Neuroimaging of sexual arousal: research and clinical utility

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The treatment of sexual dysfunction or deviancy requires an understanding of the underlying neural substrates. Neuroimaging techniques offer insight into brain regions involved in sexual arousal and inhibition. The development of robust paradigms has implications for the assessment and treatment of sexual disorder in men and women.

Sexual offence resulting from deviant behaviour impacts on the victim, perpetrator and society. Development of valid and reliable methods to identify offenders and assess treatment efficacy requires an understanding of the underlying neural substrates of human sexual behaviour. Until recently, this has largely depended on animal studies and human research involving neurosurgical lesions, head trauma or partial epilepsy (Agmo et al, 1995; Bancroft, 1999; Stoleru et al, 1999; Mendez et al, 2000; Redoute et al, 2000).

Structures implicated in arousal and/or inhibition include the hypothalamus, septal nuclei, amygdala and anterior cingulate. However, such research is limited to the study of isolated regions, which are usually damaged, rather than functioning systems in healthy brains. Moreover, animal studies are unable to account for important evolutionary differences between humans and lower mammals.

With the development of psychophysiological and neuroimaging techniques, it may be possible to gain a complete understanding of the neuroanatomy of human sexual behaviour, which can be applied in a clinical setting.

ASSESSMENT OF SEXUAL FUNCTIONING

Previous research used psychophysiological measures such as penile plethysmography (PPG) (Lawson, 2000; Looman, 2000) and electroencephalography (EEG) (Tucker and Dawson, 1984; Cohen et al, 1985; Howard et al, 1994) to study sexual functioning. More recent techniques measure vaginal and minor labial oxygen tension (Sommer et al, 2001), enabling the study of female sexual arousal. Psychophysiological techniques have some success in diagnosing sexual dysfunction and deviance (Howard et al, 1994; Lawson, 2000). However, their ability to accurately measure the function of crucial underlying neural structures is limited. This may curtail diagnostic precision; Looman (2000) found that only 25% of rapists were detected using PPG.

Neuroimaging techniques seem more capable of accurately and repeatedly measuring the function of multiple brain regions involved in sexual arousal and inhibition systems in vivo in healthy human subjects, and hold promise for research and clinical utility.

NEUROIMAGING STUDIES

Imaging studies of sexual arousal have employed single photon emission computed tomography (SPECT) (Tiihonen et al, 1994), positron emission tomography (PET) (Rauch et al, 1999; Stoleru et al, 1999; Redoute et al, 2000; Bocher et al, 2001) or functional magnetic resonance imaging (fMRI) (Rislinger et al, 1999; Bartels and Zeki, 2000; Garavan et al, 2000; Beauregard et al, 2001; Park et al, 2001a,b; Arnow et al, 2002) (*Table 1*).

The activation or deactivation of brain regions involved in sexual arousal is indicated by respective increases or decreases in regional cerebral blood flow (CBF) (in the case of PET or SPECT), or deoxygenation (in the case of fMRI) (see article by Sheringham et al, 2002). Such change is seen in response to sexually evocative stimuli such as orgasm or ejaculation (Tiihonen et al, 1994), erotic visual stimuli such as films (Stoleru et al, 1999; Garavan et al, 2000; Redoute et al, 2000; Arnow et al, 2002) and static images (Rislinger et al, 1999; Redoute et al, 2000), or script-driven imagery (Rauch et al, 1999). The response is then compared with the

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reaction to neutral stimuli (e.g. nature scenes, blank screen) or stimuli evoking other positive, non-sexual emotions, such as competitive arousal (Rauch et al, 1999; Arnow et al, 2002), humour (Stoleru et al, 1999; Redoute et al, 2000) or cocaine craving (Garavan et al, 2000).

Correlations between brain activation and other measures of arousal (e.g. subjective feelings, PPG, heart rate, lateral frontalis electromyograms, plasma testosterone or skin conductance) have also been examined. *Table 2* presents anterior, posterior and subcortical regions activated in response to sexually arousing stimuli. *Figure 1* shows the number of reports demonstrating activation in brain areas using PET, SPECT or fMRI. Relevant anterior, posterior and subcortical regions are further detailed.

TABLE 1.
Details of imaging studies of sexual arousal

Reference	Imaging technique	Stimuli	Other measures	Participant details: Sample size Male	Female	Handedness Right	Left	Age (years) (mean)
Tiihonen et al (1994)	SPECT	Ejaculation	S	8	0	8	0	29–39
Rislinger et al (1999)	fMRI	Static images	S	5	0	not reported		not reported
Rauch et al (1999)	PET	Scripts	S, HR, GSR, EMG	8	0	8	0	21–32 (25)
Stoleru et al (1999)	PET	Film	S, P, T	8	0	8	0	21–25 (23)
Redoute et al (2000)	PET	Static images/film	S, P, HR, BP	9	0	9	0	21–39 (30.7)
Bartels and Zeki (2000)	fMRI	Static images	S	6	11	16	1	21–37 (24.5)
Garavan et al (2000)	fMRI	Film	S	23*	8†	26	2	19–44
Bocher et al (2001)	PET	Film	S	10	0	10	0	24–32 (27)
Beauregard et al (2001)	fMRI	Film	S	10	0	not reported		20–42 (23.5)
Park et al (2001a)	fMRI	Film	S	0	6	6	0	25–41 (33)
Park et al (2001b)	fMRI	Film	S, P	14‡	0	14	0	21–25 (23)
Arnow et al (2002)	fMRI	Film	S,P	14	0	14	0	18–30

BP = blood pressure; EMG = electromyogram from lateral frontalis; fMRI = functional magnetic resonance imaging; GSR = galvonic skin response; HR = heart rate; P = penile response; PET = positron emission tomography; S = subjective report; SPECT = single-photon emission computed tomography; T = plasma testosterone.* Includes 14 cocaine users; †Includes 3 cocaine users; ‡ Includes 12 sexually potent and 2 hypogonadal men

TABLE 2.
Left and right anterior, posterior and subcortical brain regions found to be activated in response to sexually arousing stimuli in 12 studies

	Anterior areas							Posterior areas						Subcortical areas							
Reference	GO	INS	GCa[1]	GCa[2]	M/SF	I/PrC	TP/U	LPs	LPi	PC	IT	IT/O	CB	BS	CC	HY	HI	AM	TH	BG	NC
Tiihonen et al (1994)					R																
Rislinger et al (1999)												LR									
Rauch et al (1999)		L		R			L							L						R	
Stoleru et al (1999)	R	R	L								L	R									R
Redoute et al (2000)	R	LR	L	R		L		R	L			L						L	LR	LR	R
Bartels and Zeki (2000)		LR	LR										LR				LR			LR	LR
Garavan et al (2000)	R	LR	L	R	LR	R	L	R	L	LR		LR	R						LR		LR
Bocher et al (2001)		R						R	L		LR	LR									
Beauregard et al (2001)			R		R	L	R	LR			LR	R	L			LR		R			
Park et al (2001a)		LR	L			LR					LR	LR			LR				LR	LR	LR
Park et al (2001b)		LR	LR			LR				LR		LR			LR				LR	LR	LR
Arnow et al (2002)		LR	LR	LR	R	R					R					R				LR	L

L = left hemisphere; R = right hemisphere; GO = orbitoprefrontal (BA47/BA11); INS = insula/claustrum; GCa[1] = cingulate (BA24/BA32); GCa[2]= cingulate/medial frontal (BA9/BA32); M/SF = middle/superior frontal (BA8/BA9/BA10); I/PrC = inferior frontal/precentral (BA44/6,4); TP/U = temporal pole/uncus (BA38); LPs = superior parietal (BA7,BA5); LPi = inferior parietal (BA40); PC = cingulate (BA23); IT = inferior temporal (BA19); IT/O = inferior temporal/middle occipital (BA37); CB = cerebellum; BS = brainstem; CC = corpus callosum; HY = hypothalamus; HI = hippocampus; AM = amygdala; TH = thalamus; BG = basal ganglia; NC = caudate nucleus

Anterior regions

At least two different anterior networks have been proposed to guide behaviour in response to reward, respectively recruiting ventrolateral and dorsomedial striatopallidothalamic systems. An orbital network, involving the orbitoprefrontal cortex (GO) and insula, serves to integrate viscerosensory information with affective signals, while a medial visceromotor system, involving the anterior cingulate (GCa) and medial prefrontal cortex (GFd), provides frontal cortical influence over autonomic and endocrine functions associated with sexual response (Price, 1999).

Orbitoprefrontal cortex (GO): The GO is thought to be involved in the integration of sensory information with affective information, as well as in the evaluation of biologically relevant and potentially rewarding stimuli (Rolls, 2000).

Damage to the GO often leads to alteration in response to social reinforcers/punishers, such as sexual stimuli (Rolls, 2000). Activation in the GO is usually less prominent and less frequently seen than in the GCa, basal ganglia or insula. It may occur with sensory integration from different modalities (Price, 1999; Rolls, 2000), such as sound and vision from films (Stoleru et al, 1999; Garavan et al, 2000; Redoute et al, 2000), or integration of pleasant bodily changes with visual information (Redoute et al, 2000). In addition, GO activation may be seen when greater load is placed on evaluation processes, such as processing facial attractiveness or expression (Rolls, 2000).

For example, Redoute et al (2000) found right GO activation in response to moderately but not highly arousing static images of women. They suggest that moderately arousing images may have required subjects to evaluate more beauty stimuli to determine their reward value and sex appeal.

Insula/claustrum: One of the most robust findings from imaging studies of sexual arousal is bilateral activation of the insula and bordering claustrum. These structures are implicated in motivational processes and visceral sensations involved in primary biological drives, such as hunger and thirst (Redoute et al, 2000). Insula activation correlates with subjective arousal and PPG (Redoute et al, 2000), perhaps reflecting somatosensory processing and recognition of erection (Arnow et al, 2002). Right insula activation may represent cross-modal information transfer of visual input to imagined tactile stimulation (Arnow et al, 2002).

Using script-driven imagery alone, Rauch et al (1999) reported left without right insula activation. They also cited the left insula as one of the few regions, along with the brainstem, in which activation distinguishes sexual arousal from competitive arousal.

The only recent study not to report activation near the insula or claustrum is one of the few to report activation in the amygdala, hypothalamus and anterior temporal pole (Beauregard et al, 2001). Regulation of these latter arousal-related structures, perhaps at the automatic level, is performed by the insula (Bush et al, 2000), whereas conscious suppression of sexual arousal appears to activate the GCa (Beauregard et al, 2001).

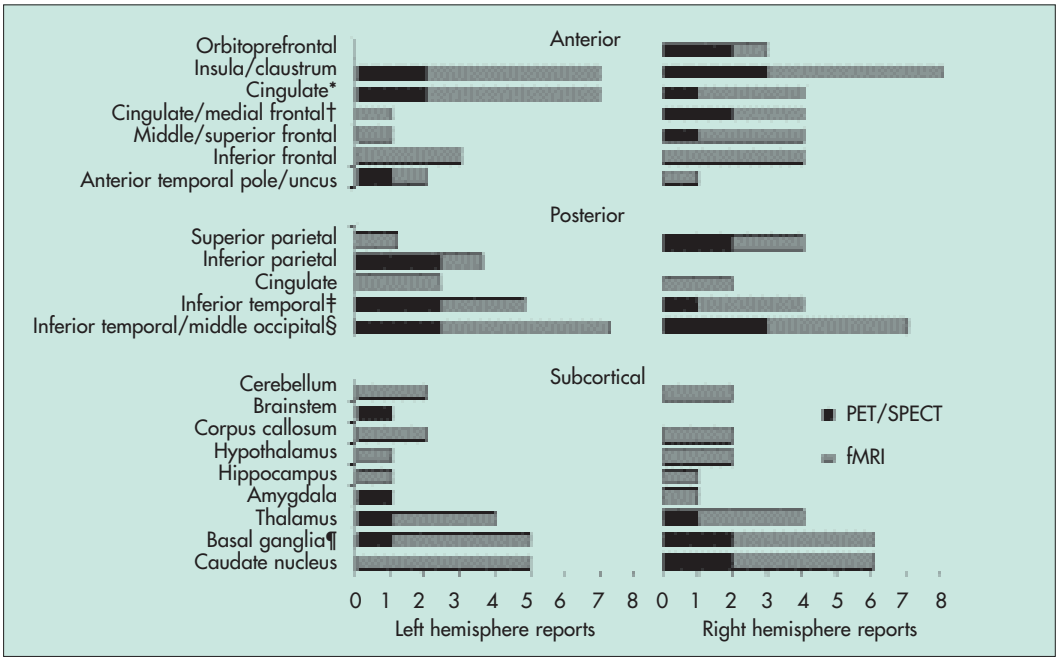

*Figure 1. Number of reports of activation in left and right, anterior, posterior and subcortical areas in response to sexual arousal in five positron emission tomography (PET)/single-photon emission computed tomography (SPECT) and seven functional magnetic resonance imaging (fMRI) studies. *Brodmann area 24/32; †Brodmann area 9/32; ‡Brodmann area 37; §Brodmann area 19; ¶including lenticular/putamen and globus pallidus.*

Future studies should assess the contribution of insula and claustrum damage to abnormal sexual response in disorders such as frontotemporal dementia (Mendez et al, 2000).

Anterior cingulate (GCa)/medial frontal: GCa has been shown to be crucial for the initiation of sexual behaviour (Agmo et al, 1995). The activated area tends to centre around Brodmann area (BA)32, extending to BA24 bilaterally but predominantly left, and to BA9 predominantly right. This extensive activation reflects its role in a number of functions, including the interpretation of biologically significant stimuli, awareness of arousal or urge to act (Redoute et al, 2000), and regulation of attention, affect or physiological processes through facilitation or suppression of conflicting responses (Lane et al, 1999; Redoute et al, 2000; Beauregard et al, 2001). Left GCa (BA 24/32) activation correlates positively with both subjective arousal and PPG (Redoute et al, 2000; Arnow et al, 2002).

Caudal GCa conducts executive functions controlling multiple competing inputs, while its rostral part (BA9/32) is involved with mediating affective and motivational processes (Bush et al, 2000; Redoute et al, 2000; Beauregard et al, 2001). As mentioned, while the insula may be involved in more automated control processes, the GCa is part of an effortful control system (Bush et al, 2000), and is activated with conscious inhibition of sexual arousal (Beauregard et al, 2000).

Rostral GCa activation is probably related to the level of perceived emotion rather than sexual quality of emotion. Redoute et al (2000) found no activation in this area compared with a control condition of humour. Likewise, Rauch et al (1999) demonstrated GCa activation to sexual and competitive arousal. GCa is also activated in response to other avoidance and approach behaviours, including cocaine craving (Wexler et al, 2001), hunger or thirst (Redoute et al, 2000), pain (Peyron et al, 2000) and anxiety (Chua et al, 1999).

Posterior regions

Occipitotemporal: Intense bilateral activation of temporo-occipital areas (i.e. primary and secondary visual cortex, BA19,37) in response to sexual stimuli is seen in most studies. Of the three studies not reporting activation in this area, one used script-driven imagery (Rauch et al, 1999), another employed portraits of romantic partners (Bartels and Zeki, 2000), and the third scanned subjects after ejaculation (Tiihonen et al, 1994). Temporo-occipital activation is not specific to sexual arousal, rather elicited by the most emotion-evoking visual stimuli (Lane et al, 1999). The region activated is close to that involved in processing human body images and is important for the perceptual processing of biologically relevant visual information (Downing et al, 2001).

Two not incompatible theories are proposed. The first suggests that extrastriate activation results from the cooperativity of multiple, single, predominantly local, visual modules in a bottom-up fashion (Bocher et al, 2001). Alternatively, a top-down theory suggests that once biologically significant stimuli are identified, the limbic regions involved in attention and motivation (e.g. GCa, GO and amygdala) may prime activation in sensory areas, enhancing early processing (Lane et al, 1999; Stoleru et al, 1999).

Parietal: Inferior parietal lobe (LPi) (BA40) contains secondary somatosensory cortex (SII). Its activation may reflect the awareness of bodily changes in response to arousal, such as penile tumescence (Redoute et al, 2000). The right superior parietal (LPs) (BA5, BA7) lobe is implicated in awareness and sustained attention (Beauregard et al, 2001). Beauregard et al (2001) suggest that LPs activation derives from the impact of emotional arousal on attentional mechanisms grounded neurally in this area. This is supported by Redoute et al's (2000) finding that activation in BA7 correlates highly with subjective perception of sexual arousal. The LPi and LPs are implicated in the mental representation of topographical knowledge of body, posture and movement in space (Graziano et al, 2000; Le Clec'H et al, 2000). Activation of these areas may therefore reflect subjects 'mirroring', i.e. imagining themselves in the erotic situation, an ability that also requires inferolateral frontal function (Bocher et al, 2001).

Subcortical regions

Basal ganglia and thalamus: As mentioned earlier, both orbital and medial networks recruit the basal ganglia and thalamus. Their activation may represent involvement in reward, arbitration and/or inhibitory mechanisms (Pardo et al, 1990; Redoute et al, 2000; Rolls, 2000). Activation of the right caudate and left putamen correlates with both perceived sexual arousal and penile tumescence (Redoute et al, 2000; Arnow et al, 2002). Imaging techniques may be used in future to study hypersexuality such as that resulting from caudate lesions (Richfield et al, 1987).

Amygdala, brainstem and hypothalamus: Amygdala, brainstem and hypothalamus activation are uncommon findings in

neuroimaging studies of sexual arousal. This is surprising, as they are implicated in sexual arousal by animal, neuropsychology and epilepsy research (Bancroft, 1999; Davidson and Irwin, 1999; Redoute et al, 2000). Activation in these areas may be dependent on a stage and/or intensity of arousal not reached in many studies, for instance when ejaculation is approached (Szechtman et al, 1978). In accordance, Beauregard et al (2001) found amygdala, hypothalamic and temporal pole activation when subjects allowed themselves to be aroused, compared with attempted suppression.

Brainstem activation is found with sexual arousal, but not competitive arousal evoked by script-driven imagery (Rauch et al, 1999). Also, although no difference was seen between sexual arousal and control conditions in brainstem activation, Bocher et al (2001) found it to correlate positively with erection sensation, as does hypothalamus activation (Redoute et al, 2000; Arnow et al, 2002).

CONCLUSION, IMPLICATIONS AND FUTURE RESEARCH

Neuroimaging studies have clarified and extended findings from previous animal and human research, demonstrating activation in brain areas in response to sexual arousal. Robust regions of activation include bilateral inferior temporal/middle occipital, left inferior parietal, right superior parietal, right GO, bilateral GCa, bilateral insula/claustrum, bilateral thalamus and basal ganglia. Surprisingly, certain areas previously thought crucial to animal sexual behaviour (e.g. amygdala, hypothalamus and brainstem) seem relatively less important for human sexual arousal. Inconsistent activations may reflect methodological differences.

KEY POINTS

- A number of anterior, posterior and subcortical brain areas are implicated in sexual behaviour.
- Deviant sexual behaviour may occur in response to abnormalities in one or more of these areas.
- Psychophysiological techniques have been successful in diagnosing sexual dysfunction and deviance. However, their ability to accurately measure the involvement of underlying neural structures is limited.
- Neuroimaging techniques enable more precise, repeated assessments of many brain regions, and may be used in both healthy subjects and in patient populations.
- Neuroimaging techniques offer an invaluable tool for research in human sexual arousal. Development of techniques may lead to their clinical use for the assessment and treatment of sexual deviancy or dysfunction in both men and women.

Imaging techniques offer invaluable research tools, enabling comparisons between brain regions involved in sexual arousal and those recruited in response to other emotions. Future studies should delineate substructures and/or activation patterns unique to sexual arousal. Such differentiation might be in the distinctive pattern of activated areas in response to sexual arousal and/or the activation of subregions within broader areas (Redoute et al, 2000).

Future research should attempt to separate perceptual, cognitive, emotional and physiological processes involved in sexual behaviour (Redoute et al, 2000) by placing a greater load on a particular function (e.g. Beauregard et al, 2001) or temporally disabling it with techniques such as transcranial magnetic stimulation. For instance, respective lesions to anterior cingulate (controlled regulation) and insula (automatic regulation) could be modelled and compared. To this end, a study of patient populations may also be insightful.

Neuroimaging techniques offer opportunity to understand the much-neglected female sexual response and draw comparisons between genders. Developments in psychophysiological techniques to measure female sexual arousal would be important in this endeavour.

Development of neuroimaging techniques to assess arousal and inhibitory mechanisms has implications for the diagnosis and assessment of treatment programmes for sexual dysfunction (Park et al, 2001b), including sexual offending. Identification of these mechanisms may be useful in treating some patients with mental illness or retardation for whom sexual dysfunction or deviation is a problem (Murrey et al, 1992; Mendez et al, 2000; Seidman and Roose, 2000; Park et al, 2001b). HM

Conflict of interest: none.

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