Neuroscience and Biobehavioral Reviews 68 (2016) 530–536

Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

A neural circuit encoding sexual preference in humans

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ARTICLE INFO

Article history:
Received 17 April 2016
Received in revised form 15 June 2016
Accepted 17 June 2016
Available online 23 June 2016

Keywords:
Sexual behavior
Sexual preference
Neuroimaging
Brain imaging
Meta-analysis
Activation likelihood estimation

ABSTRACT

Sexual preference determines mate choice for reproduction and hence guarantees conservation of species in mammals. Despite this fundamental role in human behavior, current knowledge on its target-specific neurofunctional substrate is based on lesion studies and therefore limited. We used meta-analytic remodeling of neuroimaging data from 364 human subjects with diverse sexual interests during sexual stimulation to quantify neural regions associated with sexual preference manipulations. We found that sexual preference is encoded by four phylogenetically old, subcortical brain structures. More specifically, sexual preference is controlled by the anterior and preoptic area of the hypothalamus, the anterior and mediodorsal thalamus, the septal area, and the perirhinal parahippocampus including the dentate gyrus. In contrast, sexual non-preference is regulated by the substantia innominata. We anticipate the identification of a core neural circuit for sexual preferences to be a starting point for further sophisticated investigations into the neural principles of sexual behavior and particularly of its aberrations.
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Contents

1. Introduction

Sexuality is a central component of human behavior. In both animals and humans, "nature displays an interesting range of sexual behaviors, some of which may offend some of us" (Gross, 2014). These behaviors are significantly affected by individual sexual preferences. In humans, sexual preferences refer to the favored way of reaching orgasm and to corresponding preferred sexual activities or preferred types of sexual partners (Langevin, 1983; Quinsey, 2003). These preferences hence reflect the ultimate choice of a sexual activity/partner over another that one would make (Bailey, 2009). Albeit often conflated, researchers make efforts to distinguish between sexual preference and sexual orientation. While sexual orientation is considered a "stable and enduring internal preference for same- versus opposite-sex sexual interactions and partnering", sexual preference is assumed to represent "the manifestation of behavioral choices rather than a stable internal predisposition" (Bailey and Zuk, 2009). Yet, the nomenclatural shift from sexual preference to sexual orientation has also been chal-

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http://dx.doi.org/10.1016/j.neubiorev.2016.06.025
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lenged. Particularly, it has been noted that it may overemphasize biological determination while neglecting psychological and sociocultural dimensions, but on the other hand also disregard that "choices are seldom if ever entirely volitional" (De Cecco and Parker, 1995). The debate on definitions seems heated at times, and it has been noted that a consistent definition of sexual orientation is still lacking (Moser, 2016). Nobody may disagree that hetero- and homosexuality represent sexual orientations (Moser, 2016). However, the notion of, for instance, asexuality (Bogaert, 2015) and pedophilia (Seto, 2012) as sexual orientations or the consideration of absence of sexual orientation in women (Bailey, 2009) are highly controversial. This mini-review is not limited to same-sex and opposite-sex preferences (i.e., sexual orientation) but includes also sexual preferences relating to other variables such as age (i.e., disorders of sexual preference). Therefore, it employs the term and refers to sexual preference as the preferred way of reaching orgasm concerning particular sexual activities or types of partners (Langevin, 1983; Quinsey, 2003).

Evidence for influence of epi-/genetic mechanisms but also of emotional maternal bond have fueled the controversial debate over the origin of sexual preferences, which has centered on the nature vs. nurture dichotomy (Hamer et al., 1993; Kendrick et al., 1998; Liu et al., 2011; Majerus et al., 1982; Ngun and Vilain, 2014). A quasi intermediate model between the 'nature' and 'nurture' view on the basis of genetic, hormone, and birth order studies proposes that sexual preference in humans may be stipulated in neural circuitry during early fetal development (Rahman, 2005). It has therefore been advocated for a future focus on elucidating "the fundamental neural architecture underlying the target-specific direction of human sexual orientation" (Rahman, 2005). A postmortem study had reported that the interstitial nuclei of the anterior hypothalamus (group 3; INAH 3) were twice as large in heterosexual men as not only in heterosexual women but also in homosexual men (LeVay, 1991). The inferred thesis of neuroanatomical sexual dimorphism being a biological substrate for sexual preference was further tested using modern neuroimaging techniques. Positron emission tomography (PET) and magnetic resonance imaging (MRI) showed sex-atypical (i.e., opposite-sex-like) cerebral asymmetry and functional connections (of the amygdala) in homosexual subjects (Savic and Lindström, 2008). The findings of these pioneering experiments seem plausible, given that homosexual subjects' sexual preference is similar to that of their opposite sex. The results however leave open whether these sexually dimorphic structures are significantly involved in the functional *brain response to sexual stimuli* that is specific to one's sexual preference, i.e., the neural basis underlying its *target-specific direction*.

Notably, the only MRI study that explicitly aimed at unraveling the functional neural correlates of sexual orientation in humans found stronger neuronal response to preferred as compared to non-preferred visual sexual stimuli in the reward and motor system (including ventral striatum, centromedian thalamus, and ventral premotor cortex) but not in the suggested candidate regions (Ponseti et al., 2006). The data currently available regarding consistently recruited areas mediating sexual preferences hence seems contradictory and the initial question remains unresolved. When however reviewing the rich corpus of studies investigating human brain response to sexual stimuli, we noticed that a considerable proportion implicitly also assessed brain activations related to sexual preference by comparing preferred with relatively non-preferred sexual stimuli, which were used as control stimuli, in various subject groups. In other words, we became aware of the existence of an extensive data pool that seemed ideally suited for identifying neural regions associated with sexual preference manipulations when recapitulated and re-analyzed in this context.

This meta-analytic mini-review reassesses if sexual preference-related brain activity is actually found in regions where previous neuroanatomical studies located sexual preference-related changes in brain anatomy. The overlap and link between brain structure and function might serve as evidence that the candidate regions are indeed functionally involved in encoding sexual preference and related neuroanatomical variations not merely epiphenomena. Such spatial localization could provide further hints at the temporal manifestation of sexual preferences and confine the spectrum of neurotransmitters and receptors that regulate this aspect of personality (LeVay, 1991).

2. Methods

2.1. Data selection

We applied a similar search and selection strategy as a previous meta-analysis of neural sexual stimulus processing in men (Poeppl et al., 2014). A stepwise procedure to identify the relevant experimental studies was used. First, we selected studies through a standard search in the PubMed (http://www.pubmed.gov) and ISI Web of Science (http://apps.isiknowledge.com) databases using the terms 'sexual' or 'erotic' in combination with 'fMRI', 'functional MRI', 'functional magnetic resonance', 'PET', 'positron emission', 'ASL', 'arterial spin labeling', 'MEG', 'magnetoencephalography', 'neuroimaging', or 'imaging'. Second, further studies were found by means of the 'related articles' function of the PubMed database and by tracing the references from the identified papers and review articles. Experiments were considered relevant when they were intended to sexually stimulate subjects. In addition, experiments had to (implicitly) isolate sexual preference or non-preference. According to the aforementioned notion that sexual preference should reflect the ultimate choice of a sexual activity/partner that one would make, sexual preference and non-preference were operationalized by the following two scenarios: (1) Experiments contrasting a sexually preferred vs. a sexually non-preferred stimulus (or vice versa for relative sexual non-preference) within a group of subjects ('sexually preferred vs. sexually non-preferred' or vice versa). (2) Experiments comparing two subject groups having different sexual preferences during adequate sexual stimulation of only one group (embodied in contrasting a sexual stimulus preferred by only one group vs. a non-sexual control stimulus). In other words, we considered (1) within-subjects contrasts that compared processing of a sexually preferred stimulus with that of a non-preferred one and (2) between-subjects contrasts that compared two groups with diverging sexual preferences during processing of a sexual stimulus preferred by only one group. Subjects were included irrespective of sex, gender, and sexual preference, including gender identity disorders and disorders of sexual preference. Stimuli were included irrespective of sensory modality. Additionally, only experiments reporting results of whole-brain group analyses with coordinates referring to a standard reference space (Talairach-Tournoux or Montreal Neurological Institute (MNI)) were included. Results of region-of-interest analyses and studies not reporting stereotaxic coordinates were excluded.

On the basis of these search criteria, 17 studies were found to be eligible for inclusion into the meta-analyses (Supplementary Table 1). Only functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) but no arterial spin labeling (ASL) or magnetoencephalography (MEG) studies fulfilled our search criteria. Conceptually, it is unproblematic to include both fMRI and PET techniques because there should be no systematic bias. Although cluster sizes may be larger in PET than in fMRI, activation peaks should not systematically differ (Eickhoff et al., 2009; Feng et al., 2004; Nickerson et al., 2001; Xiong et al., 1998). Since the here employed meta-analytic method relies on activation peaks (but not cluster sizes), no distortion of results by the inclusion of

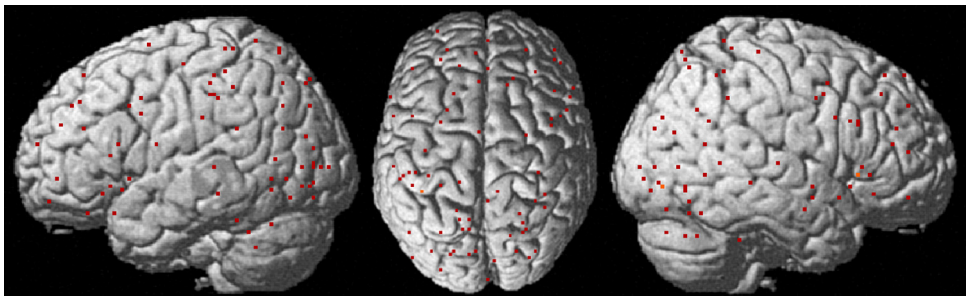

Fig. 1. Summary of the 312 activation foci reported in all 48 experiments included in the meta-analyses.

both imaging methods is to be expected. Non-preference of stimuli in the identified studies concerned (non-preferred) sex or age of the respective sexual stimulus. Together, these studies reported 275 activation foci obtained from 37 experiments isolating sexual preference and 37 activation foci obtained from 11 experiments isolating sexual non-preference (with a 'study' referring to a paper, an 'experiment' referring to an individual contrast reported in this paper) (Fig. 1). All subject and stimulus types were pooled in the two meta-analyses, respectively. Since transsexual and paraphilic samples may be more heterogeneous, however, we additionally computed a sub-meta-analysis of experiments addressing sexual preference without these subject groups. The corresponding meta-analysis with respect to sexual non-preference was not possible because of a too small number of available experiments. Differences in coordinate spaces (Talairach-Tournoux vs. MNI space) were accounted for by transforming coordinates reported in Talairach-Tournoux space into MNI coordinates using a linear transformation (Laird et al., 2010; Lancaster, 2007).

2.2. Activation likelihood estimation (ALE)

All meta-analyses were carried out using the revised ALE algorithm for coordinate-based meta-analysis of neuroimaging results (Eickhoff et al., 2012; Turkeltaub et al., 2012). This algorithm aims to identify areas with a convergence of reported coordinates across experiments that is higher than expected from a random spatial association. Reported foci are treated as centers of 3D Gaussian probability distributions capturing the spatial uncertainty associated with each focus (Eickhoff et al., 2012). Here, the between-subject variance is weighted by the number of participants per study, since larger sample sizes should provide more reliable approximations of the "true" activation effect and should therefore be modeled by "narrower" Gaussian distributions.

Subsequently, probabilities of all foci reported of a given experiment were combined for each voxel, yielding a modeled activation (MA) map (Fig. 2) (Turkeltaub et al., 2012). Voxelwise ALE scores (union across these MA maps) then quantified the convergence across experiments at each location in the brain. To distinguish "true" from random convergence, ALE scores were compared to an empirical null distribution reflecting a random spatial association among all MA maps. The resulting random-effects inference focuses on the above-chance convergence across studies rather than the clustering within a particular study (Eickhoff et al., 2009). This null hypothesis was derived by computing the distribution that would be obtained when sampling a voxel at random from each of the MA maps and taking the union of these values in the same manner as for the (spatially contingent) voxels in the original analysis (Eickhoff et al., 2012). The p value of a "true" ALE score was then given by the proportion of equal or higher values obtained under the null distribution. The resulting nonparametric p values were then assessed at a familywise error (FWE) corrected threshold of $p < 0.05$ on cluster level (cluster-forming threshold: $p < 0.001$ at voxel level) and transformed into z scores for display (Eickhoff et al., 2012).

2.3. Anatomical labeling

For anatomical labeling, we capitalized on cytoarchitectonic maps of the human brain provided by the Statistical Parametric Mapping (SPM) Anatomy Toolbox (Eickhoff et al., 2005, 2006, 2007). Clusters were thus assigned to the most probable histologically defined area at the respective location. This probabilistic histology-based anatomical labeling is reported in the results table. References to details regarding cytoarchitecture are given in the table notes.

3. Results

We systematically collected the appropriate studies. We then used activation likelihood estimation (ALE) (Fox et al., 2014) to meta-analytically remodel available neuroimaging data from 364 subjects including healthy hetero- and homosexual individuals as well as individuals with gender identity and sexual preference disorders (i.e., transsexualism and pedophilia). Our analyses identified a robust neural pattern of activity, idiosyncratic for encoding sexual preference, that converged in four regions.

Probabilistic and histology-based anatomical allocation revealed activation peaks in the septal area, the anterior and mediodorsal thalamus, the anterior and preoptic area of the hypothalamus, and the perirhinal parahippocampus including the dentate gyrus (Fig. 3, Table 1). In the subanalysis without transsexual and paraphilic subjects, convergence in the para-/hippocampus was not significant anymore, which may be due to lower statistical power or greater heterogeneity of the excluded groups. Experiments involving male, female, heterosexual, homosexual, pedophilic, and transsexual subjects contributed to the first cluster of convergent activation (septum, thalamus, hypothalamus), the second cluster (para-/hippocampal) was based on experiments involving male, female, heterosexual, homosexual, and pedophilic subjects. Both experiments using visual and experiments using olfactory stimuli contributed to both clusters of convergent activation regarding sexual preference.

In addition, we investigated the activity pattern underlying sexual non-preference, operationalized by the contrast 'sexually non-preferred vs. sexually preferred'. Here, convergence of activation localized to the substantia innominata (Fig. 3, Table 1). This cluster resulted from experiments comprising male, heterosexual, homosexual, and transsexual subjects. Only experiments using visual stimuli contributed to the cluster related to sexual non-preference.

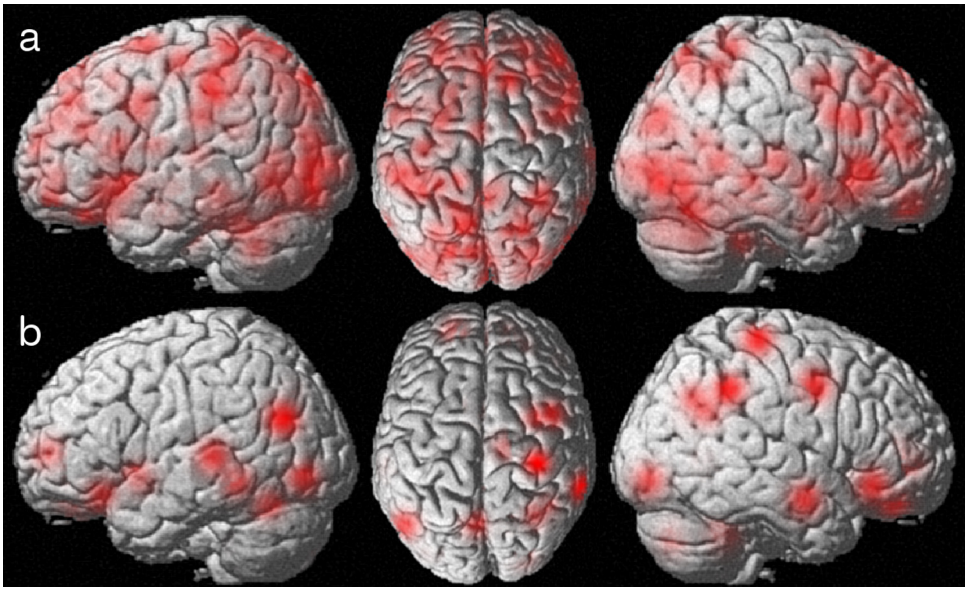

Fig. 2. Activation likelihood estimates (ALE), reflecting, for each voxel, the union of the modeled activation (MA) maps across all experiments related to sexual preference (a) and sexual non-preference (b).

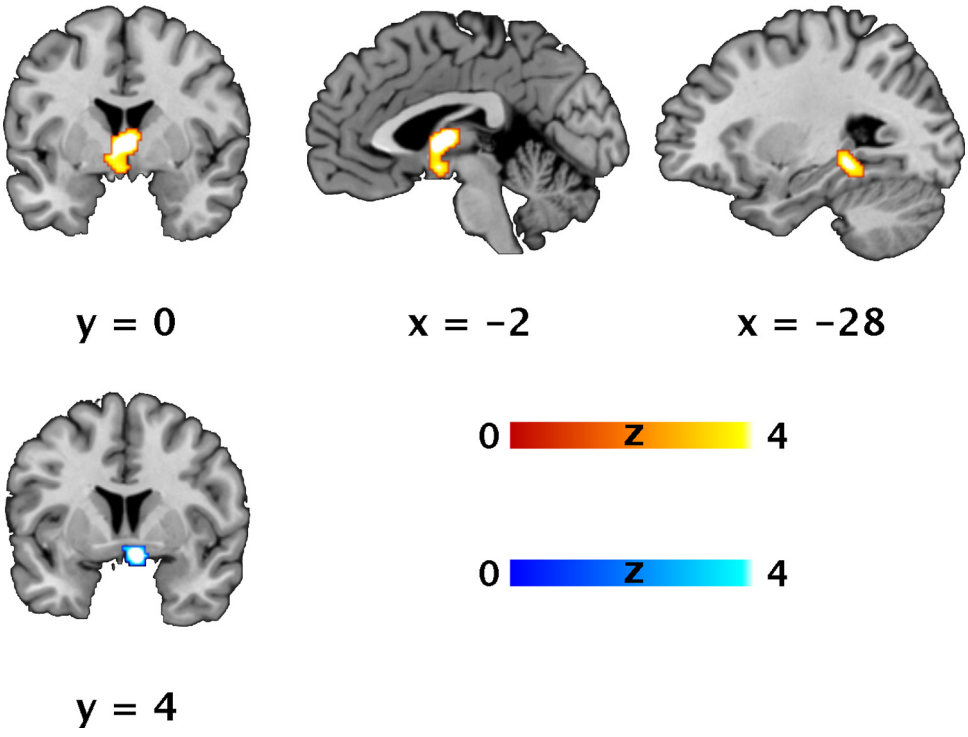

Fig. 3. Brain regions encoding sexual preference (orange) and sexual non-preference (blue). Significant clusters where the ALE analysis revealed convergence of brain activations in corresponding experiments ($p < 0.05$, FWE corrected; cf. Table 1): septal area ($y = 0$), anterior and mediodorsal thalamus as well as anterior and preoptic area of the hypothalamus ($x = -2$), and dentate gyrus in the parahippocampal region ($x = -28$); substantia innominata ($y = 4$). Brain slices are shown at coordinates (x, y, z) in MNI space. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article).
ALE, activation likelihood estimation; FWE, family-wise error; MNI, Montreal Neurological Institute.

4. Discussion

It is remarkable that the identified neural circuit encoding sexual preference exclusively encompasses phylogenetically old, subcortical brain structures, but no regions of the neocortex. In the light of Haeckel's notion that ontogenesis is a brief and rapid recapitulation of phylogenesis (Haeckel, 1899), this distinctive neuroanatomical feature supports the view of an *in utero* determination of sexual preference during early fetal development (Bao and Swaab, 2011). The lack in involvement of cognitive cortical regions may in addition account for the immutability of sexual preferences according to current state of research. It is not surprising that the here specified regions are components of the functional neuroanatomy of psychosexual arousal (Poeppl et al., 2014; Stoléru et al., 2012). Neural networks underlying psychosexual arousal however involve also the lateral prefrontal cortex and superior parietal lobules, which

Table 1
Brain activations related to sexual preference or non-preference.

Analysis	Macroanatomical Location	Cytoarchitectonic Location	Cluster Size in Voxels	MNI Coordinates x	y	z	Z Score
Preference	Septal area		419	2	0	2	5.29
	Thalamus (Temporal)			−2	−6	4	5.28
	Hypothalamus			−2	−2	−12	4.06
	Para-/Hippocampus	DG	127	−28	−38	−10	4.25
Non-preference	Substantia innominata	BF (Ch 1–3)	87	6	4	−14	5.30

Convergent brain activations related to sexual preference according to ALE across 37 experiments featuring 275 foci and related to sexual non-preference according to ALE across 11 experiments featuring 37 activation foci comprising 364 subjects in total. For all analyses, FWE correction on cluster level ($p < 0.05$) with a cluster forming threshold of $p < 0.001$ (uncorrected) was applied.
ALE, activation likelihood estimation; FWE, familywise error; MNI, Montreal Neurological Institute.
For detailed information on cytoarchitectonics and conncectivity, see publications by Amunts (DG), Behrens (Thalamus-Temporal), Zaborszky (BF), and colleagues (Amunts et al., 2005; Behrens et al., 2003; Zaborszky et al., 2008).

have been implicated in top-down control in this context (Poeppl et al., 2014). This neural specificity of the sexual preference network within the psychosexual arousal network could furthermore explain why sexual arousal can be contained, while sexual preference per se is not subject to deliberate control.

Our results for the first time validate preliminary evidence for the critical role of septal region and hypothalamus in human sexual behavior from lesion studies. Damage to these regions resulted not only in changes of sexual drive but also in altered sexual preferences including a variety of paraphilias (Baird et al., 2007). That also the hippocampus is part of the delineated circuit may point to a mutability of sexual preferences, given known hippocampal neurogenesis following sexual stimulation in rodents (Mak et al., 2007). More specifically, such hippocampal neuroplasticity could be the neural substrate for discussed shaping of sexual preferences during puberty. However, the sexual hormone-related sexual dimorphism of the hippocampal subregion (i.e., the dentate gyrus) where we pinpointed convergence of activity already exists prior to puberty and therefore seems to contradict this assumption (Roof, 1993). The corresponding cluster of convergent activity also comprised the left perirhinal cortex. Interestingly, gray matter of this region displays a more male-like structural pattern in homosexual women (Ponseti et al., 2007). Together, these findings can be interpreted as support for sex-atypical prenatal androgenization in homosexual women and for early determination of sexual preference in the fetal stage on the basis of hormonal influence in general. Finally, the involvement of the (anterior and mediodorsal) thalamus is somewhat unexpected. Yet, small bilateral ischemic and isolated lesions in these thalamic subregions have been reported in a patient to cause Klüver-Bucy syndrome (Müller et al., 1999). This syndrome is characterized by a tendency to seek sexual stimulation from unusual or inappropriate objects and typically results from lesions of the medial temporal lobe and subsequent disinhibition. Our probabilistic anatomical allocation demonstrated convergence of sexual preference-activity in a thalamic subregion that holds strong connectivity with the temporal cortices. The thalamus might hence serve as a relay communicating sexual preference to the temporal lobes and therefore be essential for behavioral transformation of its specificity.

In addition to this thalamic mechanism ensuring specificity of mate choice, the substantia innominata encodes sexual non-preference according to our meta-analysis. This finding is in line with the observation that olfactory cues in rodents, which choose mating partners by using the olfactory system, get to the basal forebrain including the substantia innominata (Sakuma, 2008). It might furthermore explain that mesoscopic gray matter alterations in this region can be associated with a sexual preference for children, i.e., subjects that are normally perceived as aversive in a sexual context (Schiltz et al., 2007). It has to be noted that no experiments involving female subjects contributed to convergence of activation in this region. This potential lack of distinct sexual non-preference-related brain activity, possibly based on regional sex-differences of structural asymmetry (Amunts, 2007), may be seen in line with "the idea that women are less contrained than men by a focused sexual arousal pattern" (Bailey, 2009). That is, one could reason that this latitude of sexual arousal patterns in women is rooted in the absence of a neural mechanism of inhibition that directs sexual preference. However, only two of the eleven experiments (≈18%) included in the meta-analysis of sexual non-preference involved female subjects. The findings with respect to potential sex differences and the drawn conclusion have to be seen with caution because they could be explained by this imbalance.

It has to be acknowledged that our meta-analysis is not able to capture potential differences in neural activity between subjects groups that are homogeneous with regard to both sex and sexual orientation within the group. Given findings showing greater fluidity in heterosexual women's behavioral responses to sex-related stimuli than is evident in homosexual women, heterosexual men, or homosexual men (Chivers et al., 2015; Dawson and Chivers, 2014), also group differences in the neural correlates of sexual preference might exist. However, there is also evidence for gender-specific genital and subjective responses in heterosexual women (Spape et al., 2014). A fair pool of experiments comparing such uniform groups during stimulation with their preferred sexual stimuli (contrasted with their non-preferred stimuli) would be needed to allow for authoritative conclusions on this matter. The same applies to the type of sexual stimuli, given evidence for sex- and sexual orientation-differences in behavioral responses to sexual stimuli depending on features such as gender and intensity of sexual stimuli (Chivers and Bailey, 2005; Chivers et al., 2007).

Our results also seem to indicate that neural systems encoding sexual preference and non-preference are clearly distinct. In this context, they extend previous findings demonstrating that subjective sexual pleasure is associated with hypothalamus and thalamus activation, while subjective sexual disgust is linked to activity in the basal forebrain (Borg et al., 2014; Walter et al., 2008). Despite this spatial segregation, however, both systems likely exchange information, given that the basal forebrain projects to hypothalamus and hippocampus via cholinergic neurons (Mesulam et al., 1983). Although the direction of the (mutual) interference must remain unclear, it can be noted that sexual preferences are probably based on a complex functional interaction of hypothalamus, thalamus, septal nuclei, hippocampus, and substantia innominata.

Our findings demonstrate that regions featuring previously identified, sexual preference-related anatomical variations are indeed key regions for functionally encoding sexual preference. It cannot be inferred from this overlap if reported morphologic differences are cause for or consequence of specific sexual preferences. However, our data specify target regions for further studies on the relationship between neuroanatomical and neuroendocrine as

well as neurochemical systems in the control of partner preference (Pfaus, 1999). These could address not only the neurodevelopment of sexual preference but also its upkeeping over life time.

In summary, we identified a unique, phylogenetically old neural signature of sexual preference in humans. This fingerprint of evolution cannot dissolve the nature/nurture dichotomy of sexual preferences. Yet, our findings support the notion that mate choice and sexual preferences are strongly biologically anchored (Grosjean et al., 2008). This delineation of a core neural circuit for sexual preferences can serve as a solid basis for further detailed investigations into various aspects of sexual behavior, e.g., the largely unknown neural fundament of paraphilias and of their enigmatic, virtual specificity to men.

Acknowledgements

The authors thank Sylvia Dorner-Mitschke and Ines Poeppl for assistance in data keying. This study was in part supported by the Deutsche Forschungsgemeinschaft (DFG; BZ 2/2-1, BZ 2/3-1, EI 816/4-1, EI 816/6-1, LA 3071/3-1), the National Institute of Mental Health (R01-MH074457), the Helmholtz Portfolio Theme "Supercomputing and Modeling for the Human Brain" and the European Union Seventh Framework Programme (FP7/2007-2013) under grant agreement no. 604102 (Human Brain Project).

All authors report no potential conflicts of interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.neubiorev.2016.06.025.

References

Amunts, K., Kedo, O., Kindler, M., Pieperhoff, P., Mohlberg, H., Shah, M.J., et al., 2005. Cytoarchitectonic mapping of the human amygdala, hippocampal region and entorhinal cortex: intersubject variability and probability maps. Anat. Embryol. (Berl.) 210, 343–352.

Amunts, V.V., 2007. Structural asymmetry of the basal nucleus of Meynert in men and women. Neurosci. Behav. Physiol. 37, 517–521.

Bailey, N.W., Zuk, M., 2009. Same-sex sexual behavior and evolution. Trends Ecol. Evol. 24, 439–446.

Bailey, J.M., 2009. What is sexual orientation and do women have one? Nebr. Symp. Motiv. 54, 43–63.

Baird, A.D., Wilson, S.J., Bladin, P.F., Saling, M.M., Reutens, D.C., 2007. Neurological control of human sexual behaviour: insights from lesion studies. J. Neurol. Neurosurg. Psychiatry 78, 1042–1049.

Bao, A.M., Swaab, D.F., 2011. Sexual differentiation of the human brain: relation to gender identity, sexual orientation and neuropsychiatric disorders. Front. Neuroendocrinol. 32, 214–226.

Behrens, T.E., Johansen-Berg, H., Woolrich, M.W., Smith, S.M., Wheeler-Kingshott, C.A., Boulby, P.A., 2003. Non-invasive mapping of connections between human thalamus and cortex using diffusion imaging. Nat. Neurosci. 6, 750–757.

Bogaert, A.F., 2015. Asexuality: what it is and why it matters. J. Sex Res. 52, 362–379.

Borg, C., de Jong, P.J., Georgiadis, J.R., 2014. Subcortical BOLD responses during visual sexual stimulation vary as a function of implicit porn associations in women. Soc. Cogn. Affective Neurosci. 9, 158–166.

Chivers, M.L., Bailey, J.M., 2005. A sex difference in features that elicit genital response. Biol. Psychol. 70, 115–120.

Chivers, M.L., Seto, M.C., Blanchard, R., 2007. Gender and sexual orientation differences in sexual response to sexual activities versus gender of actors in sexual films. J. Pers. Soc. Psychol. 93, 1108–1121.

Chivers, M.L., Bouchard, K.N., Timmers, A.D., 2015. Straight but not narrow; within-gender variation in the gender-specificity of women's sexual response. PLoS One 10, e0142575.

Dawson, S.J., Chivers, M.L., 2014. Gender-specificity of solitary and dyadic sexual desire among gynephilic and androphilic women and men. J. Sex. Med. 11, 980–994.

De Cecco, J.P., Parker, D.A., 1995. The biology of homosexuality: sexual orientation or sexual preference? J. Homosex. 28, 1–27.

Eickhoff, S.B., Stephan, K.E., Mohlberg, H., Grefkes, C., Fink, G.R., Amunts, K., Zilles, K., 2005. A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. Neuroimage 25, 1325–1335.

Eickhoff, S.B., Heim, S., Zilles, K., Amunts, K., 2006. Testing anatomically specified hypotheses in functional imaging using cytoarchitectonic maps. Neuroimage 32, 570–582.

Eickhoff, S.B., Paus, T., Caspers, S., Grosbras, M.H., Evans, A.C., Zilles, K., Amunts, K., 2007. Assignment of functional activations to probabilistic cytoarchitectonic areas revisited. Neuroimage 36, 511–521.

Eickhoff, S.B., Laird, A.R., Grefkes, C., Wang, L.E., Zilles, K., Fox, P.T., 2009. Coordinate-based activation likelihood estimation meta-analysis of neuroimaging data: a random-effects approach based on empirical estimates of spatial uncertainty. Hum. Brain Mapp. 30, 2907–2926.

Eickhoff, S.B., Bzdok, D., Laird, A.R., Kurth, F., Fox, P.T., 2012. Activation likelihood estimation meta-analysis revisited. Neuroimage 59, 2349–2361.

Feng, C.M., Narayana, S., Lancaster, J.L., Jerabek, P.A., Arnow, T.L., Zhu, F., et al., 2004. CBF changes during brain activation: fMRI vs. PET. Neuroimage 22, 443–446.

Fox, P.T., Lancaster, J.L., Laird, A.R., Eickhoff, S.B., 2014. Meta-analysis in human neuroimaging: computational modeling of large-scale databases. Annu. Rev. Neurosci. 37, 409–434.

Grosjean, Y., Grillet, M., Augustin, H., Ferveur, J.F., Featherstone, D.E., 2008. A glial amino-acid transporter controls synapse strength and courtship in Drosophila. Nat. Neurosci. 11, 54–61.

Gross, M., 2014. Paraphilia or perversion? Curr. Biol. 24, R777–R780.

Haeckel E. (1899): Die Welträthsel. Gemeinverständliche Studien über monistische Philosophie. Bonn, Germany : Emil Strauß.

Hamer, D.H., Hu, S., Magnuson, V.L., Hu, N., Pattatucci, A.M., 1993. A linkage between DNA markers on the X chromosome and male sexual orientation. Science 261, 321–327.

Kendrick, K.M., Hinton, M.R., Atkins, K., Haupt, M.A., Skinner, J.D., 1998. Mothers determine sexual preferences. Nature 395, 229–230.

Laird, A.R., Robinson, J.L., McMillan, K.M., Tordesilla-Gutiérrez, D., Moran, S.T., Gonzales, S.M., 2010. Comparison of the disparity between Talairach and MNI coordinates in functional neuroimaging data: validation of the Lancaster transform. Neuroimage 51, 677–683.

Lancaster, J.L., 2007. Bias between MNI and Talairach coordinates analyzed using the ICBM-152 brain template. Hum. Brain Mapp. 28, 1194–1205.

Langevin, R., 1983. Sexual Strands: Understanding and Treating Sexual Anomalies in Men. Erlbaum, Hillsdale, New Jersey.

LeVay, S., 1991. A difference in hypothalamic structure between heterosexual and homosexual men. Science 253, 1034–1037.

Liu, Y., Jiang, Y., Si, Y., Kim, J.Y., Chen, Z.F., Rao, Y., 2011. Molecular regulation of sexual preference revealed by genetic studies of 5-HT in the brains of male mice. Nature 472, 95–99.

Müller, A., Baumgartner, R.W., Röhrenbach, C., Regard, M., 1999. Persistent Klüver-Bucy syndrome after bilateral thalamic infarction. Neuropsychiatry Neuropsychol. Behav. Neurol. 12, 136–139.

Majerus, M.E.N., O'Donald, P., Weir, J., 1982. Female mating preference is genetic. Nature 300, 521–523.

Mak, G.K., Enwere, E.K., Gregg, C., Pakarainen, T., Putanen, M., Huhtaniemi, I., Weiss, S., 2007. Male pheromone-stimulated neurogenesis in the adult female brain: possible role in mating behavior. Nat. Neurosci. 10, 1003–1011.

Mesulam, M.M., Mufson, E.J., Levey, A.I., Wainer, B.J., 1983. Cholinergic innervation of cortex by the basal forebrain: cytochemistry and cortical connections of the septal area, diagonal band nuclei, nucleus basalis (substantia innominata), and hypothalamus in the rhesus monkey. J. Comp. Neurol. 214, 170–197.

Moser, C., 2016. Defining sexual orientation. Arch. Sex. Behav. 45, 505–508.

Ngun, T.C., Vilain, E., 2014. The biological basis of human sexual orientation: is there a role for epigenetics? Adv. Genet. 86, 167–184.

Nickerson, L.D., Martin, C.C., Lancaster, J.L., Gao, J.H., Fox, P.T., 2001. A tool for comparison of PET and fMRI methods: calculation of the uncertainty in the location of an activation site in a PET image. Neuroimage 14, 194–201.

Pfaus, J.G., 1999. Neurobiology of sexual behavior. Curr. Opin. Neurobiol. 9, 751–758.

Poeppl, T.B., Langguth, B., Laird, A.R., Eickhoff, S.B., 2014. The functional neuroanatomy of male psychosexual and physiosexual arousal: a quantitative meta-analysis. Hum. Brain Mapp. 35, 1404–1421.

Ponseti, J., Bosinski, H.A., Wolff, S., Peller, M., Jansen, O., Mehdorn, H.M., 2006. A functional endophenotype for sexual orientation in humans. Neuroimage 33, 825–833.

Ponseti, J., Siebner, H.R., Klöppel, S., Wolff, S., Granert, O., Jansen, O., et al., 2007. Homosexual women have less grey matter in perirhinal cortex than heterosexual women. PLoS One 2, e762.

Quinsey, V.L., 2003. The etiology of anomalous sexual preferences in men. Ann. N. Y. Acad. Sci. 989, 144–153.

Rahman, Q., 2005. The neurodevelopment of human sexual orientation. Neurosci. Biobehav. Rev. 29, 1057–1066.

Roof, R.L., 1993. The dentate gyrus is sexually dimorphic in prepubescent rats: testosterone plays a significant role. Brain Res. 610, 148–151.

Sakuma, Y., 2008. Neural substrates for sexual preference and motivation in the female and male rat. Ann. N. Y. Acad. Sci. 1129, 55–60.

Savic, I., Lindström, P., 2008. PET and MRI show differences in cerebral asymmetry and functional connectivity between homo- and heterosexual subjects. Proc. Natl. Acad. Sci. U. S. A. 105, 9403–9408.

Schiltz, K., Witzel, J., Northoff, G., Zierhut, K., Gubka, U., Fellmann, H., 2007. Brain pathology in pedophilic offenders: evidence of volume reduction in the right amygdala and related diencephalic structures. Arch. Gen. Psychiatry 64, 737–746.

Seto, M.C., 2012. Is pedophilia a sexual orientation? Arch. Sex. Behav. 41, 231–236.

Spape, J., Timmers, A.D., Yoon, S., Ponseti, J., Chivers, M.L., 2014. Gender-specific genital and subjective sexual arousal to prepotent sexual features in heterosexual women and men. Biol. Psychol. 102, 1–9.
Stoléru, S., Fonteille, V., Cornélis, C., Joyal, C., Moulier, V., 2012. Functional neuroimaging studies of sexual arousal and orgasm in healthy men and women: a review and meta-analysis. Neurosci. Biobehav. Rev. 36, 1481–1509.
Turkeltaub, P.E., Eickhoff, S.B., Laird, A.R., Fox, M., Wiener, M., Fox, P., 2012. Minimizing within-experiment and within-group effects in activation likelihood estimation meta-analyses. Hum. Brain Mapp. 33, 1–13.
Walter, M., Bermpohl, F., Mouras, H., Schiltz, K., Tempelmann, C., Rotte, M., et al., 2008. Distinguishing specific sexual and general emotional effects in fMRI–subcortical and cortical arousal during erotic picture viewing. Neuroimage 40, 1482–1494.
Xiong, J., Rao, S., Gao, J.H., Woldorff, M., Fox, P.T., 1998. Evaluation of hemispheric dominance for language using functional MRI: a comparison with positron emission tomography. Hum. Brain Mapp. 6, 42–58.
Zaborszky, L., Hoemke, L., Mohlberg, H., Schleicher, A., Amunts, K., Zilles, K., 2008. Stereotaxic probabilistic maps of the magnocellular cell groups in human basal forebrain. Neuroimage 42, 1127–1141.