Assessment of Sexual Orientation Using the Hemodynamic Brain Response to Visual Sexual Stimuli

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ABSTRACT

Introduction. The assessment of sexual orientation is of importance to the diagnosis and treatment of sex offenders and paraphilic disorders. Phallometry is considered gold standard in objectifying sexual orientation, yet this measurement has been criticized because of its intrusiveness and limited reliability.
Aim. To evaluate whether the spatial response pattern to sexual stimuli as revealed by a change in blood oxygen level-dependent (BOLD) signal can be used for individual classification of sexual orientation.
Methods. We used a preexisting functional MRI (fMRI) data set that had been acquired in a nonclinical sample of 12 heterosexual men and 14 homosexual men. During fMRI, participants were briefly exposed to pictures of same-sex and opposite-sex genitals. Data analysis involved four steps: (i) differences in the BOLD response to female and male sexual stimuli were calculated for each subject; (ii) these contrast images were entered into a group analysis to calculate whole-brain difference maps between homosexual and heterosexual participants; (iii) a single expression value was computed for each subject expressing its correspondence to the group result; and (iv) based on these expression values, Fisher's linear discriminant analysis and the κ-nearest neighbor classification method were used to predict the sexual orientation of each subject.
Mean Outcome Measure. Sensitivity and specificity of the two classification methods in predicting individual sexual orientation.
Results. Both classification methods performed well in predicting individual sexual orientation with a mean accuracy of >85% (Fisher's linear discriminant analysis: 92% sensitivity, 85% specificity; κ-nearest neighbor classification: 88% sensitivity, 92% specificity).
Conclusion. Despite the small sample size, the functional response patterns of the brain to sexual stimuli contained sufficient information to predict individual sexual orientation with high accuracy. These results suggest that fMRI-based classification methods hold promise for the diagnosis of paraphilic disorders (e.g., pedophilia). **Ponseti J, Granert O, Jansen O, Wolff S, Mehdorn H, Bosinski H, and Siebner H. Assessment of sexual orientation using the hemodynamic brain response to visual sexual stimuli. J Sex Med **;**:**–**.**

Key Words. fMRI; Sexual Orientation; Phallometry; Pedophilia; Classification

Introduction

Assessment of sexual orientation is an important topic in the context of paraphilias and sexual offending. Treatment strategies and treatment outcome are likely to depend on the diagnosis of a specific paraphilia established at the beginning of the treatment. For instance, phallometrically measured sexual attraction to children was found to be one of the single best predictors of sexual recidivism among sex offenders [1]. Phallometry involves the measurement of penile responses to different types of potentially sexual stimuli, like naked male or female adults, adolescents, or children. Phallometry was developed by Kurt Freund who first demonstrated that this tool was able to discriminate between heterosexual and homosexual men [2]. Later, phallometry was principally used to study and assess sexual preferences in different types of sex offenders and paraphilic men (see for reference [3]). Because forensic evaluation seeks objective information, phallometry is used to increase the validity of self-reports. Several studies demonstrated that phallometry is a valid tool for the measurement of sexual orientation in pedophiles [4,5]. For instance Freund and Watson [5] demonstrated sensitivity rates of 78% for heterosexual pedophiles and 89% for homosexual pedophiles, and specificity rates of 81% using a normal control group.

Despite the consistent evidence supporting phallometric testing, the procedure has been criticized for its lack of reliability [6,7]. Furthermore, phallometry has been criticized because of its high number of nonresponders (about one-third of men) and because of its intrusiveness. Probands are required to place a device around their penis and have their erectile responses recorded. From a neuroscientific perspective, phallometric testing resembles measurement of a peripheral response which is predominantly under the control of the central nervous system. This consideration motivates current efforts to assess sexual orientation by means of functional brain mapping [3]. A neuroimaging approach assessing the brain activation pattern to different types of stimuli is less intrusive and possibly less susceptible to faking than phallometry.

Functional MRI (fMRI) studies which mapped regional changes in the blood oxygen level-dependent (BOLD) signal in response to visual sexual stimuli have considerably advanced our knowledge about the functional systems involved in the processing of sexual stimuli [8]. Based on this research, a neuro-functional model of sexual stimulus processing has been proposed in which various stages of sexual stimulus processing are allocated in defined brain areas [9]. Another important finding has been that in male and female heterosexual and homosexual individuals, some brain areas show a neural response to sexual stimuli of the preferred sex [10–12]. A recent study extended these findings by showing preference-specific brain activation in homosexual pedophiles [13]. While these studies identified regional differences in the way the brain processes sexual stimuli at a group level, they did not clarify whether these preference-related differences in brain activation are predictive of sexual preference in individual subjects.

In recent years, the application of automated classification techniques to whole-brain MRIs has attracted considerable interest as a tool to facilitate physician diagnosis in neurological and psychiatric diseases [14–17]. For instance, automated classification of individual structural MRIs has been successfully applied in patients with early Alzheimer's disease [15,16] and obsessive–compulsive disorder [14]. Using a support vector machine classifier, patients with Alzheimer's disease were accurately classified in >95% based on their structural MRIs [15,16]. Soriano-Mas and colleagues calculated an individual expression value of each structural brain image and obtained a mean classification accuracy of 93% in patients with obsessive–compulsive disorder [14]. Automated classification methods can readily be applied to fMRI data sets to use the pattern of cerebral activity over the whole brain to identify or predict functional states at an individual level [18]. For instance, the spatial pattern of BOLD signal changes during the processing of sad faces correctly classified up to 84% of patients with a major episode of depression (sensitivity) and 89% of control subjects (specificity), corresponding to a mean accuracy of 86% [19].

Aim

The aim of this study was to examine whether automated pattern classification of fMRI data can be used to predict sexual orientation at an individual level in heterosexual and homosexual men. We hypothesized that individual maps reflecting regional differences in the BOLD response to male or female genital stimuli across the whole brain should be indicative of individual sexual orientation. To this end, we used an fMRI data set that had been gathered in a previous fMRI study on sexual orientation [11], and applied two different classification analyses to this data set.

Materials and Methods

Subjects

Subject and stimuli characteristics have been described in detail elsewhere [11]. Out of a set of four subject groups (heterosexual and homosexual males and females) fMRI data sets of 12 heterosexual men (mean age 26.8, SD 7.5 years) and 14 homosexual men (mean age 27.4, SD 4.1 years) were subjected to pattern classification. In prescan interviews, we verified that they were mentally not distressed [20]; right-handed [21];

heterosexual or homosexual (i.e., Kinsey rating of fantasy and behavior of 0 and 1, or 5 and 6, respectively) [22]; and had no history of substance abuse, sexual dysfunction, gender identity disorder, paraphilia, or sexual offences. All participants gave their written informed consent before participation in the experiment. The study was approved by the local ethics committee.

Stimuli and Procedure

The sexual stimuli used in the study were pictures of either male or female genitals displaying signs of sexual arousal. This kind of core sexual stimuli was selected in order to avoid confounding brain activation related to neuronal processing of faces, gestures, or social interactions. The sexual stimuli were preselected based on ratings obtained by 22 male and 55 female volunteers who did not participate in the study. Out of a set of 141 photographs, we selected 30 male and 30 female sexual stimuli which were rated as being sexually attractive. In the fMRI session, nonsexual pictures were also presented; however, brain responses to these stimuli were not submitted to this classification analysis.

Thirty stimuli of each category (male, female, nonsexual) were presented in a pseudorandom order. The stimuli were presented employing a fast event-related design using an interstimulus interval of 2,700 ms. Photographs were presented for 300 ms in a pseudorandomized order.

fMRI Data Acquisition and Preprocessing

MRI scanning was performed on a 1.5 tesla Philips Intera scanner (Amsterdam, Netherlands). We first obtained a structural T1-weighted MRI scan to exclude anatomical abnormalities. We then performed whole-brain echo-planar imaging to measure regional changes in the BOLD signal as an index of regional neuronal activity (TR = 3.100 ms; TE = 50 ms; flip angle 90°; 64 × 64 matrix; FOV 220 mm; 33 axial slices; slice thickness 3.5 mm; inter-slice gap: 0.3 mm). One hundred twenty-one volumes of the whole brain were acquired per session.

Data preprocessing and statistical analysis were performed with SPM2 software (http://www.fil.ion.ucl.ac.uk/spm/). Images were realigned to the first image, spatially normalized to the standard EPI template of the Montreal Neurological Institute (2 × 2 × 2 mm voxels). The normalized images were spatially smoothed with a Gaussian kernel of full-width half-maximum 10 mm to reduce intersubject differences in anatomy and enable the application of Gaussian random field theory.

Statistical Analysis and Subject Classification

Pattern classification of cerebral activity over the whole brain involved four steps:

- Step 1: A general linear model (GLM) was specified for individual fMRI time series using separate regressors for each trial type. Each regressor was convolved by a hemodynamic response function. Regression coefficients (parameter estimates) for all regressors were estimated in a subject-specific fixed effects model [23]. Low-frequency drifts in BOLD signal were removed by a high-pass filter with a cutoff of 128 s using appropriate linear contrasts. Based on the individual GLM, we calculated a *t*-statistics map subtracting the BOLD response to male sexual stimuli from the BOLD response to female stimuli for each voxel in the brain. This *t*-statistics map reflected the spatial pattern of regional differences in the BOLD response to male as opposed to female sexual stimuli across the whole brain.
- Step 2: The individual difference maps were entered in a two-sample *t*-test to quantify regional differences in the preferential BOLD response to male as opposed to female sexual stimuli between heterosexual and homosexual individuals (Figure 1).
- Step 3: We then assessed how much the individual difference map of each individual expressed the spatial pattern of difference in BOLD response as revealed by the between-groups comparison [14]. To this end, each voxel of the individual *t*-statistical difference map (male > female) was multiplied by the corresponding voxel of the group *t*-statistical difference map.
- Step 4: The resulting expression values were finally submitted subsequently to two different pattern classification algorithms: Fisher's linear discriminant analysis and the κ-nearest neighbor classification taking into account the "seven nearest neighbors" [24].

Both classification methods were cross-validated using the leave-one-out method. This was done by omitting one proband at a time form the original study sample. For the remaining 25 subjects, a new group *t*-statistical difference map was calculated (step 2). An individual expression value was then calculated for the left-out-subject (step 3) and classified subsequently by means of Fisher's linear dis-

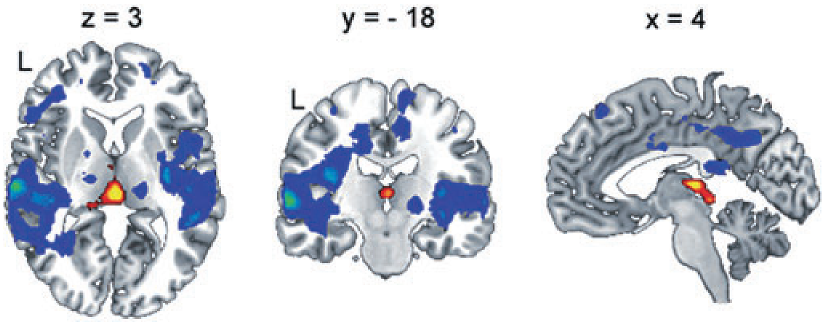

Figure 1 Homosexual men vs. heterosexual men. In this *t*-statistical map, voxels with positive *t*-values ($P < 0.001$ in red—yellow, uncorrected) indicated regions in the brain where homosexual individuals showed a relative stronger blood oxygen level-dependent (BOLD) signal than heterosexual individuals in response to male sexual stimuli as opposed to female stimuli. Conversely, voxels with negative *t*-values ($P < 0.001$ in blue—cyan, uncorrected) highlighted areas where heterosexual individuals displayed a stronger BOLD response than homosexual individuals to male sexual stimuli relative to female stimuli. Homosexual probands show significant increases in posterior thalamus. Heterosexual men show significant increased bilateral activity predominantly in insula and posterior cingulate cortex.

criminant and κ-nearest neighbor analysis (step 4). This procedure was done repeatedly (26 times), accounting for all subjects. The predictive power of the classification procedure was specified by calculating the specificity (true negative) and sensitivity (true positive) values. The average of sensitivity and specificity values was calculated as an index of mean classification accuracy.

Results

Figure 1 and Table 1 summarize the between-groups differences between heterosexual and homosexual individuals in the regional hemodynamic response to male or female sexual stimuli including all individuals of the sample. Compared to heterosexual men, homosexual men displayed stronger activation in response to male than female sexual stimuli in posterior thalamus and in right superior parietal cortex. In heterosexual men, extended areas of left and right insula, and posterior cingulate cortex, as well as right prefrontal cortex, were stronger in response to male sexual stimuli relative to female stimuli.

Individual expression values were mostly negative in the homosexual group and predominantly positive in heterosexual probands (Figure 2). Cross-validation showed that both classification methods performed equally well. Mean classification accuracy (average of sensitivity and specificity values in percent) was 88.5% using Fisher's linear discriminant analysis with a sensitivity of 92%

Table 1 Brain regions showing a relative increase in blood oxygen level-dependent (BOLD) signal during passive viewing of male sexual stimuli vs. female sexual stimuli

			Peak difference			
			Coordinates			
Area	Side	Cluster extent	*x*	*y*	*z*	*Z*-score
Heterosexual men > homosexual men (male > female)						
Insula	L	2,895	–62	–20	0	4.97
Superior frontal gyrus	R	1,596	20	50	22	4.77
Insula	R	1,772	34	–16	–8	4.64
Posterior cingular gyrus	L	109	–16	–46	46	4.09
Dorsal premotor cortex	R	117	44	–14	40	4.07
Posterior cingular gyrus	R	122	10	–50	38	4.04
Homosexual men > heterosexual men (male > female)						
Superior parietal lobule	R	44	26	–70	56	3.54
Posterior thalamus	M	34	4	–26	6	3.40

Regional differences in BOLD signal change are characterized by the cluster extent, stereotactic MNI coordinates, and *Z*-scores of the voxel showing maximal signal change within the cluster.
$P < 0.001$ (uncorrected).
R = right; L = left; M = mesial.

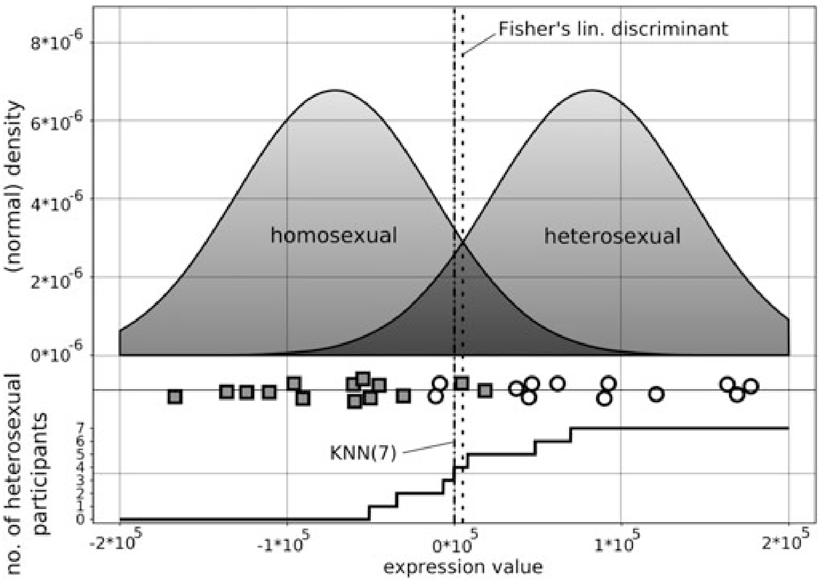

Figure 2 Classification of heterosexual and homosexual expression values according to Fisher's discriminant and κ-nearest neighbor analysis. In the middle of the figure, the original expression values of homosexual participants (filled squares) and of heterosexual participants (white circles) are plotted. Top: estimated normal density functions of the homosexual and heterosexual expression values. Fisher's discriminant analysis classifies expression values which were right from the vertical dotted line (decision boundary) as members of the heterosexual participant group. Bottom: number of "heterosexual neighbors" of each individual expression value (out of the seven nearest neighbors). Expression values at the left side of the graph have zero "heterosexual neighbors," and the function increases until all of the seven nearest neighbors are members of the heterosexual group. According to the κ-nearest neighbor analysis, expression values with more than three "heterosexual neighbors" were classified "heterosexual" (KNN(7) decision boundary). Note: Leaving one subject out (cross-validation) results in slightly different values and decision boundaries.

(two false positives) and specificity of 85% (four false negatives) (Table 2). The κ-nearest neighbor method reached a classification accuracy of 90% with a sensitivity of 88% (three false positives) and specificity of 92% (two false negatives) (Table 2).

Discussion

We show that functional activation maps derived from fMRI during the exposure to pictures of sexually aroused male or female genitals can be used for the assessment of sexual orientation. Although functional brain scans were not recorded to classify sexual preference, mean classification was accurate in approximately 9 out of 10 cases. Hence, classification accuracy is comparable with the classification accuracy gathered by phallometric procedures. This observation is consistent with a recent attempt to classify sexual orientation on the basis of functional brain images [25]. Extending the findings of that study, we cross-validated our results showing that the classification procedure also performs well when using individual fMRI activation maps of individuals who have not been included when training the classifier.

Table 2 Classification accuracy of Fisher's linear discriminant and κ-nearest neighbor analysis

	Fischer	KNN (7)
False positives (sensitivity)	2 (92%)	3 (88%)
False negatives (specificity)	4 (85%)	2 (92%)
Mean accuracy (%)	88.5%	90%

Total number of false positive and false negative classified probands (out of 26 participants) and corresponding sensitivity and specificity values in percent. KNN (7) = κ-nearest neighbor analysis taking into account the seven nearest neighbors.

Standard voxel-wise comparison of stimulus-driven brain activation at the group level revealed elevated activity of posterior thalamus in response to male sexual stimuli in homosexual probands. This is in accordance with the results found in the original sample from which this subsample was selected [11]. In the original sample (consisting of heterosexual and homosexual males and females), thalamus and superior parietal areas were activated by sexually preferred stimuli. A specific feature of our fMRI paradigm was the very short period of stimulus presentation (300 ms). Therefore, the functional brain response to sexually preferred stimuli can be attributed to early stimulus appraisal within the framework of contemporary emotion theory [26]. On the other hand, heterosexual men displayed increased brain activity in insula and cingulate cortex when viewing male sexual stimuli. This response pattern is more difficult to interpret. Because insula and cingulate cortex activity can be activated by disgusting pictures [27], it is conceivable that the observation of an erected penis triggered brain activity related to disgust in the heterosexual probands.

For the purpose of automatic classification, it is not necessary to know why a given brain area is activated by a particular stimulus. The only issue that matters is that a stimulus evokes different patterns of brain responses in different groups. This applies in particular to the feature extraction algorithm we choose for classification. It gives an individual expression value based on the whole-brain response, and hence, classification is entirely driven by the data. This is a critical difference to classification based on averaging the signal in predefined regions-of-interests (ROIs) [25] which is much more dependent on theoretical assumptions and anatomical distortions.

It is of interest that given the short stimulus presentation time in our fMRI session, the net stimulus exposure time was only 27 seconds (without inter-stimulus interval, but including the nonsexual stimuli). According to phallometric studies [4,28] net stimulus exposure time was about 1,500 seconds, and according to Safron and colleagues [25], net stimulus exposure time was about 1,400 seconds. In our study, we achieved a similar classification accuracy by using only a fraction of time as previous researchers needed to test sexual orientation. How can this be explained?

In phallometric research, it has been shown that short stimulus events are not able to elicit penile responses [29]. Therefore, long-lasting and consistent stimulus presentation is necessary. In phallometric assessment, additional efforts were realized in order to prevent subject manipulation, which is enabled by longer presentation times. With regard to fMRI-based classification, our results demonstrate that it is not necessary to present stimuli more than 1 second. Presentation times above 1 second particularly trigger sexual arousal in the participant, adding no more information to the stimulus appraisal which takes place within the first 500 ms after stimulus onset. As fMRI is able to detect sexual stimulus appraisal [11], presentation times below 1 second are justified. An advantage of short presentation time is that it enables a further increase in classification accuracy by increasing numbers of stimuli used in one fMRI session without overburdening the participants. Furthermore, short presentation times can be expected to be less prone to subject manipulations, as the subject has no time to elicit prepared responses to the varying stimuli within an event-related fMRI setting.

In summary, we argue that automatic classification of brain activity triggered by preference-specific sexual stimuli in heterosexual vs. homosexual males is as accurate as phallometric classification in pedophiles vs. heterosexual males. Measurement of brain activity is much less intrusive and much faster than phallometry. Our classification was based on only 27 seconds of stimulus exposure by means of a 1.5 tesla scanner. The classification accuracy is expected to further improve with increasing stimulus numbers, increasing participant numbers, and increasing signal-to-noise ratio (i.e., by means of a 3 tesla scanner).

We successfully classified heterosexual and homosexual men. In doing so, we only were interested in the accuracy of the technique, because objective measurements for the classification of homosexual vs. heterosexual orientation are of no clinical interest. Further research should test if this approach is feasible for a reliable diagnosis of paraphilias. Much of the phallometric research was done by assessing denying pedophiles. This is the crucial sample with which fMRI-based classification of sexual orientation is to be tested in future research.

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Statement of Authorship

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