participant. At the group level, we tested with one-sample, one-sided t-tests (as it is common in MVPA, for example, Hebart et al. 2012; Reverberi et al. 2012) to learn whether the average classification accuracy among the participants for the binary comparison in question was significantly greater than the chance level (50%). The comparisons between groups were performed using two-sided t-tests.

Cross-Categorization MVPA

We performed a stronger test for shared processes in processing faces and X-rays in FFA. We first trained the binary classifier on all possible faces versus room comparisons and tested on completely different stimuli—X-rays versus rooms (see Fig. 2A). If face and radiological perception share similar processes and play a role in FFA's functioning, then FFA should be sensitive even if the learned patterns are tested on different comparisons involving face and radiological stimuli. The same procedure was performed on the second neutral stimuli—tools.

Searchlight Analysis

Here, we wanted to check for the sensitivity of the whole brain to the classification of different binary comparisons. We applied the so-called searchlight approach (Haynes and Rees 2006; Kriegeskorte et al. 2006), as implemented in the Decoding Toolbox (Görgen et al. 2012), on the whole brain. The searchlight approach examines the information in small spherical voxel clusters, here 6 mm, at specified positions in the brain. It produces a map of classification accuracies across the whole brain for the normal binary comparisons and cross-classification comparisons in each participant. We used these individual maps in the group analysis by spatially warping them, affine transforming them to the MNI space, and spatially smoothing them using a 6-mm FWHM Gaussian kernel. The group analyses used one-sample, one-sided t-tests to identify the voxels within the occipital and temporal lobes that were sensitive to the normal binary classification comparisons and cross-categorization procedures.

Localizer Analysis

In order to isolate FFA, we modeled the blocks for each condition in the localizer run whereas the baseline was implicitly modeled in a GLM. We then compared the blocks with faces with the blocks with rooms. The voxels in the vicinity of the posterior right fusiform gyrus that survived the $P < 0.0001$ (uncorrected) threshold were then taken as the FFA ROI (see Supplementary Fig. 1 for visualization of the group FFA). In 2 of the radiologists and 1 medical student, we used a less stringent threshold ($P < 0.001$) to identify the right FFAs. The right FFA was on average larger in radiologists ($M = 461 \pm SE = 60$ mm³) than that in medical students (370 ± 37 mm³). The difference, however, was not significant ($t_{29} = 1.3$; $P = 0.21$), and the analyses accounting for the ROI size produced the same pattern of results as the analyses without controlling for the ROI size presented in the main text.

The first control ROI was another face area on the right side, the posterior part of the superior temporal sulcus (pSTS) (Campanella and Belin 2007). In all participants, only voxels that were significantly more active when viewing faces than rooms (the same comparison for FFA) at $P < 0.001$ in the localizer task were included in the ROI (see Supplementary Fig. 1 for visualization of the group pSTS). The identified pSTSs in radiologists ($M = 377 \pm SE = 59$ mm³) were not significantly different from those identified in medical students (393 ± 45 mm³—$t_{29} = 0.2$; $P = 0.83$).

We also tried to isolate the occipital face area (OFA) as an additional face control ROI (Gauthier et al. 2000). However, we could only unambiguously identify OFA in 8 radiologists and 9 medical students (also, please note that OFA was not obtained in the group-based analysis presented in Supplementary Fig. 1). Even in those several instances, the anatomical location varied substantially across individuals (see also Pitcher et al. 2011). We therefore refrained from reporting the incomplete data and refer the interested readers to the whole-brain searchlight maps in the result section.

The second control ROI was the intraparietal sulcus, an area responsible for top-down attention (Corbetta and Shulman 2002). We used this ROI to control for attentional effects in our experiments. Given that face processing is associated with areas in the right hemisphere (Kanwisher and Yovel 2006), just like sustaining top-down attention (Pardo et al. 1991; Lawrence et al. 2003), we focused our analysis on right-hemisphere areas. The IPS was identified in localizer by exploiting the attentional properties and working memory maintenance in the one-back task (see also Bilalić et al. 2011). In all participants, we only considered voxels that were significantly more active during the one-back task (regardless of the stimuli) than during baseline at $P < 0.05$ (FWE) level (see Supplementary Fig. 1 for visualization of the group IPS). The volume of IPS in radiologists was on average 344 ± 27 mm³ and in medical students 395 ± 51 mm³ (the differences between the ROIs in the 2 groups was not significant: $t_{29} = 0.9$; $P = 0.37$).

There were no differences in the size of the 3 ROIs (ROI × Expertise 3 × 2 ANOVA, main effect ROI—$F_{2,90} = 0.6$; $P = 0.58$) nor did radiologists have larger-sized ROIs (main effect Expertise—$F_{1,90} = 0.14$; $P = 0.71$). The interaction between ROIs and expertise was also not significant ($F_{2,90} = 1.2$; $P = 0.31$). The size of the ROIs also did not correlate with the success rate of the MVP (neither within groups nor within both groups together).

Results

Behavioral Analysis

Radiologists were better at noticing repetition among upright X-rays than medical students ($d' = 3.05 \pm SE = 0.06$ for radiologists,

and $d' = 2.59 \pm 0.11$ for students; $t_{29} = 3.03$; $P = 0.005$). The same expertise effect was found with inverted X-rays ($d' = 2.91 \pm SE = 0.08$ for radiologists, and $d' = 2.43 \pm 0.11$ for students; $t_{29} = 2.93$; $P = 0.007$). The radiologists' superiority was limited to the domain stimuli—there were no differences between them and the medical students with faces ($d' = 2.95 \pm SE = 0.06$ for radiologists, and $d' = 2.83 \pm 0.06$ for students; $t_{29} = 1.45$; $P = 0.16$), rooms ($d' = 3.06 \pm SE = 0.05$ for radiologists, and $d' = 3.02 \pm 0.06$ for students; $t_{29} = 0.56$; $P = 0.58$), and tools ($d' = 3.04 \pm SE = 0.04$ for radiologists, and $d' = 3.06 \pm 0.05$ for students; $t_{29} = 0.22$; $P = 0.83$). There were no differences in the RT between radiologists and medical students in any of the 5 categories (see Supplementary Fig. 2).

Univariate Analysis

The individual right FFAs were not sensitive to radiological expertise in the univariate analysis (see Supplementary Fig. 3), thus confirming previous findings (Harley et al. 2009). The control ROIs (pSTS and IPS) also failed to differentiate between radiologists and medical students (see Supplementary Fig. 3).

Multivariate Analysis

With the MVPA, we checked whether it was possible to differentiate between upright X-rays and rooms on the one side, and upright X-rays and tools on the other, above the chance level when the whole pattern of activation in the FFA was taken into account (Fig. 1A). We were interested in seeing whether the FFA in

experienced radiologists could distinguish better between domain-specific stimuli (upright X-rays) and other stimuli categories (rooms and tools) than the FFA of inexperienced medical students. The inversion effect was investigated by comparing upright X-rays with inverted X-rays in FFA of radiologists and medical students. At the same time, we wanted to show the exclusivity of the FFA's relation to radiological expertise and have used the same MVPA analysis on the control ROI (pSTS). Finally, we controlled the attentional effects by investigating the patterns in the right IPS, an area generally believed to be sensitive to effort and attention (Corbetta and Shulman 2002).

Figure 1B shows that the FFA in both radiologists and medical students could distinguish between X-rays and rooms above the chance level ($t_{15} = 8.1$; $P < 0.001$ and $t_{14} = 4.5$; $P < 0.001$ for radiologists and medicals students, respectively). Similarly, both groups' FFA could distinguish between X-rays and tools ($t_{15} = 7.8$; $P < 0.001$ and $t_{14} = 3.9$; $P = 0.001$ for radiologists and medicals students, respectively). The FFA in radiologists, however, distinguished more accurately between X-rays and rooms ($t_{29} = 3.3$; $P = 0.002$) and X-rays and tools ($t_{29} = 2.3$; $P = 0.028$) than the FFA in students.

The expertise effect, however, was restricted to the FFA (Fig. 1C). The right pSTS just failed to distinguish between X-rays and rooms among radiologists ($t_{15} = 1.7$; $P = 0.055$) as well as among medical students ($t_{14} = 1.6$; $P = 0.063$). There were also no differences between radiologists and medical students in the level of pSTS sensitivity ($t_{29} = 0.1$; $P = 0.91$). The same pattern of results was found in the pSTS when we used tools instead of rooms. The X-ray–Tool comparison in the pSTS were not significantly
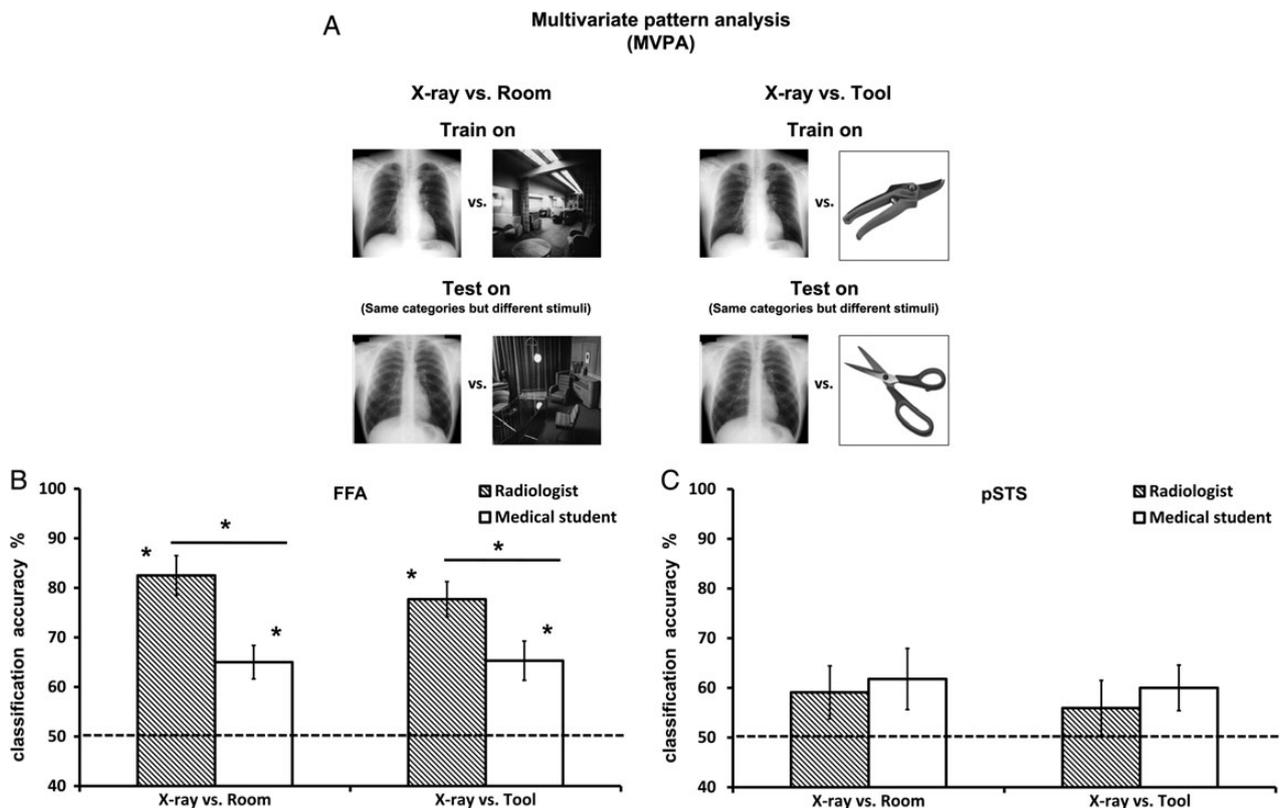
Figure 1. MVPA results. (A) Illustration of the binary comparison employed. FFA and pSTS' sensitivity to radiological images was tested by 2 binary comparisons: 1) X-ray vs. Room and 2) X-ray versus Tool. The learning process used all stimuli pairs but one that was then used for testing the learned patterns of activation. (B) Classification accuracy presented as percentage of correctly classified instances (50% is a chance level—see the dotted line) of the binary comparisons with rooms and tools for the FFA. (C) Classification accuracy presented as percentage of correctly classified instances (50% is a chance level—see the dotted line) of the binary comparisons with rooms and tools for the pSTS. *$P < 0.05$. Error bars indicate SEM.

more successful than chance in both radiologists ($t_{15} = 1.1$; $P = 0.015$) and students ($t_{14} = 1.1$; $P = 0.016$). The difference between the groups was not significant ($t_{29} = 0.2$; $P = 0.86$).

So far, we have compared upright X-rays with rooms and tools. We can also compare faces with X-rays and see whether FFAs in radiologists are more difficult to categorize these 2 stimulus categories because of the shared processes needed for perception of faces and X-rays. This indeed seemed to be the case, since the radiologists' FFA is worse at distinguishing between faces and upright X-rays ($M = 85\% \pm SE = 4.6$) than the FFA of medical students ($M = 93.8\% \pm SE = 3$). The difference was not quite significant ($t_{29} = 1.9$; $P = 0.07$), which can be explained by a very high level of successful categorization in FFA. The ceiling effect in the FFA for comparisons involving faces is expected, given that the FFA had previously been localized based on face stimuli. That is why we believe that the above-presented comparisons involving radiological images and non-face stimuli are more informative (for results of other comparisons involving faces, for all 3 ROIs, see Supplementary Fig. 4).

Attentional Effects

It is possible that experts are more drawn to the stimuli from their domain, which in turn may influence their activation patterns (Wojciulik et al. 1998; Harel et al. 2010). We believe this possibility is unlikely as we found an expertise effect in FFA but not in pSTS although the same comparisons were used in both ROIs. In addition, the behavioral responses (d' on upright X-rays) were not

significantly correlated with the MVPA classification accuracy in FFA (for X-ray–Room comparison: Spearman's $r_{(30)} = 0.16$, ns, for whole sample, and $r_{(15)} = -0.09$, ns for radiologists and $r_{(30)} = -0.17$, ns for students; for X-ray–Tool comparison: $r_{(30)} = 0.06$, ns, for whole sample, and $r_{(15)} = 0.38$, ns for radiologists and $r_{(30)} = 0.01$, ns for students). To further exclude this possibility, we analyzed whether the right IPS, often used as an attentional index, could differentiate between radiologists and medical students on the same stimuli comparison. The IPS turned out to be sensitive to the X-ray–Room comparison in both groups ($M = 68.4\% \pm SE = 4.3$; $t_{15} = 4.1$; $P < 0.001$ for radiologists and $M = 70.7\% \pm SE = 2.9$; $t_{14} = 6.1$; $P < 0.001$ for students) as well as to the X-ray–Tool comparison ($M = 66.6\% \pm SE = 3.9$; $t_{15} = 4.3$; $P < 0.001$ for radiologists and $M = 71.3\% \pm SE = 4.1$; $t_{14} = 5.3$; $P < 0.001$ for students). There were, however, no significant differences between the groups in the X-ray–Room comparison ($t_{29} = 0.7$; $P = 0.49$) and X-ray–Tool comparison ($t_{29} = 0.85$; $P = 0.40$).

Cross-Categorization (MVPA) Analysis

As the ultimate test of the FFA role in radiological expertise, we employed the cross-categorization procedure in the MVPA. If X-rays share similar expertise processes as faces, then the obtained patterns of activation in the FFA based on faces (versus rooms) should be able to differentiate between X-rays and rooms among radiologists (Fig. 2A). Similarly, the Face–Tool comparison should produce a possible basis for success in the X-ray–Tool comparison among radiologists. Figure 2B shows
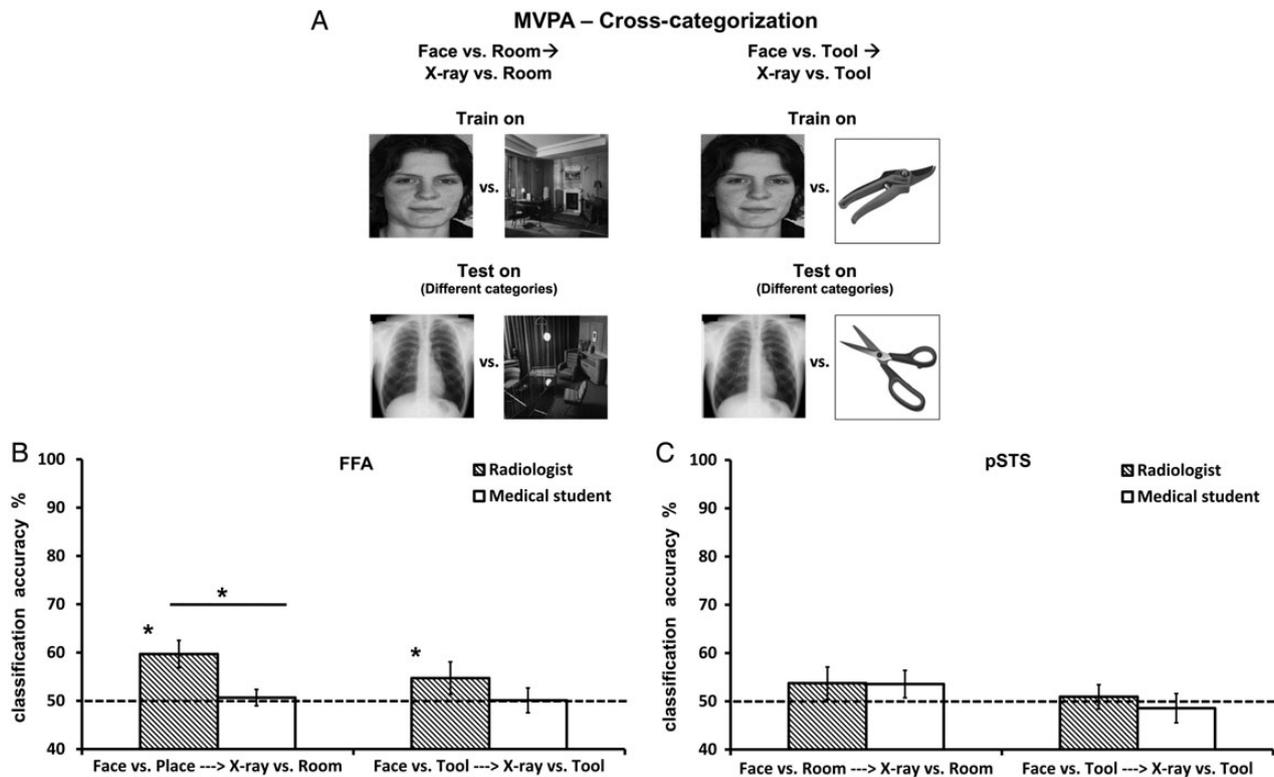
Figure 2. MVPA cross-categorization results. (A) Illustration of the cross-categorization procedure. Instead of training and testing on the same categories (but different instances of the same categories—see Figure 1A), we trained on one type of category and tested on a different type of category. We first trained the classification algorithm on the binary comparison of faces and rooms. Then, we tested the learned patterns on the binary comparison involving a new category—X-rays. The same procedure was done for the tools (instead of rooms—right hand side) (B) Classification accuracy for cross-categorization procedure presented as percentage of correctly classified instances (50% is a chance level—see the dotted line) of the binary comparisons with rooms and tools for the FFA. (C) Classification accuracy for cross-categorization procedure presented as percentage of correctly classified instances (50% is a chance level—see the dotted line) of the binary comparisons with rooms and tools for the pSTS. *$P < 0.05$. Error bars indicate SEM.

that the radiologists' FFA could distinguish between X-rays and rooms even when it had used previously learned pattern of activation based on the comparison between faces and rooms ($t_{15} = 3.4$; $P = 0.002$). In contrast, the same cross-categorization procedure was not successful in medical students ($t_{14} = 0.5$; $P = 0.65$), which underlined the FFA's sensitivity to expertise ($t_{29} = 2.8$; $P = 0.009$). The cross-categorization with tools (Fig. 2B) was also successful among radiologists ($t_{15} = 2.8$; $P = 0.007$) but was not better than chance with students ($t_{14} = 0.1$; $P = 0.46$). There was a trend for the expertise effect in cross-categorization with tools, but it did not reach the significance levels ($t_{29} = 1.6$; $P = 0.12$).

The cross-categorization procedure for rooms was not successful in the pSTS (Fig. 2C) of radiologists ($t_{15} = 1.1$; $P = 0.14$) and that of medical students ($t_{14} = 1.3$; $P = 0.12$). There were no significant differences between radiologists and medical students ($t_{29} = 0.4$; $P = 0.96$). The cross-categorization with tools (instead of rooms) was unsuccessful in the pSTS of radiologists ($t_{15} = 0.4$; $P = 0.36$) and students ($t_{14} = 0.5$; $P = 0.33$) at differentiating upright X-rays from tools. The difference between the 2 groups in the success rate was also not significant ($t_{29} = 0.6$; $P = 0.54$).

Finally, the IPS could not differentiate between X-rays and rooms based on the patterns obtained by the Face–Room comparison among either radiologists ($M = 55\% \pm SE = 4.1$; $t_{15} = 1.2$; $P = 0.12$) or medical students ($M = 54\% \pm SE = 3.2$; $t_{14} = 1.1$; $P = 0.14$), which resulted in no significant expertise effect ($t_{29} = 0.25$; $P = 0.80$). The same pattern was observed in the IPS cross-categorization with tools. Neither could the IPS in radiologists ($M = 55\% \pm SE = 4.1$; $t_{15} = 0.7$; $P = 0.24$) or students ($M = 47\% \pm SE = 3$; $t_{14} = 1.1$; $P = 0.14$) successfully differentiate between X-rays and tools based on the patterns obtained by the face–tool comparison. There were no significant differences between the 2 groups in the success rate ($t_{29} = 1.2$; $P = 0.24$).

Searchlight Analysis

So far, we have demonstrated expertise effects in the FFA and not in other control ROIs. To further check whether the FFA is indeed the focus of radiological expertise, and to uncover other areas which may be important for radiological expertise, we have searched the whole brain with the searchlight procedure in the MVPA (Haynes and Rees 2006; Kriegeskorte et al. 2006). The areas that were sensitive to expertise (more successful prediction in radiologists than medical students) in the comparison X-ray–Room are presented in Figure 3A. There are a number of areas that show expertise effects in both hemispheres (see Supplementary Table 1 for the complete list), but the focal points in both hemispheres are in the fusiform gyrus, in the same area that is identified as the FFA in the localizer. The same pattern of results we find in the comparison X-ray–Tool (see Supplementary Fig. 5 for visualization and Supplementary Table 3 for the list of areas). There are fewer areas sensitive to radiological expertise than in the previous comparison with rooms, but the focal points again are in the both fusiform gyrus, near the group FFA found in the localizer.

The cross-categorization from Face–Room comparison to X-ray–Room comparison (Fig. 3B) indicates that both fusiform gyri in the vicinity of the FFA differentiate between experts and novices. The focal points, however, seem to be in the occipital lobe and posterior superior temporal gyri (Supplementary Table 2 lists all areas in Fig. 3B). The cross-categorization procedure from Face–Tool comparison to X-ray–Tool comparison produced much fewer sensitive areas to radiological expertise (see Supplementary Fig. 6 for visualization and Supplementary

Table 4 for the list of areas). None of these was near the group FFA identified in the localizer task—thus confirming the previous MVPA cross-categorization procedure for the FFA.

Inversion Effect

One of the hallmarks of face perception is more difficult processing of inverted faces, the so-called inversion effect (Fig. 4A). This effect is thought to be a consequence of holistic processing that should characterize processing of other non-face stimuli for which people have developed expertise (Tanaka and Gauthier 1997; Maurer et al. 2002; Wong et al. 2009, 2011; Curby and Gauthier 2010; Wong and Gauthier 2010a; Chen et al. 2013). Here, in the simple 1-back paradigm, the upright X-rays were better perceived than the inverted ones (main effect of position: $F_{1,29} = 5.1$; $P = 0.031$), but there was no interaction between the position of stimuli and expertise ($F_{1,29} = 0.1$; $P = 0.94$). In other words, experts performed better than novices on the inverted X-rays to the same extent as they were better with the upright X-rays. Both groups thus demonstrated inversion effects when the accuracy (d') was measured. Unsurprisingly, radiologists performed better on both types of stimuli (main effect of expertise: $F_{1,29} = 10.8$; $P = 0.003$).

When we used RT instead of accuracy, we found the inversion effect in radiologists (694 ms for upright vs. 775 ms for inverted X-rays—see Supplementary Fig. 2) but not in medical students (730 ms for upright vs. 740 ms for inverted X-rays). This resulted in the interaction between expertise and position of stimuli ($F_{1,29} = 9.7$; $P = 0.004$) and main effect of position ($F_{1,29} = 16.5$; $P < 0.001$), although the main effect of expertise was not significant ($F_{1,29} = 0.1$; $P = 0.94$). It seems that radiologists compensated their accuracy on inverted X-rays by using up more time. That way their accuracy did not suffer as much it would have if they were responding as quickly as they did for upright X-rays. The consequence was that their inversion effect was as pronounced as that of medical students when only the accuracy was considered.

The univariate analysis failed to find differences between upright and inverted stimuli in either group in the FFA or any other control ROI (see Supplementary Fig. 3). The MVPA, however, was more successful. The activation patterns in the FFA in radiologists (Fig. 4B) reached the significance level of above chance differentiation between upright and inverted X-rays ($M = 61\% \pm SE = 2.1$; $t_{15} = 3.1$; $P = 0.004$). The FFA of students could not differentiate between the 2 types of X-rays above the chance level ($M = 54\% \pm SE = 3.9$; $t_{15} = 1$; $P = 0.16$). The difference between the classification levels of the 2 groups did not quite reach the significance level ($t_{29} = 1.1$; $P = 0.22$). The pSTS could not differentiate between upright and inverted X-rays in either radiologists ($t_{15} = 0.5$; $P = 0.33$) or medical students ($t_{14} = 0.4$; $P = 0.36$). The difference in the success rate between radiologists and medical students was also not significant ($t_{29} = 0.6$; $P = 0.56$). The searchlight MVPA procedure produced only a handful of areas that could successfully differentiate between upright and inverted X-rays (see Supplementary Fig. SM7). Among them was an area within the fusiform gyrus but more anterior and medial to the actual FFA identified in the localizer task (see Supplementary Table 5).

Discussion

We tackled the brain modularity issue by investigating the role of the FFA, an area believed to be specialized exclusively for faces, in radiological expertise. Radiology is a suitable domain to test the expertise view of the FFA function because we can compare experienced and skilled people, like radiologists, with people who
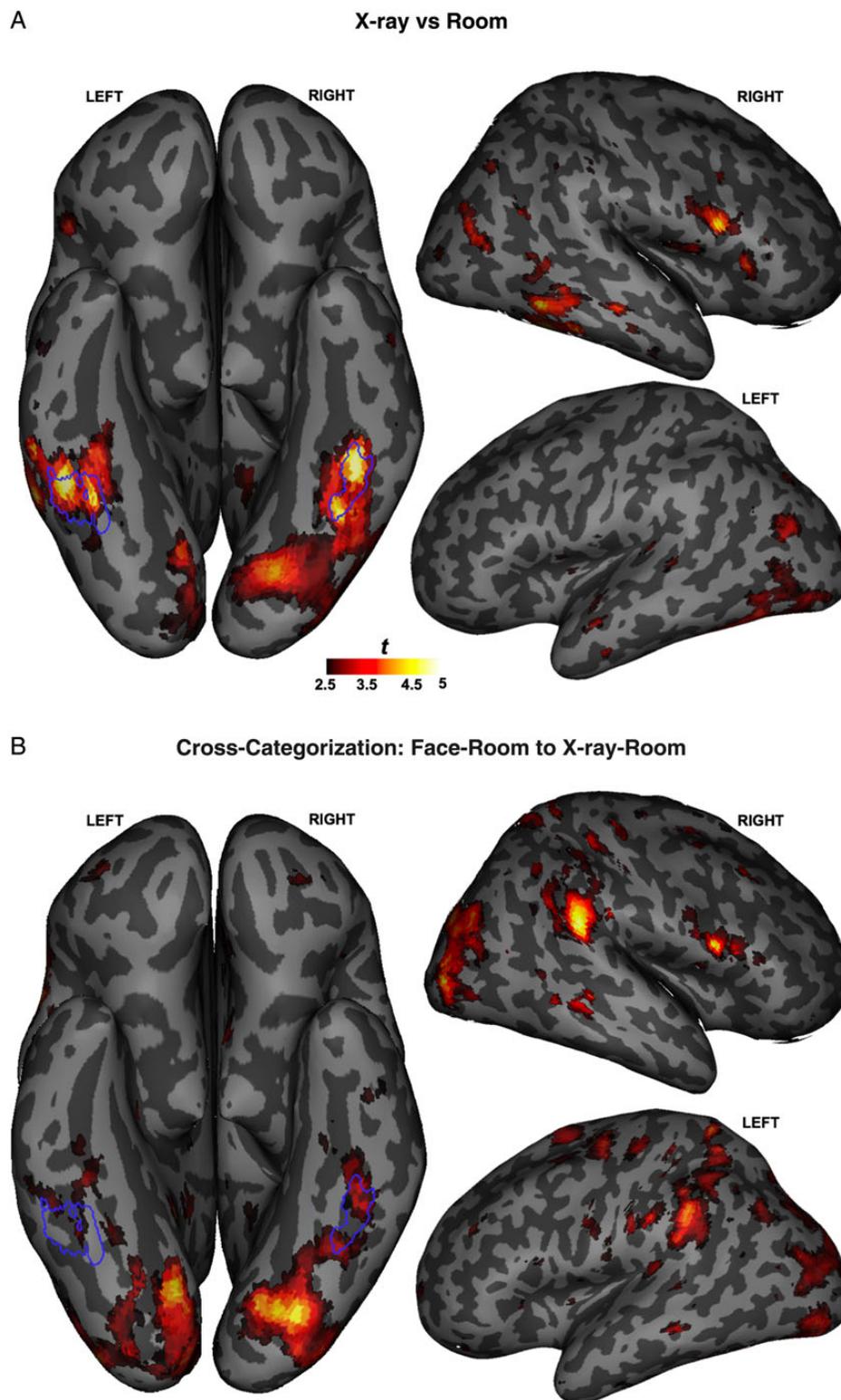
Figure 3. Searchlight maps for radiological expertise effect. (A) Areas in the searchlight procedure that were more successful in radiologists than medical students in differentiating between X-rays and rooms. The right and left FFA obtained from the localizer (group analysis—see Fig. SM1) were superimposed on the inferior brain searchlight maps (white blue color). The list of all areas can be found in Supplementary Table 1. (B) Areas in the searchlight procedure that were more successful in radiologists than medical students in differentiating the cross-categorization procedure Face–Room to X-ray–Room. The right and left FFA obtained from the localizer (group analysis—see Supplementary Fig. 1) were superimposed on the inferior brain searchlight maps (white blue color). The list of all areas can be found in Supplementary Table 1. Error bars indicate SEM.
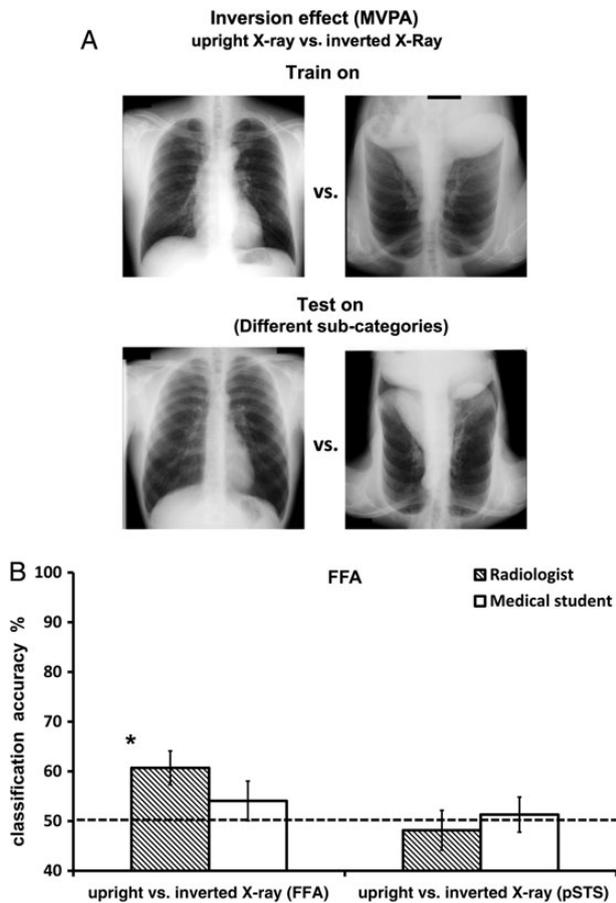
Figure 4. Inversion effect—MVPA results. (A) Illustration of the binary comparison employed to test the inversion effect. The FFA's sensitivity to the inversion effect was tested by two binary comparisons between upright and inverted X-rays. The learning process used all stimuli pairs but one that was then used for testing the learned patterns of activation. (B) Classification accuracy for cross-categorization procedure presented as percentage of correctly classified instances (50% is a chance level—see the dotted line) of the binary comparisons with upright and inverted X-ray for the FFA (left) and the pSTS (right). *P < 0.05. Error bars indicate SEM.

lack experience and necessary skills, like medical students. Most importantly, radiological images, such as thorax X-rays, do not bear any visual resemblance to faces, a problem that has plagued previous research on the FFA. We can therefore be certain that a possible overlap is not a result of similarity in appearance, as is the case with other stimuli.

Our results indicate that radiological expertise modulates FFA's neural response. Radiologists' FFA was more sensitive in differentiating X-rays from control stimuli such as rooms and tools than the same area in medical students. It should be noted, however, that even medical students with their limited exposure to radiological stimuli achieved differentiation between X-rays and control stimuli significantly above chance level in the FFA. This fact underlines the sensitivity of the MVPA procedure as X-rays may constitute a more homogeneous category than the categories used in comparisons. Alternatively, the success of students' FFA may point toward the possible role of the FFA in the early stages of development of radiological expertise. This possibility could be investigated with an additional group of participants who are not familiar with X-rays. In any case, the expertise effects were restricted to only the FFA and not other face control areas. This indicates that the FFA difference between

radiologists and medical students is driven by experience and expertise with radiological stimuli.

The strongest evidence in the similarity between faces and radiological images is provided by the cross-categorization procedure. It is 1 thing to successfully predict stimulus category in the binary comparison based on activation patterns of the other stimuli belonging to the very same category, as is the case in the classical MVPA. It is much more difficult to predict the same stimulus category using activation patterns of completely different categories as is done in the cross-categorization procedure. The fact that the FFA differentiated between X-rays and rooms using the Face–Room comparison among radiologists but not medical students, additionally highlights the similarities between faces and radiological images.

The lack of expertise differences in the control ROIs in the MVPA and cross-categorization procedures confirms the exclusive role of the FFA in the processing of radiological images. While the IPS control area could differentiate between radiological images and control stimuli, the face specific pSTS could not differentiate successfully between radiological and other images. Importantly, however, there were no differences in the level of success between radiologists and medical students in both control ROIs.

The searchlight analyses provided additional evidence for the importance of the FFA in radiological expertise by examining the whole brain for expertise effects instead of focusing on individual areas. The highest differentiation levels between X-rays on the one hand, and rooms and tools on the other, among radiologists and medical students were found in the fusiform gyri at the area where FFA is situated (Fig 3A). The cross-categorization searchlight map for rooms (Fig. 3B) provides numerous different areas that differentiate between radiologists and novices but among them, once again, is the FFA area. The whole-brain analyses through searchlight thus add another layer of evidence for the crucial role of the FFA in radiological expertise.

It should be noted that only comparisons with rooms produced clear-cut support for the role of FFA in radiological expertise. Radiologists' FFA was successful in differentiating tools from X-rays (Fig. 1), but the comparisons with tools failed in searchlight procedures (Fig. 2 and Supplementary Figs SM5 and SM6). One of the reasons for the lack of success in the differentiation of tools may lie in the proximity of the areas that support perception of tools to the FFA. Unlike rooms that are supported at the parahippocampal place area (Epstein and Kanwisher 1998; Epstein et al. 1999), tools are supported with more lateral areas in the fusiform gyrus in the vicinity of the FFA (Mahon et al. 2007; Noppeney 2008). Another possibility is that rooms constitute a more homogeneous category than tools in general and so are easier to differentiate. In any case, the results demonstrate the need for use of more than one control category in MVPA procedures.

Why is FFA modulated by radiological expertise? Radiological stimuli do not have much in common with faces when it comes to appearance, but they are both processed in a similar manner. Just as people need a mere glimpse to recognize a person, experienced radiologists often report that they only need a single glance to grasp the whole stimulus. Current theories of radiological expertise (e.g. Kundel et al. 2007) suppose that radiologists have acquired an impressive wealth of knowledge about radiological images due to their extensive exposure to visual images within their specialization. This knowledge enables radiologists to automatically obtain a global impression of the image and thus rapidly inspect suspicious areas (Nodine and Mello-Thoms 2000; Reingold and Sheridan 2011). Radiological expertise is thus characterized by holistic processing that is not unlike the holistic

processing of faces (e.g. Myles-Worsley et al. 1988; Harley et al. 2009). The holistic processing in radiological expertise may therefore be one of the underlying factors behind the FFA's sensitivity to X-rays.

One of the ways to check this hypothesis about holistic processing further is the inversion effect in radiology. The inversion effect is taken as evidence of holistic processing that is characteristic not only for face processing but also for skillful processing of any other stimuli (Tanaka and Gauthier 1997; Maurer et al. 2002; Wong et al. 2009, 2011; Curby and Gauthier 2010; Chen et al. 2013). Our evidence, however, is inconclusive. The inversion effect had some behavioral effect on the performance of participants in our study but was present in both radiologists and students when the accuracy was considered. Reaction time revealed that radiologists compensated for the difficulty of processing inverted radiological images by using more time. On a neural level, we found that the FFA in radiologists can reliably distinguish between upright and inverted X-rays unlike the FFA in students. However, there were no differences between the 2 groups in the differentiation levels in FFA (Fig. 4B). The searchlight maps also did not produce any other candidate areas for the neural implementation of the inversion effect (see Supplementary Fig. 7).

It is difficult to believe that medical students have already developed holistic processing of X-rays, as FFA was clearly inferior in differentiating X-rays from rooms and faces. It is more likely that the inversion effect in radiology is less pronounced and thus more difficult to detect when compared with the expertise effect. The study on diagnosing targeted nodules (patches of X-ray images) also failed to find either behavioral or neural differences between upright and scrambled X-rays among radiologists and non-radiologists (Harley et al. 2009). The difficulty in connecting the FFA with the neural implementation of the inversion effect in face processing is well documented (Yovel and Kanwisher 2005). Furthermore, there are different opinions about the exact nature of holistic processing (Richler and Gauthier 2014). The use of a relatively simple paradigm (1-back task) with the inversion paradigm may not be perfectly suited to eliciting holistic processing. Some researchers believe that inverted faces are just processed slower but not in a qualitatively different manner (Willenbockel et al. 2010; Richler et al. 2011). In other words, inverted stimuli may require more time to process from experts, but they are eventually processed holistically. Other paradigms such as composite task (Young et al. 1987) and part–whole task (Tanaka and Farah 1993) may be better suited for uncovering holistic processing. All these factors may explain why we could not fully pinpoint the neural basis of the inversion effect in radiology even with a sensitive technique such as MVPA.

Although radiological images are seemingly visually distinct from faces, both categories depict curved shapes. It is possible that the FFA is not responsible for holistic processing after all but simply responds to curved shapes. This possibility gains ground when one considers that perception of curvature is disrupted in prosopagnosic patients (Kosslyn et al. 1995). Another study (Wilkinson et al. 2000) found that concentric patterns activated the FFA more than identical linear patterns (see also Tsao et al. 2006; Ohayon et al. 2012). Similarly, the thorax is a body part and one wonders whether the fusiform body area (FBA; Downing et al. 2001; Schwarzlose 2005), a neighboring area to the FFA, may be driving the activation in and around the FFA. The searchlight map (Fig. 3A) shows areas around the FFA, including lateral parts that correspond to the FBA, which also distinguish between radiological images and control stimuli. Our study did not localize the FBA and so cannot unambiguously pinpoint the role of the

FBA in radiological expertise. We also used only oval-shaped X-rays as radiological stimuli and cannot rule out the possibility that the shape is driving the FFA response in experts. Future studies should use other radiological stimuli that are not curved, such as bones (e.g. hand and foot) or blood vessels, in addition to independent FBA localizers, to provide more conclusive answers to these questions.

The whole-brain searchlight analyses do not only corroborate the MVPA analyses used on the individual FFAs but also provide clues about other areas involved in radiological expertise. Among the areas that differentiated between radiologists and medical students were the posterior middle temporal gyrus (pMTG) and posterior cingulate gyrus (called retrosplenial cortex, RSC), the inferior and medial frontal gyri (IFG and MFG), as well as the area in the lingual gyrus posterior to the FFA. The temporal areas pMTG and RSC are known to play a role in retrieval and application of knowledge in knowledge-based domains (Bar 2004, 2009). These two areas were activated when radiologists were asked to diagnose X-rays in another radiological study (Melo et al. 2011). The area in bilateral lingual gyri posterior to the FFA seems to be one of the main focal points of radiological expertise besides the FFA since it also present in cross-categorization (Fig. 3B). The lingual gyrus is a part of the ventral stream (Mishkin et al. 1983) and is associated with visual processes such as word recognition (Kuriki et al. 1998; Booth et al. 2008). It is worth mentioning that the lingual gyrus projects connections to both the lateral temporal areas and the fusiform gyrus (Catani et al. 2003) that were responsive to radiological expertise.

While temporal areas are important in expertise because of domain-specific knowledge stored there, the role of frontal areas is more difficult to pinpoint. It is telling, however, that in the aforementioned study (Melo et al. 2011), similar frontal areas were more activated in radiologists when they diagnosed X-rays than when they named objects (animals and letters). Complex skills such as radiological expertise feature numerous cognitive processes that work together to enable experts' efficient performance (Gobet et al. 2001; Reingold and Sheridan 2011; Bilalić and McLeod 2014). It is unlikely that they engage only a single area, even if that area is the FFA (Harel et al. 2010, 2013, 2014; Wong and Gauthier 2010b; Wong and Wong 2014). Future studies on radiological expertise, and expertise in general, should try to connect the temporal knowledge-based areas, including the FFA and lingual gyrus, with frontal areas, to enable full insight into expertise processing (Kelly and Garavan 2005; Guida et al. 2012, 2013).

In this study, we combined the expertise approach (Bilalić et al. 2010, 2012) with the MVPA to demonstrate that FFA is indeed sensitive to radiological stimuli such as thorax X-rays. Our results are important for several reasons. They pinpoint a possible neural basis behind an enormously important real world skill and thus provide a starting point in understanding the cognitive and neural mechanisms behind visual skills in general. They also offer support for the expertise view in the FFA controversy by avoiding the confounding factor of face similarity that had vitiated previous studies. Finally, they shift the emphasis in the modularity debate. The FFA may indeed be a brain module, but it seems more likely to be connected to visual features such as curved shapes or holistic processing in general rather than serving exclusively to process faces.

Supplementary Material

Supplementary Material can be found at http://www.cercor. oxfordjournals.org/online.

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Notes

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