

·Review·

Role of the brain in the control of erection

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Abstract

In contrast to the spinal control of erection, relatively little is known about the brain control. In the present review, we have outlined the role of brain structures involved in penile erection and provided a synopsis on the brain circuit of erection. Findings from both animal and human studies are discussed. Evidence suggests that the most important structures are the frontal lobe, cingulate gyrus, amygdala, thalamus and hypothalamus. Within the brain circuit of erection, the thalamus serves as a gate-controller in which all relevant information is evaluated and further processed to higher and lower centres. (*Asian J Androl* 2006 May; 8: 259–264)

Keywords: penile erection; brain; spinal; circuit

1 Introduction

Penile erection is a complex event controlled by vascular, hormonal and neuronal systems [1, 2]. The neuronal system involved in erection can be divided into spinal network and supraspinal network. Evidence suggests that the spinal network directly controls erection and that the brain modulates this control mechanism through different ascending and descending pathways [3]. The spinal cord integrates information from somatic and autonomic afferents, and supplies the penis with regulatory efferents [4]. The main intraspinal centers involved in this process are the sacral parasympathetic nucleus (Spn), the thoracolumbar sympathetic nuclei (intermediolateral cell

column and dorsal gray commissure) and the pudendal motoneurons [4]. In contrast to the spinal control, relatively little is known about the brain control of erection. An excitatory pathway has recently been identified from the lumbosacral spinal cord to the oxytocin-secreting parvocellular region of the paraventricular nucleus (PVN) of the hypothalamus [5]. Furthermore, reciprocal connections between the striatum, hypothalamus, thalamus, amygdala and various cortical areas are likely to be involved in the brain control of erection [6]. The introduction of apomorphine, a proerectile drug acting at supraspinal levels, in the clinical treatment of erectile dysfunction (ED) [7–10] and the report of changes in penile erection following deep brain stimulation (DBS) of the thalamus have raised the question of what extent direct central modulation of erection is possible [7, 8, 11]. In the present review, we outline the role of the brain in the control of erection. Both the findings of animal studies and studies involving human subjects are discussed.

2 Brain regions

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2.1 Cortical structures

2.1.1 Animal studies

At the level of the cortex, specific parts of the frontal lobe have been reported to be involved in erection. MacLean and associates [12] carried out several experiments in which primates (*Saimiri sciureus*) received electrical brain stimulation. They were actually among the first investigators to map the proerectile regions in the brain. Using stereotactic procedures, electrical stimulations were carried out at the level of several neuroanatomical loci and the effects on the size of erection was investigated. Erection was graded on a six-point scale. One of the brain regions that was shown to be proerectile was the medial frontal lobe [13].

A second cortical region involved in erection is the cingulate gyrus. Dua and MacLean [13] performed a brain-stimulation study on the squirrel monkey in which attention was focused specifically on sexual responses. The experimental set-up of this study was similar to the previous investigation [12]. Stimulations at the level of the anterior cingulate gyrus elicited erection. This finding was confirmed a few years later by others in a comparable experiment with monkeys [14].

2.1.2 Human studies

Human studies have also provided evidence that cortical structures are involved in erection. Park and associates [15] found that the frontal lobe was involved in erectile functions. They described for the first time the activity of brain regions involved in penile erection as a response to visual erotic stimulation using blood oxygenation level-dependent (BOLD) functional magnetic resonance imaging (fMRI) [15]. In their patients, BOLD-fMR images demonstrated significant activation in the inferior frontal lobe. Activation was also found in the cingulate gyrus during sexual arousal and erection [15]. The latter was reproduced by another comparable neuroimaging study [16].

2.2 Subcortical structures

2.2.1 Animal studies

At the level of the subcortical regions, specific parts of the amygdala have been reported to be involved in erection. Robinson and Mishkin [14] carried out an experiment in which primates (*Macaca mulatta*) received electrical brain stimulation at specific neuroanatomical targets. The effect of electrical stimulations on erection was studied. Electrical stimulation of the corticomедial nucleus of the amygdala resulted in a profound erection

[14]. The bed nucleus of the stria terminalis (BNST), which is similar to the central nuclear group of the amygdala [17], has also been reported to be involved in erection. Valcourt and Sachs [18] showed that rats with lesions in the BNST were accompanied with severe deficits in noncontact erection. Noncontact erections are erections that occur in the presence of inaccessible estrous females and are analogous to human "psychogenic erections". Several years later, Bialy and Sachs [19] published their results on the effects of androgen implants into the medial amygdala of male rats. Androgens delivered to the medial part of the amygdala restored some of the erectile deficits caused by castration. These findings suggest that different parts of the amygdala are involved in the facilitation of erectile functions.

The thalamus also is a subcortical structure involved in erection. Electrical brain stimulation studies conducted by MacLean and co-workers showed that proerectile responses could be evoked by stimulation at the levels of the thalamic tubercle and the rostral pole of the thalamus [12], and from the medial dorsal (MD) nucleus to the posterior parts of the thalamus [20]. Robinson and Mishkin [14] found, in their electrical stimulation study, proerectile responses at the level of the midline thalamus. The involvement of the MD nucleus of the thalamus in erection was also demonstrated in rodents by Sapolsky and Eichenbaum [21]. Lesions in the MD nucleus of the thalamus inhibited odor-guided erection and intercourse in hamsters. These data are in favor of the hypothesis that thalamic nuclei have a facilitatory role in erection.

Another important subcortical structure involved in erection is the hypothalamus. Different areas of the hypothalamus have been reported to be involved in erectile functions in different ways. One of the areas is the PVN. Electrical stimulation of the PVN of the hypothalamus resulted in erection in primates [12]. In another study, bilateral electrolytic lesions of the PVN in rats induced a shorter latency to the first erection [22]. These data suggest that the PVN has a facilitatory role in erection, as excitation of this nucleus by electrical stimulation has a proerectile effect and inhibition of this nucleus by lesioning has a negative effect on erectile performance. The second hypothalamic region involved in erection is the lateral hypothalamus. Lesions at the level of the lateral hypothalamus facilitated noncontact erections in rats, suggesting an inhibitory role on erection of this part of the hypothalamus [23]. The third hypothalamic region related to erectile functions is the preoptic area [24]. Pre-

optic areas are considered to be part of the anterior hypothalamus. Robinson and Mishkin [14] reported large erections following stimulation of the primate medial and lateral preoptic regions. The same finding was also documented in rodents [24]. Electrical stimulation of the hypothalamic medial preoptic area (MPOA) reliably elicited erectile responses. These data suggest a facilitatory role for the preoptic areas in erection. The fourth hypothalamic region involved in erection is the mamillary body, found in the posterior parts of the hypothalamus. Different results have been found in studies with stimulations of the mamillary bodies. MacLean and Ploog [12] found proerectile responses in primates, whereas Robinson and Mishkin [14] could not find any effect of stimulation on erection in the same species. Therefore, it is unclear whether the mamillary bodies have a facilitatory or inhibitory effect on erection.

Three other subcortical structures have been described to be involved in erectile functions: nucleus accumbens, fornix and striatum. Kippin and associates [23] performed excitotoxic lesions at the level of the nucleus accumbens in rats. During exposure to an inaccessible receptive female, these lesioned animals displayed impaired erections. MacLean and Ploog [12] found that stimulations at the level of the lateral and medial aspects of the fornix induced erections in non-human primates. Robinson and Mishkin [14] saw a similar effect in monkeys with stimulations at the level of the dorsal putamen and anterior parts of the internal capsule.

2.2.2 Human studies

In human, parts of the thalamus and hypothalamus have been documented to be involved in erection. In two patients who underwent thalamic DBS for intractable Tourette's syndrome (TS), unexpected changes in erectile functions were observed [25, 26]. DBS electrodes were implanted bilaterally in the medial parts of the thalamus at the level of the nucleus ventrooralis internus, centromedian nucleus (Cm, as a part of the intralaminar thalamic nuclei) and substantia periventricularis (as a part of the midline thalamic nuclei). Despite considerable reduction of TS symptoms, the patients experienced substantial changes in penile erection. Penile erection was measured using an electromechanical strain gauge in stimulation *on* and *off* conditions. Patients were shown selected clips from erotic films. With stimulation, the speed of erection and amplitude of penile circumference was remarkably increased in patient 1. In patient 2, turning the stimulation on prac-

tically inhibited erection. The authors explained these different penile reactions to visual erotic stimuli by differences in electrode positions. In patient 1, the location of the left electrode was 2 mm lateral and the right electrode 2 mm medial in relation to the position of the electrodes in patient 2. Different electrode positions could therefore give rise to these opposing effects, as a result of a possible differential organization of "inhibitory" and "excitatory" projections in this area. Additionally, Park *et al.* [15] found that the thalamus showed bilateral activation during erection in response to visual erotic stimuli in their fMRI study.

Regarding hypothalamic areas, ablative neurosurgical procedures have been performed at the levels of the medial and ventromedial preoptic areas in male volunteers with the aim of suppressing sexual behaviors such as pedophilia and rape [27–29]. These procedures often resulted in an overall impairment in sexual functions.

The involvement of the striatum in erection was confirmed by two neuroimaging studies, which found activation in the striatum during sexual arousal and penile erection [15, 16].

2.3 Other brain structures

Few studies, all of them experiments with animals, have shown that midbrain structures are involved in erection. DBS experiments have revealed that electrical stimulations at the level of the ventral tegmental area (VTA), lateral aspects of the substantia nigra (SN), and the medial forebrain bundle elicited penile erection in primates [12, 13, 20]. There is limited evidence showing the involvement of the brainstem in erection.

3 Synopsis

Data from animal and human studies, as outlined above, show that within the cortical areas, parts of the frontal lobe (medial and inferior) [13, 15] and cingulate gyrus (anterior) [13–16], and within the subcortical areas, parts of the amygdala (corticomedial, medial and BNST) [14, 18, 19, 30], thalamus (MD, and Cm–parafascicular [Pf] complex), hypothalamus (PVN, medial and lateral, POAs and mamillary bodies) [14, 20, 22–24, 27], nucleus accumbens [23], fornix [12] and striatum [14–16] are reported to be involved in erection. The spatial organization of these structures is schematically shown in Figure 1.

Data from the aforementioned studies support the view that brain centers are potent modulators of the spi-

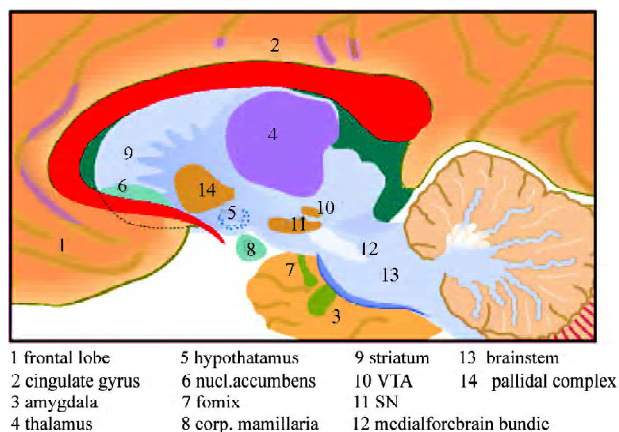


Figure 1. Spatial organisation of brain regions that have been documented to be involved in penile erection. SN, substantia nigra; VTA, ventral tegmental area.

nal centers responsible for the generation of penile erection. In some studies, these effects are so acute and great that one could even argue that brain centers are indeed generators of erection [11, 12, 14]. The spinal cord contains the autonomic and somatic nuclei at the origin of efferent and afferent pathways to the penis [4]. The information flow to and from the penis and perigenital areas is concentrated at the level of the Spn, thoracolumbar sympathetic nuclei and pudendal motoneurons. This information is, in turn, directed to the thalamus through both the anterolateral and dorsal column-medial lemniscus systems [32, 33]. The main thalamic centres involved in the information processing at this level are the MD nucleus and the Cm–Pf complex. Within the functional organisation of the brain circuit of erection, the thalamus seems to have a central role [32]. On its way to the thalamus, these projections from the spinal centers pass through the brainstem. The importance of this relay mechanism at the level of the brainstem remains unclear. Several other structures are also projecting to the MD and Cm–Pf complex of the thalamus. One of these structures is the nucleus accumbens, which is considered to be part of the ventral pallidum [34]. The nucleus accumbens, in turn, receives projections from the striatum and VTA [17]. Another structure that projects to the MD nucleus of the thalamus is the amygdala, through the ventral amygdalofugal pathway [17]. After passing through the thalamic stations, the thalamocortical pathways are directed to the frontal cortical areas and the anterior cingulate gyrus [34].

The descending pathways most probably originate

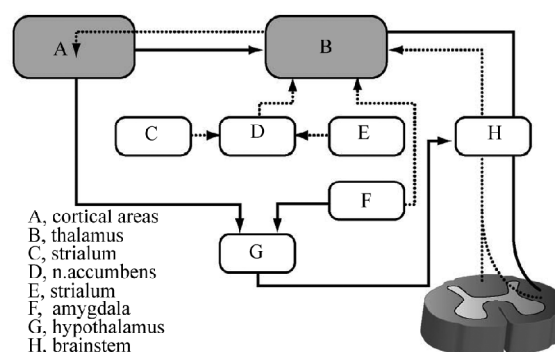


Figure 2. Functional organisation of the brain areas involved in penile erection. The information from the spinal cord is directed through the brainstem to the thalamus, which has a central role in the functional organisation of the brain circuit of erection. Several other structures also project to the thalamus, including the nucleus accumbens which, in turn, receives projections from the striatum and ventral tegmental area. Another structure that projects to the thalamus is the amygdala. After passing the thalamic stations, the thalamocortical pathways are directed to the frontal cortical areas and cingulate gyrus. The descending pathways most probably originate at the level of the frontal cortical areas and project to both the thalamus and hypothalamus. From the thalamus, projections pass through the brainstem and travel to the spinal centers. At the level of the hypothalamus, projections from the amygdala also provide input. Subsequently, this information is transmitted through the brainstem to the spinal cord.

at the level of the frontal cortical areas. These pathways project to both the thalamus and hypothalamus. From the thalamus, projections pass through the brainstem and travel all the way to the spinal centers. At the level of the hypothalamus, projections from the amygdala also provide an input. Subsequently, this information is transmitted through the brainstem to the spinal centers. Figure 2 represents the schematic functional organisation of neuronal structures involved in penile erection.

4 Future perspectives

The importance of certain brain areas in the control of erection is also clinically evidenced by the occurrence of ED in neurodegenerative disorders such as Parkinson's disease (PD), which is characterised by a selective progressive degeneration of dopaminergic neurons in the midbrain [35]. Treatment of PD patients with dopaminergic drugs such as apomorphine, levo-dopa (*L*-DOPA) or bromocriptine may elevate libido and increase erections [36–41]. Dopamine seems to play a major role in erection. In a study of patients with impotence, many of

the patients responded to subcutaneous and sublingual formulation of apomorphine [42–46]. Despite these recent developments in the treatment of ED with centrally-acting drugs, there is surprisingly little known about the central control of erection when compared to the peripheral control. Future studies, basic and clinical, using a variety of approaches including molecular (neuro-mediators), electrophysiological (pathways) and behavioral (both) techniques, are needed to uncover the mechanisms involved in the brain control of erection.

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