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Meta-analytic Evidence for Neural Dysactivity Underlying Sexual Dysfunction

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Abstract

Background: About 30–40% of the population report sexual dysfunction. Although it is well-known that the brain controls sexual behavior, little is known about the neural basis of sexual dysfunction.

Aims: To assess convergence of altered brain activity associated with sexual dysfunction across available functional imaging studies.

Methods: We used activation likelihood estimation (ALE) meta-analysis to quantify interstudy concordance across 14 functional imaging studies reporting 179 foci from 40 individual analyses involving 191 subjects with sexual dysfunction and 123 controls.

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Conflict of Interest: The authors declare no conflict of interest.

Outcomes: ALE scores were used to assess convergence of findings.

Results: Consistently decreased brain activity associated with sexual dysfunction was identified in the dorsal anterior cingulate cortex, ventral striatum, dorsal midbrain, anterior midcingulate cortex, and lateral orbitofrontal cortex.

Clinical Translation: These findings can serve as a basis for further studies on the pathophysiology of this highly common disorder with the view to development of more specific treatment strategies.

Strengths & Limitations: Findings are based on an observer-independent meta-analysis that provides robust evidence for and anatomical localization of altered brain activity related to sexual dysfunction. Our analysis cannot distinguish between the putative sources of sexual dysfunction but provides a more ubiquitous and general pattern of related altered neural activity.

Conclusion: The identified regions have previously been shown to be critically involved in mediating sexual arousal and to be part of the sympathetic division of the autonomic nervous system. This suggests that the disturbance of brain activity associated with sexual dysfunction primarily affects sexual arousal already at early stages that are controlled by the sympathetic nervous system.

Keywords

Activation likelihood estimation; ALE; functional neuroimaging; meta-analysis; neural dysactivity; sexual dysfunction

INTRODUCTION

About 31% of men and 43% of women report sexual dysfunction.[1] Aphrodisiacs have enjoyed great popularity since ancient times and modern compounds are a billion dollar business. As it is well-known that sexual behavior is reflected in brain activity[2], it should be assumed that sexual dysfunction is based on altered neural activity. However, is there reliable evidence to draw this conclusion?

MATERIALS AND METHODS

To investigate whether there is converging evidence from functional neuroimaging studies for altered brain activity linked to sexual dysfunction, we conducted a quantitative coordinate-based meta-analysis using activation likelihood estimation (ALE[3]). A principled procedure to identify the relevant experimental studies was used. First, we selected studies through a standard search in the PubMed (https://www.ncbi.nlm.nih.gov/pubmed/) and ISI Web of Science (https://www.webofknowledge.com) databases using the terms “sexual”, “hyposexual” or “sexual dysfunction” in combination with “fMRI”, “functional MRI”, “functional magnetic resonance”, “PET”, “positron emission”, “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. Included were functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) studies on brain activity during sexual stimulation that (1) reported direct group comparisons between subjects with and subjects without (or less)

symptoms of sexual dysfunction and (2) presented corresponding results of whole-brain group analyses with coordinates referring to a standard reference space (Talairach or Montreal Neurological Institute [MNI]). Excluded were studies (1) involving subjects with sexual dysfunction due to an organic disease such as hypogonadism or (2) restricting analyses to a priori defined brain regions of interest.

According to these criteria, 14 papers were found to be eligible for inclusion into the meta-analysis (Supplementary Table). Together, these studies involved 314 subjects (191 with sexual dysfunction and 123 controls) and reported 179 foci obtained from 40 individual comparisons (experiments). Only seven of these 40 experiments (36 foci) showed *increased* activity associated with sexual dysfunction, excluding further analysis due to insufficient statistical power[3]. In contrast, from the 22 experiments assessing decreased activity, only four achieved non-significant results. Convergence across the 18 experiments reporting *decreased* activity (143 foci; cf., Figure 1A) was quantified by the union across each experiment's modeled activation maps (Figure 1B), i.e. by voxel-wise ALE scores, using a random effects approach[3]. Statistical significance was assessed at $p<0.05$, corrected for multiple comparisons using threshold-free cluster enhancement (TFCE).

RESULTS

Eleven of the 18 experiments assessing *increased* activity found no alterations. Hence, there was no evidence for reliably *increased* brain activity related to sexual dysfunction. Consistently *decreased* brain activity associated with sexual dysfunction was identified in the dorsal anterior cingulate cortex (dACC), ventral striatum (VS), dorsal midbrain (dMB), anterior midcingulate cortex (aMCC), and right lateral orbitofrontal cortex (lOFC) (Figure 1C).

DISCUSSION

These regions have been shown to be critically involved in processing of sexual stimuli and mediating sexual arousal.[1,4] A neurophenomenological model based on functional neuroimaging results postulated four components of sexual arousal.[4] Altered activity according to our meta-analysis particularly affects the cognitive (lOFC), motivational (aMCC, ventral striatum), and autonomic (dACC) components of this model[4]. Moreover, these regions are essential for sympathetic arousal, while parasympathetic processing includes activity of the posterior part of the cingulate cortex, several temporal cortices, and hypothalamus.[5] Interestingly, the regions emerging from our meta-analysis thus appear to be part of a subsystem for the sympathetic rather than the parasympathetic division of the autonomic nervous system.[5] This is somewhat unexpected given the major role of parasympathetic control in penile erection and vaginal lubrication. However, it has to be kept in mind that sexual arousal is a complex reaction that implies "a differential change in the activity of both branches of the autonomic nervous system, in which neither the parasympathetic nor the sympathetic nervous system may be considered dominant".[6] Our results suggest that the disturbance of brain activity associated with sexual dysfunction primarily affects sexual arousal already at early stages that are controlled by the sympathetic nervous system.

To the best of our knowledge, this is the first observer-independent meta-analysis of altered brain activity related to sexual dysfunction. It provides robust evidence for and anatomical localization of these consistent functional aberrances. However, also its limitations have to be acknowledged. Our analysis cannot distinguish between the putative sources of sexual dysfunction. More specifically, it comprises hypoactive sexual desire disorder, vaginism, dyspareunia, psychogenic erectile dysfunction, sexual dysfunction in the context of depression, and side effects of psychopharmacological treatment. In addition, it is not able to account for potential sex differences in the neural basis of sexual dysfunction, which have been reported in healthy sexual behavior[1]. While it seems likely that there are also disorder- and sex-specific effects, our meta-analysis provides a more ubiquitous and general pattern of altered neural activity related to sexual dysfunction. The identified regions could serve as targets for therapeutic interventions such as medication, psychotherapy or, in terms of cortical areas (lOFC and ACC), non-invasive brain stimulation. Given the involvement of the regions in the reward circuit[7], our results support a focus on dopaminergic compounds. Recently, it was also shown that cognitive behavioral therapy, which is capable of modulating cingulate and orbitofrontal cortical activity[8], can improve erectile dysfunction in men[9]. In addition, high-frequency repetitive transcranial magnetic stimulation (rTMS) over the lOFC or the ACC (using a double cone coil) might be worth being evaluated.

CONCLUSIONS

In sum, we showed that sexual dysfunction is reflected in decreased brain activity during sexual stimulation in brain regions that are crucial at an early stage of sexual arousal. These findings might serve as a basis for further studies on the pathophysiology of this highly common disorder with the view to development of new treatment strategies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

1. Laumann EO, Paik A and Rosen RC (1999) Frequency of sexual dysfunction in “normal” couples. JAMA 281:537–544. [PubMed: 10022110]
2. Poeppl TB, Langguth B, Rupprecht R, Safron A, Bzdok D, Laird AR and Eickhoff SB (2016) The neural basis of sex differences in sexual behavior: A quantitative meta-analysis. Front Neuroendocrinol 43:28–43. [PubMed: 27742561]
3. Eickhoff SB, Nichols TE, Laird AR, Hoffstaedter F, Amunts K, Fox PT, Bzdok D and Eickhoff CR (2016) Behavior, sensitivity, and power of activation likelihood estimation characterized by massive empirical simulation. Neuroimage 137:70–85. [PubMed: 27179606]

4. Stoléru S, Fonteille V, Cornélis C, Joyal C and 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. [PubMed: 22465619]
5. Beissner F, Meissner K, Bär KJ and Napadow V (2013) The autonomic brain: An activation likelihood estimation meta-analysis for central processing of autonomic function. J Neurosci 33:10503–10511. [PubMed: 23785162]
6. Wenger MA, Averill JR and Smith DB (1968) Autonomic activity during sexual arousal. Psychophysiology 4:468–478. [PubMed: 5662817]
7. Schultz W (2000) Multiple reward signals in the brain. Nat Rev Neurosci 1:199–207. [PubMed: 11257908]
8. Franklin G, Carson AJ, Welch KA (2016) Cognitive behavioural therapy for depression: Systematic review of imaging studies. Acta Neuropsychiatr 28:61–74. [PubMed: 26122039]
9. Khan S, Amjad A, Rowland D (2019) Potential for Long-Term Benefit of Cognitive Behavioral Therapy as an Adjunct Treatment for Men with Erectile Dysfunction. J Sex Med 16:300–306. [PubMed: 30770073]

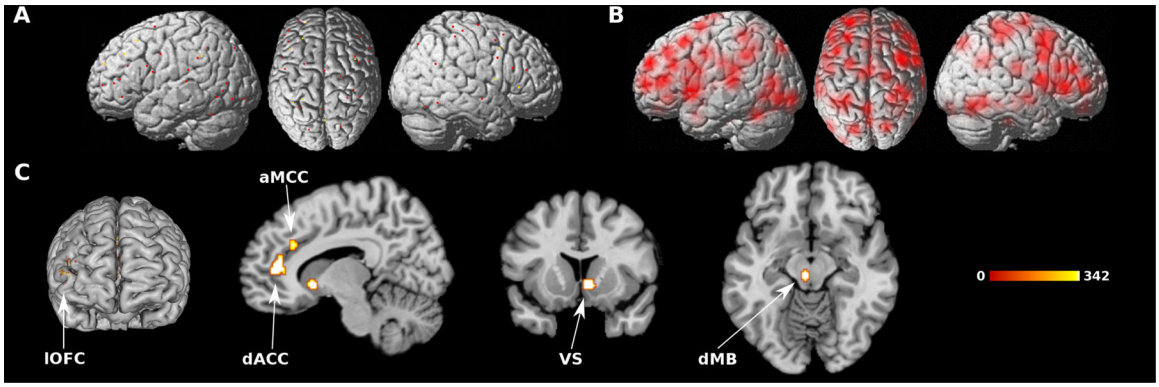

Figure 1.

A: Summary of the 143 deactivation foci reported in all 18 experiments reporting decreased activity associated with sexual dysfunction. B: Activation likelihood estimates (ALE), reflecting, for each voxel, the union of the modeled activation (MA) maps across all experiments related to sexual dysfunction. C: Decreased brain activity associated with sexual dysfunction. Significant clusters where the meta-analysis revealed significant convergence of altered brain activity associated with sexual dysfunction during sexual stimulation (abbreviation; peak voxel coordinates x, y, z; TFCE score): dorsal anterior cingulate cortex (dACC; 12, 44, 6; 422.08), ventral striatum (VS; 8, 12, −6; 455.58), dorsal midbrain (dMB; −4, −24, −14; 394.19), anterior midcingulate cortex (aMCC; 10, 28, 26; 338.03), and right lateral orbitofrontal cortex (lOFC; 32, 46, 6; 384.68). The color bar reflects threshold-free cluster enhancement (TFCE) scores.