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# The Functional Neuroanatomy of Male Psychosexual and Physiosexual Arousal: A Quantitative Meta-Analysis

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**Abstract:** Reproductive behavior is mandatory for conservation of species and mediated by a state of sexual arousal (SA), involving both complex mental processes and bodily reactions. An early neurobehavioral model of SA proposes cognitive, emotional, motivational, and autonomic components. In a comprehensive quantitative meta-analysis on previous neuroimaging findings, we provide here evidence for distinct brain networks underlying psychosexual and physiosexual arousal. Psychosexual (i.e., mental sexual) arousal recruits brain areas crucial for cognitive evaluation, top-down modulation of attention and exteroceptive sensory processing, relevance detection and affective evaluation, as well as regions implicated in the representation of urges and in triggering autonomic processes. In contrast, physiosexual (i.e., physiological sexual) arousal is mediated by regions responsible for regulation and monitoring of initiated autonomic processes and emotions and for somatosensory processing. These circuits are interconnected by subcortical structures (putamen and claustrum) that provide exchange of sensorimotor information and crossmodal processing between and within the networks. Brain deactivations may imply attenuation of introspective processes and social cognition, but be necessary to release intrinsic inhibition of SA. *Hum Brain Mapp 35:1404–1421, 2014.* 

**Key words:** male sexual arousal; penile erection; neuroimaging; activation likelihood estimation; ALE

## INTRODUCTION

The sexual instinct is mandatory for conservation of species as it provides the basis on which reproductive behavior occurs. The sexual act is mediated by a state of sexual arousal (SA) that is associated with emotional and bodily reactions. Despite or due to the difficulty of its conceptualization, SA has consistently been the focus of such endeavors from different, yet complementary perspectives.

Singer [1984] proposed a trichotomy of SA, meant "to provide starting points for theory and research", that distinguished aesthetic, approach, and genital responses. According to this model, the aesthetic response is conceived as a

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stimulus-induced hedonic feeling leading to active orientation toward the sexual incentive. The approach response includes not only body movements toward a sexual object but also the desire to achieve physical contact. With increasing proximity and likewise general somatic arousal, the approach may shade into the genital response, i.e., genital tumescence, accompanied by other autonomic–somatic reactions.

Emphasizing its cognitive aspects, Janssen et al. [2000] divided the process of SA into two main information processing stages: an appraisal stage and a response generation stage. Both stages together form the model's central pathway, which is assumed to operate automatically. As a third component, attentional processes reciprocally influence appraisal and response generation. The evoked genital response and subjective experience of SA themselves become part of the sexual stimulus and feed back into the central pathway, thus closing the circuitry of the interactive process.

Corresponding to McKenna's [1999] notion that "the brain is the master organ in sexual function", Stoléru [1999], Redouté [2000] and colleagues were the first to monitor cerebral activity during visual sexual stimulation using positron emission tomography (PET). Activations were observed in the orbitofrontal cortex (OFC), claustrum, anterior cingulate cortex (ACC), caudate, putamen, and hypothalamus. On the basis of these results, the authors postulated a neurobehavioral model of SA, consisting of cognitive, emotional, motivational, and autonomic components. Despite its plausibility, one major drawback of this theory, particularly with respect to the attribution of brain structures to its components, is that it is based on the findings of merely two studies assessing only a few subjects.

Since then, however, the number of studies investigating SA by functional neuroimaging has remarkably increased [see Stoléru et al., 2012, for an overview]. Sexual stimulation was performed through further sensory modalities such as the auditory system [e.g., Rauch et al., 1999], olfaction [e.g., Savic et al., 2001], and tactile perception [e.g., Georgiadis et al., 2010]. The subjects' brain response to sexual stimuli was assessed with respect to not only miscellaneous control stimuli and subjective SA [e.g., Bocher et al., 2001] but also physiological measures such as penile tumescence [e.g., Arnow et al., 2002] and plasma levels of sexual hormones [Seo et al., 2009]. In the same vein, the range of implicated brain areas has likewise enormously broadened. By now, it can be stated that almost any brain region has been implicated in SA. This heterogeneity of findings is most likely due to specific design properties. For instance, differences between event-related and block design employing erotic stimuli have been shown, while keeping all remaining experimental parameters constant [Bühler et al., 2008]. Similarly, divergences in imaging techniques, sample sizes, significance thresholds, regressors, and, last but not least, variation in the applied contrasts as well as the presented erotic stimuli imply heterogeneous results. Although variations in the employed experimental paradigms are expedient and necessary to assess different aspects of SA, they may complicate the identification of key regions. A summary of the hitherto existing data is thus highly needed to delineate neural networks of SA.

Mere reviews, however, run the risk of being subjective and lack the capability of quantitative assessment. For an objective assessment of interstudy concordance, automated meta-analyses that quantify the level of concordance and allow to locate the "hot-spots" (i.e., brain regions) of significant convergence in a testable manner are hence preferable. Activation likelihood estimation (ALE) as introduced to neuroimaging by Turkeltaub et al. [2002] and subsequently refined [Eickhoff et al., 2009, 2011, 2012; Laird et al., 2005; Turkeltaub et al., 2012] meets these demands and represents the most widely used approach for such quantitative integration of neuroimaging findings.

Given its complexity, the phenomenon of SA is very likely to originate from differing neural networks responsible for specific aspects of sexual behavior [Georgiadis and Kringelbach, 2012]. These networks should be dissociable, a statistical separation has not been undertaken though. In this regard, the fundamental question raises: How can the networks be isolated in a conceptually meaningful way? Such endeavor seems complicated, since SA can be divided into neurophenomenological components [Stoléru et al., 2012] but also different stages [Georgiadis and Kringelbach, 2012]. However, although the introduced psychological concepts of SA [Janssen et al., 2000; Singer, 1984] differ in certain aspects, they share common ground by assuming psychic (from here on referred to as "psychosexual") and physical (from here on referred to as "physiosexual") processes. Hence, disentangling brain regions related to psychosexual arousal from those related to physiosexual arousal was the main objective of the present study.

A meta-analysis on psychosexual arousal aimed to represent the neural correlates of the core mental operations during the processing of sexual stimuli. According to Singer [1984], SA "may take place through central processes, independent of somatic and visceral sensation". It thus also includes early automatic appraisal and attentional phenomena, which may eventually "lead to subjective experience of sexual arousal and genital response" [Janssen et al., 2000]. Consequently, all experiments that contrasted sexual stimuli against (nonsexual) control stimuli, irrespectively of stimulus duration, were assumed to represent psychosexual arousal. As there seems to be consensus that penile tumescence and turgidity are not only the most obvious but also valid indicators of male physiosexual arousal [Freund et al., 1974; Furr, 1991; Harris et al., 1992; Kuban et al., 1999; McAnulty and Adams, 1992; McConaghy, 1989; Wheeler and Rubin, 1987], results of studies aiming to identify brain areas whose activity was correlated with penile erection (PE) were meta-analytically assessed to delineate the neural basis of physiosexual arousal. To disentangle the corresponding neural networks, we then tested for differences and significant overlap between these analyses. To bring into focus brain deactivations during SA, which have been rather neglected

in the literature, we additionally tested for significant convergence of reported deactivated brain regions during SA. The assessment of brain deactivations during SA may provide illuminating insights especially into regulatory mechanisms and antagonistic networks and hence potentially also into the potential pathologies of SA such as syndromes involving hypersexuality [Stoléru et al., 2012].

In contrast to previous reports [Kühn and Gallinat, 2011; Stoléru et al., 2012], we excluded experiments (within a particular study, i.e., paper) focusing on the neural correlates of subjective SA [cf., Stoléru et al., 2012] to increase homogeneity, since the present meta-analysis of psychosexual arousal aimed to reflect mental processes during sexual stimulation in general, independently from subjective emotional intensity. However, we did not restrict the study selection to a certain imaging technique [unlike Kühn and Gallinat, 2011] to maximize statistical power.

## METHODS

### Study Selection

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 "erotic", "sexual", "penile tumescence", "penile turgidity", or "penile erection" 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 review articles and the identified papers. Experiments were considered relevant when they were intended to induce SA by visual sexual stimulation (1) and/or measured PE (2) in heterosexual men, applying the following constraints:

1. Activation and deactivation data resulting from subtractions between sexual and control conditions were included if the subjects' primary task was to merely view the visual stimuli. Experiments focusing on other tasks such as the inhibition of SA during visual sexual stimulation [e.g., Beauregard et al., 2001] were excluded.
2. Activation and deactivation data related to PE were included if an external variable such as penile turgidity had been collected in the experiments. Excluded were studies that did not relate the external variable to imaging data [e.g., Tsujimura et al., 2006]. Please note that here sexual stimulation was not restricted to the visual system.

Additional inclusion and exclusion criteria were as follows:

- Only studies reporting results of whole-brain group analyses as coordinates referring to a standard reference space [Talairach/Tournoux or Montreal Neurological Institute (MNI)] were included. Reports including less than five subjects [e.g., Montorsi et al., 2003b], results of region-of-interest analyses [e.g., Stark et al., 2005], and studies not reporting stereotaxic coordinates [e.g., Montorsi et al., 2003a] were excluded.
- Only data from healthy men were included, while results from patients and contrasts comparing healthy heterosexual men with another group (e.g., women) were excluded. However, when studies of the latter comprised a group of healthy heterosexual men, their data were included if separately reported or if the authors provided us with the necessary information upon being contacted.
- Data from conditions with pharmacological manipulations were excluded.
- Since virtually all paradigms of papers on PE were found to induce SA using visual stimuli, studies employing olfactory or acoustic sexual stimulation were excluded to allow for a well-balanced comparison between psychological and physiological components of SA. Moreover, restriction to VSS assured homogeneity among studies by preventing heterogeneity associated with the few experiments employing other stimulus modalities. Such restriction is also in line with the strong visual bias in human sexual behavior [Georgiadis and Kringelbach, 2012].

Based on these criteria, 20 studies were found to be eligible for inclusion into the meta-analysis (cf., Table I). Only fMRI and PET but no MEG (which might considerably differ from fMRI and PET with regard to spatial uncertainty) studies fulfilled our search criteria. Conceptually, it is unproblematic to include both fMRI and PET techniques, because there should be no systematic shift in precision. 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]. Some studies also concomitantly gathered other physiological data such as respiration rate [Arnow et al., 2002], heart rate [Arnow et al., 2002; Redouté et al., 2000], blood pressure [Redouté et al., 2000], skin conductance [Klucken et al., 2009], and testosterone levels [Redouté et al., 2000], but did not relate those to the imaging data. Together, these studies reported 827 activation foci obtained from 41 individual experiments (with a "study" referring to a paper, an "experiment" referring to an individual contrast reported in this paper) as well as 132 deactivation foci obtained from 20 individual experiments. Differences in coordinate spaces (Talairach vs. MNI space) were accounted for by transforming coordinates reported in Talairach space into MNI coordinates using a linear transformation [Laird et al., 2010; Lancaster et al., 2007]. As noted above, convergence of reported activation coordinates was analyzed for the main effects of visually evoked

**TABLE I. Studies included in the meta-analysis**

| First author | Year | Subjects | Imaging method | Experiment/Regressor | Foci | |
|---|---|---|---|---|---|---|
| | | | | | Activations | Deactivations |
| Arnow | 2002 | 11 | fMRI | Penile turgidity | 21 | 0 |
| Beauregard | 2001 | 10 | fMRI | VSS > Neutral | 6 | N/A |
| Bocher | 2001 | 10 | PET | VSS > Baseline | 8 | 8 |
| | | 10 | PET | VSS > Nature | 7 | 8 |
| | | 10 | PET | VSS > Talkshow | 6 | 6 |
| | | 10 | PET | Sensation of erection | 9 | N/A |
| Brunetti | 2008 | 18 | fMRI | VSS > Sport | 26 | N/A |
| Bühler | 2008 | 10 | fMRI | VSS > Neutral (block) | 9 | 1 |
| | | 10 | fMRI | VSS > Neutral (event) | 14 | 0 |
| Ferretti | 2005 | 9 | fMRI | VSS > Sport (videos) | 28 | N/A |
| | | 9 | fMRI | VSS > Sport (pictures) | 17 | N/A |
| | | 9 | fMRI | Penile turgidity | 28 | N/A |
| | | 9 | fMRI | Onset of erection | 10 | N/A |
| | | 9 | fMRI | Sustained erection | 8 | N/A |
| Georgiadis | 2010 | 16 | ASL | Penile circumference | 16 | 10 |
| | | 16 | ASL | Penile circumferential change | 14 | 4 |
| Hu | 2008 | 10 | fMRI | VSS > Baseline | 32 | N/A |
| Kagerer | 2011 | 10 | fMRI | VSS > Neutral | 38 | 1 |
| Karama | 2002 | 10 | fMRI | VSS > Neutral | 18 | N/A |
| Karama | 2011 | 18 | fMRI | VSS > Neutral | 71 | N/A |
| | | 18 | fMRI | VSS > Neutral/Humor/Disgust | 18 | N/A |
| Kim | 2006 | 10 | fMRI | VSS > Sport | 13 | N/A |
| Klucken | 2009 | 20 | fMRI | VSS > Neutral | 12 | 2 |
| Moulier | 2006 | 10 | fMRI | VSS > Neutral | 24 | 3 |
| | | 6 | fMRI | Penile tumescence (lag = 0 s) | 31 | 21 |
| | | 6 | fMRI | Penile tumescence (lag = 20 s) | 21 | N/A |
| Mouras | 2008 | 8 | fMRI | VSS > Neutral/Humor (block) | 4 | N/A |
| | | 8 | fMRI | VSS > Neutral/Humor (event) | 18 | N/A |
| | | 8 | fMRI | Penile tumescence (lag = 0 s) | 48 | 3 |
| | | 8 | fMRI | Penile tumescence (lag = 20 s) | 41 | 13 |
| Paul | 2008 | 12 | fMRI | VSS > Neutral | 15 | N/A |
| Redouté | 2000 | 9 | PET | VSS > Neutral | 20 | 16 |
| | | 9 | PET | VSS > Neutral/Humor (HA) | 14 | 14 |
| | | 9 | PET | VSS > Neutral/Humor (MA) | 7 | 2 |
| | | 9 | PET | Penile circumference | 29 | 20 |
| | | 9 | PET | Penile circumference[a] | 3 | N/A |
| Seo | 2009 | 12 | fMRI | VSS > Nonerotic | 39 | 0 |
| Seo | 2010 | 12 | fMRI | VSS > Nonerotic | 26 | 0 |
| Sundaram | 2010 | 14 | fMRI | VSS > Baseline (early stage) | 19 | N/A |
| | | 14 | fMRI | VSS > Baseline (mid stage) | 19 | N/A |
| | | 14 | fMRI | VSS > Baseline (late stage) | 20 | N/A |

ASL, arterial spin labeling; fMRI, functional magnetic resonance imaging; HA, highly arousing; MA, moderately arousing; N/A, not available; PET, positron emission tomography; VSS, visual sexual stimuli.
[a]Corrected for effect of conditions.

SA (28 experiments, 548 foci) and PE (13 experiments, 279 foci), respectively, as well as for their differences and commonalities. In addition, the convergence of reported deactivation foci was separately assessed. Since relatively few papers presented deactivations, it was not possible to distinguish between deactivations related to visual sexual

stimulation and those to PE, but foci from both were pooled. Hence, areas of convergent deactivation relate to both aspects of SA.

### 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., 2009; 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., 2009]. 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 [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 family-wise error (FWE) corrected threshold of $P < 0.05$ on cluster level [cluster-forming threshold: $P < 0.001$ at voxel level, cf., Eickhoff et al., 2012] and transformed into $Z$ scores for display.

### Differences and Conjunction Analyses

Differences between psychosexual and physiosexual arousal were tested by first performing separate ALE meta-analyses for both (visual sexual stimulation minus visual control stimulation/correlations with measures of PE) and computing the voxelwise difference between the ensuing ALE maps. The experiments contributing to either analysis were then pooled and randomly divided into two groups of the same size as the sets of contrasted experiments [Eickhoff et al., 2011]. Voxelwise ALE scores for these two randomly assembled groups were subtracted from each other and recorded. Repeating this process 10,000 times yielded an empirical null distribution of ALE-score differences between the two conditions. Based on this permutation procedure, the map of true differences was then thresholded at a posterior probability of $P > 0.95$ for a true difference between the two samples. Surviving voxels were inclusively masked by the respective main effect, i.e., the significant effect of the ALE analysis for the minuend [Caspers et al., 2010; Eickhoff et al., 2011; Rottschy et al., 2012]. In addition, a cluster extent threshold of $k \geq 10$ voxels was applied to eliminate minor, presumably incidental findings. A conjunction analysis testing for convergence between the two different meta-analyses (visual sexual stimulation minus visual control stimulation/correlations with measures of PE) employed inference by the minimum statistic, i.e., computing intersection of the thresholded $Z$ maps [Caspers et al., 2010]. Here, the significance threshold was set to $P < 0.05$, FWE corrected on cluster level (cluster-forming threshold: $P < 0.001$ at voxel level).

### Anatomical Labeling

Resulting brain regions were macroanatomically labeled by reference to the probabilistic Harvard-Oxford atlas [Desikan et al., 2006] included with FSLView v3.1 (http://www.fmrib.ox.ac.uk/fsl/fslview/index.html). For a more precise allocation, we made use of cytoarchitectonic maps of the human brain provided by the SPM Anatomy Toolbox [Eickhoff et al., 2005, 2006d, 2007]. Hereby, activations and deactivations were assigned to the most probable histologically defined area at the respective location. This probabilistic and histology-based anatomical labeling is reported in each table; references to details of the cytoarchitecture are given in the respective table notes.

## RESULTS

### Psychosexual Arousal (Visual Sexual Stimulation Minus Visual Control Stimulation)

Across 28 experiments (i.e., individual contrasts), convergent brain activations during SA induced by visually presented erotica were observed in a widespread network of cortical and subcortical brain areas (cf., Fig. 1 and, also for histological assignment, Table II). Corresponding to the visual stimulus modality and in spite of the fact that virtually all included experiments represented contrasts controlling for visual input, robust activity was found in inferior temporal and lateral occipital visual association cortices. In addition, the superior parietal lobules (SPLs) and lateral prefrontal cortex (LPFC), mainly comprising the middle and inferior frontal gyri, exhibited bilaterally increased activity. Significant convergence of activation on

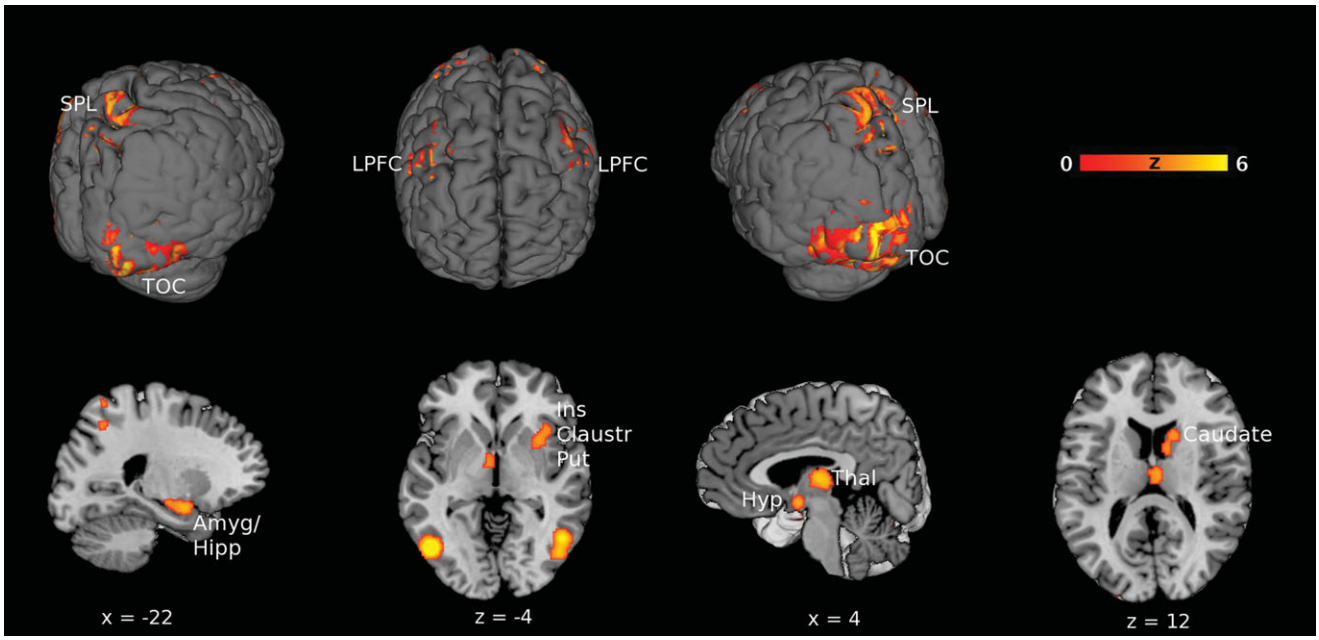


**Figure 1.**

Brain map of male psychosexual (i.e., mental sexual) arousal. Significant clusters where the ALE analysis revealed convergence of brain activation ($P < 0.05$, FWE corrected) during male heterosexual arousal induced by visual sexual stimuli (VSS) (cf., Table II). Brain slices are shown at coordinates ($x$, $y$, $z$) in Montreal Neurological Institute (MNI) space. Amyg, amygdala; Claustr, claustrum; Hipp, hippocampus; Hyp, hypothalamus; Ins, insula; LPFC, lateral prefrontal cortex; Put, putamen; SPL, superior parietal lobule; Thal, thalamus; TOC, temporo-occipital cortex.

**TABLE II. Brain map of male psychosexual arousal**

| Macroanatomical location | Cytoarchitectonic location | Cluster size in voxels | MNI coordinates | | | Z score |
|---|---|---|---|---|---|---|
| | | | $x$ | $y$ | $z$ | |
| R + L Thalamus (Th-Temporal/Prefrontal) | | 698 | 4 | −16 | 8 | 5.08 |
| L + R Hypothalamus | | | −4 | −2 | −12 | 4.65 |
| R Putamen/Claustrum | | | 32 | 12 | −4 | 4.10 |
| R Insular cortex | | | 38 | 18 | −4 | 3.79 |
| R Inferior lateral occipital cortex | | 695 | 50 | −64 | −8 | 6.26 |
| R Temporal occipital fusiform cortex | | | 46 | −54 | −20 | 5.30 |
| L Inferior lateral occipital cortex | | 584 | −48 | −68 | −4 | 8.23 |
| l Occipital fusiform gyrus | | | −38 | −78 | −16 | 4.51 |
| L Hippocampus | FD/CA | 261 | −18 | −16 | −14 | 5.25 |
| L Amygdala | SF/LB | | −22 | −4 | −20 | 4.71 |
| L Superior parietal lobule | 7A/hIP3/7PC | 248 | −30 | −56 | 50 | 5.18 |
| L Inferior lateral occipital cortex | | 170 | −28 | −90 | 6 | 4.63 |
| R Inferior/Middle frontal gyrus | Area 44 | 132 | 50 | 12 | 32 | 4.39 |
| R Superior parietal lobule | 7PC/7A/hIP3 | 128 | 34 | −52 | 56 | 4.84 |
| R Caudate | | 108 | 16 | 14 | 12 | 3.91 |
| L Inferior temporooccipital cortex | | 105 | −44 | −52 | −18 | 5.00 |
| L Precentral/Inferior frontal gyrus | Area 44 | 104 | −50 | 8 | 30 | 4.69 |

Convergent brain activations during sexual arousal induced by visual sexual stimuli (VSS) according to activation likelihood estimation (ALE) across 28 experiments in healthy heterosexual men. FWE corrected on cluster level ($P < 0.05$) with a cluster-forming threshold of $P < 0.001$ (uncorrected). Coordinates ($x$, $y$, $z$) represent peaks of convergence within a cluster. For detailed information on cytoarchitectonics and connectivity, see: Amunts et al. [1999] (Area 44), [2005] (CA, FD, LB, SF); Behrens et al. [2003] (Th-Prefrontal, Th-Temporal); Scheperjans et al. [2008a,b] (7A, 7PC, hIP3).
L, left; MNI, Montreal Neurological Institute; R, right.

**TABLE III. Brain map of male physiosexual arousal**

| Macroanatomical location | Cytoarchitectonic location | Cluster size in voxels | MNI coordinates | | | Z score |
|---|---|---|---|---|---|---|
| | | | x | y | z | |
| R Insular cortex | | 572 | 44 | −2 | 4 | 5.25 |
| R Putamen/Claustrum | | | 32 | 4 | −6 | 4.46 |
| R Insular cortex | | | 46 | 12 | −6 | 3.81 |
| L Insular cortex | | 461 | −44 | −2 | 6 | 5.90 |
| L Claustrum | | | −32 | 8 | 0 | 3.94 |
| L Insular cortex | | | −34 | 18 | 0 | 3.42 |
| L Parietal opercular cortex | OP 1/PFop | 259 | −54 | −22 | 18 | 5.85 |
| aMCC | | 131 | 2 | 16 | 36 | 5.12 |
| R Parietal opercular cortex | OP 1/PFop | 117 | 56 | −20 | 20 | 4.88 |
| sgACC | | 102 | 4 | 26 | −12 | 4.38 |

Convergent brain activity positively correlating with penile erection (PE) according to activation likelihood estimation (ALE) across 13 experiments in healthy heterosexual men. FWE corrected on cluster level ($P < 0.05$) with a cluster-forming threshold of $P < 0.001$ (uncorrected). Coordinates ($x$, $y$, $z$) represent peaks of convergence within a cluster. For detailed information on cytoarchitectonics, see: Caspers et al. [2006, 2008] (PFop); Eickhoff et al. [2006a,b] (OP 1).
aMCC, anterior midcingulate cortex; L, left; MNI, Montreal Neurological Institute; R, right; sgACC, subgenual anterior cingulate cortex.

the (anterior) insular cortex, in contrast, was restricted to the right hemisphere. The respective large cluster also extended into the right claustrum and putamen as well as thalamus and hypothalamus. Although some voxels (~5% of the cluster) were histologically allocated to the right amygdala, no local maximum could be observed in the latter region. The left amygdala, however, featured a distinct local maximum of convergence, even though this cluster likewise extended further into the hippocampus. Finally, there was also significant convergence of VSS-induced activity in the right caudate.

## Physiosexual Arousal (Correlations With Measures of Penile Erection)

Our meta-analysis identified several areas where brain activity was consistently positively correlated with PE (cf., Table III). Bilateral convergent activation was observed in the insular cortex. Significant convergence extended further into the claustrum bilaterally and into the basal ganglia (putamen) on the right hemisphere, showing distinct local maxima, respectively. There was also significant convergence in the anterior midcingulate cortex (aMCC) and

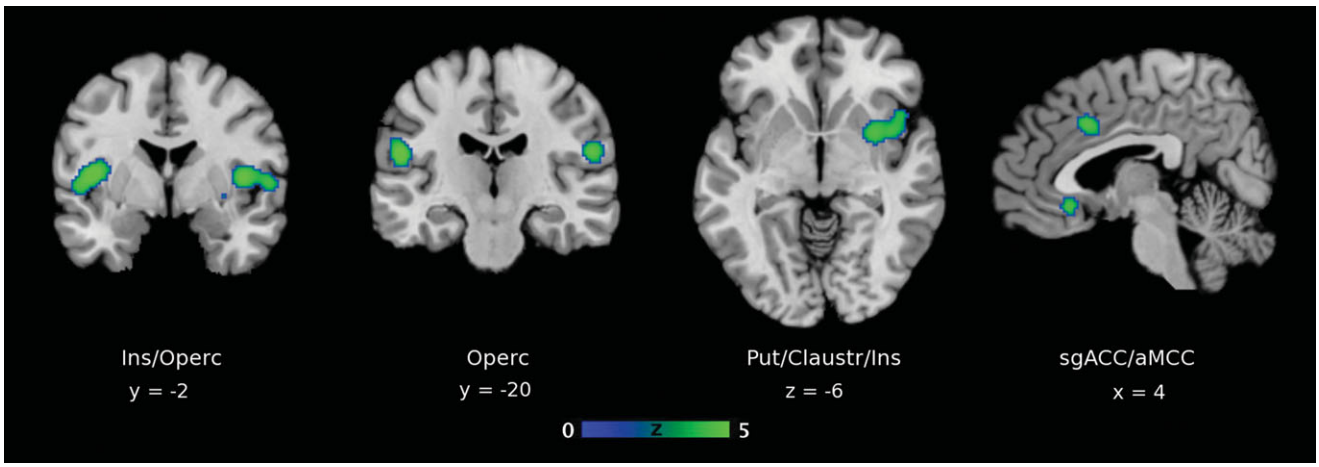


**Figure 2.**
Brain map of male physiosexual (i.e., physiological sexual) arousal. Significant clusters where the ALE analysis revealed convergence of brain activity ($P < 0.05$, FWE corrected) positively correlating with penile erection (PE) in heterosexual men (cf., Table III). Brain slices are shown at coordinates ($x$, $y$, $z$) in Montreal Neurological Institute (MNI) space. aMCC, anterior midcingulate cortex; Claustr, claustrum; Ins, insula; Operc, operculum; sgACC, subgenual anterior cingulate cortex.

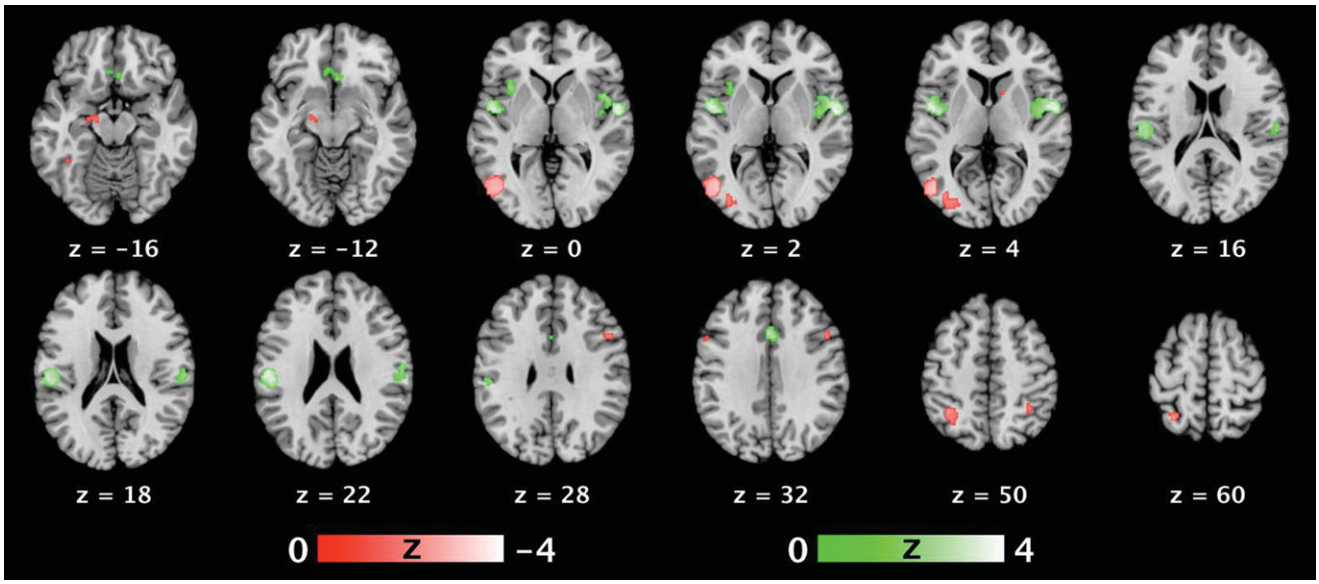


**Figure 3.**

Differences between psychosexual and physiosexual arousal. Comparison of brain activity between psychosexual (VSS) and physiosexual (PE) arousal as revealed by subtraction [VSS > PE (red) and PE > VSS (green)] analyses (cf., Table IV). Brain slices are shown at coordinates (*x*, *y*, *z*) in Montreal Neurological Institute (MNI) space. Significance threshold set to $P > 0.95$ posterior probability, cluster size $k \geq 10$ voxels. PE, penile erection; VSS, visual sexual stimulation.

subgenual portion of the ACC (sgACC) (cf., Fig. 2). The labeling of the latter region has been somewhat inconsistent in the literature, and also "ventromedial prefrontal cortex (vmPFC)" and "medial orbitofrontal cortex (mOFC)" have been used. To avoid ambiguities, we stick to Palomero-Gallagher et al. [2009], who count not only area 25 but also the most ventral portions of areas 24, 32, and 33 among "sgACC". Furthermore, significant convergence of activation related to physiosexual arousal was found in the parietal operculum. Since PET as compared with fMRI might produce less artifacts in prefrontal regions such as sgACC, we rerun the analysis leaving out the PET experiments. However, the results did not change.

## Comparison Between Psychosexual and Physiosexual Arousal

Subtraction analyses between brain activations elicited by VSS and those related to PE revealed significantly differently strong convergence in most of the areas mentioned in sections "Psychosexual Arousal" and "Physiosexual Arousal" (cf., Fig. 3 and Table IV). While VSS-induced SA was significantly stronger associated with activity in the visual cortex, left amygdalohippocampal complex and midbrain, bilateral SPL, right caudate, and right LPFC, PE was significantly stronger associated with activity in the bilateral insular and opercular cortex as well as in the aMCC and sgACC. Notably, no significant differences emerged in thalamus, hypothalamus, right claustrum, or putamen. It has to be considered that experiments on both psychosexual and physiosexual arousal employed quite variable durations of sexual stimulation. A comparison of stimulation durations between the experiments pertaining to psychosexual with those to physiosexual arousal barely reached significance ($P = 0.048$, two-tailed). The mean stimulation durations ($M = 93 \pm 71$ s vs. $144 \pm 82$ s), however, indicated that both experimental paradigms involve tonic rather than phasic attention. Hence, the observed differences are unlike to primarily emerge from a systematic discrepancy in stimulus duration and associated appraisal and attentional phenomena.

The conjunction analysis revealed a significant overlap between the meta-analyses on psychosexual and physiosexual arousal in the right basal ganglia. In particular, the right putamen and adjacent claustrum appeared to be consistently active in both aspects of SA, that is, VSS and PE (cf., Fig. 4 and Table IV).

## Deactivations During Sexual Arousal

A main effect for convergent brain deactivation during SA was found in the temporal and parietal lobes (cf., Table V and Fig. 5): The left superior temporal gyrus (STG) and right inferior temporal sulcus (ITS) showed constantly reduced activity across experiments. Furthermore, significant convergence of deactivation was observed in a cluster located in the left middle hippocampus. Further deactivations converged in two clusters in the left angular gyrus (parietal

**TABLE IV. Comparison between psychosexual and physiosexual arousal**

| Contrast | Macroanatomical location | Cytoarchitectonic location | Cluster size in Voxels | MNI coordinates | | | Z score |
|---|---|---|---|---|---|---|---|
| | | | | *x* | *y* | *z* | |
| VSS > PE | L Inferior lateral occipital cortex | | 304 | −46 | −76 | 2 | 3.22 |
| | L Superior parietal lobule | 7A/hIP3/7PC | 140 | −30 | −58 | 60 | 2.50 |
| | L Inferior lateral occipital cortex | | 65 | −38 | −78 | 4 | 2.56 |
| | R Superior parietal lobule | 7PC/hIP3 | 46 | 36 | −50 | 50 | 2.01 |
| | R Caudate | | 32 | 12 | 10 | 4 | 2.18 |
| | R Inferior frontal gyrus, opercular | Area 44 | 28 | 48 | 14 | 28 | 2.06 |
| | L Amygdala/Midbrain | SF | 26 | −14 | −12 | −16 | 2.02 |
| | L Hippocampus | CA | | −22 | −14 | −16 | 1.70 |
| PE > VSS | R Insular/Opercular cortex | | 348 | 58 | −6 | 2 | 4.04 |
| | L Insular/Opercular cortex | | 294 | −50 | −4 | 4 | 3.78 |
| | L Parietal opercular cortex | OP 1/PFop | 249 | −56 | −18 | 22 | 3.60 |
| | aMCC | | 115 | 0 | 16 | 32 | 3.00 |
| | R Parietal opercular cortex | OP 1/PFop | 75 | 62 | −20 | 18 | 2.62 |
| | sgACC | | 39 | 4 | 22 | −12 | 2.27 |
| | L Insular cortex | | 27 | −36 | 14 | 0 | 2.59 |
| VSS ∩ PE | R Claustrum | | 55 | 32 | 10 | −4 | 3.81 |
| | R Putamen | | | 30 | 6 | −6 | 3.59 |

Subtraction (VSS > PE, PE > VSS) and conjunction (VSS ∩ PE) analyses of activation likelihood estimation (ALE) maps between psychosexual (VSS) and physiosexual (PE) arousal. Significance threshold set to $P > 0.95$ posterior probability, cluster size $k \geq 10$ voxels, for the subtraction analysis. For the conjunction analysis, FWE correction on cluster level ($P < 0.05$) with a cluster-forming threshold of $P < 0.001$ (uncorrected) was applied. Coordinates ($x$, $y$, $z$) represent peaks of convergence within a cluster. For detailed information on cytoarchitectonics, see: Amunts et al. [1999] (Area 44), [2005] (CA, SF); Caspers et al. [2006, 2008] (PFop); Eickhoff et al. [2006a,b] (OP 1); Scheperjans et al. [2008a,b] (7A, 7PC, hIP3).
aMCC, anterior midcingulate cortex; L, left; MNI, Montreal Neurological Institute; PE, penile erection; R, right; sgACC, subgenual anterior cingulate cortex; VSS, visual sexual stimulation.

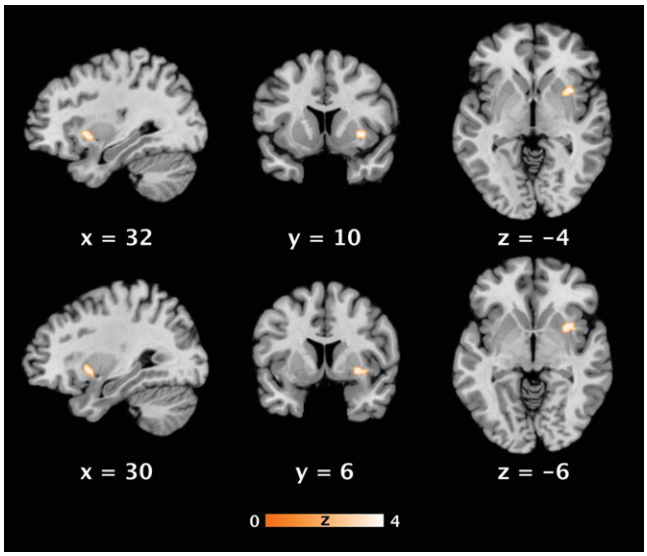


**Figure 4.**
Overlap of psychosexual and physiosexual arousal. Location of significant convergent brain activity ($P < 0.05$, FWE corrected) in both psychosexual (VSS) and physiosexual (PE) arousal as revealed by conjunction (VSS ∩ PE) analysis (cf., Table IV). Brain slices are shown at coordinates ($x$, $y$, $z$) in Montreal Neurological Institute (MNI) space. PE, penile erection; VSS, visual sexual stimulation.

cortex) and the retrosplenial cortex (RSC) (posterior cingulate gyrus).

## DISCUSSION

### A Neural Network for Sexual Stimulus-Driven Processing

The present study sought to disentangle brain activity related to psychosexual arousal from that related to physiosexual arousal. ALE meta-analyses of functional neuroimaging studies on SA revealed two statistically dissociable neural networks relating to psychological and physiological aspects. Moreover, it could be shown that both networks share putamen and claustrum as common structures. In addition, a limited set of brain areas, located in the temporal and parietal cortices, was found to be deactivated during SA.

#### *Corticolimbic pathway*

The meta-analysis of psychosexual arousal demonstrates that visual sexual stimulation recruits a broad network of cortical and subcortical brain areas in heterosexual men. Convergence of activation foci in the temporo-occipital visual cortex most likely reflects attentional enhancement of

**TABLE V. Cerebral deactivations during male sexual arousal**

| Macroanatomical location | Cytoarchitectonic location | Cluster size in voxels | MNI coordinates | | | Z score |
|---|---|---|---|---|---|---|
| | | | x | y | z | |
| R Superior temporal gyrus | | 207 | 52 | −8 | −12 | 5.12 |
| L Angular gyrus | PGp/PGa | 203 | −52 | −56 | 24 | 4.50 |
| L Hippocampus | CA | 122 | −36 | −18 | −22 | 4.96 |
| L Retrosplenial cortex | | 117 | −18 | −54 | 14 | 5.97 |
| L Anterior inferior temporal sulcus | | 110 | −58 | −8 | −32 | 4.88 |

Convergent cerebral deactivations according to activation likelihood estimation (ALE) across 20 experiments in healthy heterosexual men during psychosexual (VSS) and physiosexual (PE) arousal. FWE corrected on cluster level ($P < 0.05$) with a cluster-forming threshold of $P < 0.001$ (uncorrected). Coordinates ($x$, $y$, $z$) represent peaks of convergence within a cluster. For detailed information on cytoarchitectonics, see: Amunts et al. [2005] (CA); Caspers et al. [2006, 2008] (PGa, PGp).
L, left; MNI, Montreal Neurological Institute; PE, penile erection; R, right; VSS, visual sexual stimulation.

visual processing that should be triggered by the behavioral saliency of the sexual material but not be specific to it [Kastner et al., 1999]. The same holds true for the SPLs that have been shown to modulate activity in the visual system by top-down signals, thus representing a source of attentional control [Culham and Kanwisher, 2001] over the visual cortex [Kastner et al., 1999]. It may be speculated that the attention modulation during SA mediated by the SPL is triggered by the LPFC, where the stimulus is evaluated and categorized as a sexual incentive. Such a view would be endorsed by the pivotal role of the LPFC in categorization of visual stimuli [Freedman et al., 2001]. Moreover, lateral prefrontal neurons have been shown to encode category-based reward information [Pan et al., 2008]. In addition, the importance of the hippocampus has been suggested for retrieving stimuli from well-established categories, among which also visual erotica may be counted. This hippocampal function in making category judgments is fairly automatic [DeGutis and D'Esposito, 2007] and would be in line with the observed convergent activation in the hippocampus in response to visual stimuli from a sexual category. However, it must be acknowledged that there is also some evidence that the LPFC is implicated in the inhibition of fully developed SA [Beauregard et al., 2001], thus exercising cognitive control in this context. Control mechanisms may particularly be activated in a situation in which the subject assumes that his SA is observed by the investigator. Relating to this, also feelings of guilt and shame might be represented in the LPFC [Finger et al., 2006; Michl et al., 2012].

### *Limbic modulation*

The cluster of consistent activation comprising the hippocampus, which fMRI as well as PET studies and block-

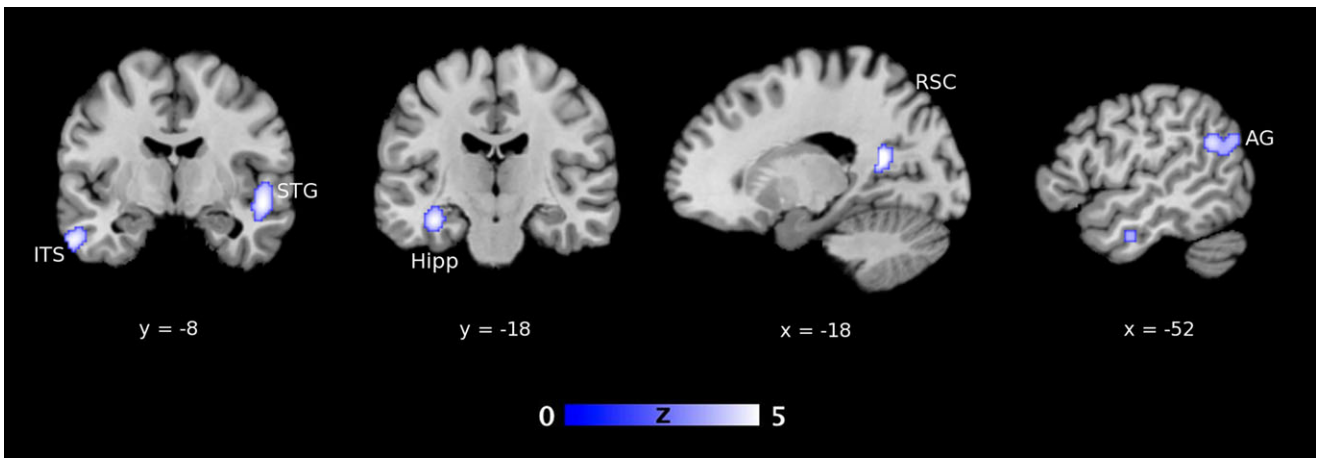


**Figure 5.**
Cerebral deactivations during male sexual arousal. Significant clusters where the ALE analysis revealed convergence of brain deactivation ($P < 0.05$, FWE corrected) during psychosexual (VSS) and physiosexual (PE) arousal in heterosexual men (cf., Table V). Brain slices are shown at coordinates in Montreal Neurological Institute (MNI) space. AG, angular gyrus; Hipp, hippocampus; ITS, inferior temporal sulcus; PE, penile erection; RSC, retrosplenial cortex; STG, superior temporal gyrus; VSS, visual sexual stimulation.

as well as event-related-designed experiments contributed to [Brunetti et al., 2008; Ferretti et al., 2005; Karama et al., 2002, 2011; Klucken et al., 2009; Redouté et al., 2000; Seo et al., 2009; Sundaram et al., 2010], extended into the amygdala showing a local maximum. The amygdala, which we found to respond consistently to VSS, might act as an impellent factor of attention modulation in SA. Amygdala activity during visual sexual stimulation also fits well with the involvement of the amygdala in social and emotional relevance detection irrespective of the modality of sensory input [Ball et al., 2007; Bzdok et al., 2011]. It has thus been proposed that in affective visual processing, the amygdala primarily coordinates the function of brain networks evaluating stimulus significance [Pessoa and Adolphs, 2010]. In addition, there is strong evidence that amygdala activity is associated only with a general emotional component during SA but not modulated by the stimulus' specific sexual intensity [Walter et al., 2008b].

### *Diencephalic processing*

A general feeling of pleasure during SA presumably also relates to convergent activation observed in the mediodorsal thalamus: Similarly to the amygdala, activity within this part of the thalamus has been shown to correlate with subjective emotional involvement during SA, whereas a relationship with perceived sexual intensity is not evident [Walter et al., 2008b]. Furthermore, a previous meta-analysis including subjective aspects of SA revealed a large cluster of convergent activation in the mediodorsal thalamus [Stoléru et al., 2012], and a recent meta-analysis has shown that subjective pleasantness in general is associated with thalamic activation [Kühn and Gallinat, 2012].

While brain regions mentioned thus far seem to relate to rather nonspecific components of cognitive and emotional processing during SA, it stands to reason that also the particular sexual quality of stimuli should be reflected in brain activity. In this context, the hypothalamus may play a key role in representing more specific effects of sexual intensity as its activity has been shown to correlate with subjective sexual valence [Karama et al., 2002; Walter et al., 2008b]. This specificity seems reasonable, given the hypothalamus' fundamental role in sexual preferences [LeVay, 1991; Swaab, 2008] and behavior [Balthazart and Ball, 2007]. Furthermore, the hypothalamus is assumed to trigger autonomic responses to sexual stimuli [Ferretti et al., 2005].

### *Subcortical telencephalic routing*

Similarly, the striatum, i.e., caudate and putamen, that were likewise revealed by our analysis, are putatively involved in specific processing of sexual intensity [Walter et al., 2008b]. Moreover, the caudate has been implicated in the regulation of sexual urge [Karama et al., 2002; Redouté et al., 2000; Stoléru et al., 1999], which is supported by the observation of a reduced caudatal response to VSS in persons with impaired sex drive [Redouté et al., 2005; Stoléru et al., 2003]. On a more general level, these subcortical telencephalic structures like the basal ganglia and claustrum also seem to represent important nodes of the functional anatomy of urges [Jackson et al., 2011] and might thus contribute to development of such urges, i.e., desires, in the context of sexually relevant sensory stimuli.

### *Insular integration*

It has been proposed that awareness is a defining feature of an urge [de Haan, 2011], which is certainly true for sexual desires. In this context, the insular cortex has been shown to be reliably activated in paradigms inducing an urge to act [Jackson et al., 2011]. More precisely, activity of the anterior insula cortex is assumed to be particularly associated with the awareness of such "urges for action" [Jackson et al., 2011]. While stimulus-driven processes of appraisal and emotion generation may run unconsciously during SA [Damasio et al., 2000; Janssen et al., 2000], it seems therefore likely that awareness of the resulting bodily and particularly affective state is engendered in the (right) anterior insula [Craig, 2010; Kurth et al., 2010]. Such awareness of the arising sexual urges may also be seen as a consequence of changes in the involuntary nervous system that are monitored in the anterior insular cortex [Craig, 2011]. Notably, the convergence of activation foci in the right (but not left) anterior insular cortex is in line with the hypotheses of an asymmetric involvement of the insula in emotional processing, as it has been argued that in particular the right-sided insula may represent "aroused" or "sympathetic" emotional feelings [Craig, 2005], which would match the processes of SA.

In summary, the ALE results suggest a brain network of psychosexual (i.e., mental sexual) arousal formed by several distinct neurofunctional components. Based on the meta-analytic findings, we propose the following sequence of sexual stimulus-driven processing: A potentially sexual stimulus is categorized through cognitive and memory-guided evaluation (LPFC, hippocampus), which induces attention focusing on the sexual target and top-down modulation of sensory processing (temporo-occipital cortex, SPL). These processes are presumably triggered by relevance detection and affective evaluation (amygdala, thalamus). It may be speculated that, based on autonomic responses (hypothalamus), the thereby resulting sexual urge (basal ganglia) finally ends in the awareness of SA (anterior insula).

## A Neural Network for Sexual Autonomic Regulation

It is striking that the ALE meta-analysis on the neural correlates of PE revealed convergence of activation in several regions that are distinct from those related to

processing of VSS. The objectivization of differential activity by the ALE subtraction analysis is noteworthy, since visual sexual stimulation may also lead to autonomic–somatic arousal. Such difference indicates that contrasting VSS against control stimuli primarily assesses psychological processes associated with SA (i.e., psychosexual arousal), whereas regression analyses on PE encompass the bodily changes (i.e., physiosexual arousal). Furthermore, the functional segregation of SA indicates the coexistence of specific networks. A recent and exhaustive review of brain imaging studies on the human sexual response even provides strong evidence for the existence of subnetworks within the networks of psychosexual and physiosexual arousal, pertaining to different phases of the sexual response cycle [Georgiadis and Kringelbach, 2012].

### *Somatosensory processing*

Bilateral activation of the parietal opercular cortex (specifically area OP 1) has been reported during tactile, nonsexual stimulation of the penis [Kell et al., 2005]. Accordingly, activation of this region might also be regarded as the somatosensory representation of (increasing) PE. On the other hand, tactile stimulation by the apparatus measuring PE cannot be ruled out. Hence, activation of the opercula could simply represent an artifact produced from the experimental setting, referring rather to external stimulation than to the erection itself. This possibility would correspond with the observation that manual stimulation of the erect penis leads to significantly stronger opercular activation than erection alone [Georgiadis et al., 2010]. However, the neural correlates of tactile penile stimulation include activity in the primary somatosensory cortex [Georgiadis et al., 2009, 2010; Kell et al., 2005]. The lack of convergent activity in the primary somatosensory cortex thus suggests that the parietal opercular cortex may be the site processing the sensory feedback of PE. Thereby, it may particularly be reflective of the vegetative aspects of erection.

### *Insular integration*

The middle insular cortex, where the present ALE analysis on PE revealed strong convergence of activity, processes both somatosensory and viscerosensory information [Eickhoff et al., 2006c]. To assume that PE, representing interoceptive information of hedonic quality, is processed in the middle insular cortex, is consistent with Craig's [2010] remark that "the mid-insula seems to integrate afferent activity associated with all aspects of somatic function". Furthermore, convergent peak activation correlating with PE was also observed in the anterior insula, which supports the proposal of a posterior-to-anterior sequence in insular neural processing [Craig, 2011]. According to the model, the anterior insular cortex would generate awareness of increasing PE in an emotional context. Such immediate relatedness of subjective feelings to homeostatic sensory integration [Craig, 2011] fits the James–Lange theory saying that feelings emerge from bodily states [James, 1884] and likewise Damasio's [1994] "somatic marker" hypothesis. In addition, it is noteworthy that ALE revealed a lateralization of anterior insular activity to the left hemisphere (PE > VSS, Table IV). Keeping in mind the parasympathetic regulation of PE (in particular, the filling of the cavernous bodies), this asymmetry resonates well with the concept that "parasympathetic" feelings are associated with left-sided activation [Craig, 2005]. In contrast, right-sided insular activity is observed during ejaculation, which is controlled by the sympathetic nervous system [Holstege et al., 2003]. Such interpretation regarding emerging feelings during SA is limited by the nonconsideration of correlations with subjective SA in the present meta-analyses. However, previous literature on the topic suggests that perceived erotic pleasure is positively correlated with activity in the insular cortex [Georgiadis et al., 2010; Sescousse et al., 2010].

### *Cingulate regulation*

Also in line with the parasympathetic regulation of PE is the convergence of activation foci in the sgACC. Critchley [2004] suggested that sgACC activity is a correlate of parasympathetic rather than sympathetic drive. He moreover argued that it may also reflect arousal associated with reward-based emotional/motivational processing that goes without the need of attention. This view is based on evidence of neuroanatomical and neurofunctional connections between the sgACC and areas implicated in autonomic and emotion regulation, such as hypothalamus and laterobasal amygdala [Barbas et al., 2003; Freedman et al., 2000; Teves et al., 2004], as well as sgACC deactivation during attention focusing [Raichle et al., 2001]. The prominent role of the sgACC in emotion regulation [Diekhof et al., 2011] is supported by its dysfunction in mood disorders [Drevets et al., 1997]. Moreover, sgACC response to emotional stimuli is likely modulated by serotonin transporter genotype [O'Nions et al., 2011]. The evidence of serotonergic regulation may also explain why serotonin uptake inhibitors (SSRI) induce sgACC hypoactivity during sexual stimulation that is accompanied by subjective sexual dysfunction [Abler et al., 2011].

It is noteworthy that the sgACC has been proposed to be functionally dissociable from dorsal parts of the ACC and the aMCC in the context of limbic modulation of behavior [Critchley, 2004]. This functional segregation corresponds to differences in anatomical connectivity: The sgACC holds strong connections to key players in emotion processing, such as hypothalamus and amygdala, and is therefore regarded as crucial for interaction with the limbic system. In contrast, dACC and MCC seem rather connected to premotor areas and LPFC [Beckmann et al., 2009; Etkin et al., 2011], suggesting their important role in the regulation and elicitation of behavioral responses [Etkin et al., 2011]. In particular, the aMCC is involved

conjointly with premotor areas and the LPFC in intentional initiation of behavior [Hoffstaedter et al., 2013]. Correspondingly, aMCC activity increasing with rising penile tumescence resonates well with the notion that PE is mandatory for the initiation of copulatory behavior and hence the realization of sexual desires. Concordant with this assumption, MCC as well as putamen, claustrum, and insula belong to the so-called "urge-for-action network" [Jackson et al., 2011] and notably, the latter regions were also consistently active during both PE and visual sexual stimulation. Furthermore, the region corresponding to the aMCC cluster of our ALE analysis on PE has been shown to be embedded in a network including the LPFC, anterior insula, thalamus, caudate, putamen, and amygdala [Yu et al., 2011]. It is striking that all these brain areas showed convergent activity in response to VSS, and further that the putamen showed convergence of activation during both visual sexual stimulation and PE. This indicates a contingent interconnection of the networks for sexual stimulus-driven processing and sexual autonomic regulation.

Taken together, our quantitative meta-analysis on PE suggests a neural network of physiosexual (i.e., bodily sexual) arousal, primarily consisting of regulatory components. Autonomic and concomitant emotion regulation is mirrored by activity in the sgACC, while the aMCC controls the initiation of (copulatory) behavior, i.e., action toward sexual urges. These in turn may be represented primarily in the putamen and claustrum as well as in the anterior insular cortex, where awareness of both the rising sexual desire and the bodily reaction is engendered. To this end, the insular cortex should also integrate, in a posterior-to-anterior sequence, somatosensory information from the opercular cortex, which monitors the bodily, physiosexual changes during SA.

## Interplay of Psychosexual and Physiosexual Arousal

Bodily sexual reactions are usually observed in causal and temporal sequence to a sexual stimulus [Janssen et al., 2000; Singer, 1984]. It is thus undoubted that central circuits of sexual stimulus processing (i.e., mediating psychosexual arousal) and of autonomic response generation (i.e., inducing physiosexual arousal) are necessarily linked. Janssen and colleagues [2000] proposed a bidirectional relationship between sexual stimulus processing and sexual response. More specifically, they state that "both the activation of genital responses and the awareness of becoming sexually aroused become part of the stimulus event and feed back into the central pathway" of SA. Following this view, there has to exist a two-way communication between the described networks of psychosexual and physiosexual arousal (cf., sections "A Neural Network for Sexual Stimulus-Driven Processing" and "A Neural Network for Sexual Autonomic Regulation"). The neurofunctional representation, putatively fulfilling such an interconnection task, seems to be rooted in the right claustrum and putamen, as indicated by the conjunction analysis between both meta-analyses.

The putamen as a part of the basal ganglia has predominantly been implicated in various aspects of motor control. To cope with such tasks, it receives topographic projections from (pre)motor and somatosensory areas as well as parietal association areas [Alexander and Crutcher, 1990]. The putamen is also an essential part of the corticostriatal motor loop, which communicates with visual, executive, and motivational loops linking basal ganglia with cerebral cortex (including prefrontal, limbic, and temporo-occipital areas) via feedback processing [Seger, 2008]. Accordingly, the putamen and more general corticostriatal loops may serve as a gateway in SA by connecting and integrating the neural networks for stimulus-driven processing, autonomic regulation, and behavioral responses. In addition, apart from PE as an objective measure of SA, activity in the putamen has also been shown to positively correlate with subjective SA [Redouté et al., 2000]. Furthermore, direct electrical stimulation of the putamen evokes erection in nonhuman primates [Robinson and Mishkin, 1968]. Also orgasm, representing the peak of SA, is associated with activation of the putamen [Holstege et al., 2003]. Bringing these observations together, it might be argued that increasing subjective SA leading to PE and eventually ejaculation may be mediated by the putamen as a key relay of corticostriatal loops.

The second maximum within the single cluster of convergent activation in the conjunction analysis emerged in the right claustrum: a thin, irregular, sheet-like neuronal structure whose function is enigmatic [Crick and Koch, 2005]. Activation of the claustrum in VSS as well as PE has been a matter of conjecture with conflicting findings. These inconsistencies may to some extent be attributable to technical limitations due to relatively low resolution in common functional imaging, making it difficult to anatomically differentiate the claustrum from adjacent structures such as putamen or insula. However, high-resolution neuroimaging of SA at 7 T indicates that activation of the claustrum represents a distinct feature of the functional neuroanatomy of SA [Walter et al., 2008a]. Diffusion tensor imaging (DTI)-based tractography shows the claustrum connecting with various cortical areas as well as subcortical structures of the limbic system and suggests a distant transcortical interconnection through the claustrum [Fernández-Miranda et al., 2008]. Concordant with this broad range of communication pathways, the claustrum has been associated with crossmodal processing [Calvert, 2001]. Moreover, Crick and Koch [2005] conclude in their exhaustive review "that the claustrum may contain specialized mechanisms that permit information to travel widely within its anterior-posterior and ventral-dorsal extent to synchronize different perceptual, cognitive and motor modalities". Thus, the authors regard the claustrum as a "conductor coordinating a group of players in the orchestra" (i.e., various brain areas) and adumbrate its significant

contribution to consciousness [Crick and Koch, 2005; Stevens, 2005]. Considering the complex psychological and physiological processes that are necessary for the full development of SA, the involvement of a coordinator like the claustrum seems mandatory. We therefore propose that the claustrum not only interconnects the neural networks of psychosexual and physiosexual arousal but also acts as a crossmodal coordinator within both of these networks.

Finally, we would like to comment on the role of the hypothalamus, that was reported to respond to VSS and contribute to PE in a previous review [Kühn and Gallinat, 2011]. In contrast to this finding, our more comprehensive quantitative meta-analysis on PE failed to demonstrate convergence of activation foci in the hypothalamus. Given the importance of the hypothalamus for autonomic regulation, this observation nevertheless needs to be discussed. The hypothalamus shows activity predominantly during the initial phase of SA [Sundaram et al., 2010; Walter et al., 2008b]. It is furthermore activated mainly during the onset of PE, while its role during maintenance of erection seems less relevant [Ferretti et al., 2005]. Such an "initiating role" of hypothalamic activity and its modulation by sexual stimulus intensity may thus indicate that the hypothalamus is activated by a (new) sexually relevant stimulus and primarily responsible for triggering the autonomic response to it. Its activity may hence decrease once the autonomic processes have been initiated. The lack of convergent hypothalamic activation may hence well be explained by the fact that most of the experiments in our meta-analysis on PE employed long blocks during which PE was measured. Another straightforward explanation for the nonconvergence in the hypothalamus might be the more stringent correction for multiple comparisons (FWE) that has been employed in the present meta-analysis compared with previous analyses [Kühn and Gallinat, 2011; Stoléru et al., 2012] and which most likely also accounts for the observed lack of convergent activation in the ACC during psychosexual (i.e., mental sexual) arousal and in a similar vein in the thalamus during PE, as opposed to those previous findings.

Summing up, the conjunction analysis identified two regions that connect the neural networks of psychosexual and physiosexual arousal with potentially dissociable functions. While the putamen might orchestrate the integration of sensorimotor information in the context of rising sexual lust, the claustrum may be primarily responsible for crossmodal processing between and within the networks of SA.

## Implications of Deactivated Brain Regions in Sexual Arousal

Only a rather limited set of brain areas was found to be consistently deactivated during SA. In this regard, the striking disproportion between studies on SA only reporting activations and those reporting both activations and deactivations must be raised. Whether this is conditional upon a lack of deactivations or simply omitting these results, however, remains unclear.

The consistently deactivated RSC, together with the medial prefrontal cortex, superior temporal cortex, and posterior parahippocampal cortex, has been discussed to form a circuit that may be involved in introspective self-monitoring [Price, 2005]. Moreover, together with the hippocampus, the RSC is essential for recollection of personal experiences, and also contributes to other cognitive functions such as imagination and planning for the future [Vann et al., 2009]. In addition, the RSC is involved in metacognitive evaluation of both oneself and others [Schmitz et al., 2004]. In line with these findings, neurophilosophy considers the RSC a part of cortical midline structures that are mandatory for the constitution of the self [Northoff and Bermpohl, 2004]. Deactivation of RSC and middle hippocampus might therefore imply a downregulation of introspective and self-reflexive processes in the context of SA.

Convergence of deactivations observed in the left angular gyrus overlaps with activity of a network of unconstrained cognition and sociocognitive tasks that do not include primarily self-referential processing [Schilbach et al., 2012]. Interestingly, this region has also been considered a key region of the neural correlates of moral cognition, contributing to morality, theory of mind, and empathy [Bzdok et al., 2012]. Hence, in more general terms, the angular gyrus seems to be also involved in social cognition and reasoning about people, presupposing an interaction between self- and other-reflection. In combination with the RSC deactivation, its decreased activity therefore indicates attenuation of both egocentric and allocentric processes during SA and the sexual act.

In the temporal cortex, deactivations were observed in the right STG and left ITS. Temporal lesions seem to be associated with various disturbances in sexual appetite [Braun et al., 2003; Stein et al., 2000] and are in general are assumed to be accompanied by hypersexuality [Stein et al., 2000]. Reminiscent of patients suffering from Klüver–Bucy syndrome [Klüver and Bucy, 1937], individuals with disturbances of the temporal lobes may not only exhibit an increased sex drive but also seek sexual stimulation from nonsexual or inappropriate objects. Accordingly, pedophilic behavior has been related to temporal lesions [Mendez and Shapira, 2011; Mendez et al., 2000], and abnormal temporal activity during SA has been shown in pedophilic patients [Poeppl et al., 2011]. This might provide evidence for the importance of the temporal cortex in the intrinsic inhibition of SA and the necessity of the release of temporocortical inhibition for developing SA. The latter hypothesis is supported by the observation of an inverse relationship between activity in the temporal cortex and subjective sexual pleasure [Georgiadis et al., 2006] as well as of widespread temporal deactivations in orgasm [Georgiadis et al., 2006, 2009].

In summary, the consistent deactivations during SA may implicate impaired metacognitive introspective and self-reflexive processing (angular gyrus, hippocampus,

RSC) as well as a release of intrinsic inhibition of SA (ITS, STG).

## Conclusions

The present ALE meta-analysis corroborates the existence of specific networks related to different components of SA. Sexual stimulus-driven processing recruits brain areas known to be crucial for cognitive evaluation, top-down modulation of attention and sensory processing, relevance detection and affective evaluation, inducement of a conscious sexual urge, and triggering of autonomic processes. The bodily reactions associated with SA are mediated by brain regions responsible for autonomic and emotion regulation and somatosensory processing. Both networks seem to be interconnected by the putamen and claustrum, presumably coordinating sensorimotor information and providing crossmodal processing between and within the networks. Deactivations may imply attenuation in introspective processes and social cognition, but be necessary to release intrinsic inhibition of SA.

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