

Editorial:

# Ventrolateral Preoptic Nucleus of Hypothalamus: A Possible Target for Deep Brain Stimulation for Treating Sexual Dysfunction



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## ABSTRACT

Sexual function and orientation is a complex platform of human personality which is being modulated by several brain circuitries which is less understood currently. Recently, several studies have demonstrated interesting results regarding the role of several brain locations in sexual behaviors and orientation. Sexual arousal in homosexual men are associated with activation of the left angular gyrus, left caudate nucleus, Ventrolateral Preoptic (VLPO) Nucleus of Hypothalamus and right pallidum; while it is associated with bilateral lingual gyrus, right hippocampus, and right parahippocampal gyrus in heterosexual men. We postulate that sexual-orientation behaviors are being mediated by several circuits in the brain in the center of which the VLPO is playing an indistinguishable role. We hypothesize that the different aspects of the sexual dysfunction could be associated with innate or acquired lesions of VLPO. Accordingly, the electrical stimulation of the nucleus in those with sexual dysfunction would be a treatment option. Thus the VLPO could be considered a target for Deep Brain Stimulation (DBS) in individuals with impaired sexual function.

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The basic neuroscientific infrastructure of the sexual orientation and the gender disorders have been the matter of several studies without clear evidence and physiology [1]. Recently, Eprecht et al. [2] have addressed an important issue in patients with Subarachnoid Hemorrhage (SAH) which affects the quality of life to a great extent. The results of this study demonstrated that sexual dysfunction is a common problem

even after good grade SAH. Decreased sexual desire and loss of orgasmic experience were among the most common reported problems. The results of this study along with our own experience and other lines of evidence, lighted up an idea regarding the sexual function and sexual orientation.

Sexual function and orientation is a complex platform of human personality which is being modulated by sev-

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eral brain circuitries which is less understood currently. Recently, several studies have demonstrated interesting results regarding the role of several brain locations in sexual behaviors and orientation [3-5]. Accordingly, Weitekamp et al. demonstrated that expression of genes encoding nonapeptides and sex steroid receptors are upregulated in the familiar male context [3]. Their investigations have demonstrated critical role for preoptic gene expression, as well as circulating steroid hormone levels, in encoding information from the social environment and in shaping adaptive behavior [3, 6].

The Ventrolateral Preoptic Nucleus (VLPO) of the hypothalamus is currently believed to play a central role in regulating the social behavior and the reward-pleasure circuit [7]. From an anatomical and historical point of view, the VLPO has been found to be dimorphic in many species including humans [8, 9]. Several lines of evidence have demonstrated high expression of gonadal steroid hormone receptors in VLPO being associated with regulation of sexually differentiation and orientation [4]. Indeed, neuronal numbers or densities, synaptic organizations, distributions of innervating fibers, and gene expression patterns in the VLPO are all found to be sexually dimorphic [10]. Interestingly, it has been demonstrated that the dimorphic features of the VLPO are amenable to perinatal hormonal changes and affect the future sex-specific behaviors [5].

Recently, McHenry et al. demonstrated that the activity of the Medial Preoptic Area (MPA) correlate with sexually dimorphic display of male-typical mounting and female-typical pup retrieval [11]. In addition, the electrical stimulation of the MPA results in similar display of mounting and pup retrieval in both males and females [5]. These result indicate that the VLPO of the hypothalamus plays an important role in same sex orientation through olfactory stimulations. We would like to add some additive points to build a clinical milestone accordingly. Coria-Avila et al. demonstrated that male rats conditioned with quinpirole expressed about 60% more Fos-Immunoreactivity (IR Fos) in the MPA compared to controls [4]. In addition, exposure for the first time to the same sex scent induced a high activation of cells in the MPA, while repeated exposure results in less activation.

Interestingly, the MPA did not decrease its response when repeated exposure to the odor. Previously, Panzica and et al. demonstrated that the sexual-oriented behaviors in Quail are associated with hormonal changes and expression of estrogen receptors in VLPO [12]. The complementary results of Wei and et al confirmed these results and showed that the expression estrogen

receptor alpha (Esr1) in VLPO is essential for sexual-oriented behavior [5]. In an experimental study, Kindon et al. demonstrated that bilateral destruction of the VLPO in male rats results in sexual orientation toward the same sex [13]; this finding was also consistent in rats that lacked the dopaminergic neurons in VLPO [13]. In the same way, Wei et al. demonstrated that acute inhibition of VLPO Esr1 along with neurons destruction, results in disruption of sexual behavior and sexual-orientation in both male and female rats [5].

Functional Magnetic Resonance Imaging (fMRI) studies have demonstrated that different areas of the brain are activated during the sexual arousal and orgasm in heterosexual and homosexual individuals [8, 14]. Sexual arousal in homosexual men are associated with activation of the left angular gyrus, left caudate nucleus, VLPO and right pallidum; while it is associated with bilateral lingual gyrus, right hippocampus, and right parahippocampal gyrus in heterosexual men. None of these areas were activated in either group [8].

Cognitive dysfunction in identical brain location after TBI has also been reported previously [15]. In addition, Eprecht et al. demonstrated that anterior circulation was the most common site of aneurysm probably with SAH into the suprasellar cisterns and a great proportion of the patient had parenchymal defects [2]. These demonstrate that injury to the hypothalamic nuclei located in suprasellar regions could be responsible for sexual dysfunction.

Taking all these findings together, this can be postulated that sexual-orientation behaviors are being mediated by several circuits in the brain in the center of which the VLPO is playing an indistinguishable role. We hypothesize that the different aspects of the sexual dysfunction could be associated with innate or acquired lesions of VLPO. Accordingly, the electrical stimulation of the nucleus in those with sexual dysfunction would be a treatment option. Thus the VLPO could be considered a target for Deep Brain Stimulation (DBS) in individuals with impaired sexual orientation.

## Ethical Considerations

### Compliance with ethical guidelines

There was no ethical considerations to be considered in this research.

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### Authors contributions

Both authors contributed equally to this editorial.

### Conflict of interest

The authors declared no conflict of interest.

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