

Brain Processing of Audiovisual Sexual Stimuli Inducing Penile Erection: A Positron Emission Tomography Study

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Purpose: Penile erection is dependent on commands from the central nervous system. Although basic studies of animals and neuroimaging studies of humans have been conducted to identify key brain regions associated with sexual arousal, to our knowledge no reliable studies of the first excitation phase of sexual arousal leading to penile erection have been reported.

Materials and Methods: We used H₂¹⁵O-positron emission tomography to analyze regional cerebral blood flow just before penile erection in heterosexual volunteers. The subjects viewed 3 different types of audiovisual materials—sexually explicit clips, nonsexual neutral clips and dynamic mosaic image control clips—presented in random order, and penile rigidity was monitored in real time with a RigiScan® Plus device. Positron emission tomography scanning was initiated simultaneously when each clip was started, and images obtained when the subjects showed appropriate penile response were analyzed and compared.

Results: The advanced audiovisual cortices and cerebellar vermis in the right hemisphere were activated for sexually explicit-dynamic mosaic image control clip contrast, and only the right middle frontal gyrus was activated for sexually explicit-nonsexual neutral clip contrast. Several primary visual and audio regions were activated for dynamic mosaic image control-sexually explicit clip contrast and nonsexual neutral-sexually explicit clip contrast.

Conclusions: We speculate that advanced audiovisual activity with imagination, not primary visual and audio activity, occurs when men experience sexual arousal inducing penile erection. Furthermore, the cerebellar vermis may be a key region for induction of penile erection in humans.

Key Words: arousal, penile erection, central nervous system, positron-emission tomography

Erectile dysfunction is defined as the inability to achieve or maintain an erection sufficient for satisfactory sexual performance. It can be classified as psychogenic, organic (neurogenic, hormonal, arterial, cavernous or drug induced) or both psychogenic and organic. Psychogenic ED is caused by various mental factors including psychiatric disorders such as depression and schizophrenia, performance anxiety, a strained relationship and lack of sexual arousal.¹ It is well known that penile erection is dependent on commands from the CNS. Since the introduction in 1998 of sildenafil citrate, a selective inhibitor of phosphodiesterase type 5 that prevents the degradation of cyclic guanosine monophosphate in the corpus cavernosum of the penis, this drug has been the main tool for treatment of psychogenic ED.² Although phosphodiesterase type 5 inhibitors are effective for psychogenic ED, they cannot increase sexual arousal themselves. It was reported that the

greatest increases in the International Index of Erectile Function scores by treatment with sildenafil citrate were observed in the domain scores for erectile function, intercourse satisfaction and overall satisfaction with sex life, and the smallest increases were observed in the sexual desire domain scores.³ The precise mechanism of CNS induced sexual arousal and penile erection has not been elucidated.

Recent development of neuroimaging techniques has allowed the investigation of psychogenic function in several disorders and diseases. With the use of these techniques, male sexual response to visual sexual stimuli has been investigated. Although previous results are informative with respect to identifying key regions of the CNS involved in sexual activity in humans, it is unknown whether these activated regions are involved in real sexual arousal to induce penile erection.⁴⁻¹² The human male psychosexual cycle is divided into 4 phases according to penodynamic changes: excitement into latency and tumescence (excitation phase), plateau into erection and rigidity (plateau phase),

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orgasm into emission and ejaculation (orgasm phase), and resolution into detumescence and refractoriness (resolution phase).^{13,14} Most previous neuroimaging studies have focused on the role of the CNS in the plateau phase.^{4–7,9} A recent study showed that the mesodiencephalic transition zone and cerebellum are activated at the time of orgasm and ejaculation (orgasm phase),¹⁵ but little has been reported on regions activated during the excitation phase. We conducted an experimental study designed to identify regions activated only during the excitation phase. The study was based on audiovisual sexual stimulation, PET and a RigiScan® Plus device for evaluation of penile status.

MATERIALS AND METHODS

Participants

Six healthy, right-handed, heterosexual volunteers (mean age 35.5 ± 3.1 years, range 31 to 39) gave written informed consent according to the Declaration of Helsinki, and the procedures were approved by the Regional Ethics Committee of Osaka University Graduate School of Medicine. None of the volunteers had any history of physical, psychiatric or sexual disorders. All of the subjects were shown to have normal erectile function according to the short version of the International Index of Erectile Function, as well as normal endocrinological profiles before the study. The volunteers were expressly asked not to move.

Sexual Stimuli and Monitoring of Penile Rigidity

The subjects viewed 3 categories of audiovisual materials—sexually explicit clips (S condition), nonsexual neutral clips (N condition) and dynamic mosaic image control clips (M condition)—each lasting 3 minutes, in random order. The sexually explicit clips featured heterosexual intercourse. The nonsexual neutral clips included dances, sports, car races and talk shows. The mosaic image clips were created from corresponding sexually explicit clips to provide the same brightness, color information and auditory stimuli, with sandstorm-like sounds, as of the original sexually explicit clips. A RigiScan® Plus device was used for continuous real-time monitoring of penile rigidity while the subjects were viewing the video clips. Rigidity at the tip and base of the penis (percentage of linear displacement of the loops due to constant force) was determined and charted.

PET Scanning and Data Analysis

PET scanning was performed with a Headtome V scanner (Shimazu, Kyoto, Japan) in the 3-dimensional acquisition mode. The subjects underwent 12 regional cerebral blood flow measurements (4 per condition, each lasting 90 seconds) after a slow intravenous bolus injection of $H_2^{15}O$ (259 MBq per scan). The attenuation corrected data were reconstructed into 3-dimensional images with a voxel resolution of $2 \times 2 \times 3.125$ mm, which were then analyzed using statistical parametric mapping software (SPM2, Wellcome Department of Cognitive Neurology, London, United Kingdom). The images were realigned using the first image, transformed into the standard stereotactic space devised by the MNI and smoothed using an isotropic 12 mm full width half maximum Gaussian kernel. When each clip was started, PET scanning was initiated simultaneously regardless of erectile status. The order in which clips were pre-

sented was random and counterbalanced. Mean blood flow was normalized to a common mean value of 50 ml/100 g per minute. After the appropriate design matrix and comparison vectors were specified, the main effects and interactions were estimated in comparisons of adjusted task means with the use of the *t* statistic transformed into a normally distributed *z* statistic. Statistical significance was analyzed for comparisons of S-M, S-N, M-S and N-S. Statistical significance was set at $p < 0.05$, corrected for multiple comparisons. Activated brain regions were estimated according to the Talairach and Tournoux method, after adjustment for differences between MNI and Talairach coordinates.

RESULTS

A schematic of the audiovisual presentations together with PET scanning and representative penile rigidity data are shown in figure 1. Data were excluded from analysis when a subject could not achieve significant penile erection in response to sexually explicit clips or when the RigiScan® Plus device showed increased penile rigidity in response to mosaic or nonsexual clips. A total of 19 scans for sexually explicit clips, 23 scans for mosaic clips and 22 scans for nonsexual clips were analyzed. The latency time—duration between the first response and the plateau of penile erection in response to sexually explicit clips—was 129.5 ± 32.1 seconds. Furthermore, nobody in our volunteers reached the plateau of the erection within 90 seconds after the beginning of the sexually explicit clips. In addition, the first response of penile erection was usually recorded at 15 to 30 seconds after the beginning of the sexually explicit clips. Thus, PET scanning in our protocol was actually performed during the excitement phase of penile erection.

To elucidate brain activity patterns inducing penile erection, PET data of the S condition were compared with those of the N and M conditions (table 1). For S-M contrast (fig. 2) large regions of prominently increased activation were identified in the middle occipital gyrus (BA19) in the right hemisphere and inferior occipital gyrus (BA19) in the left hemisphere. The most activated locus was identified in the right cerebellar vermis (fig. 2). For S-N contrast specific activity was identified in the right middle frontal gyrus (BA11). Possible clusters that may have a role in inhibiting sexual arousal were also analyzed (table 2). For M-S contrast calcarine sulcus (BA17), inferior frontal gyrus (BA47), inferior parietal gyrus (BA7) and medial frontal gyrus (BA8) were seen only in the left hemisphere (fig. 3). For N-S contrast the middle temporal gyrus (BA21) and inferior temporal gyrus (BA20) in the left hemisphere, and middle frontal gyrus (BA6) in the right hemisphere were noted.

DISCUSSION

Sexual dysfunction is important with respect to quality of life. Specific regions of the human brain involved in the induction of penile erection are receiving increased attention. Basic studies of animals have revealed that the medial preoptic arc, the paraventricular nucleus of the hypothalamus and the hippocampus are brain loci that elicit penile erection when stimulated.¹⁶ However, little is known about the relation between brain activation and sexual behavior in humans. The human psychosexual response has unique characteristics that distinguish it from homologous behavior

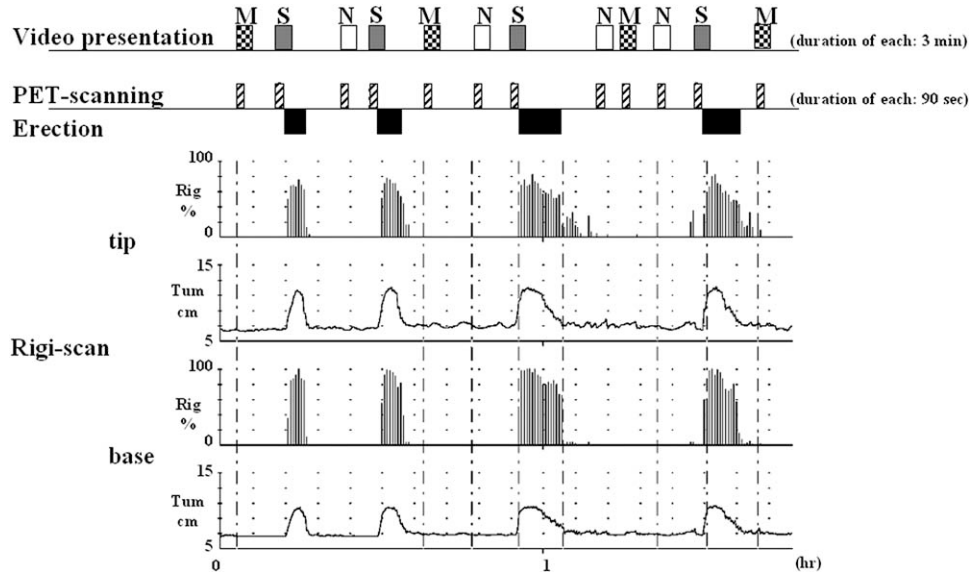


FIG. 1. Schematic of experimental design. Three categories of audiovisual stimuli are represented as gray box—sexually explicit clip (S), white box—nonsexual neutral clip (N) and mosaic box—dynamic mosaic image control clip (M). Each video was presented in random order and lasted 3 minutes. PET scanning is indicated by striped bars. When each clip was started PET scanning was initiated simultaneously regardless of erectile status. Durations of penile erection are indicated by black boxes below scanning bars. Typical graph of RigiScan® Plus data indicating rigidity (Rig) and tumescence (Tum) of tip (upper 2 graphs) and base (lower 2 graphs) of penis shows percentage of linear displacement of loops due to constant force and changes in penile circumference.

in other species because cognitive aspects of sexuality, such as sexual imagery, are likely to be much more important in humans than in other species. The advent of functional neuroimaging has provided powerful tools, including PET and fMRI, for the study of neural substrates of normal emotions as well as those involved in the pathophysiology of psychiatric disorders. With use of these techniques several studies have been conducted to identify key regions of the CNS involved in sexual arousal. Previous PET and fMRI studies have identified the cingulate gyrus, caudate, putamen, claustrum, sensorimotor region, premotor region and hypothalamus as important for sexual arousal.^{4–12} The identification of many regions is likely due to various methodologies for evaluation of sexual arousal. Sexual arousal in normal men results in penile erection. However, most studies have evaluated penile status without reliable tools. These studies, excluding 3 studies with plethysmography to monitor penile circumference^{6,8} or a custom-built pneumatic pressure cuff,⁹ assessed only subjective penile erection. Although a subject reports sexual arousal during the viewing of sexually explicit films or clips, this may not be true sexual arousal unless penile erection occurs. Even the use of questionnaires to evaluate mental state cannot guarantee true sexual arousal. We believe that it is necessary to evaluate

penile status regardless of subject reports of sexual arousal. In this study we used a RigiScan® Plus device, which is the most reliable and widely used tool for real-time monitoring of penile tumescence and rigidity.¹⁷

A previous neuroimaging study of the early stage of sexual arousal was conducted by comparing 8 healthy men and 7 patients with hypoactive sexual desire disorder by PET with plethysmography.⁸ Activation in control subjects and deactivation or unchanged activity in patients was found in the inferior parietal lobules, anterior cingulate gyrus and frontal lobes, which are related to emotional and motor imagery processes or premotor processes. The cerebellar vermis was not activated in normal subjects. However, these results may not represent the excitation phase because PET data acquisition was initiated 60 seconds after the visual stimulation began. Another interesting fMRI study of the early stage of sexual arousal was conducted with 8 healthy men to evaluate emotional changes in response to sexual stimuli.¹² Regional cerebral blood flow was increased in the parietal and frontal premotor areas, which are involved in attentional processes directed toward motivationally relevant stimuli, and in motor preparation and motor imagery. Activation of the cerebellar vermis was not identified.

TABLE 1. Stereotaxic coordinates of S-M and S-N contrast

Location		MNI Coordinate (mm)			Z-Score*
		x	y	z	
S-M contrast:					
Rt	Cerebellar vermis	4	-74	-22	5.62
Rt	Middle occipital gyrus (BA19)	46	-86	4	5.48
Lt	Inferior occipital gyrus (BA19)	-44	-84	-8	5.28
S-N contrast:rt					
	Middle frontal gyrus (BA11)	26	58	-18	5.27

The height threshold was $t = 5.26$ ($p < 0.05$ corrected for multiple comparisons).
* Activations are reported as Z-scores (conversion of normal distribution).

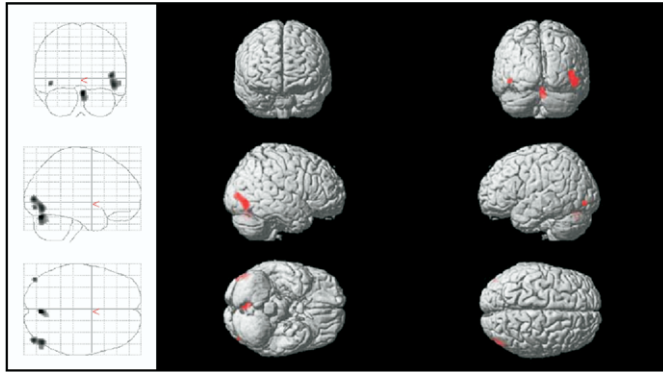


FIG. 2. Neocortical activation for S-M contrast. Large regions of prominently increased activation were identified in middle occipital gyrus (BA19) in right hemisphere and inferior occipital gyrus (BA19) in left hemisphere. Most activated locus was identified in right cerebellar vermis.

However, the sexual stimuli in this study were photographs, and the emotional condition was evaluated with a series of questions regarding desire and erection. In the present study we initiated PET scanning when each clip was started regardless of consequent erectile status, and data were excluded when the subjects did not show expected penile response by the RigiScan® Plus device. Therefore, we were able to focus on regions activated during the excitation phase.

Our results clearly showed right side dominant activation of the middle and inferior occipital gyri (BA19), which are highly advanced audiovisual cortices for S-M contrast (table 1). This finding is similar to the results of previous studies of the plateau phase.^{4-7,9-11} A positive correlation has been reported between signal intensity in the right middle occipital gyrus and magnitude of penile tumescence in response to visual sexual stimuli.⁹ However, a recent review indicated that activation of the middle and inferior occipital gyri might not be related specifically to sexual arousal but rather to visual stimulation itself.¹⁸ Furthermore, the middle frontal gyrus (BA11) in the right hemisphere, which is related to emotional impulses, was only activated for S-N contrast in the present study. The viewing of sexually explicit clips appears to involve more physiological impulses than the viewing of nonsexual clips involves. Interestingly, specific activation in response to S-M contrast was identified in the right cerebellar vermis during the excitation phase. The cerebellum has traditionally been viewed as dedicated to motor control, but recent evidence has shown that it is

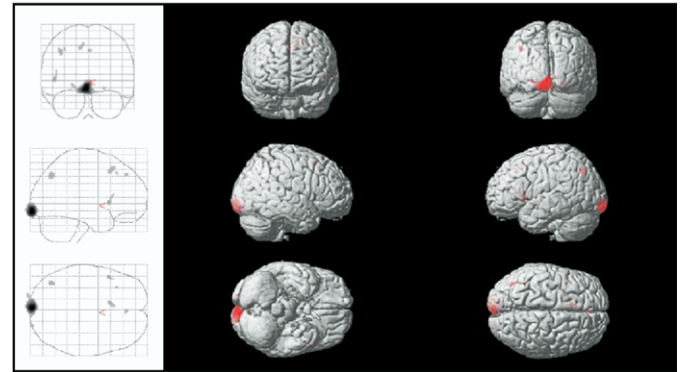


FIG. 3. Neocortical activation for M-S contrast. Activity in sulcus (BA17), inferior frontal gyrus (BA47), inferior parietal gyrus (BA7) and medial frontal gyrus (BA8) was seen only in left hemisphere.

involved in nonmotor operations as well. Deficits after cerebellar lesions include disturbances in executive function, learning, memory, attention, visuospatial function, language and personality change. Thus, the cerebellum is not limited to motor control. It also has important roles in cognition and emotion.^{19,20} Sexual arousal has cognitive, motivational, emotional and autonomic components.⁶ The cognitive component comprises a process of appraisal through which stimuli are categorized as sexual incentives and quantitatively evaluated as such, attention to stimuli evaluated as sexual is increased, and motor imagery related to sexual behavior is increased. In addition, imagination of previous sexual experiences may affect this process in humans. We suggest that the cerebellar vermis is a key region for sexual arousal in human males.

In contrast, almost all regions activated for M-S contrast and N-S contrast were in the left hemisphere (table 2). This asymmetric activity of the hemispheres relative to sexual arousal is consistent with findings of previous PET studies.⁴⁻¹² Among regions activated for M-S contrast and N-S contrast, the calcarine sulcus (BA17), inferior parietal gyrus (BA7), medial frontal gyrus (BA8) and middle frontal gyrus (BA6) may be associated with primary visual stimulation and with visuospatial attention. In addition, inferior frontal gyrus (BA47) activated for M-S contrast, and the middle and inferior temporal gyri (BA20 and BA 21) for N-S contrast are associated with primary audio stimulation such as that of spoken language. These findings indicate that regions associated with primary visual and audio activity are inactivated in the sexual condition, and are activated in the nonsexual condition.

TABLE 2. Stereotaxic coordinates of M-S and N-S contrast

Location	MNI Coordinate (mm)			Z-Score*	
	x	y	z		
M-S contrast:					
Lt	Calcarine sulcus (BA17)	-2	-98	-10	6.48
Lt	Inferior frontal gyrus (BA47)	-48	16	2	5.11
Lt	Inferior parietal gyrus (BA7)	-40	-68	42	5.04
Lt	Medial frontal gyrus (BA8)	-8	20	50	4.99
N-S contrast:					
Lt	Middle temporal gyrus (BA21)	-44	6	-22	6.00
Lt	Inferior temporal gyrus (BA20)	-46	-18	-34	5.21
Rt	Middle frontal gyrus (BA6)	46	2	50	4.85

The height threshold was $t = 5.26$ ($p < 0.05$ corrected for multiple comparisons).

* Activations are reported as Z-scores (conversion of normal distribution).

CONCLUSIONS

We found that advanced audiovisual regions and the cerebellar vermis are activated, and that primary visual and audio regions are inactivated during the excitation phase of sexual arousal. We speculate that the advanced audiovisual activity involved in imagination, not primary visual and audio activity, occurs when men experience sexual arousal. Furthermore, we believe that the cerebellar vermis is a key region involved in sexual arousal inducing penile erection in humans. Our findings will aid in understanding how the human brain controls sexual arousal and penile erection.

Abbreviations and Acronyms

CNS	=	central nervous system
ED	=	erectile dysfunction
fMRI	=	functional magnetic resonance imaging
M	=	dynamic mosaic image control clip
MNI	=	Montreal Neurological Institute
N	=	nonsexual neutral clip
PET	=	positron emission tomography
S	=	sexually explicit clip

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