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Review article

Stroke and sexual dysfunction — A narrative review

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ABSTRACT

Sexual function is an essential part of quality of life in adults. However, sexual dysfunction (SD) in stroke survivors is a common but under-recognized complication after stroke. It is frequently neglected by patients and clinicians. The etiology of post-stroke SD, which is multifactorial includes anatomical, physical and psychological factors. Complete return of sexual function is an important target for functional recovery after stroke, so clinicians need to be aware of this issue and take a lead role in addressing this challenge in stroke survivors. Accurate diagnosis and prompt treatment of post-stroke SD should be routinely incorporated into comprehensive stroke rehabilitation. This narrative review article, outlines the anatomy and physiology of sexual function, discusses various factors contributing to post-stroke SD, and proposes directions for future research.

Contents

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1. Introduction

Stroke is a leading cause of disability that can impair physical, linguistic, cognitive and sexual function [1]. Of all post-stroke disabilities, sexual dysfunction (SD) is considerably under-recognized. SD can present as decreased libido, impotence or inability to ejaculate in males or decreased libido, lack of vaginal lubrication, arousal problems or orgasmic dysfunction in females. Understandably stroke patients are often embarrassed to discuss SD issues with their physicians. Patient reticence and physician ignorance have arguably led to a relative neglect of post-stroke SD, thereby limiting our ability to explore underlying mechanisms and identify appropriate therapeutic strategies [2].

Normal sexual function relies on a complex network of central and peripheral nervous system pathways involving autonomic (sympathetic/parasympathetic), spinal, and somatic nervous systems [2]. However, little is known about the impact of stroke on sexual activity or which specific psychological or organic factors contribute to SD after stroke.

In this narrative review, we first outline the physiology and anatomical correlations of sexual activity; secondly, we discuss the various factors contributing to post-stroke SD; and finally, we propose directions for future research.

2. Physiology of the sexual response cycle

There are three ways that neurobiological systems are involved in sexual response [2,3]: (1) physiologic input systems for inducing sexual arousal, (2) spinal and mesodiencephalolimbic in mediating sexual arousal, and (3) physiologic response in the genital region by sympathetic/parasympathetic nervous system necessary for priming and executing a sexual activity.

In males, the neurotransmitters and neuropeptides facilitating penile erections are oxytocin, dopamine, glutamic acid, opioid peptides, hexarelin peptides, and pro-VGF peptides [4]. The paraventricular nucleus (PVN) of the hypothalamus [4] is the most sensitive area for the pro-erectile effect of oxytocin. It projects oxytocinergic neurons to extra-hypothalamic brain areas (e.g., septum, hippocampus, amygdala, ventral tegmental area, medulla oblongata and spinal cord). The PVN is considered as a cardinal integration center between the central and peripheral autonomic nervous systems [5]. During sexual arousal, oxytocin-induced penile erection is mediated by Ca^{2+} influx into the oxytocinergic neurons in PVN. This causes nitric oxide by activation of nitric oxide-synthase. Nitric oxide in turn leads to the activation of oxytocinergic neurons, which project to extra-hypothalamic brain areas, thereby inducing penile erection and copulatory behavior [4,5]. Oxytocinergic pathways from PVN to extra-hypothalamic brain areas that mediate penile erection are illustrated in Fig. 1. Furthermore, oxytocin also activates mesolimbic dopaminergic neurons. Dopamine released in the nucleus accumbens (NAcc) in turn stimulates neural pathways leading to the activation of incerto-hypothalamic dopaminergic neurons in the PVN involved in erectile function [4].

On the contrary, little is known about precise mechanisms that mediate female sexual response.

Male genital apparatus is innervated mainly by pudendal nerves, which contain the primary afferent sensory and motor pathways to the penis, and by cavernous nerves, which contain the primary efferent sympathetic and parasympathetic pathways [5]. Cavernous nerves are innervated by hypogastric nerves, pelvic nerves, and paravertebral sympathetic ganglia chain of the thoracic–lumbar tract (T11–L2) [5]. In males, penile erection is mediated by pelvic parasympathetic activity while ejaculation is controlled by thoracolumbar sympathetic system [6]. In females, sexual stimulation increases blood flow to the vagina resulting in lubrication and erection of the cavernous tissues and clitoris, which are innervated by the pudendal nerve [7]. Sexual function in females proceeds in a more complex and circuitous manner than males and is more vulnerable to psychosocial factors [8].

3. Anatomical locations responsible for sexual dysfunction (Table 1)

3.1. Mesodiencephalolimbic system

The thalamus may play a crucial role in penile erection. Jeon et al. investigated the correlation of erectile dysfunction (ED) with stroke lesion(s) in 44 ischemic stroke patients [9]. Thalamic lesions were found to be more associated with ED compared to lesions in other locations. In an fMRI study, the thalamus was bilaterally activated during erection in 10 out of 12 subjects [10]. In another study, eleven healthy heterosexual young volunteers underwent positron emission tomography (PET) to measure increases in regional cerebral blood flow (rCBF). During ejaculation, the mesodiencephalolimbic system, including the ventral tegmental area, lateral central tegmental field, subparafascicular nucleus, and the medial/ventral thalamus recorded the most intense activation [11]. However, another study found no specific activation in the thalamus or hypothalamus to the genital part of the primary somatosensory cortex during sexual intercourse [12].

The NAcc is a part of the mesolimbic system and regulates dopamine-driven pleasure and sexual activity [13]. Studies of NAcc relating to sexual behavior have shown conflicting results. In a study with male rats, bilateral NAcc lesions caused inability to have an erection and intromission [14], but other studies showed only minor impairment of sexual behavior or limited change after NAcc damage [15,16]. Moreover, increased rCBF was not observed in NAcc in a human study [12].

The amygdala was found to be closely associated with ejaculation in human studies [11,17]. Contrary to other limbic system studies, the amygdala seems to have an inverse relationship between euphoric psychological states and amygdala activation during human male ejaculation [11].

3.2. Cerebral hemisphere, cortex and subcortex (Striatum)

The right hemisphere is more likely to play a dominant role in activation/attention of libido and erectile functionality [18,19]. Sexual reaction time is more impaired in right hemispheric stroke than left [19]. In a PET study [12] to measure rCBF during various stages of sexual performance, sexual stimulation of the penis increased rCBF in the posterior insular and adjacent posterior part of the secondary somatosensory cortex of the right hemisphere. In the neocortex, the activated regions were primarily on the right side. The right hemisphere also dominates in sensing emotional stimuli, as a result, right parietal lesions frequently cause hemi-inattention [18] and increase susceptibility to emotional disorders [20,21]. Patients with right hemispheric stroke likely have difficulty in responding to erotic sensations because of sensory and perceptual neglect [22]. Therefore, it is conceivable that right parietal lesions are more closely associated with the development of SD.

However, studies are not consistent regarding the laterality of hemispheric lesion and SD. Monga et al. reported that females with right-hemispheric lesions were more likely to experience a decline in sexual function when compared to those with left-hemispheric lesions [23]. Another study suggested that left hemispheric lesions play an important role in post-stroke SD (diminished libido or satisfaction) among male patients [24]. Post-stroke depression occurs more commonly with left hemispheric stroke and is closely related to SD, but these studies failed to show a relationship between the lesion side and SD [25–27].

3.3. Cerebellum

The cerebellum is involved with motor coordination, emotional processing [28] and sexual arousal [17]. Large portions of cerebellum, including deep cerebellar nuclei, vermis, and hemispheres are activated during ejaculation, especially the left side [11]. Jung et al. showed that right cerebellar lesions were associated with ejaculation disorder in a