Supplementary Information

Neural substrates of sexual arousal are not sex-dependent

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Report of data mining process for meta-analysis and systematic review according to PRISMA guidelines

Search Strategy: The online portal of the National Library of Medicine (http://www.ncbi.nlm.nih.gov/pubmed/) including PubMed, PubMed Central and MEDLINE was used as the platform for literature research. A systematic screening of the original research articles published until January 2019 was performed based on the keywords: *heterosexual (OR) homosexual (OR) bisexual (OR) transsexual (OR) MRI (OR) visual (OR) fMRI (OR) sexual (OR) stimulus (OR) stimuli*. For the systematic review related to structural sex differences, the research article screening was based on the following keywords similar to previous meta-analyses (1): *(Insula OR anterior cingulate cortex/gyrus OR ACC) AND MRI AND grey AND matter AND (sex OR gender OR (male AND female) OR (males AND females)).* In addition, the reference sections of identified papers as well as review and meta-analysis articles were then screened for further relevant citations.

Study Selection: Two reviewers (EM and HRN) independently screened titles and abstracts of articles and reviewed the full text of any title or abstract deemed potentially eligible by either reviewer. Reviewers resolved disagreements by discussion. Among these studies, only peer-reviewed original research articles in English language were chosen for data mining. For the meta-analysis of functional response patterns to visual sexual stimuli studies were included if they provided analysis of brain responses (i.e. exact coordinates or explicit identification of the reactive brain regions) to visual stimuli (i.e. pictures and videos) either within a group with self-identified sexual orientation of the same or different sex, or between such individuals and subjects with a different sexual orientation. For the systematic review of sex differences in grey matter volume in insula and anterior cingulate, data was extracted only from studies that provided coordinates for the regions of interest as well as the results of statistical tests in terms of t- or Z-levels. If raw or corrected (with respect to total brain volume) mean ± SD volume were provided, then the study was also selected for meta-analysis. All participants were un-medicated healthy volunteers with no Axis I disorders. Axis I disorders, as defined in the Diagnostic and Statistical Manual (DSM-IV), include all psychological diagnostic categories, barring mental retardation and personality problems. Additional exclusion criteria for all groups were: lifetime diagnosis of schizophrenia or psychotic episodes; diagnosis of manic disorder, obsessive compulsive disorder, alcohol use disorders, substance dependent disorder or post-traumatic stress disorder; treatment for mental disorders other than pathological gambling in the past 12 months; use of psychotropic medication; history or current treatment for neurological disorders, major internal disorders, brain trauma, or exposure to neurotoxic factors. Resting-state fMRI and other scanning modalities were excluded. Abstracts and unpublished studies were not included. Authors were contacted if critical information was missing or only partially provided in their articles.

Quality Assessment: Pairs of reviewers independently assessed the risk of bias and the reporting quality of individual studies by means of the 83-item checklist adapted from the guidelines for reporting an fMRI study (2). A minimum score of 15 out of 83 was assumed as an inclusion criterion.

Data Extraction: The following variables and parameters were extracted from relevant publications into a standardized template and used for further analysis:

1. **Publication Variables:** PubMed Identification Number (PMID), first author, year of publication, country;
2. **Demographic Variables:** Number of study participants, mean and standard deviation of the age, percentage of male individuals, sexual orientation, Kinsey scale, handedness, medications history, and in case of comparative studies number of participants in opposite group, and matching criteria;
3. **Experimental Variables:** Scanning modalities (i.e. machine power, number of channels per RF head coil, data type e.g. T2*-weighted/ T1-weighted/ T2-weighted, spatiotemporal resolution, and in case of structural data: voxel-based morphometry etc.), stimulus type (picture or video), contrast stimulus type (e.g. couples engaged in non-sexual activity, sport activity, landscapes), cue presentation paradigm (block-design or event-related);

Analysis Parameters: Analysis software and version, statistical analysis (whole brain or ROI-based), coordinates of activated brain regions (in Montreal Neurological Institute (MNI) or Talairach coordinates), if provided mean ± SD volume of the brain regions and the level of activation/deactivation.

Figure S1. Detailed flow diagram of study selection according to PRISMA guidelines.

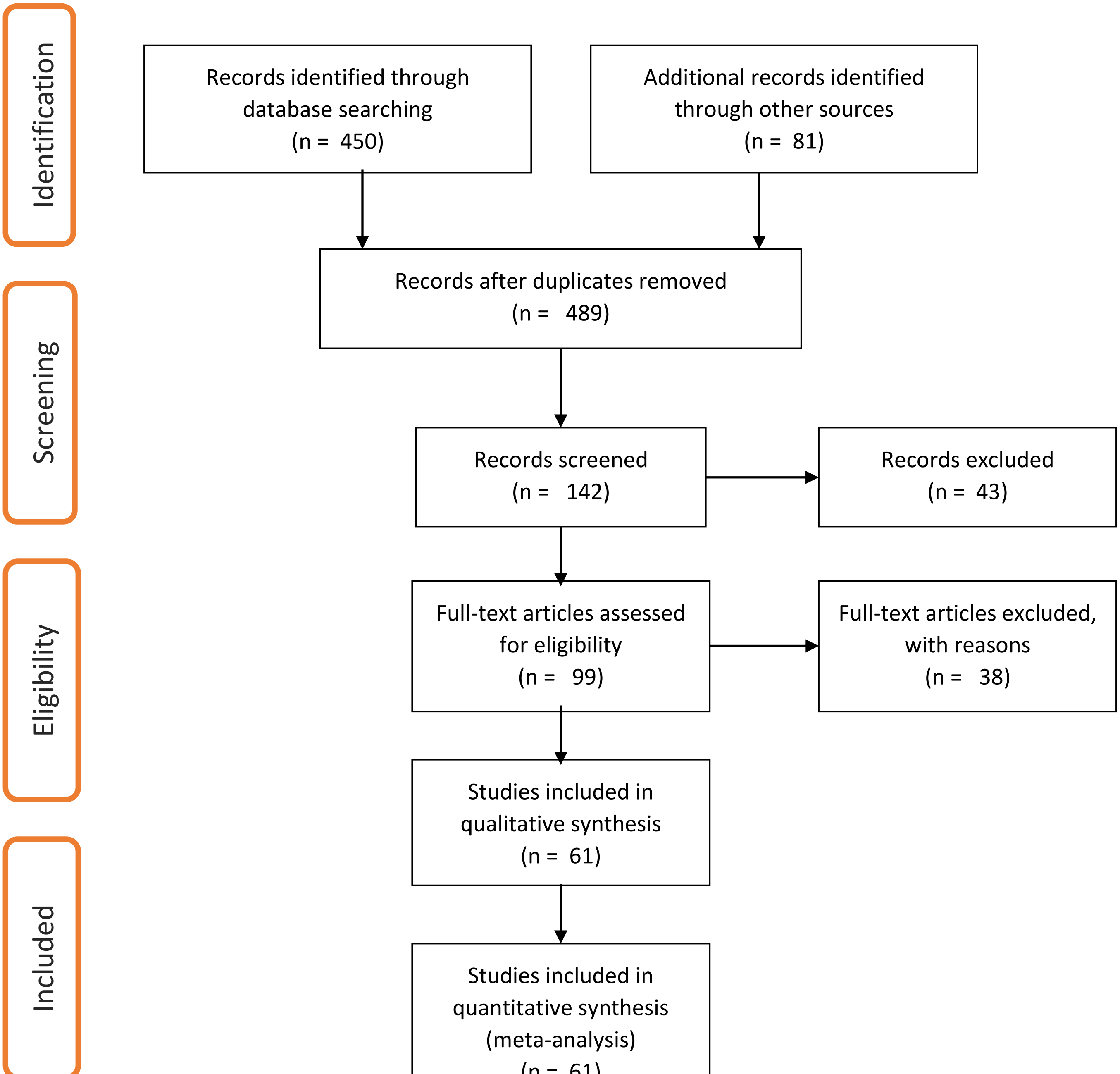

Figure S2. Axial presentation of the differences in neural response patterns between heterosexuals and homosexuals. Visual sexual stimuli induce a larger lateralized neuronal activation towards the left hemisphere in heterosexual in comparison with homosexual individuals. The significant clusters are colored according to their ALE score ranging from 0.013 to 0.042.

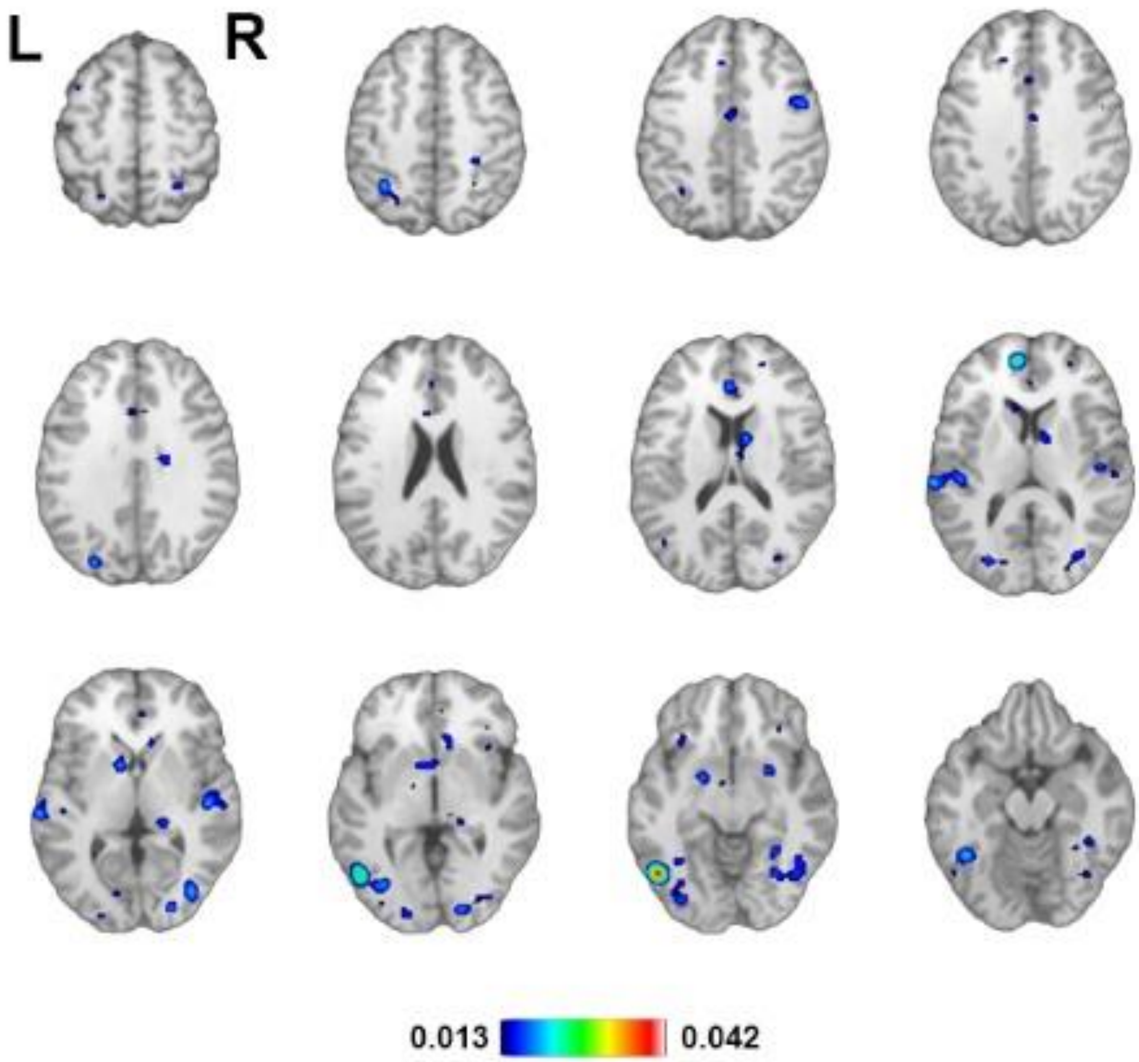

Figure S3. The tree-based classification model of the data. It classifies cases into groups or predicts values of a dependent (target) variable based on values of independent (predictor) variables. Two step clustering algorithm suggests stimulus/cue type (picture or video) as the predictor of maximal importance. Thus, the decision tree is based on cue type as main predictor.

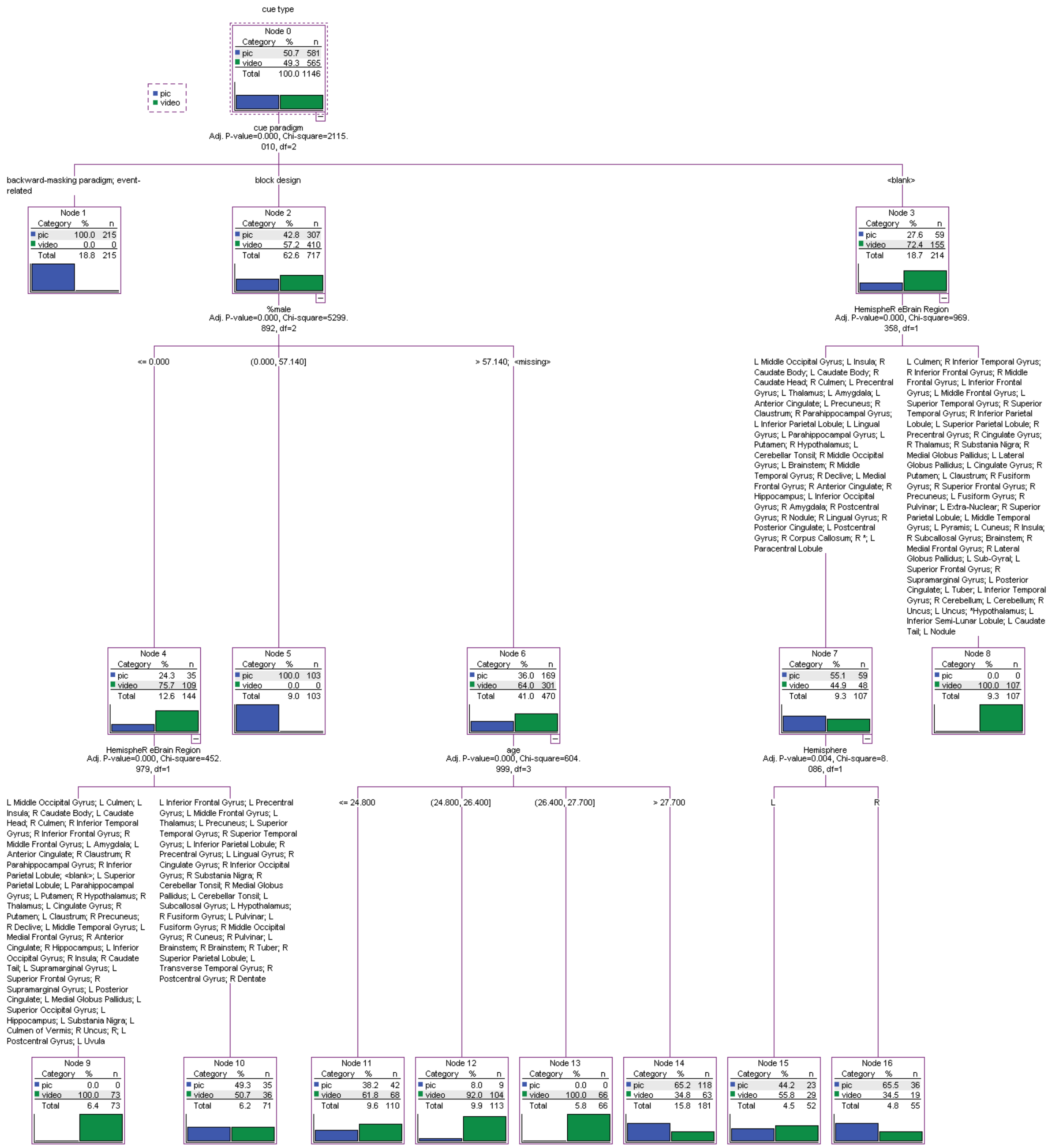

Table S1. Overall estimates of the included studies. In relation to transsexual individuals, FTM and MTF refer to female (F) to male (M) and male to female transformation, respectively. Duplicates are excluded from the number of study participants (n).

Groups	Sex	# Studies	n	Mean Age ± SD (y)
Bisexual	F	Safron et al. 2018 (3)	21	30.3 ± 6.4
	M	Safron et al. 2017 (4)	19	37.5 ± 6.4
Heterosexual	F	Safron et al. 2018 (3); Strahler et al. 2018 (5); Borg et al. 2014a,b (6, 7); Wehrum-Osinsky et al. 2014 (8); Kim et al. 2013 (9); Sylva et al. 2013 (10); Wehrum et al. 2013 (11); Woodard et al. 2013 (12); Demos et al. 2012 (13); Gillath et al. 2012 (14); Bianchi-Demicheli et al. 2011 (15); Arnow et al. 2009 (16); Klucken et al. 2009 (17); Savic and Lindstrom 2008 (18); Walter et al. 2008 (19); Sabatinelli et al. 2007 (20); Ponseti et al. 2006 (21); Stark et al. 2005 (22); Hamann et al. 2004 (23); Sabatinelli et al. 2004 (24); Karama 2002 (25)	560	26.0 ± 4.0
	M	Unterhorst et al. 2018 (26); Strahler et al. 2018 (5); Jordan et al. 2018 (27); Safron et al. 2017 (4); Wernicke et al. 2017 (28); Brand et al. 2016 (29); Seok et al. 2016 (30); Graf et al. 2014 (31); Oei et al. 2014 (32); Kühn and Gallinat, 2014 (33); Mascaro et al. 2014 (34); Wehrum-Osinsky et al. 2014 (8); Costumero et al. 2013 (35); Kim et al. 2013 (9); Wehrum et al. 2013 (11); Oei et al. 2012 (36); Kagerer et al. 2011 (37); Zhang et al. 2011 (38); Hu et al. 2011 (39); Seo et al. 2010 (40); Sundaram et al. 2010 (41); Metzger et al. 2010 (42); Gizewski et al. 2009 (43); Klucken et al. 2009 (17); Ponseti et al. 2009 (44); Seo et al. 2009 (45); Brunetti et al. 2008 (46); Bühler et al. 2008 (47); Hu et al. 2008 (48); Savic and Lindstrom 2008 (18); Paul et al. 2008 (49); Schiffer et al. 2008 (50); Walter et al. 2008 (19); Sabatinelli et al. 2007 (20); Safron et al. 2007 (51); Gizewski et al. 2006 (52); Kim et al. 2006 (53); Moulier et al. 2006 (54); Ponseti et al. 2006 (21); Ferretti et al. 2005 (55); Stark et al. 2005 (22); Hamann et al. 2004 (23); Sabatinelli et al. 2004 (24); Mouras et al. 2003 (56); Arnow et al. 2002 (57); Karama et al. 2002 (25); Beauregard et al. 2001 (58); Park et al. 2001 (59)	1054	28.5 ± 6.6
Homosexual	F	Safron et al. 2018 (3); Savic et al 2008 (18); Ponseti et al. 2006 (21)	55	28.0 ± 1.9
	M	Safron et al. 2017 (4); Hu et al. 2011 (39); Zhang et al. 2011 (38); Hu et al. 2008 (48); Savic and Lindstrom 2008 (18); Paul et al. 2008 (49); Ponseti et al. 2006 (21)	109	30.9 ± 3.2
Transsexual	FTM	Kim et al. 2016 (60)	11	41.5 ± 5.5
	MTF	Oh et al. 2012 (61); Gizewski et al. 2009 (43)	21	37.9 ± 2.6
Overall			1850	29.4 ± 6.0

Table S2. Brain regions associated with sexual arousal. Healthy individuals exposed to erotic pictures and videos show accentuated neural activation patterns in contrast to neutral visual stimulation. In particular, ALE meta-analysis (corrected for false discovery rate pID <0.05) suggests activations of insula, middle and inferior occipital and fusiform gyrus, amygdala, caudate, claustrum, globus pallidus, pulvinar, and substantia nigra. Coordinates are presented in Talairach space. For clusters with sub-peaks, primary peak is bolded and sub-peaks are italicized. Clusters with relative importance less <5% are shaded. While these clusters have a volume larger than 200 mm^3, their cumulative ALE scores are outside the 95% quantile.

Anatomical Region	Weighted Center (x,y,z)			Brodmann Area	Volume (mm^3)	ALE score	Relative Importance (%)
L Lateral Globus Pallidus	-1.3	-1.2	-2.3		23944	0.071458	29.1
L Caudate Head						0.071275	
R Medial Globus Pallidus						0.063293	
R Caudate Head						0.060864	
L Amygdala						0.055921	
L Thalamus						0.047616	
R Caudate Body						0.042929	
L Pulvinar						0.030309	
L Pulvinar						0.024629	
L Substantia Nigra						0.024496	
L Middle Occipital Gyrus	-42.8	-67.4	-6.6	37	7656	0.080538	10.1
L Inferior Occipital Gyrus				19		0.036159	
L Culmen						0.028757	
L Middle Occipital Gyrus				18		0.026369	
R Fusiform Gyrus	42.8	-62.3	-7.5	37	6144	0.056005	7.1
R Fusiform Gyrus				37		0.032246	
R Declive						0.031727	
R Lingual Gyrus	25.6	-83.6	9.8	17	2664	0.041032	5.7
R Middle Occipital Gyrus				19		0.032548	
R Lingual Gyrus				17		0.022856	
R Precuneus	27.1	-55.6	48.2	7	2440	0.053713	7.3
R Precuneus				7		0.023799	
R Precuneus				7		0.023032	
R Precuneus				7		0.022488	
L Anterior Cingulate	-0.9	33.5	12.6	24	2248	0.047023	2.8
L Claustrum	-27.4	19.7	-9.7		2104	0.035937	6.5
L Inferior Frontal Gyrus				47		0.028184	
L Inferior Frontal Gyrus				47		0.025215	
L Insula				13		0.021274	
R Claustrum	26	13.8	-5.3		1832	0.039797	2.3
L Superior Parietal Lobule	-30.3	-54.2	45.3	7	1440	0.036688	3.4
L Precuneus				7		0.020758	
R Pulvinar	16.6	-30.4	3.1		1256	0.034267	3.3
R Thalamus						0.021186	

L Inferior Frontal Gyrus	-45.7	1.1	30.4	6	1056	0.038055	2.2
R Inferior Occipital Gyrus	37.3	-78.8	-0.1	19	696	0.025747	1.5
L Insula	-39.6	-3	4.3	13	672	0.031169	1.8
R Inferior Frontal Gyrus	44	3.3	28.2	9	640	0.030416	1.8
R Insula	39.5	-4.4	3.9	13	472	0.023476	2.7
R Insula				13		0.02307	
R Culmen	30.3	-50.4	-11.6		432	0.030895	1.8
L Cuneus	-26.2	-81.6	22.8	19	408	0.027583	1.6
L Cingulate Gyrus	-2.9	18	27.1	24	392	0.02577	1.5
L Inferior Parietal Lobule	-44.7	-33.2	40.8	40	352	0.026356	1.6
R Middle Frontal Gyrus	30.2	-9.5	48.3	6	304	0.027036	1.6
R Substantia Nigra	9.8	-22	-9.1		296	0.024097	2.7
R Substantia Nigra						0.021254	
R Postcentral Gyrus	55.7	-24.8	35.5	2	200	0.025426	1.5

Table S3. Regions in which sexual cues induced significantly different activation responses than contrasted neutral cues in male participants. *$p < .05$, corrected, voxelwise, for the false discovery rate. ALE = activation likelihood estimate. Coordinates are in Talairach space. For clusters with sub-peaks, primary peak is bolded and sub-peaks are italicized.

Anatomical Region	Weighted Center (x,y,z)			Brodmann Area	Volume (mm^3)	ALE score	Relative Importance (%)
L Amygdala	-5.1	-0.7	-1		11224	0.047921382	38.5
L Thalamus						0.042276394	
L Caudate Head						0.039614864	
R Caudate Head						0.038639594	
L Amygdala						0.036768116	
L Hypothalamus						0.03509055	
R Caudate Body						0.027035099	
L Amygdala						0.020057363	
R Inferior Temporal Gyrus	43.8	-59.2	-8.4	19	2824	0.032368105	8.4
R Fusiform Gyrus				37		0.03047994	
L Middle Occipital Gyrus	-47.3	-65.5	-4.3	37	2816	0.048047878	11.1
R Amygdala	22.7	-1.3	-12.2		1840	0.035074487	
R Lingual Gyrus	24	-87.5	2.4	17	952	0.03782408	5.1
L Culmen	-41.7	-50.7	-18.7		880	0.027779741	3.7
L Inferior Parietal Lobule	-30.3	-52	43.4	40	808	0.027705273	3.7
R Superior Parietal Lobule	27.3	-52.4	46.9	7	712	0.030980863	4.1
L Insula	-40.2	-3.6	5.4	13	648	0.029987777	4.0
L Inferior Occipital Gyrus	-33.8	-73.6	-4.8	19	560	0.025050608	3.4
R Insula	31.6	13.4	-6.1	13	424	0.020162899	2.7
L Inferior Parietal Lobule	-45.5	-33	39.3	40	368	0.024424419	3.3
L Cuneus	-25.3	-90.6	2.2	18	280	0.022239197	3.0
R Postcentral Gyrus	55.8	-25.1	35.9	2	240	0.02440132	3.3
R Anterior Cingulate	1.6	32.2	17.4	24	232	0.021947337	2.9
L Inferior Frontal Gyrus	-47.3	4	29	9	200	0.021348292	2.9

Table S4. Regions in which sexual cues induced significantly different activation responses than contrasted neutral cues in female participants. **p* < .05, corrected, voxelwise, for the false discovery rate. ALE = activation likelihood estimate. Coordinates are in Talairach space. For clusters with sub-peaks, primary peak is bolded and sub-peaks are italicized.

Anatomical Region	Weighted Center (x,y,z)			Brodmann Area	Volume (mm^3)	Extrema Value	Relative Importance (%)
L Fusiform Gyrus	-46.5	-66.1	-9.6	19	408	0.025985	27.2
R Declive	30.6	-65.5	-11.4		384	0.024251	25.3
L Amygdala	-20.9	0.1	-18.6		360	0.023228	24.3
L Precentral Gyrus	-45	-0.9	29.9	6	248	0.022212	23.2

Table S5. Regions in which sexual cues induced significantly different activation responses than contrasted neutral cues in male participants. Relaxed $p < .01$, uncorrected, voxelwise. ALE = activation likelihood estimate. Coordinates are in Talairach space. For clusters with sub-peaks, primary peak is bolded and sub-peaks are italicized.

Anatomical Region	Weighted Center (x,y,z)			Brodmann Area	Volume (mm^3)	Extrema Value	Relative Importance (%)
L Amygdala	1.2	1.6	-1.3		30912	0.047921	34.4
L Thalamus						0.042276	
L Caudate Head						0.039615	
R Caudate Head						0.03864	
L Amygdala						0.036768	
L Hypothalamus						0.035091	
R Amygdala						0.035074	
R Caudate Body						0.027035	
R Anterior Cingulate				24		0.021947	
L Substania Nigra						0.02178	
R Insula				13		0.020163	
L Amygdala						0.020057	
R Caudate Head						0.018996	
L Anterior Cingulate				24		0.017096	
R Anterior Cingulate				24		0.016765	
R Anterior Cingulate				24		0.015814	
L Pulvinar						0.014819	
L Middle Occipital Gyrus	-43.4	-63.9	-7.6	37	9336	0.048048	7.4
L Culmen						0.02778	
L Inferior Occipital Gyrus				19		0.025051	
R Inferior Temporal Gyrus	42.7	-60.5	-7.3	19	7168	0.032368	7.5
R Fusiform Gyrus				37		0.03048	
R Middle Occipital Gyrus				19		0.021093	
R Culmen						0.017845	
R Lingual Gyrus	25	-85.8	5.5	17	2720	0.037824	5.1
R Middle Occipital Gyrus				19		0.017955	
R Cuneus				19		0.014014	
L Inferior Parietal Lobule	-28.4	-53.4	43.9	40	2688	0.027705	4.4
L Precuneus				7		0.019235	
L Superior Parietal Lobule				7		0.013809	
L Insula	-41.2	-5.1	3.9	13	1968	0.029988	3.4
L Superior Temporal Gyrus				22		0.016637	
R Parahippocampal Gyrus	19.2	-22.9	-8.5	35	1936	0.019631	4.2
R Parahippocampal Gyrus				35		0.019019	
R Thalamus						0.018146	
R Superior Parietal Lobule	27.6	-52.4	45.9	7	1760	0.030981	2.3
R Middle Frontal Gyrus	43.1	3.1	34.2	6	1688	0.017586	3.5

R Inferior Frontal Gyrus				9		0.015845	
R Inferior Frontal Gyrus				9		0.014833	
L Insula	-34.6	16.8	-7	13	1512	0.021049	4.0
L Inferior Frontal Gyrus				47		0.018876	
L Extra-Nuclear				13		0.015262	
L Cuneus	-26.5	-89.7	1.7	18	1392	0.022239	1.6
L Inferior Parietal Lobule	-46.8	-32.6	38.8	40	1312	0.024424	1.8
L Inferior Frontal Gyrus	-45	2.8	30.5	9	1256	0.021348	2.7
L Precentral Gyrus				6		0.015735	
R Insula	39	-2.4	2.5	13	984	0.02084	2.6
R Claustrum						0.014883	
R Postcentral Gyrus	55.6	-25.4	35.7	2	752	0.024401	1.8
R Cingulate Gyrus	1.3	-8.5	38.5	24	696	0.01916	1.4
L Cuneus	-25.6	-81.4	25	19	536	0.022288	1.6
L Anterior Cingulate	-14.1	36	3.7		472	0.016645	1.2
R Nodule	0.8	-47	-32.6		464	0.019786	1.4
R Precuneus	20.9	-69.2	42.7	7	464	0.017063	1.2
L Inferior Frontal Gyrus	-24.8	30.2	-11	47	328	0.015729	1.2
R Pulvinar	16.2	-27.3	15.9		296	0.019004	1.4
L Medial Frontal Gyrus	-7.4	38.1	-14.1	11	272	0.016948	1.2
L Middle Temporal Gyrus	-43.5	-67.6	17.3	39	272	0.017951	1.3
R Caudate Body	15	23.6	10.1		240	0.016361	1.2

Table S6. Regions in which sexual cues induced significantly different activation responses than contrasted neutral cues in female participants. Relaxed $p < .01$, uncorrected, voxelwise. ALE = activation likelihood estimate. Coordinates are in Talairach space. For clusters with sub-peaks, primary peak is bolded and sub-peaks are italicized.

Anatomical Region	Weighted Center (x,y,z)			Brodmann Area	Volume (mm^3)	Extrema Value	Relative Importance (%)
L Amygdala	-17.8	0.4	-12.2		6096	0.023228	11.5
L Caudate Head						0.014976	
L Putamen						0.014933	
L Medial Globus Pallidus						0.014092	
Hypothalamus						0.012619	
L Inferior Frontal Gyrus				47		0.010018	
L Putamen						0.009215	
R Declive	32.8	-61.7	-10.3		4896	0.024251	8.6
R Declive						0.018973	
R Fusiform Gyrus				37		0.017041	
R Inferior Temporal Gyrus				37		0.013412	
L Anterior Cingulate	-4.7	41.1	12.4	24	3136	0.018261	6.1
L Medial Frontal Gyrus				10		0.017215	
L Anterior Cingulate				24		0.01706	
L Fusiform Gyrus	-45.3	-64.4	-9.9	19	2408	0.025985	5.3
L Declive						0.010554	
L Declive						0.00904	
R Middle Occipital Gyrus	26.5	-79.2	17.9	19	1912	0.01817	4.1
R Middle Occipital Gyrus				19		0.016638	
R Medial Globus Pallidus	14.2	-4.6	-8.1		1432	0.016132	3.4
R Parahippocampal Gyrus				34		0.01277	
L Precentral Gyrus	-45.4	-0.9	30.6	6	1360	0.022212	2.6
R Inferior Occipital Gyrus	38	-79.9	-2.6	19	1056	0.01693	2.0
R Superior Parietal Lobule	30.5	-54.3	54.1	7	1040	0.018536	2.2
L Inferior Occipital Gyrus	-34.7	-82.1	-8.1	18	984	0.015102	3.2
L Middle Occipital Gyrus				18		0.01245	
R Inferior Frontal Gyrus	43.3	2.3	27.6	9	944	0.018094	2.1
R Insula	47	-14.3	5.8	13	928	0.013525	3.0
R Superior Temporal Gyrus				22		0.012021	
R Inferior Frontal Gyrus	33	6.9	-14	47	872	0.012579	2.8
R Superior Temporal Gyrus				38		0.011043	
L Precuneus	-30	-63	37.2	7	864	0.010695	4.6
L Superior Parietal Lobule				7		0.009996	
L Angular Gyrus				39		0.009965	
L Middle Temporal Gyrus				39		0.008836	
L Parahippocampal Gyrus	-39.3	-30.1	-6.4	36	728	0.015787	1.8
R Middle Frontal Gyrus	29.7	-9.3	46.9	6	704	0.014209	1.7

R Pulvinar	14.7	-27.2	5.9		688	0.015783	2.9
R Inferior Parietal Lobule				40		0.009163	
L Cingulate Gyrus	-2.1	17.2	27.4	32	624	0.011723	2.4
R Anterior Cingulate				24		0.008873	
L Superior Temporal Gyrus	-61.4	-27.8	6.8	42	560	0.015704	2.9
L Superior Temporal Gyrus				41		0.008975	
L Substania Nigra	-11.5	-23.2	-11.9		488	0.011965	2.5
L Parahippocampal Gyrus				35		0.009697	
L Lingual Gyrus	-9.5	-78.4	-1.4	18	480	0.016565	1.9
L Inferior Parietal Lobule	-58	-29	31	40	448	0.015293	1.8
R Precuneus	21.1	-72.3	34.3	19	432	0.015318	1.8
R Thalamus	10.4	-15.9	14.9		408	0.011492	2.4
R Thalamus						0.008713	
R Supramarginal Gyrus	51.5	-53.4	32.9	40	368	0.012415	1.4
R Uncus	19.9	0	-21.9	28	352	0.012511	1.5
R Substania Nigra	8	-22	-10.4		328	0.012413	1.4
L Thalamus	-3.4	-13.1	7.4		304	0.00949	3.2
L Thalamus						0.008968	
L Thalamus						0.008905	
L Middle Frontal Gyrus	-26.4	-10.4	46	6	304	0.011852	1.4
L Superior Temporal Gyrus	-49.7	-11.8	3.9	22	296	0.011732	1.4
L Transverse Temporal Gyrus	-41.5	-28.5	9.5	41	296	0.011241	1.3
R Inferior Occipital Gyrus	14	-92	-6.4	17	288	0.011489	1.3
L Cingulate Gyrus	-2.6	-22.6	34	24	256	0.010929	1.3
L Middle Occipital Gyrus	-26.7	-80.5	11.9	19	232	0.01033	1.2
R Putamen	24.9	3.8	1.2		200	0.010045	1.2

Table S7. Regions in which erotic visual stimulation (pictures and videos) induced significantly different responses than contrasted cues among bisexual study participants. Coordinates are in Talairach space. For clusters with sub-peaks, primary peak is bolded and sub-peaks are italicized.

Anatomical Region	Weighted Center (x,y,z)			Brodmann Area	Volume (mm^3)	Extrema Value
R Sub-Gyral Parietal Lobe	30.1	-41.1	44.6		3544	0.012177
R Inferior Parietal Lobule						0.009981
R Precuneus				7		0.008566
R Precuneus				7		0.008564
R Supramarginal Gyrus	48.1	-58.5	32.8	40	2264	0.009437
R Middle Temporal Gyrus				39		0.00918
R Inferior Parietal Lobule				39		0.008735
R Superior Temporal Gyrus	53	-19	4.7	41	1864	0.008335
R Superior Temporal Gyrus				22		0.008193
R Superior Temporal Gyrus				22		0.008082
R Superior Temporal Gyrus				22		0.007959
R Middle Occipital Gyrus	27.4	-79.2	15.9	19	1680	0.01375
R Middle Occipital Gyrus				19		0.012356
L Superior Temporal Gyrus	-48.3	-13.7	4.1	22	1184	0.008911
L Superior Temporal Gyrus				22		0.00876
R Declive	29.3	-52.1	-11.8		464	0.008444
L Precentral Gyrus	-24	-19.1	57.9	4	464	0.008312
R Declive	32.3	-66.3	-10.7		448	0.00841
R Precentral Gyrus	26	-16.6	56.5	6	448	0.008442
L Middle Occipital Gyrus	-37.1	-80.2	-10.4	18	440	0.008321
R Inferior Occipital Gyrus	37.6	-78.3	-3.3	19	440	0.008357
R Middle Occipital Gyrus	29.1	-87.4	3.8	18	440	0.008229
L Superior Temporal Gyrus	-53.8	-25.2	8.3	41	440	0.008216
R Cingulate Gyrus	12.4	-52.9	25.6	31	432	0.008245
L Inferior Parietal Lobule	-35	-62.2	37.3	39	432	0.008128
L Superior Parietal Lobule	-32.5	-52.6	51.9	7	432	0.008424

L Inferior Occipital Gyrus	-23.3	-89	-8	18	424	0.008201
L Lingual Gyrus	-9.5	-78.3	-1.4	18	424	0.008365
L Declive	-23.3	-79.7	-15.3		416	0.008238
L Middle Occipital Gyrus	-29	-84	0.4	18	416	0.008231
R Middle Occipital Gyrus	23.9	-81.1	-1.1	18	416	0.008175
L Cingulate Gyrus	-1.4	-25.3	33.3	31	416	0.008202
R Fusiform Gyrus	43.3	-60.8	-9.8	37	408	0.008225
L Superior Temporal Gyrus	-42.8	-22.8	8.7	13	408	0.007894
L Angular Gyrus	-48.9	-64.8	34.1	39	408	0.008153
L Inferior Parietal Lobule	-35.1	-40.9	50.2	40	408	0.008024
R Lingual Gyrus	12.8	-94.7	-8.1	17	400	0.008267

Table S8. Regions in which erotic visual stimulation (pictures and videos) induced significantly different responses than contrasted cues among transsexual study participants. Coordinates are in Talairach space. For clusters with sub-peaks, primary peak is bolded and sub-peaks are italicized.

Anatomical Region	Weighted Center (x,y,z)			Brodmann Area	Volume (mm^3)	Extrema Value
L Putamen	-26.4	-8.6	-4.4		3336	0.006951
L Amygdala						0.006914
L Lateral Globus Pallidus						0.006377
R Hypothalamus	-1.5	-0.3	-0.1		2968	0.006995
L Caudate Head						0.006279
L Caudate Head						0.006161
R Caudate Body	13.6	2.9	15.9		1544	0.006277
R Caudate Body						0.006269
R Claustrum	29.1	8.1	1.1		1032	0.006561
R Cingulate Gyrus	2.7	20.5	28.7	32	1032	0.006648
R Amygdala	22.5	-2	-11		1008	0.006698
R Hippocampus	23.5	-39.5	-1.5		1000	0.006792
L Thalamus Medial Dorsal Nucleus	-5.6	-13.2	10.6		992	0.00615
L Cingulate Gyrus	-11.2	13.6	36.6	32	992	0.006097
R Cerebellar Tonsil	9	-47.1	-34.5		984	0.005979
L Caudate Body	-18.8	-15.7	22.8		984	0.006088
L Substania Nigra	-13.5	-17.6	-11.8		976	0.006268
R Parahippocampal Gyrus	9.7	-38	9	30	960	0.006154
R Claustrum	34	-10.9	5.9		928	0.006216

Table S9. Regions in which erotic visual stimulation (pictures and videos) induced significantly different responses than contrasted cues among homosexual study participants. Coordinates are in Talairach space. For clusters with sub-peaks, primary peak is bolded and sub-peaks are italicized. Clusters with relative importance less <5% are shaded.

Anatomical Region	Weighted Center (x,y,z)			Brodmann Area	Volume (mm^3)	ALE Extrema Value	Relative Importance
L Middle Occipital Gyrus	-42.1	-67	-8.8	37	3080	0.018343	12.82
L Inferior Occipital Gyrus				19		0.009292	
L Fusiform Gyrus				37		0.008545	
L Inferior Occipital Gyrus				18		0.008522	
L Declive						0.008402	
L Fusiform Gyrus				37		0.006892	
R Superior Temporal Gyrus	49.2	-19.7	6.7	13	1696	0.013117	8.41
R Insula				13		0.009015	
R Superior Temporal Gyrus				41		0.00878	
R Superior Temporal Gyrus						0.008443	
L Superior Temporal Gyrus	-49.9	-28	6.1	41	1560	0.013436	6.71
L Middle Temporal Gyrus				22		0.009074	
L Superior Temporal Gyrus				42		0.008893	
R Postcentral Gyrus	29	-38.8	46.6	3	1360	0.015611	6.66
R Inferior Parietal Lobule				40		0.008847	
R Postcentral Gyrus				5		0.006681	
R Fusiform Gyrus	44	-60.9	-7.2	37	952	0.009207	5.26
R Fusiform Gyrus				19		0.008555	
R Middle Occipital Gyrus				37		0.006857	
R Nodule	-2.2	-46.6	-31		944	0.011283	4.23
L Cerebellar Tonsil						0.008523	
R Culmen	29.7	-49.3	-11.6		864	0.013309	2.84
L Cuneus	-25.4	-81.6	24.9	19	760	0.01277	2.73
L Middle Occipital Gyrus	-32.7	-77.5	7.4	19	664	0.009403	3.77
L Middle Occipital Gyrus				18		0.008228	
L Superior Temporal Gyrus	-56.5	-15	2.3	22	592	0.008597	3.58
L Superior Temporal Gyrus				22		0.008148	
R Precentral Gyrus	27.5	-10.2	52.9	6	424	0.0085	3.61
R Sub-Gyral Frontal Lobe				6		0.008389	
R Inferior Occipital Gyrus	37.6	-81.2	-1	19	336	0.008821	1.89
L Middle Occipital Gyrus	-23.5	-93.3	7.4	18	264	0.008428	1.80

L Cingulate Gyrus	-23.8	-37.3	39.9	31	256	0.008838	1.89
L Precuneus	-21.3	-60.4	48.5	7	256	0.008411	1.80
R Anterior Cingulate	4.7	40.4	-3.6	32	248	0.008564	1.83
L Superior Parietal Lobule	-29.6	-52	49.3	7	248	0.008652	1.85
R Inferior Parietal Lobule	56.8	-45.3	35.1	40	232	0.008187	1.75
R Culmen	-1	-54	-18		224	0.008433	1.80
L Lingual Gyrus	-12.5	-78.8	3.9	18	224	0.008374	1.79
R Cuneus	29.4	-76.6	10	30	224	0.008188	1.75
R Anterior Cingulate	18.3	27.3	14.2	32	224	0.008362	1.79
L Caudate Body	-20.6	-13.4	26		224	0.008287	1.77
L Lingual Gyrus	-18	-92.2	-2.7	17	216	0.008277	1.77
R Lingual Gyrus	29.5	-67.9	5.7	19	216	0.008268	1.77
L Caudate Body	-9.5	19.7	7.9		216	0.008406	1.80
R Caudate Body	15.2	-13.4	26.8		216	0.008253	1.76
R Lingual Gyrus	15.5	-89.3	-4.8	17	208	0.008018	1.71
R Supramarginal Gyrus	54	-53	26.2	40	208	0.008314	1.78
R Superior Parietal Lobule	20.2	-64	54.3	7	208	0.008529	1.82
R Precentral Gyrus	31.6	-11.1	59.8	6	208	0.008268	1.77
R Declive	29.7	-66	-13.3		200	0.008244	1.76
R Inferior Parietal Lobule	37.3	-31.6	38.9	40	200	0.008058	1.72

Table S10. Regions in which erotic visual stimulation (pictures and videos) induced significantly different responses than contrasted cues among heterosexual study participants. Coordinates are in Talairach space. For clusters with sub-peaks, primary peak is bolded and sub-peaks are italicized. Clusters with relative importance less <5% are shaded.

Anatomical Region	Weighted Center (x,y,z)			Brodmann Area	Volume (mm³)	ALE Extrema Value	Relative Importance
L Lateral Globus Pallidus	-12	-1.8	-5.7		6984	0.025848	10.32%
L Anterior Cingulate				25		0.020094	
L Lateral Globus Pallidus						0.019862	
L Hypothalamus						0.014821	
L Anterior Cingulate	-2.2	19.2	25.6	24	4136	0.027938	7.02%
L Cingulate Gyrus				32		0.01523	
L Medial Frontal Gyrus				9		0.011701	
R Medial Globus Pallidus	24.6	0.7	-5.8		4032	0.018982	12.65%
R Putamen						0.018413	
R Claustrum						0.014189	
R Insula				13		0.013846	
R Parahippocampal Gyrus				34		0.012696	
R Putamen						0.011387	
R Uncus				34		0.009357	
R Thalamus Anterior Nucleus	6.7	-6.6	14.3		2136	0.017197	3.99%
R Thalamus Medial Dorsal Nucleus						0.014021	
L Middle Occipital Gyrus	-47.9	-65.3	-6.2	37	2064	0.025041	4.52%
L Inferior Temporal Gyrus				37		0.010269	
R Middle Occipital Gyrus	28.9	-81.9	2.7	19	1840	0.016963	5.53%
R Middle Occipital Gyrus				18		0.016054	
R Middle Occipital Gyrus				18		0.010216	
L Medial Frontal Gyrus	-5.9	50	8.6	10	1160	0.020771	2.66%
L Inferior Frontal Gyrus	-32.7	19.2	-12.4	47	1064	0.016455	3.94%
L Inferior Frontal Gyrus				47		0.014365	
R Caudate Head	9.9	18.7	-0.4		1040	0.016194	2.07%
L Culmen	-40.2	-52.2	-18.7		984	0.019781	2.53%
R Middle Frontal Gyrus	43.4	-0.2	39.7	6	920	0.015579	1.99%
R Thalamus	17.3	-31.8	0.2		792	0.014727	1.88%
L Superior Temporal Gyrus	-58.4	-27.4	7.6	42	776	0.013504	4.70%
L Superior Temporal Gyrus				22		0.012007	
L Superior Temporal Gyrus				41		0.011193	
L Inferior Parietal Lobule	-31.4	-56.5	42.8	7	720	0.016438	2.10%
R Precuneus	27.4	-53.8	49.4	7	656	0.014613	1.87%
L Lingual Gyrus	-30.9	-72	-5.2	18	576	0.015714	2.01%
R Medial Frontal Gyrus	23.4	47.2	12.3	10	528	0.0126	3.21%

R Superior Frontal Gyrus				10		0.012496	
R Inferior Frontal Gyrus	32	27.1	-5.6	47	496	0.012795	1.64%
R Superior Temporal Gyrus	60.5	-52.6	13.1	22	464	0.014865	3.04%
R Supramarginal Gyrus				40		0.008883	
R Fusiform Gyrus	40.7	-66	-12.4	19	336	0.01074	1.37%
R Superior Temporal Gyrus	48.7	-18.1	2.8	22	320	0.011945	1.53%
L Middle Temporal Gyrus	-42.8	-67.1	17	39	320	0.012808	1.64%
R Precentral Gyrus	23	-13.3	65.5	6	320	0.013695	1.75%
L Middle Frontal Gyrus	-36.7	8.6	53.2	6	304	0.013529	1.73%
R Middle Temporal Gyrus	47.7	-60.7	5.2	37	264	0.011431	1.46%
R Caudate Body	21.6	-14.5	28.6		248	0.011605	1.49%
R Fusiform Gyrus	39.3	-44.9	-14.5	37	232	0.012154	1.56%
L Middle Frontal Gyrus	-20.7	9.2	59.6	6	232	0.011485	1.47%
L Anterior Cingulate	-0.8	33.2	18.3	32	216	0.010404	1.33%
R Cingulate Gyrus	2	-4	42.8	24	208	0.010483	1.34%
L Middle Occipital Gyrus	-31.8	-82.1	-10.7	18	200	0.010795	1.38%
L Thalamus Lateral Posterior Nucleus	-17.1	-17.7	15.2		200	0.011536	1.48%
R Medial Frontal Gyrus	2.5	37.6	29	9	200	0.011035	1.41%
R Postcentral Gyrus	55.6	-21.6	33.5	2	200	0.01069	1.37%

Table S11. Regions in which erotic visual stimulation (pictures and videos) induced significantly stronger activation in heterosexuals than in homosexuals. Coordinates are in Talairach space. For clusters with sub-peaks, primary peak is bolded and sub-peaks are italicized. Clusters with relative importance less <5% are shaded.

Anatomical Region	Weighted Center (x,y,z)			Brodmann Area	Volume (mm^3)	ALE Score	Relative Importance (%)
L Middle Occipital Gyrus	-42	-65.1	-9.1	37	6528	0.042287	11.49
L Fusiform Gyrus				37		0.021754	
L Lingual Gyrus				18		0.01764	
L Middle Occipital Gyrus				18		0.015223	
L Declive						0.014738	
L Inferior Temporal Gyrus				37		0.010483	
L Lateral Globus Pallidus	-12	-1.7	-5.8		5520	0.025848	7.59
L Anterior Cingulate				25		0.020095	
L Lateral Globus Pallidus						0.019863	
L Hypothalamus						0.014821	
L Anterior Cingulate	-1.1	21.6	23	24	4840	0.027985	9.08
L Anterior Cingulate				24		0.016668	
L Cingulate Gyrus				32		0.015287	
L Cingulate Gyrus				32		0.013315	
L Medial Frontal Gyrus				9		0.011701	
R Anterior Cingulate				24		0.011596	
R Middle Occipital Gyrus	29.3	-81.1	3.3	19	3152	0.018849	6.16
R Lingual Gyrus				17		0.017129	
R Middle Occipital Gyrus				18		0.01616	
R Middle Occipital Gyrus				19		0.013286	
R Medial Globus Pallidus	24.1	0.8	-5.5		2720	0.018984	8.42
R Putamen						0.018413	
R Claustrum						0.014189	
R Insula				13		0.013846	
R Parahippocampal Gyrus				34		0.012696	
R Putamen						0.011387	
R Thalamus	7.8	-6.4	13.5		2400	0.019309	3.46
R Thalamus Medial Dorsal Nucleus						0.017437	
L Superior Temporal Gyrus	-54.4	-27.2	6.6	42	2376	0.020599	3.62
L Superior Temporal Gyrus				41		0.017829	
R Declive	38.7	-64.4	-9.2		1960	0.015524	4.15
R Fusiform Gyrus				19		0.01492	
R Fusiform Gyrus				37		0.013699	
R Superior Temporal Gyrus	49.7	-19	4.9	13	1760	0.01926	4.28
R Superior Temporal Gyrus						0.013315	
R Superior Temporal Gyrus				41		0.01293	

L Inferior Parietal Lobule	-28.5	-57.3	45.2	40	1352	0.017847	4.09
L Precuneus				7		0.014824	
L Superior Parietal Lobule				7		0.01079	
L Medial Frontal Gyrus	-6.6	49.6	8.5	10	1296	0.026735	2.52
R Nodule	-1.5	-45.9	-31.7		992	0.018206	2.89
L Cerebellar Tonsil						0.012562	
R Precentral Gyrus	44.2	-0.5	39	6	880	0.016193	1.52
L Inferior Frontal Gyrus	-32.8	19.5	-12.6	47	848	0.016497	2.91
L Inferior Frontal Gyrus				47		0.014462	
R Culmen	32.4	-48.7	-12.2		848	0.015621	2.71
R Fusiform Gyrus				37		0.013204	
R Caudate Head	9.8	18.6	-0.5		752	0.016195	1.52
L Middle Occipital Gyrus	-19.8	-79.8	7.2	19	744	0.015672	3.72
L Lingual Gyrus				18		0.01239	
L Cuneus				17		0.011452	
R Cingulate Gyrus	1.2	-8.1	38	24	704	0.01336	1.26
R Thalamus	17.4	-32.4	0.8		608	0.01495	1.41
L Cuneus	-26.3	-80.7	25.2	19	584	0.018596	1.75
L Lingual Gyrus	-18.8	-92.1	-1.1		544	0.013651	1.28
R Caudate Body	19.3	-14.4	27.6		480	0.014418	1.36
R Precuneus	27.1	-53.9	49.5	7	464	0.01464	1.38
R Medial Frontal Gyrus	23.2	47.5	12.6	10	320	0.0126	2.36
R Superior Frontal Gyrus				10		0.012496	
R Superior Temporal Gyrus	61	-53.2	12.8	22	304	0.014867	1.40
R Inferior Frontal Gyrus	31.9	27.4	-6	47	280	0.012795	1.20
L Caudate Body	-8.7	17.6	7.8		264	0.012747	1.20
R Postcentral Gyrus	27.5	-37.7	43.5	3	264	0.01566	1.47
R Precentral Gyrus	23.2	-13.4	65.2	6	256	0.013846	1.30
L Middle Frontal Gyrus	-36.9	8.8	53	6	240	0.013529	1.27
L Middle Temporal Gyrus	-42.5	-67.4	16.9	39	216	0.012974	1.22

Table S12. Systematic review of studies reporting sex differences in grey matter volume (GMV) of insula (Ins) and anterior cingulate (ACC). Hereby, women (w) show larger GMV in Ins and ACC than men (m). These studies represent approximately 20% of structural investigations of regional GMV differences between healthy male and females. The majority of publications report inconsistent findings. Most publications do not report significant sex differences in the Ins and ACC, while differences in other brain areas are observed (see as an example (62)). Δ represents differences. w* means that this study identified differences between women on contraceptives and men but no differences between w and m could be observed for Ins and ACC. Coordinate, if reported in MNI, were transformed and are presented in Talairach-space.

Publication	**N(f)**	**Age (yrs)**	**Δ**	**Brain region**	**Cluster size (voxels)**	**x**	**y**	**z**	**t/F score**	**Z**
Lotze et al 2019 (63)	2838	52.4±13.7	w>m	R ACC	3087	8	41	6	9.22	
			w>m	L ACC	3087	-8	38	20	8.05	
			w>m	R pIns	349	36	-17	3	8.31	
			w>m	L pIns	199	-40	-15	.34	6.48	
Yang et al 2017 (64)	82(53)	27.7±8.0	w>m	R Ins	1380	38	12	-1	26.84	
			w>m	L Ins	772	-33	11	-1	20.63	
Lentini et al 2013 (65)	86(45)	35±7	w>m	ACC	1.6 cm^3	-16	19	-10		4.8
Paus et al 1996 (66)	105(42)	25.2±7.7		R ACC	F: 6.22 ccm M: 5.81 ccm				4.86	
Pletzer et al 2010 (67)	28(14)	24.3±4.1	w*>m	L/R ACC	189502	-7	56	18	11.45	
Yamasue et al 2008 (68)	155(66)	28.5±4.3	w>m	L Ins	9160	-53	-22	16		4.04
				R Ins	11616	47	-22	21		3.89
				L ACC	64	-14	46	12		3.33
Chen et al 2007 (69)	411(227)	46.7±1.4	w>m	ACC, dorsal		-1	4	46	5.81	

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