Human Brain Activation during Sexual Stimulation of the Penis

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ABSTRACT
Penile sensory information is essential for reproduction, but almost nothing is known about how sexually salient inputs from the penis are processed in the brain. We used positron emission tomography to measure regional cerebral blood flow (rCBF) during various stages of male sexual performance. Compared to a passive resting condition (without penile erection), sexual stimulation of the penis increased rCBF in an area of the right hemisphere encompassing the posterior insula and adjacent posterior part of the secondary somatosensory cortex (SII) and decreased rCBF in the right amygdala. No activation was observed in either the thalamus, genital part of primary somatosensory cortex (SI), or hypothalamus. Based on these results we put forward the concept that during sexual performance the salience of the stimulus, represented by activation of the insula and SII, is of greater significance than the exact location of the stimulus, encoded in SI. The absence of activation in the hypothalamus indicates that this region is more important for the onset of sexual arousal than for the resulting sexual performance. Deactivation of the amygdala during sexual stimulation of the penis corresponds with a decrease of vigilance during sexual performance. J. Comp. Neurol. 493:33–38, 2005. © 2005 Wiley-Liss, Inc.

Indexing terms: positron emission tomography; human; penile stimulation; insula; secondary somatosensory cortex; amygdala

Many sexual health problems originate in the central nervous system (CNS), but very little is known about how the human brain organizes sexual behavior. Only recently, researchers have begun to explore this unknown territory, with the focus on sexual arousal (Stoleru et al., 1999; Rauch et al., 1999; Redoute et al., 2000; Bocher et al., 2001; Arnow et al., 2002; Karama et al., 2002; Hamann et al., 2004) rather than on sexual consumption or performance. Our research focuses on the consummatory aspects of sexual behavior and our findings regarding ejaculation have recently been published (Holstege et al., 2003). The build-up towards ejaculation usually consists of stimulation of the erect penis, providing the brain with information crucial for performing ejaculation. Reproduction, therefore, depends heavily on this penile sensory information, but nothing is known about how these penile inputs are processed in the human CNS.

Penile tissue possesses characteristics of skin and of viscer a and particularly the glans penis contains an unusually high number of free nerve endings innervated by A6 fibers (Halata and Munger, 1986; Johnson and Halata, 1991). These fibers travel through the dorsal penile nerve, a branch of the pudendal nerve. In cat, primary afferents from the penis terminate in laminae V, VII, and X of spinal segments S1–S2 (Ueyama et al., 1984; Thor et al., 1989). Human somatosensory innervation of the genitals resembles that of cat, because sacral root recordings, performed before surgical rhizotomies, identified the S2 roots to carry the fibers involved in genital sensation (Huang et al., 1997).

Above the level of the spinal cord, physiological experiments in rats have demonstrated that neurons in the medullary reticular formation (especially in the paragigantocellular nucleus) and in various thalamic nuclei (medial–dorsal, ventral, lateral, intralaminar, posterior, and reticular) respond to stimulation of the dorsal penile nerve (Hubscher and Johnson, 1996, 2003). The representation of the external genitals on the primary somatosensory cortex (SI) is on the interhemispheric surface of the postcentral gyrus, which, in humans, was discovered by...

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stimulating the cortex of patients undergoing brain surgery (Penfield and Rasmussen, 1950). Recently, this location has been confirmed using magnetic encephalography during electrical stimulation of the dorsal penile nerve (Nakagawa et al., 1998; Makela et al., 2003). Other regions activated by this dorsal penile nerve stimulation were the secondary somatosensory cortex (SII) and the insula (Makela et al., 2003).

However, these human stimulation studies as well as the animal tracing and stimulation studies mentioned above lack important features of male sexual activity, namely, penile erection and sexual arousal. In the present study the context was sexually salient for the volunteers, because their penis was stimulated by their own female partner during the experiment. Thus, for the first time we have investigated which brain regions are activated or deactivated by sexually salient penile stimulation.

SUBJECTS AND METHODS

Participants

Eleven healthy right-handed heterosexual male volunteers (mean age 33, range 19–45) participated in the study together with their female partner after giving written informed consent according to the Declaration of Helsinki. The procedures were approved by the Groningen University Hospital Medical Ethics Committee. None of the volunteers had any history of physical, psychiatric, or sexual disorders.

PET protocol

Measurements were made with a CTI/Siemens Ecat Exact HR+ (CTI/Siemens, Knoxville TN, USA). This 32 ring PET scanner with an axial field of view of 15.5 cm, operated in 3D-mode to have maximum sensitivity, simultaneously images a total of 63 planes with a spatial resolution of 4–5 mm full width at half maximum (FWHM) in all three directions. The tracer \([^{15}\text{O}]\text{-H}_2\text{O}\) was used to measure regional cerebral blood flow (rCBF). To allow for the decay of the \([^{15}\text{O}]\) (half-life 122 seconds), consecutive scans were made with an interval of ~8 minutes. For each scan 500 MBq of \([^{15}\text{O}]\text{-H}_2\text{O}\) was injected into the right median antebrachial vein and flushed with saline with a total volume of 32 ml at a speed of 8 ml/s. Except for the first scan, PET-scanning began 30 seconds prior to the injection in order to acquire background correction information. After injection of the radioactive bolus, data were collected for 2 minutes. A scan-specific calculated attenuation correction was performed to minimize interscan displacement-induced variance (Reinders et al., 2002).

Experimental tasks

We measured brain activation during: 1) a passive resting condition (no erection), 2) penile erection, 3) stimulation of the erect penis, and 4) ejaculation. To create a sexually salient context during the experiment, the volunteers' female partner manually provided the penile stimulation before and during sexual conditions. The penis was erect during all conditions except the passive resting state. Eight scans were obtained, consisting of two runs of the four tasks (Fig. 1). A consequence of this set-up is that we collected pre- as well as postejaculatory scans of the experimental conditions of rest, penile erection, and stimulation of the erect penis.

The volunteers' head was maintained in position with a head-restraining adhesive band and, in order to minimize visual input, volunteers were asked to keep their eyes closed. Prior to the experiment we again explained the precise procedure to the volunteers and their female partners and we made great effort to let the volunteers feel relaxed during the experiments. After the experiment the volunteers did not report important differences between their sexual experience under normal circumstances and in the scanner. Some volunteers reported using imagery during the sexual conditions.

Data processing and statistical analysis

The 1999 version of Statistical Parametric Mapping (SPM99) software was used for spatial transformation and statistical analysis of the data (Talairach and Tournox, 1988; Friston et al., 1995a,b). The data were realigned, stereotactically normalized into Talairach space, and, to increase the signal-to-noise ratio, the data were smoothed using an isotropic Gaussian kernel of 10 mm FWHM. An analysis of variance (ANOVA) with subject and experimental condition as factors, leaving 52 degrees of freedom, was performed on the data to estimate the parameters. The data were normalized for global effects by means of proportional scaling. Differences in regional cerebral activity due to sexual stimulation of the penis were tested by performing a Student's \(t\)-test on each voxel \((2 \times 2 \times 2 \text{ mm})\) of the brain, testing against the null hypothesis that states that there
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is no difference between the parameters sexual stimulation and passive rest. We investigated rCBF increases (activations: stimulation scans minus rest scans) as well as decreases (deactivations: rest scans minus stimulation scans), testing both parameter contrasts at \( P < 0.05 \). Because many \( t \)-tests are performed with this kind of analysis, multiple comparisons correction is necessary. We used the FDR (false discovery rate) correction (Genovese et al., 2002).

Clusters that were significantly activated and deactivated (\( P < 0.05 \), corrected for multiple comparisons) are listed in Table 1. For visualization of the results, activations and deactivations are displayed in Figures 2 and 3, respectively. The size of reported and displayed clusters is at least 8 voxels. For color scaling of activations and deactivations in Figures 2 and 3 we used the medical imaging tool AMIDE (free download at: http://amide.sourceforge.net). After transformation to Talairach coordinates, the cortical regions were identified using the Talairach atlas (Talairach and Tournoux, 1988).

RESULTS

Activations

Comparison of stimulation of the erect penis with rest resulted in significantly increased rCBF in an area in the right hemisphere encompassing the posterior part of the secondary somatosensory cortex (SII) and the posterior part of the insula (Table 1; Fig. 2B,C). The medial part of the activated cluster possibly involves the lateral posterior part of the basal ganglia (claustrum and putamen).

Deactivations

Comparison of stimulation of the non-erect penis with non-sexual rest resulted in decreased rCBF in the right amygdala (Table 1; Fig. 3A,B) and also in the left inferior temporal lobe (BA 20; Table 1).

DISCUSSION

The results show that sexual stimulation of the penis strongly activates the right posterior insula and adjacent posterior secondary somatosensory cortex (SII) and deactivates the right amygdala. No activation was observed in the thalamus, the genital part of the primary somatosensory cortex (SI), or in the hypothalamus. The right-sided dominance of rCBF changes corresponds to the clinical observation that sexual dysfunction occurs more frequently after strokes in the right hemisphere than after strokes in the left hemisphere (Coslett and Heilman, 1986).

Activation of insula and SII

Recently, it has been proposed that the insula creates a cortical image of the physiological condition of all tissues of the body, a concept called interoception (for a review, see Craig, 2002). Indeed, various tasks and conditions activate neurons in the insula. Examples in humans are vibrotactile stimulation (Burton et al., 1993), cocaine usage (Breiter et al., 1997), pleasant and aversive taste (O’Doherty et al., 2001), romantic love (Bartels and Zeki, 2000), hunger for air (Brannan et al., 2001), and sexual arousal (Arnow et al., 2002).

In the present study the posterior part of the right insula was activated. The posterior insula is involved in general arousal, contrary to the anterior insula, which has an important function in the processing of gustatory information in rats (Cechetto and Saper, 1987) and in hu-
mans (O’Doherty et al., 2001; Small et al., 2004). Sexual performance implies heightened arousal, i.e., elevated blood pressure, respiration, and heart rate (Kruger et al., 1998), which explains the activation of the posterior insula in the present study.

In a very elegant functional MRI (fMRI) case study, hair brushing of the forearm elicited insula activation in a patient without large myelinated afferents (Olausson et al., 2002). The patient stated that the brushing felt pleasant, but she was unable to determine what part of her body was touched. This kind of stimulation probably excites free nerve endings innervated by small-diameter fibers. Such free nerve endings are numerous in the penis (Halata and Munger, 1986; Johnson and Halata, 1991), and, indeed, our study also shows activation in the insula.

The secondary somatosensory cortex, located in the lateral-sulcal opercular cortex, has reciprocal connections with the insula (Friedman et al., 1986) and is thought to be concerned with the intensity of somatosensory stimuli (Bushnell et al., 1999). Because of its reciprocal connections with temporal lobe limbic structures, SII presumably also functions as a relay for somatosensory information to the limbic system (Friedman et al., 1986). An important feature of the present study is that only the posterior part of SII is activated. Recent studies in humans have shown involvement of the posterior SII during painful stimulation of the median and the tibial nerve, representing the hand and foot, respectively (Ferretti et al., 2003, 2004). In contrast, nonpainful stimulation of these nerves activated separate regions for “hand” and “foot” in the anterior SII (Ferretti et al., 2004). Apparently, only a salient stimulus (be it pain or a sexual stimulus) results in activation of the posterior SII.

Electrical stimulation of the dorsal penile nerve in humans activated SII together with insula and SI (Makela et al., 2003), whereas in the present study we find activation in insula and SII, but not in SI. Similarly, in another study (Lotze et al., 2001) distension of the rectum also activated SII and the insula but failed to activate SI, suggesting that visceral input has direct access to insula and SII without projecting to SI. This might be relevant in the present study because penile skin, which contains numerous free nerve endings, possesses characteristics of viscera (Halata and Munger, 1986; Johnson and Halata, 1991). Maybe in a sexually salient context it is the visceral information that drives the brain response.

**Deactivation of the amygdala**

The present study shows that blood flow in the amygdala decreases during stimulation of the erect penis relative to nonsexual rest. Currently, evidence exists that in certain brain areas, including the amygdala, blood flow is generally higher during a passive resting state than during goal-oriented behavior. Comparison of two such conditions, therefore, very likely leads to amygdala deactivation (Gusnard and Raichle, 2001), indicating that this phenomenon may not be specific for sexual behavior.

Still, amygdala deactivation might be crucial for sexual behavior to take place. Sexually aroused men show a diminished startle response to a sudden burst of white noise (Koukounas and McCabe, 2001), suggesting that sexual arousal goes together with attenuated vigilance and fear levels. Since an active amygdala promotes vigilance and fear (Davis and Whalen, 2001; Amaral, 2002), this attenuated vigilance during sexual arousal can be

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**Fig. 3.** Deactivations: *t*-map for rest minus stimulation of the erect penis, depicted in glass brains and superimposed on a standard *T*1-weighted MRI template (SPM99). The lines on the glass brains show the orientation and location of sections A and B. The *t*-bar indicates the level of deactivation in blue scaling (*t* = 0: white, *t* = −7: dark blue). *y*, anterior–posterior, relative to AC; *z*, superior–inferior, relative to AC.
explained by the amygdala deactivation we find in the present study. This also means that an active amygdala might preclude sexual behavior. Clinical cases provide support for this hypothesis: Patients who suffer from war- and combat-related post-traumatic stress disorder (PTSD) have a “hyperactive” amygdala (Rauch et al., 2000) and they also experience more sexual difficulties than healthy controls (Lettourneau et al., 1997).

Absence of activation in hypothalamus, thalamus, and SI

Activation is absent in the genital part of SI (Fig. 2C) and the thalamus when the erect penis is stimulated. One explanation could be that precise stimulus location of penile afferent information, encoded in SI, is not important in a sexually salient context, i.e., when the volunteers’ partner stimulates the penis. On the other hand, SI is very precisely somatotopically organized and, as a result, penile afferent information might lead to small focal activations, which might be degraded when data are smoothed and averaged across subjects (Bushnell et al., 1999).

Surprisingly, sexual stimulation of the penis also fails to activate the hypothalamus (Fig. 2A). Traditionally, the hypothalamus has been linked to every aspect of sexual behavior, but in men the hypothalamus might not be involved in the consummatory aspects of the male sexual response. Using fMRI in men, it has been shown that the hypothalamus is activated only during the onset of penile erection and not during sustained penile erection (Ferretti et al., 2005). The hypothalamus, therefore, might be involved in the motivational part of the human male sexual response, and not in the consummatory part of it.

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LITERATURE CITED


Friedman DP, Murray EA, ONeill JB, Mishkin M. 1986. Cortical connec-


Hubscher CH, Johnson RD. 1999. Responses of medullary reticular forma-
tion neurons to input from the male genitalia. J Neurophysiol 89:2–11.


hemisphere dominant activation in the second somatosensory cortex. Hum Brain Mapp 18:90–99.


