ORIGINAL ARTICLE

ONLINE FIRST

# Assessment of Pedophilia Using Hemodynamic Brain Response to Sexual Stimuli

*Jorge Ponseti, PhD; Oliver Granert, MSc; Olav Jansen, Prof MD; Stephan Wolff, MSc; Klaus Beier, Prof MD, PhD; Janina Neutze, MSc; Günther Deuschl, Prof MD; Hubertus Mehdorn, Prof MD; Hartwig Siebner, Prof MD; Hartmut Bosinski, Prof MD*

**Context:** Accurately assessing sexual preference is important in the treatment of child sex offenders. Phallometry is the standard method to identify sexual preference; however, this measure has been criticized for its intrusiveness and limited reliability.

**Objective:** To evaluate whether spatial response pattern to sexual stimuli as revealed by a change in the blood oxygen level–dependent signal facilitates the identification of pedophiles.

**Design:** During functional magnetic resonance imaging, pedophilic and nonpedophilic participants were briefly exposed to same- and opposite-sex images of nude children and adults. We calculated differences in blood oxygen level–dependent signals to child and adult sexual stimuli for each participant. The corresponding contrast images were entered into a group analysis to calculate whole-brain difference maps between groups. We calculated an expression value that corresponded to the group result for each participant. These expression values were submitted to 2 different classification algorithms: Fisher linear discriminant analysis and κ-nearest neighbor analysis. This classification procedure was cross-validated using the leave-one-out method.

**Setting:** Section of Sexual Medicine, Medical School, Christian Albrechts University of Kiel, Kiel, Germany.

**Participants:** We recruited 24 participants with pedophilia who were sexually attracted to either prepubescent girls (n=11) or prepubescent boys (n=13) and 32 healthy male controls who were sexually attracted to either adult women (n=18) or adult men (n=14).

**Main Outcome Measures:** Sensitivity and specificity scores of the 2 classification algorithms.

**Results:** The highest classification accuracy was achieved by Fisher linear discriminant analysis, which showed a mean accuracy of 95% (100% specificity, 88% sensitivity).

**Conclusions:** Functional brain response patterns to sexual stimuli contain sufficient information to identify pedophiles with high accuracy. The automatic classification of these patterns is a promising objective tool to clinically diagnose pedophilia.

*Arch Gen Psychiatry. 2012;69(2):187-194.*
*Published online October 3, 2011.*
*doi:10.1001/archgenpsychiatry.2011.130*

**Author Affiliations:** Sections of Sexual Medicine (Drs Ponseti and Bosinski) and Neuroradiology (Dr Jansen and Mr Wolff) and Departments of Neurology (Mr Granert and Drs Deuschl and Siebner) and Neurosurgery (Dr Mehdorn), Medical School, Christian Albrechts University of Kiel, Kiel, and Institute of Sexology and Sexual Medicine, Charité Universitätsmedizin, Freie University and Humboldt University, Berlin (Dr Beier and Ms Neutze), Germany; and Danish Research Center for Magnetic Resonance, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark (Dr Siebner).

According to a retrospective inquiry in Germany, 8.6% of adult women and 2.8% of adult men reported that they had been a victim of severe child sexual abuse.[1] In light of this high incidence, considerable research effort has attempted to elucidate the causes of childhood sexual offenses, develop effective treatments for child sex offenders, and develop tools to predict recidivism.

First, research in this area must take into account that some child sex offenders are pedophiles and some are not. Phallometric assessments of single-victim offenders showed that approximately half of these men are pedophiles.[2] According to the current diagnostic criteria, pedophiles experience a sustained sexual attraction to prepubescent children and have either acted on or felt distress by this sexual urge (*DSM-IV-TR* code 302.2).[3] Although the etiology of either pedophilic or nonpedophilic child sex offending is not fully understood, findings from distinct research areas suggest that there are neurodevelopmental[4-8] and social[9] causes. Moreover, morphometric magnetic resonance imaging (MRI) studies have found reduced gray matter volume in the amygdala and interconnected areas such as the hypothalamus,[10] ventral striatum, orbitofrontal cortex, and cerebellum,[11] as well as reduced white matter in the superior fronto-occipital fasciculus and right arcuate fasciculus.[12] However, these structural changes have shown little overlap across studies.

Pedophiles showed reduced neural responses to adult erotic stimuli in brain areas



©2012 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/24/2013

known to be involved in sexual processing such as the amygdala,[13] hypothalamus, and prefrontal cortex in functional MRI (fMRI) studies.[14] Exposure to sexual stimuli that matched their preferences (ie, pictures of nude children), however, evoked preference-specific activations similar to those observed in healthy heterosexual adults.[15,16] One study reported a hypoactivation of the orbitofrontal cortex and a hyperactivation of the dorsolateral prefrontal cortex; this evidence was interpreted as a sexual processing dysfunction in the prefrontal networks.[16]

Although there is not consistent evidence of an abnormal activation profile in pedophiles, preference-specific tuning of the functional activation patterns evoked by sexual stimuli could be used to assess pedophilia. Using an automatic classification algorithm, Ponseti and colleagues[17] tested whether brain activity in response to sexually preferred vs nonpreferred stimuli predicts sexual orientation in a sample of healthy heterosexual and homosexual men. They found that the algorithm's mean classification accuracy exceeded 85%, which indicates that the brain's functional response patterns to sexual stimuli contained sufficient information to predict sexual orientation with high accuracy. This finding ties in with an increasing body of research showing that automated classification techniques of whole-brain MRI scans can facilitate the diagnosis of neurological and psychiatric diseases. For example, a classification accuracy well above 85% has been obtained using structural MRI brain scans in patients with early Alzheimer disease,[18,19] obsessive-compulsive disorder,[20] and prodromal psychosis[21] or with fMRI in patients with major depression.[22]

Reliable assessment of a paraphilic sexual orientation is of great importance for the prediction of recidivism.[23] Furthermore, the effective treatment of child sex offenders relies on an accurate assessment of a paraphilic sexual orientation, given that some interventions are appropriate for pedophilic offenders but not for nonpedophilic offenders and vice versa. In cases in which forensic records and convincing reports are absent (eg, a first sexual offense), a valid assessment of sexual orientation can only be done using the phallometric measurement, the current standard to objectively assess sexual deviances.[2,24] During phallometric measurements, participants are required to place a device around their penis to have their erectile responses recorded. Phallometry has been criticized not only for its intrusiveness but also because of its high proportion of nonresponders. According to a laboratory survey, up to 40% of phallometric test results are rejected owing to low response (which are commonly considered "random variation").[25] The proportion of nonresponders can be lowered to approximately 2% using volumetric phallometry, a more sensitive and accurate assessment of penile reponses.[26] Sildenafil citrate may also increase the rate of response.[27] However, most laboratories still use circumferential phallometric measurements because they are easier to apply than volumetric phallometric measurements.

This study examined whether an automated pattern classification of fMRI data can predict paraphilic sexual orientation. We tested this using a parametric classifier (Fisher linear discriminant analysis) and a nonparametric classifier (κ-nearest neighbor analysis).[28] We hypothesized that maps reflecting regional differences in participants' blood oxygen level–dependent (BOLD) response to sexual stimuli should indicate sexual orientation.

## METHODS

### PARTICIPANTS

We recruited 25 male participants who met the diagnostic criteria for pedophilia according to the *DSM-IV-R*[3] (exclusive and nonexclusive types) from 2 outpatient departments of Sexual Medicine involved in the prevention project Dunkelfeld, which offers anonymous treatment for self-identified pedophiles.[29] The standard intake procedures of the prevention project Dunkelfeld, which include a semistructured clinical interview and a questionnaire to measure sexual interest, behavior, and child pornography consumption, assessed pedophilic interest.[30] We excluded 1 participant from further analysis because his postscan ratings of sexual stimuli revealed a preference for adult women. According to self-report, 11 of the remaining participants with pedophilia were sexually attracted to prepubescent girls (heterosexual pedophiles), and 13 were attracted to prepubescent boys (homosexual pedophiles). Of the 24 participants with pedophilia, 11 underwent phallometry to confirm the initial pedophilia diagnosis. In the remaining cases, forensic records supplied the diagnosis. Seven of the pedophilic participants declared to be sometimes sexually attracted to adults as well (ie, they were of the nonexclusive type). Five of these nonexclusive pedophiles were heterosexual pedophiles; the remaining 2 were homosexual pedophiles. Twelve participants with pedophilia had committed sexual offenses previously. We recruited 32 healthy male volunteers to serve as a control group (also referred to as teleiophiles). Eighteen controls were sexually attracted to adult women (heterosexual teleiophiles), and 14 were sexually attracted to adult men (homosexual teleiophiles). Sexual orientation was ascertained using the Kinsey ratings of fantasy and behavior of 0 and 1 or 5 and 6, respectively.[31]

Based on a structured interview, we verified that participants had no claustrophobia, implants or other metallic parts inside their body, history of head injury, sexual dysfunction, gender identity disorder, substance abuse during the last year, or any medication related to sexual functioning. In addition, we excluded control participants for having histories of paraphilia or committing sexual offenses. Six participants with pedophilia and 2 volunteers were left handed.

Groups were matched for age (mean [SD], heterosexual pedophiles, 37 [5.9] years [range, 25-46 years]; homosexual pedophiles, 33.5 [14.2] years [range, 18-64 years]; heterosexual teleiophiles, 32.4 [8.2] years [range, 22-49 years]; homosexual teleiophiles, 28.6 [5.7] years [range, 23-42 years]; $F_{3,52}=1.81$; $P=.16$) and intelligence as measured by the Wechsler Adult Intelligence Scale reasoning subtest matrix[32] (mean [SD], heterosexual pedophiles, 11 [3.1] scaled scores [range, 5-16 scaled scores]; homosexual pedophiles, 10.2 [2.9] scaled scores [range, 4-14 scaled scores]; heterosexual teleiophiles, 11.8 [2.3] scaled scores [range, 5-15 scaled scores]; homosexual teleiophiles, 11.8 [2 ] scaled scores [range, 8-14 scaled scores]; $F_{3,52}=1.25$; $P=.30$). All participants provided written informed consent before participating in this experiment. The local ethics committee of the Medical Faculty of Christian-Albrechts University approved this study.



©2012 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/24/2013

## STIMULI AND PROCEDURE

We presented 14 different picture categories during an fMRI session: nude adults and children (either whole-body frontal views, genitals only, or face only) and nonsexual pictures with either high or low arousal scores from the International Affective Picture System.[33] In each sexual picture, only 1 person (or 1 genitalia) was visible without additional context. In contrast to the child stimuli, many of the adult sexual stimuli displayed signs of genital arousal. We used this type of core sexual stimuli because research has found that these stimuli are highly selective in triggering neuronal responses according to the sexual preference of the observer.[34] We presented 35 pictures within each category for a total of 490 photographs. However, for the purpose of pattern classification only, trials with pictures depicting whole-body frontal views or genitals only entered the analysis. This corresponds to 70 pictures (35 whole-body view + 35 genital) of boys, girls, men, and women each (and a total of 280 trials in the analysis).

We presented each image for 1 second with a variable interstimulus interval (range, 1-5 seconds) in a pseudorandom order. Participants were instructed to view each stimulus attentively. To ensure that participants paid attention to the stimuli, they manually responded when an oddball stimulus (green circle) appeared on-screen. The oddball was presented 20 times during the fMRI session. Stimuli were projected to a mirror mounted on a standard head coil. Immediately afterward, participants rated the stimuli in terms of valence and arousal using the 9-point Self-Assessment Manikin Likert-type scale.[35] For each sexual stimulus, we multiplied valence and arousal ratings to obtain a combined index that we previously found to be closely correlated with sexual attractiveness ratings.[34]

## IMAGING PROCEDURE AND DATA PREPROCESSING

A 3-T whole-body MRI scanner (Achieva; Philips, Best, the Netherlands) imaged participants. A 3-dimensional spoiled gradient echo acquisition with sagittal volume excitation ($1 \times 1 \times 1$-mm voxels) acquired a structural T1 volume for each participant, followed by 3 fMRI runs. Each fMRI run consisted of 352 volumes. The functional MRI measurements of the BOLD signal were performed using an echo planar imaging (EPI) sequence with a repetition time of 2500 milliseconds, echo time of 36.8 milliseconds, and a flip angle of 90°. The field of view covered the whole brain (38 axial slices; slice thickness: 3 mm; interslice gap: 0.3 mm). We acquired axial slices parallel to the anterior-posterior commissural plane.

We performed data preprocessing and statistical analyses using SPM8 software (http://www.fil.ion.ucl.ac.uk/spm/) on Matlab 7.7.0 (MathWorks, Natick, Massachusetts). We realigned the EPI images to their mean and spatially normalized scans using the Montreal Neurological Institute template. The spatial normalization was realized by applying the SPM segmentation algorithm to individual T1-weighted images to estimate the parameters of the nonlinear spatial normalization transform. We then coregistered the realigned EPI images to the corresponding individual T1-weighted image and used the normalization parameters of the segmentation step to write normalized versions of the EPI images ($2 \times 2 \times 2$-mm voxels). This procedure optimizes spatial normalization using the high-resolution T1-weighted image to determine the complex nonlinear spatial normalization function and incorporates a bias correction to cope with potential brightness heterogeneities in the T1-weighted structural images. Finally, a gaussian kernel of full-width half-maximum 8 mm spatially smoothed the normalized EPI images to reduce anatomical differences in participants and enabled gaussian random field theory application.

## STATISTICAL ANALYSES AND SUBJECT CLASSIFICATION

Whole-brain pattern classification of cerebral activity was done using the same algorithm we previously applied to another sample.[17] This algorithm has 4 steps:

Step 1 (first-level analysis): We specified a general linear model for fMRI time series of each subject using a separate regressor for each stimulus condition (boys' body, boys' genital, men's body, men's genital, girls' body, girls' genital, women's body, women's genital) and 6 regressors with movement parameters as estimated in the realignment step. Each stimulus-related response was convolved with the standard hemodynamic response function. Regression coefficients (parameter estimates) for all regressors were estimated within a subject-specific fixed-effects model.[36] A high-pass filter with a cutoff of 128 seconds was used to remove low-frequency drifts in BOLD signal. Based on subject-specific general linear model estimates, we calculated 2 *t*-statistic maps by contrasting the stimulus conditions from (1) pictures of boys compared with pictures of men and (2) pictures of girls compared with pictures of women for each voxel. For each subject, we got 2 *t*-statistic maps: the first reflecting the spatial pattern of regional differences in the BOLD response to male-child sexual stimuli as opposed to male-adult sexual stimuli and the second reflecting regional differences in the BOLD response to female-child sexual stimuli as opposed to female-adult sexual stimuli across the whole brain.

Step 2 (second-level analysis): We built a (3-way) flexible factorial design with the parameter estimates of each stimulus condition ($n=8$) for each subject as a stimulus factor. The remaining 2 factors within this design were group (2 levels) and subject (56 levels) and as covariate of no interest, age and intelligence. The covariates age and intelligence were included to correct group differences for age- or intelligence-related variance. Both covariates were centered to the global mean value. The subject factor was aimed to capture any further subject-related variance not modeled by any of the other factors (eg, handedness). We then calculated statistical maps (*t* contrasts) between groups to quantify regional differences in the preferential BOLD response to boys vs men and to girls vs women between pedophiles and healthy volunteers.

Step 3 (*t*-map projection): To assess and quantify subject-specific effects, contrast images calculated in the first step were projected onto the group-specific difference maps determined in second-level analysis (step 2). These statistical maps express the spatial pattern of difference in BOLD response as revealed by the between-groups comparison.[20] The projection is implemented by summing up the voxelwise products of the subject-specific contrast images (boy < men and girl < women) determined in the first-level analysis (step 1) and the *t* maps of the group difference maps determined in the second-level analysis (step 2). This sum mathematically corresponds to a vector dot product. The procedure was performed separately for the boys vs men and the girls vs women difference maps. The summed voxelwise product is referred to as the "individual expression value." It represents the degree to which the brain response of one subject (ie, its *t* statistical difference map) matches the average brain response of one group (ie, the group *t* statistical difference map gathered in step 2). High individual expression values, either negative or positive, usually indicate a good correspondence with the (difference) pattern of one group. Moderate individual expression values indicate that the respective individual expresses a brain response lying somehow between the expression patterns found in the groups.

Step 4 (classification and cross-validation): Finally, we submitted the resulting individual expression values (2 values for



©2012 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/24/2013

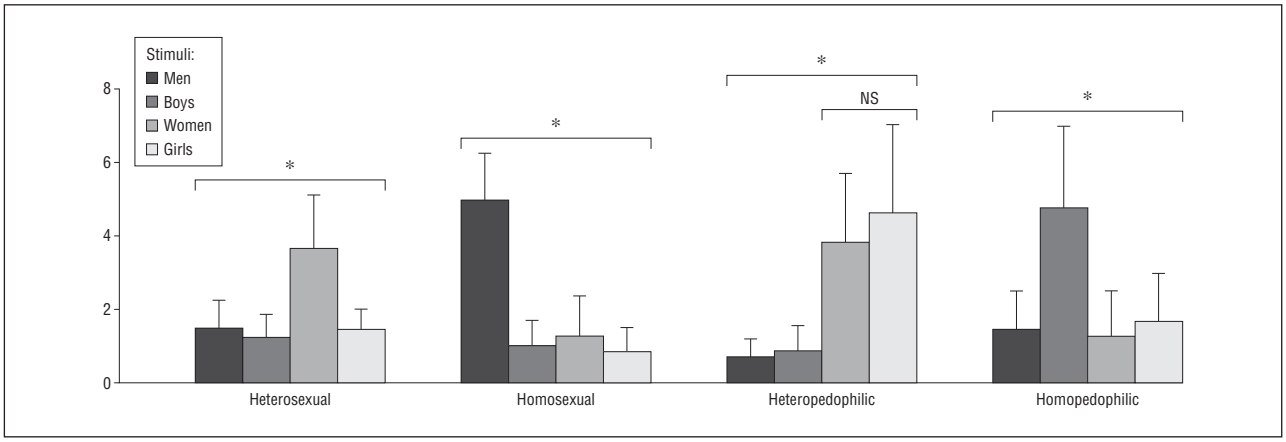


**Figure 1.** Mean ratings of sexual stimuli for groups of heterosexual, homosexual, heteropedophilic, and homopedophilic participants were in concordance with their reported sexual orientations. Nonexclusive pedophiles were primarily heteropedophilic. Error bars = 1 SD. *$P < .001$. NS indicates not significant.

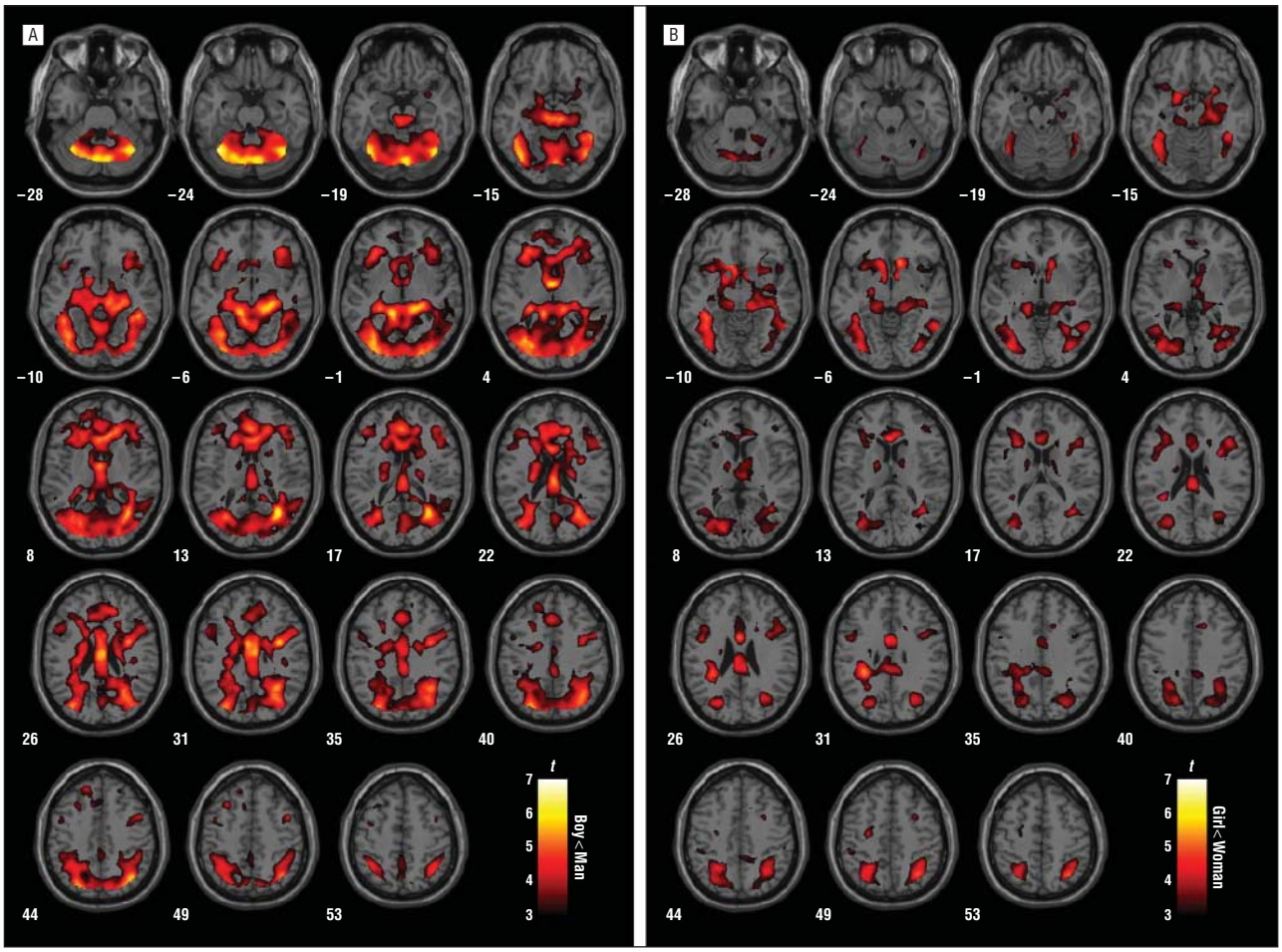


**Figure 2.** Differences in brain activity between pedophiles and healthy volunteers. The axial statistical *t*-score maps show between-group differences in functional brain activation evoked by pictures of naked children and adults (with a threshold at $P < .001$, uncorrected). Increased responses to child vs adult stimuli are presented in part A for male stimuli and in part B for female stimuli. The *t*-score maps were overlaid on a structural T1-weighted magnetic resonance image. The numbers represent the stereotactic z coordinate corresponding to each axial slice.

each subject) to 2 different pattern classification algorithms: a parametric Fisher linear discriminant analysis and a nonparametric κ-nearest neighbor classification (taking into account the 7 nearest neighbors).

To calculate the ability of classifying previously unknown data sets (test the generalization ability), we cross-validated both classification methods using the leave-one-out method (ie, we omitted 1 proband at a time from the original sample). For the remaining 55 participants, we calculated new *t* statistical difference maps (step 2). Individual expression values were then calculated for the "left-out" participant (one for the boys < men and one for the girls < women comparison; step 3). Subsequently, we classified the participant according to these values using Fisher linear discrimi-



©2012 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/24/2013

**Table 1. The Discriminative Pattern Underlying Pedophilic vs Control Group Classification[a]**

| Brain Area | Side | Cluster Size, Voxels | *t* Value Maximum | *z* Score Maximum | MNI Coordinates, mm x | y | z |
|---|---|---|---|---|---|---|---|
| Pedophiles < controls (boys < men) | | | | | | | |
| Cerebellum | L | 50 195 | 6.72 | 6.53 | –38 | –62 | –24 |
| Cerebellum | R | | 6.36 | 6.19 | 40 | –64 | –22 |
| Lingual gyrus | L | | 6.05 | 5.91 | –12 | –40 | –2 |
| Anterior thalamus | L | | 6.05 | 5.90 | –2 | –6 | 4 |
| Hippocampus | R | | 5.99 | 5.85 | 22 | –32 | –4 |
| Occipital lobe | L | | 5.96 | 5.82 | –34 | –76 | 0 |
| Lingual gyrus | R | | 5.87 | 5.74 | 14 | –34 | 0 |
| Fusiform gyrus | L | | 5.82 | 5.69 | –38 | –74 | –16 |
| Inferior temporal gyrus | R | | 5.72 | 5.60 | 46 | –44 | –12 |
| Angular gyrus | R | | 5.61 | 5.50 | 38 | –66 | 44 |
| Pedophiles < controls (girls < women) | | | | | | | |
| Nucleus caudate | R | 17 577 | 5.59 | 5.47 | 12 | 18 | –8 |
| Nucleus caudate | L | | 5.27 | 5.18 | –8 | 14 | –8 |
| Superior parietal gyrus | R | | 5.27 | 5.18 | 32 | –62 | 52 |
| Inferior temporal gyrus | L | | 5.24 | 5.14 | –42 | –44 | –10 |
| Fusiform gyrus | L | | 5.21 | 5.11 | –38 | –46 | –10 |
| Cingulate | L | | 5.07 | 4.98 | –2 | 4 | 28 |
| Occipital lobe | L | | 4.77 | 4.70 | –38 | –78 | 0 |
| Amygdala | L | | 4.75 | 4.68 | –18 | 0 | –12 |
| Superior parietal gyrus | L | | 4.66 | 4.59 | –26 | –56 | 46 |
| Fusiform gyrus | R | | 4.59 | 4.52 | 44 | –42 | –14 |
| Inferior temporal gyrus | R | | 4.51 | 4.45 | 54 | –56 | –8 |
| Insula | L | | 4.25 | 4.19 | –32 | 12 | –10 |
| Inferior frontal gyrus | R | 623 | 4.21 | 4.16 | 44 | 24 | 22 |
| Thalamus | L | 161 | 4.04 | 4.00 | –16 | –8 | 10 |
| Cerebellum | R | 116 | 3.46 | 3.43 | 28 | –48 | –30 |

Abbreviation: MNI, Montreal Neurological Institute.
[a]Significant clusters only (uncorrected threshold: $P < .001$).

nant and κ-nearest neighbor analyses (step 4). We performed this "leave-one-out" procedure 56 times to account for all participants. We specified the predictive power of the classification procedure by calculating the specificity (true negative) and sensitivity (true positive) values. We calculated the average sensitivity and specificity values and the mean classification accuracy (number of correct decisions divided by number of total decisions).

The predictive power of the individual expression values depends on the proportion of significant vs nonsignificant voxels of the group *t* statistical difference map, which was taken into account. For instance, if individual expression value calculations are based on the whole-brain *t* statistical difference map, much more "noise" would be accumulated in the individual expression values. In contrast, restricting individual expression values to significant areas of the group *t* statistical difference map would reduce the influence of noise. In the absence of previous experiences with statistical thresholds in this regard and its effect on subsequent classification accuracy, we tested 4 different thresholds (whole brain; $t > 2$; $t > 3$; and $t > 4$). Accordingly, we performed steps 3 and 4 and subsequent cross-validations based on these thresholds to determine the effect of whole-brain vs a more region-specific analysis.

## RESULTS

### BEHAVIORAL RESPONSES

Ratings corresponded to participant sexual preferences (**Figure 1**). Repeated-measures analyses of variance revealed main effects of stimulus type in the groups of heterosexual teleiophiles ($F_{3,51}=42.55$; $P<.001$), homosexual teleiophiles ($F_{3,39}=71.83$; $P<.001$), heterosexual pedophiles ($F_{3,30}=26.25$; $P<.001$), and homosexual pedophiles ($F_{3,36}=22.62$; $P<.001$). Interestingly, heterosexual pedophiles rated pictures of women and girls as sexually attractive, and the difference between these ratings was not significant ($t_{10}=1.45$; $P=.18$). This result is in accordance with the clinical assessment of our sample showing that the nonexclusive pedophiles were predominantly heterosexual pedophilic participants.

### AUTOMATIC CLASSIFICATION

Analysis of variance (step 2) revealed significant differences of the individual difference maps between pedophilic and teleiophilic participants in widespread brain areas. This was found in the boys vs men as well as the girls vs women contrast (**Figure 2** and **Table 1**). However, as shown in Figure 2 and Table 1, group differences were more extended in the boys vs men than in the girls vs women contrast.

In each participant, the individual brain response was characterized by 2 expression values, one for the girls < women contrast and one for the boys < men contrast. **Figure 3** displays the individual expression values based on whole-brain *t* maps for all 56 partici-



©2012 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/24/2013

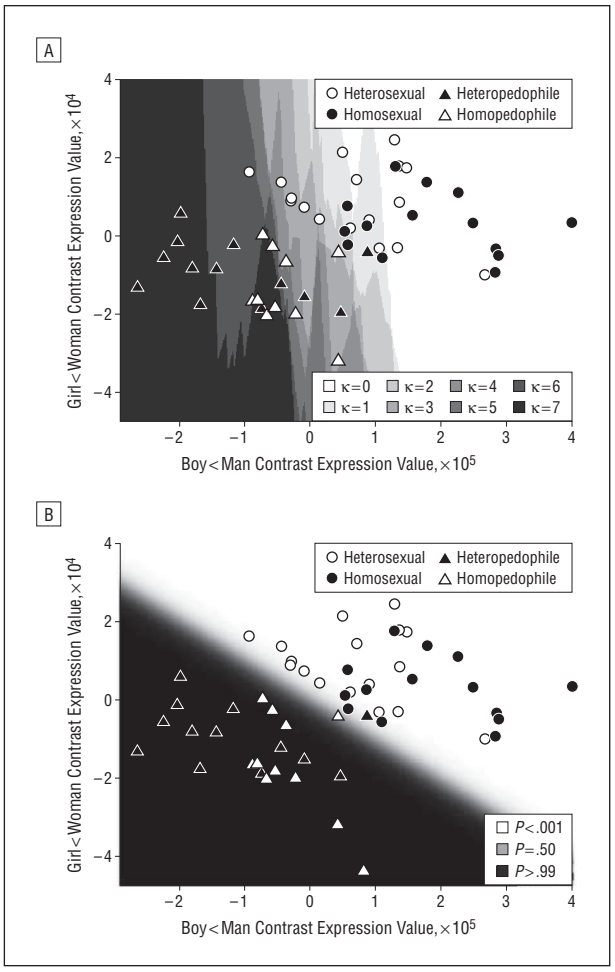


**Figure 3.** The classification of pedophiles and healthy controls using individual expression values according to both classification algorithms. A, κ-Nearest neighbor analysis. The gray areas vary according to the number of pedophilic "neighbors." Participants with more than 3 pedophilic "neighbors" were classified as pedophiles. B, Fisher linear discriminant analysis. Participants with $P_{(\text{pedophilic})}>.50$ (dark area) were classified as pedophiles.

pants (parts A and B present identical expression values). Individual expression values of those sexually attracted to a female body (heterosexual teleiophiles and heterosexual pedophiles) differed mostly in regard to the girls < women comparison (y-axis in Figure 3). Conversely, homosexual teleiophiles and homosexual pedophiles differed predominantly with respect to the boys < men comparison (x-axis in Figure 3).

We entered individual expression values into classification analyses based on whole-brain expression values. Cross-validation showed that Fisher linear discriminant analysis performed somewhat better than the κ-nearest neighbor classification (**Table 2**). Classification accuracy improved by increasing the $t$ threshold. When whole-brain difference maps were held to $t>4$, Fisher linear discriminant analysis provided the best classification results. Only 3 participants were misclassified in this case (false negatives). Of the 3 misclassified pedophiles, 2 were heterosexual and 1 was homosexual. All of them were of the nonexclusive type.

## COMMENT

To our knowledge, this study is the first to apply a neurofunctional pattern classification to assess pedophilia. Relying solely on the spatially distributed between-group differences in functional brain response to sexual stimuli, a pattern classification algorithm distinguished participants with pedophilia from healthy controls with a high degree of accuracy. Classification accuracy was robust when classifying previously unseen participant fMRI activation maps.

We chose a mixed sample of heterosexual and homosexual men who were either attracted to adults or children to test automatic classification accuracy under the realistic condition of not knowing whether a supposed pedophile is homosexual or heterosexual. By integrating these 2 comparisons (boys vs men) and (girls vs women), we were able to reliably discriminate teleiophilic participants from pedophilic participants (no matter whether the latter were exclusive pedophilic, nonexclusive pedophilic, heterosexual pedophilic, or homosexual pedophilic). As Figure 3 demonstrates, the boys vs men comparison was able to discriminate within the homosexual participants those attracted to adults from those attracted to children. Conversely, the girls vs women comparison was more sensible to discriminate with regard to the heterosexual probands.

When applying a neurofunctional pattern classification algorithm, diagnostic accuracy relies on the discriminative power of the spatially distributed brain response as triggered by stimuli. In the present study, we presented core sexual stimuli that triggered a highly discriminative response pattern in participants. This result is consistent with previous research showing that core sexual stimuli reliably trigger preference-specific responses independent of either the sex of the participant or the stimulus.[34]

We consistently found preference-specific brain activity in a distributed set of brain areas, most of them known to be involved in processing sexually arousing stimuli, such as the caudate nucleus, cingulate cortex, insula, fusiform gyrus, temporal cortex, occipital cortex, thalamus, amygdala, and cerebellum.[37] The highly consistent activation differences in these brain areas account for our algorithm's high classification accuracy, but only when classified by means of Fisher linear discriminant analysis. When we restricted the calculation of the individual expression values to these brain areas (by increasing the $t$ threshold), the mean classification accuracy improved from 89% to 95% (Table 2).

Apparently, the classification algorithm performs less optimally in cases of participants with ambiguous sexual preferences. All of the 3 misclassified participants (Fisher linear discriminant, $t>4$) (Table 2) were pedophiles of the nonexclusive type (2 heterosexual pedophiles and 1 homosexual pedophile). Most of the nonexclusive pedophiles in our sample were heterosexual (5 of 7 nonexclusive pedophiles). This might account for the smaller group differences in the girls vs women contrast in comparison with the boys vs men contrast and in turn with the misclassification of the 2 heterosexual pedophiles.



©2012 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/24/2013

**Table 2. Sensitivity and Specificity Scores of Fisher Linear Discriminant Analysis and KNN Analysis After Cross-validation for Various *t* Levels**

| Classification Algorithm | Brain Area Considered for Expression Values[a] | No. of False Positives | Specificity, % | No. of False Negatives | Sensitivity, % | Mean Accuracy, % |
|---|---|---|---|---|---|---|
| KNN | | | | | | |
| | Whole brain | 3 | 91 | 4 | 83 | 88 |
| | $t > 2$ | 2 | 94 | 3 | 88 | 91 |
| | $t > 3$ | 3 | 91 | 6 | 75 | 84 |
| | $t > 4$ | 5 | 84 | 9 | 63 | 75 |
| Fisher | | | | | | |
| | Whole brain | 4 | 88 | 2 | 92 | 89 |
| | $t > 2$ | 2 | 94 | 2 | 92 | 93 |
| | $t > 3$ | 2 | 94 | 3 | 88 | 91 |
| | $t > 4$ | 0 | 100 | 3 | 88 | 95 |

Abbreviation: KNN, κ-nearest neighbor.
[a]We calculated expression values entered into the classification algorithm with respect to either whole-brain *t* maps or *t* maps restricted by a threshold of $t > 2$ to $t > 4$.

Comparing neurofunctional pattern classification with the phallometric assessment in terms of accuracy yields a heterogeneous picture. When administered to pedophiles who admit their sexual orientation, the phallometric assessment shows perfect sensitivity (100%),[38] whereas fMRI-based classification shows a maximal sensitivity of 92%. In contrast, specificity of fMRI-based classification reaches 100%. Specificity scores of the phallometric assessment are reported to be around 81% when pedophiles were compared with a group of healthy controls.[24] In total, mean classification accuracy of the neurofunctional pattern classification approach was somewhat superior as opposed to the phallometric assessment.

However, the present study only included individuals who openly admit to pedophilia. Objective assessment of sexual preferences is generally needed when there is doubt about the subject's sexual preference, for instance, in single-victim child sexual offenders who declare not to be pedophilic. Sensitivity of the phallometric assessment in nonadmitting pedophiles is reported to be about 78% for heterosexual pedophiles and 89% for homosexual pedophiles.[24] The decrease from 100% sensitivity in admitting pedophiles to 78% and 89%, respectively, in nonadmitting pedophiles can be attributed to the ability of some men to manipulate their penile responses during the phallometric measurement. Currently, it is not known whether probands are able to manipulate their neurofunctional response during brief sexual stimulus presentation within the MRI environment.

Our findings raise the question as to whether sexual orientation in child sex offenders should be assessed using fMRI. Some considerations speak in favor of automatic fMRI classifications: first, automatic classification may be more accurate than phallometry; and second, fMRI measures are less intrusive than phallometry and can be performed in less than 20 minutes. Furthermore, fMRI-based classification has the potential to overcome some additional limitations of phallometry. The present study did not include any participant who could not be classified owing to a small response; thus, this method might be able to circumvent the problem of nonresponders in circumferential phallometry. Finally, fMRI-based classification might be less susceptible to manipulation because the participant has no time to elicit prepared responses to varying stimuli in a fast, event-related fMRI setting.

In summary, the automatic classification of functional brain response to sexual stimuli is a promising technique to assess the sexual orientation of child sex offenders; however, additional research is needed to improve classification accuracy, particularly in cases of nonexclusive pedophiles or nonadmitting pedophiles. One possibility might be just to increase sample size, given that Fisher linear discriminate accuracy improves with increasing numbers. Furthermore, the validity of this new assessment technique should be tested more extensively. For example, test-retest reliability has to be evaluated. This issue is crucial, and it has been repeatedly criticized in phallometry.[39] Moreover, future studies should include pedophiles who do not admit their sexual orientation. Finally, fMRI research should test whether participants are able to falsify their response to sexual stimuli.

**Submitted for Publication:** February 24, 2011; final revision received June 30, 2011; accepted July 28, 2011.
**Published Online:** October 3, 2011. doi:10.1001/archgenpsychiatry.2011.130
**Correspondence:** Jorge Ponseti, PhD, Section of Sexual Medicine, Christian Albrechts University, Arnold Heller Strasse 3, 24105 Kiel, Germany (ponseti@sexmed.uni-kiel.de).
**Author Contributions:** Dr Ponseti had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
**Financial Disclosure:** None reported.
**Funding/Support:** Functional MRI was performed in the MRI unit sponsored by the Federal Ministry of Education and Research. Federal Ministry of Education and Research structural grant 01 GO 0511 to NeuroImageNord sponsored Dr Siebner's research.
**Previous Presentation:** This paper was presented at the Association for the Treatment of Sexual Abusers 29th Annual Research and Treatment Conference; October 21, 2010; Phoenix, Arizona.



©2012 American Medical Association. All rights reserved.
Downloaded From: http://jamanetwork.com/ on 05/24/2013

## REFERENCES


1. Wetzels P. Prävalenz und familiäre Hintergründe sexuellen Kindesmissbrauchs in Deutschland: Ergebnisse einer repräsentativen Befragung. *Sexuologie*. 1997; 4(2):89-107.
2. Blanchard R, Klassen P, Dickey R, Kuban ME, Blak T. Sensitivity and specificity of the phallometric test for pedophilia in nonadmitting sex offenders. *Psychol Assess*. 2001;13(1):118-126.
3. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed, text revision. Washington, DC: American Psychiatric Association; 2000.
4. Blanchard R, Barbaree HE, Bogaert AF, Dickey R, Klassen P, Kuban ME, Zucker KJ. Fraternal birth order and sexual orientation in pedophiles. *Arch Sex Behav*. 2000;29(5):463-478.
5. Smallbone SW, McCabe BA. Childhood attachment, childhood sexual abuse, and onset of masturbation among adult sexual offenders. *Sex Abuse*. 2003;15(1):1-9.
6. Blanchard R, Kuban ME, Klassen P, Dickey R, Christensen BK, Cantor JM, Blak T. Self-reported head injuries before and after age 13 in pedophilic and nonpedophilic men referred for clinical assessment. *Arch Sex Behav*. 2003;32(6): 573-581.
7. Cantor JM, Blanchard R, Christensen BK, Dickey R, Klassen PE, Beckstead AL, Blak T, Kuban ME. Intelligence, memory, and handedness in pedophilia. *Neuropsychology*. 2004;18(1):3-14.
8. Schiffer B, Vonlaufen C. Executive dysfunctions in pedophilic and nonpedophilic child molesters. *J Sex Med*. 2011;8(7):1975-1984.
9. Jespersen AF, Lalumière ML, Seto MC. Sexual abuse history among adult sex offenders and non-sex offenders: a meta-analysis. *Child Abuse Negl*. 2009; 33(3):179-192.
10. Schiltz K, Witzel J, Northoff G, Zierhut K, Gubka U, Fellmann H, Kaufmann J, Tempelmann C, Wiebking C, Bogerts B. Brain pathology in pedophilic offenders: evidence of volume reduction in the right amygdala and related diencephalic structures. *Arch Gen Psychiatry*. 2007;64(6):737-746.
11. Schiffer B, Peschel T, Paul T, Gizewski E, Forsting M, Leygraf N, Schedlowski M, Krueger TH. Structural brain abnormalities in the frontostriatal system and cerebellum in pedophilia. *J Psychiatr Res*. 2007;41(9):753-762.
12. Cantor JM, Kabani N, Christensen BK, Zipursky RB, Barbaree HE, Dickey R, Klassen PE, Mikulis DJ, Kuban ME, Blak T, Richards BA, Hanratty MK, Blanchard R. Cerebral white matter deficiencies in pedophilic men. *J Psychiatr Res*. 2008; 42(3):167-183.
13. Sartorius A, Ruf M, Kief C, Demirakca T, Bailer J, Ende G, Henn FA, Meyer-Lindenberg A, Dressing H. Abnormal amygdala activation profile in pedophilia. *Eur Arch Psychiatry Clin Neurosci*. 2008;258(5):271-277.
14. Walter M, Witzel J, Wiebking C, Gubka U, Rotte M, Schiltz K, Bermpohl F, Tempelmann C, Bogerts B, Heinze HJ, Northoff G. Pedophilia is linked to reduced activation in hypothalamus and lateral prefrontal cortex during visual erotic stimulation. *Biol Psychiatry*. 2007;62(6):698-701.
15. Schiffer B, Krueger T, Paul T, de Greiff A, Forsting M, Leygraf N, Schedlowski M, Gizewski E. Brain response to visual sexual stimuli in homosexual pedophiles. *J Psychiatry Neurosci*. 2008;33(1):23-33.
16. Schiffer B, Paul T, Gizewski E, Forsting M, Leygraf N, Schedlowski M, Kruger TH. Functional brain correlates of heterosexual paedophilia. *Neuroimage*. 2008; 41(1):80-91.
17. Ponseti J, Granert O, Jansen O, Wolff S, Mehdorn H, Bosinski H, Siebner H. Assessment of sexual orientation using the hemodynamic brain response to visual sexual stimuli. *J Sex Med*. 2009;6(6):1628-1634.
18. Duchesne S, Caroli A, Geroldi C, Barillot C, Frisoni GB, Collins DL. MRI-based automated computer classification of probable AD versus normal controls. *IEEE Trans Med Imaging*. 2008;27(4):509-520.
19. Klöppel S, Stonnington CM, Chu C, Draganski B, Scahill RI, Rohrer JD, Fox NC, Jack CR Jr, Ashburner J, Frackowiak RS. Automatic classification of MR scans in Alzheimer's disease. *Brain*. 2008;131(pt 3):681-689.
20. Soriano-Mas C, Pujol J, Alonso P, Cardoner N, Menchón JM, Harrison BJ, Deus J, Vallejo J, Gaser C. Identifying patients with obsessive-compulsive disorder using whole-brain anatomy. *Neuroimage*. 2007;35(3):1028-1037.
21. Koutsouleris N, Meisenzahl EM, Davatzikos C, Bottlender R, Frodl T, Scheuerecker J, Schmitt G, Zetzsche T, Decker P, Reiser M, Möller HJ, Gaser C. Use of neuroanatomical pattern classification to identify subjects in at-risk mental states of psychosis and predict disease transition. *Arch Gen Psychiatry*. 2009;66(7): 700-712.
22. Fu CH, Mourao-Miranda J, Costafreda SG, Khanna A, Marquand AF, Williams SC, Brammer MJ. Pattern classification of sad facial processing: toward the development of neurobiological markers in depression. *Biol Psychiatry*. 2008; 63(7):656-662.
23. Hanson RK, Morton-Bourgon KE. The characteristics of persistent sexual offenders: a meta-analysis of recidivism studies. *J Consult Clin Psychol*. 2005; 73(6):1154-1163.
24. Freund K, Watson R. Assessment of the Sensitivity and Specificity of a Phallometric Test: an update of phallometric diagnosis of pedophilia. *Psychol Assess*. 1991;3(2):254-260. doi:10.1037//1040-3590.3.2.254.
25. Howes R. A survey of plethysmographic assessment in North America. *Sex Abuse*. 1995;7(1):9-24. doi:10.1007/BF02254871.
26. Kuban M, Barbaree HE, Blanchard R. A comparison of volume and circumference phallometry: response magnitude and method agreement. *Arch Sex Behav*. 1999;28(4):345-359.
27. Kolla NJ, Klassen PE, Kuban ME, Blak T, Blanchard R. Double-blind, placebo-controlled trial of sildenafil in phallometric testing. *J Am Acad Psychiatry Law*. 2010;38(4):502-511.
28. Dasarathy BV. *Nearest Neighbor Norms: NN Pattern Classification Techniques*. Vol 20. Los Alamitos, CA: IEEE Computer Society Press; 1991.
29. Beier KM, Neutze J, Mundt IA, Ahlers CJ, Goecker D, Konrad A, Schaefer GA. Encouraging self-identified pedophiles and hebephiles to seek professional help: first results of the Prevention Project Dunkelfeld (PPD). *Child Abuse Negl*. 2009; 33(8):545-549.
30. Neutze J, Seto MC, Schaefer GA, Mundt IA, Beier KM. Predictors of child pornography offenses and child sexual abuse in a community sample of pedophiles and hebephiles. *Sex Abuse*. 2011;23(2):212-242.
31. Kirk KM, Bailey JM, Dunne MP, Martin NG. Measurement models for sexual orientation in a community twin sample. *Behav Genet*. 2000;30(4):345-356.
32. von Aster M, Neubauer A, Horn R. *Wechsler Intelligenztest für Erwachsene WIE. Deutschsprachige Bearbeitung und Adaptation des WAIS-III von David Wechsler*. Frankfurt, Germany: Pearson Assessment; 2006.
33. Lang PJ, Bradley MM, Cuthbert BN. *International Affective Picture System (IAPS): Technical Manual and Affective Ratings*. Gainesville: The Center for Research in Psychophysiology, University of Florida; 1997.
34. Ponseti J, Bosinski HA, Wolff S, Peller M, Jansen O, Mehdorn HM, Büchel C, Siebner HR. A functional endophenotype for sexual orientation in humans. *Neuroimage*. 2006;33(3):825-833.
35. Bradley MM, Greenwald A, Hamm A. Affective picture processing. In: Birbaumer N, Öhman A, eds. *The Structure of Emotion*. Göttingen, Germany: Hogrefe; 1993: 48-65.
36. Friston KJ, Holmes A, Worsley KJ, Poline J, Frith C, Frackowiak RSJ. Statistical parametric maps in functional imaging: a general linear approach. *Hum Brain Mapp*. 1995;2(4):189-210. doi:10.1002/hbm.460020402.
37. Stoleru S, Mouras H. Brain functional imaging studies of sexual desire and arousal in human males. In: Janssen E, ed. *The Psychophysiology of Sex*. Bloomington: Indiana University Press; 2007:3-34.
38. Freund K, Blanchard R. Phallometric diagnosis of pedophilia. *J Consult Clin Psychol*. 1989;57(1):100-105.
39. Barbaree HE, Baxter DJ, Marshall WL. Brief research report: the reliability of the rape index in a sample of rapists and nonrapists. *Violence Vict*. 1989;4(4): 299-306.





©2012 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/ on 05/24/2013