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Review Article

A topographical, structural and functional review of the sexual dimorphic nucleus of preoptic area in hypothalamus – A descriptive review

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Abstract

Are gender identity and sexual orientation determined prenatally or do postnatal social factors play any role? These are some intriguing questions which demand more clarity. With the growing dilemma around gender identity and disputes regarding sexual dysphoria, many neuropsychologists have focused their research on studying the areas of the brain that govern and orchestrate these functions. One such area that has gained immense attention in the recent past is the sexual dimorphic nucleus of preoptic area (SDN-POA) in hypothalamus. Our descriptive review was aimed to coalesce the existing information about the human preoptic nucleus location, its anatomical description and dimorphic changes in both sexes. We have broadened our search spectrum to encompass deeper insights into the role of SDN-POA in sex regulation, orientation and sexual or gender identity. Relevant articles were obtained by a comprehensive search conducted through PubMed, Scopus, Embase and google scholar electronic database. The search was employed using keywords related to hypothalamus, medial preoptic nucleus, sexually dimorphic nucleus, and sex regulation. The review includes English language articles published between January 1980 and July 2023. With compiled data from all the published human and non-human studies, we could relatively conclude that the existing research has given ample evidence about the sexual dimorphic changes seen in SDN-POA during brain development and with aging, among sexes. Males showed larger area and neuronal size in comparison to females. Despite comprehensive review, ambiguity still persists with regards to its anatomical nomenclature, location and its function. We found it increasingly difficult to construct a clear outline of the region and establish its connection with gender identity or orientation as hypothesized by previous authors. Nevertheless, the existing body of literature offers a foundational collation of knowledge, encouraging further investigation as we continue to seek clearer answers about the region's role in the neurobiology of sexual orientation.

Keywords: Hypothalamus, Uncinate nucleus, Medial preoptic nucleus, Sexually dimorphic nucleus, Anterior hypothalamic nuclei, Sexual orientation.

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1. Introduction

Considerable progress has been achieved in understanding the sexual behavior pattern in non-human animals. These predictive patterns of behavior in animals can be linked to their inheritance and to learned components during growth. But the same could not be said about human behavior, as these are highly complex, and integrated functions, that are governed and influenced by multiple factors including developmental and social interactions.[1] Studies have shown that human behavior changes constantly and is suborned by environmental interactions.[2,3] Changes in the perception of individual's gender identity, and sexual orientation would certainly be under this category. Understanding these intricate functions has always presented its own challenges and complexities. Neurobiologists, psychologists and researchers have targeted neural circuits and areas of the brain to get better insights into these behaviors.

Gender identity – according to American Psychological Association (APA) "is an individual's sense of their own gender (e.g., as a male, female, transgender, nonbinary)" and Sexual orientation is outlined "as an often-enduring pattern of emotional, romantic, and/or sexual attractions to men, women, or both. It also refers to an individual's sense of personal and social identity based on those attractions, related

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behaviors, and membership in a community of others who share those attractions and behaviors".[4] Sexual behavior is defined as a "diverse array of activities that can be classified as masturbation, oral-genital stimulation (oral sex), penile-vaginal intercourse (vaginal sex), and anal stimulation or anal intercourse. Sexual behaviors may also include activities to arouse the sexual interest of others or attract partners".[5]

With the growing dilemma around gender identity and disputes regarding gender dysphoria, the need to understand the sexually dimorphic areas of the brain has grown exponentially. According to Hofman and Swaab[6] certain areas of the human and animal brain show sex differences, which could form the neurocircuitry source for sex-specific behavior and reproductive and non-reproductive functions. Among the several dimorphic areas of the brain like bed nucleus of stria terminalis and the anterolateral paraventricular nucleus,[7] the medial preoptic nucleus of hypothalamus has gained paramount attention in the recent past due to the compelling differences shown among sexes in non-human animals. Yet a limited number of published reviews have tailored this connection between SDN-POA with gender identity and sexual orientation.[6,7] Our review is focused towards understanding this unique nucleus and to bridge the earlier description of the nuclei by various authors with the most modern insights about its anatomical depiction, location and functional relevance of the human preoptic nucleus. This review aims to identify the precise location of the nuclei, nomenclature and the morphological features of it.

Our review process involved three important steps. The first step was to identify relevant abstracts within the PubMed, Scopus, Embase and google scholar database. This search was conducted based on keywords like hypothalamus, medial preoptic nucleus, sexual dimorphism, gender dysphoria, and fMRI. Next step included screening, during which, all *180* abstracts were divided, and distributed among the six reviewers. Each reviewer segregated the most relevant abstracts and compiled them separately. The entire process (divide, distribute and select) was repeated to avoid any selection bias. Abstracts with greatest similarity to our ideology and those selected by two reviewers were included (n - 68), and those beyond the scope of present review, duplicates and non-English language were excluded. Our review includes articles published between the year 1980 and 2023. 68 complete articles extracted from the database were redistributed among the six-member team for further scrutiny, resulting in the exclusion of 48 articles. These were non-human related, and articles focused on a different dimorphic nucleus within hypothalamus. Consequently, 20 studies met the predefined inclusion criteria and were incorporated into the final review.

2. Section 1: Anatomical considerations of preoptic nucleus

The preoptic nucleus of the hypothalamus commonly known as sexual dimorphic nucleus of the preoptic area (SDN-POA), is also referred to by different names such as the interstitial nucleus of the anterior hypothalamus (INAH),[9] uncinate nucleus (Un),[10] medial preoptic area (MPOA) and medial preoptic nucleus (MPN).[11]

2.1. Morphometric description of the SDN in preoptic region of hypothalamus:

Umpteen number of authors have described the location, and the morphological features of the SDN in non-human, but studies related to human subjects are scarce. Here we have summarised morphometric description of human SDN-POA by various authors:

Swaab, Hofman & flier,[8] were among the early researchers who have contributed greatly to the understanding of the anatomy and the dimorphic changes seen in human hypothalamus. In their investigations, they performed studies on 30 human brains, consisting of 13 males subjects with age between 27-85 years, mean of 51±6 and 17 females aged between 10-93 years, mean of 58±7. Subject's medical records showed no history of nervous system disorders or were diagnosed with any type of clinical or neuropathological dysfunction. The specimens obtained by autopsy were then fixed in formaldehyde, dehydrated and embedded in paraffin wax. Serial sections were obtained and later stained with thionine. The study was directed to analyse age related changes in SDN–POA in relation to cell number, length in specific thionine-stained slide and structural relation of volume of SDN-POA with total brain weight. Their results describe the human SDN-POA as an ovoid, densely arranged cell collection, characterized by larger cell bodies which were heavily stained as compared with the adjoining preoptic regions. The nucleus was located in the medial region of the preoptic area, between the dorso-lateral aspect of supraoptic nucleus (SON) and the rostral end of the paraventricular nucleus (PVN) (6).(**Figure 1**)

Allen et al.,[9] focused their study on the preoptic anterior hypothalamic area to understand the possible sexual dimorphic nuclei in human brain. This study was performed on 22 human brains with an age group between 4 to 81 years. No subjects were diagnosed with any underlying neurological disorders. After autopsy, all the brain specimens were fixed in formalin, embedded in gelatin, solidified and sectioned coronally. These sections were later stained with thionin. As they were unable to isolate any cell group that were identical to sexual dimorphic nucleus as in other species, they segregated them into 4 discrete groups within the targeted preoptic area. These groups were quantitatively analyzed and were opted to name them as interstitial nucleus of anterior hypothalamus (INAH1 – 4). In this study, SON was used as a control nucleus because this nucleus showed no dimorphic changes in other species was located in anterior hypothalamus and had well demarcated boundaries. Results of this study showed that the INAH nuclear aggregate was seen between SON and PVN. INAH-1 contained larger cell bodies and was located between SON and the rostral pole of

PVN. INAH-2 was twice larger in males and was composed of smaller cell bodies. Reports also showed INAH-2 was extensively larger (3.7-fold) in multiparous women. INAH-3 in males was 2.8 times larger when compared with females with larger cell bodies and was found just above the rostral pole of PVN. INAH-4 located posteromedial to INAH-3, showed no size difference in either gender.(**Figure 2**) The authors claim that INAH-2 and INAH-3 showed definitive sexually dimorphic changes in humans. A striking similarity was noted between INAH-3 in humans and SDN-POA of rats, location and cell body size. Allen and colleagues are hesitant for such comparison without further investigations. He reported that INAH1 resembles the sexual dimorphic nucleus in humans similar to earlier descriptions by Swaab and fliers, (8). Multiple factors like cell type, location, size, shape, and reduction of cell volume with aging had much resemblance between the two areas. Swaab and colleagues (6) mentioned the nucleus been 2.5 times larger in males, on the contrary, reports by Allen et al showed it to be 1.2 fold larger in males than in females. This difference would be attributed to thickness of sections, or different age group been used in the study by authors.

Braak H and Braak E, in their conclusive review on chiasmatic (preoptic) and tuberal region of hypothalamus, have described the *intermediate nucleus* (sexual dimorphic nucleus). They examined hypothalamic cell body architecture by relatively thick (100 - 400µm) Nissl preparations counterstained for interneural lipofuscin deposits. According to Braak, intermediate nucleus is a small, well defined condensed structure located at the optic chasmal level midway between the PVN and SON.(**Figure 3**, **Figure 4**) They have reported presence of similar nuclear mass in the chiasmatic region of brain of a rhesus monkey,(**Figure 5**) also endorsing the findings by Swaab and flier.[8] They also found the volumetric difference between males and females; it was found to be larger in men than in age-matched women. The intermediate nucleus is composed of a single type of neuronal form. These medium-sized bipolar nerve cells are defined by numerous large and sharply defined Nissl bodies. As these neurons lack lipofuscin deposits, this feature could aid in differentiating them from ectopic neurosecretory nerve cells, which lie in close vicinity to intermediate nucleus.[12]

Koutcherov and colleagues studied the organization of adult human medial preoptic nucleus (MPN) by using various cytological and chemoarchitectonic markers. Earlier studies have tried to establish functional similarities between human and non-human medial preoptic nucleus, but less attention was paid to the subnuclear architectural organization of MPN. The aim of the study was to expound on the internal cyto and chemo-architecture of MPN and that would aid to envision the organization of reproductive and homeostatic control mechanism from non-humans to humans. The study was conducted on human brains, with the subjects' age group ranging from 15 to 76 years. No subjects were diagnosed with any underlying neurological disorders. All eight specimens were divided into two batches, two and six brains respectively, which were subjected to different preservation techniques. Two cryoprotected brain specimens were sectioned and stained with immunohistochemical agents. Six formalin preserved paraffin embedded brains sections were treated with various neuroactive substances for immunohistochemical processing. The results showed the MPN as an "inverted comma" shaped area curved out laterally by lateral area of hypothalamus and caving in medially into para-ventricular nucleus.(**Figure 6**) The MPN was located in the cell dearth medial preoptic region (MPOA) delineating itself from the suprachiasmatic nucleus (SCN) and anterior commissure on its ventral and dorsal aspect respectively. Rostrally the nucleus was seen extending into the region between SON and SCN nuclei. And its caudal extension was seen curving from PVN towards SON nucleus. Based on cyto and chemoarchitecture, the MPN was compartmentalized into 4 regions – Medial, lateral MPN, intermediate nucleus and uncinate nucleus.(**Figure 7**) They conclude by stating that Uncinate nucleus (Un) would be the homolog of sexual dimorphic nucleus of medial preoptic area as in rats. According to them Un consists of a tight group of medium sized cell bodies, and was located between PVN (medially), medial part of MPN (laterally).[10]

Based on earlier studies by Braak and Braak, and Koutcherov et al., who proposed that INAH3 was a part of uncinate nucleus of hypothalamus, and they grouped it as sexual dimorphic nucleus.[12] In the year 2008, Garcia et al.,[13] studied changes in the interstitial nucleus of hypothalamus (INAH3) among transsexual people. They conducted studies on 42 human brains targeting the hypothalamic region. Controls group had 25 specimens, with 14 males (age group: 25 - 81) and 11 females (age group: 21- 82) with no history of neurological, endocrine or psychiatric disorders. The case group consisted of 12 transsexual individuals with age group: 26- 84 years. Formaldehyde fixed human brain specimens were embedded in paraffin and sectioned. These sections were processed with thionin and immunocytochemical staining. The nucleus was located microscopically using human brain atlas[14] and was affirmed by immunochemistry. The results showed the location of uncinate nucleus in the close proximity to third ventricle across the hypothalamic sulcus, sandwiched between fornix and optic chiasm, dorsal to anterior commissure. The nucleus mainly consisted of medium sized, oval shaped, small and compactly arranged neurons. The nucleus was bisected by fibers of fornix into INAH3 and INAH4. Based on this, three different forms of arrangement were seen, one horseshoe shaped, or either completely bisected or as a single unit.(**Figure 8**)[13]

3. Section 2: Discussion

3.1. SDN-POA role in gender identity and sexual orientation

Are gender identity and sexual orientation determined prenatally or do postnatal social factors play any role? For

centuries, we have charted the human body's development and aging, including its sexual differentiation. Numerous areas of the brain show significant size-by age trajectories between male and females in mammals like rhesus monkey,[15] quail,[16] mice, and many other species.[17-19] Investigations on non-human species have helped localize the preoptic area of the hypothalamus and affirm the sexually dimorphic characteristics in terms of size and cell number of the nucleus. The nucleus been situated in the anterior hypothalamus and superior to the optic chiasm (**Table 1**) orchestrates a vast number of activities regulating the bodily functions, however, its close association with sexual identity and sexual functions has attracted much needed attention. To fully understand the importance and role of SDN-POA in gender identity and individual's sexual orientation, we have cumulated observations, findings and outcomes of various authors. These well documented conclusions on the dimorphic changes seen in SDN-POA among different individuals (heterosexual, homosexual and transsexuals) belonging to various age groups, should facilitate us in understanding the contribution of this key area of brain in gender identity and sexual orientation.

Table 1: Anatomical description of sexual dimorphic nucleus in human hypothalamus pre-optic area by various authors

Authors	Year	Nomenclature used	Location description	Nucleus description
Swaab and Fliers.,[8]	1985	Sexual dimorphic nucleus – Pre-optic area	The SDN-POA was located in the medial region of the preoptic area, between the dorso-lateral aspect of supraoptic nucleus and the rostral end of the paraventricular nucleus	Densely arranged cell collection, characterized by larger cell bodies
Allen et al.,[9]	1989	Interstitial nucleus of anterior hypothalamus (INAH2 and INAH3)	Nuclear aggregate seen between SON and PVN.	INAH 2 - smaller cell bodies INAH3 - larger cell bodies
Braak H and Braak E,[12]	1992	Intermediate nucleus	Small, well defined condensed structure located at the optic chasmal level midway between the PVN and SON.	Medium-sized bipolar nerve cells are defined by numerous large and sharply defined Nissl bodies
Koutcherov et al.,[10]	2007	Uncinate nucleus	Located between PVN (medially), and medial part of MPN (laterally)	Tight group of medium sized cell bodies
Garcia-falgueras A and Swaab,[13]	2008	Uncinate nucleus	Located in the close proximity to the third ventricle, across hypothalamic sulcus. It was sandwiched between optic chiasm and fornix, and anterior commissure on the ventral aspect.	Medium sized, oval shaped, small and compactly arranged neurons

Table 2: Morphometry of the human sexually dimorphic nucleus

Variable[1]	Males (n=13)	Females (n=17)	Dimorphic index (%)[2]	Statistics[3]	
				t_2	U_2
Volume (mm^3)	0.182±0.0222	0.084±0.0116	73.7	4.178***	188***
Cell density ($\times 10^3$ mm^{-3})	159.4±12.05	151.9±8.06	4.82	0.536	114.5
Total cell number ($\times 10^3$)	27.56±3.172	13.20±2.152	70.5	3.877**	186**
Cell-nuclear diameter (µm)	6.36±0.149	6.49±0.136	-2.02	-0.641	127
Brain weight (g)	1400±24.4	1226±35.3	13.3	3.802***	185.5**

[1] Values are given as mean ± S.E.M.

[2] Dimorphism index = 100 $(\bar{X}m - \bar{X}f)$ / $\{(\bar{X}m + \bar{X}f)/2\}$

[3] t_s student's t test: U_s, Wilcoxon/Mann-Whitney U test

Note: ***P≤ 0.001; **0.001< P ≤0-01; *0.01 < P ≤0.05.

Adapted from: Hofman and Swaab, 1989, Copyright 1989, Society for Neuroscience

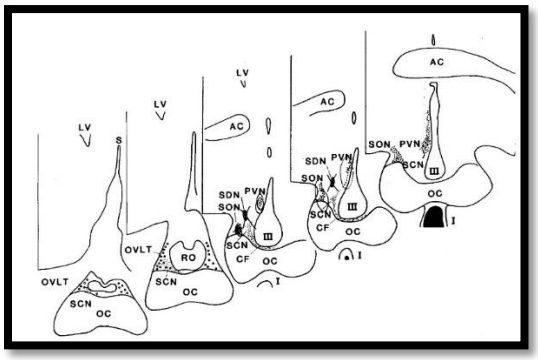

Figure 1: Topography of the sexually dimorphic nucleus (SDN) in the preoptic area of the human hypothalamus. Third ventricle, Ill; anterior commissure, AC; infundibulum, I; lateral ventricle, LV; optic chiasma, OC; organum vasculosum of the lamina terminalis, OVLT; recessus opticus, RO; septum, S; suprachiasmatic nucleus. SCN; paraventricular nucleus, PVN; supraoptic nucleus, SON; commissural fibres of the suprachiasmatic nucleus, CF. (Source: Adapted from Swaab, d. F. & fliers, E. (1985). A sexually dimorphic nucleus in the human brain. Science 228, 1112-1114. Reprinted with permission from AAAS.)

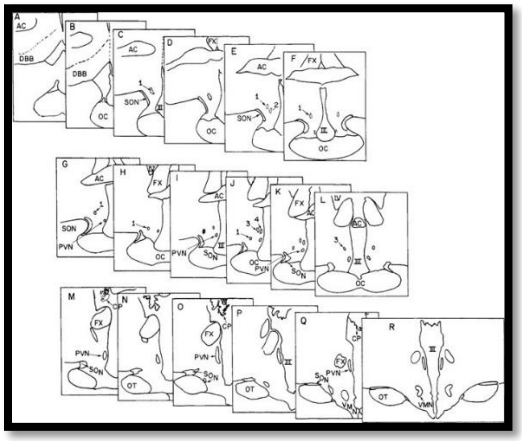

Figure 2: Schematic illustration of the nuclei analyzed in this study in the coronal plane, organized rostrally to caudally, from the diagonal band of Broca (DBB) to the ventromedial nucleus (VMN). This atlas was drawn from sections, all projected at the same magnification, from the 58year-old male from pair number 7 who was selected because of the similarity in the plane of section to his age-matched pair. There are 7 60-gm-thick sections between each section from A through C and from L through R. Between each section from C through L, which contain the INAH, there are only 2 60-gm-thick sections. Other abbreviations: anterior commissure, AC; optic chiasm, OC; INAH-I, 1; fornix, FX; third ventricle, Ill; INAH-2, 2; supraoptic nucleus, SON; paraventricular nucleus, PVN; INAH-3, 3; INAH-4, 4; lateral ventricle, LV•, choroid plexus, cp; and optic tract, OT. (Source: Adapted from Allen LS, Hines M, Shryne JE, Gorski RA. Two sexually dimorphic cell groups in the human brain. J Neurosci. 1989 Feb;9(2):497-506. Copyright 1989, Society for Neuroscience)

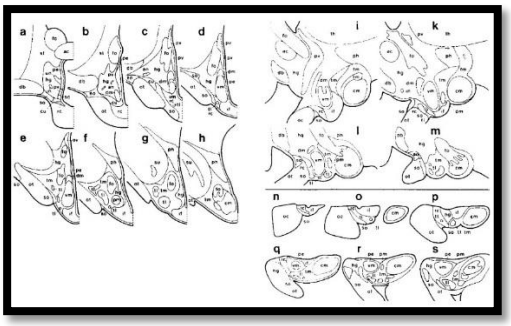

Figure 3: Chiasmatic and tuberal region of the proper hypothalamus in the human adult. The diagram shows the main landmarks and nuclear grays that are encountered as coronal sections are traced antero-posteriorly *(u - h),* sagittal sections mediolaterally *(i - m)* and horizontal sections infero-superiorly *(n* -s). Each of the sections is spaced apart by *800* pm. *uc,* Anterior commissure; *an,* accessory neurosecretory nucleus; *em,* corpus mamillare; *cu,* cuneate nucleus; *db,* nucleus of the diagonal band; *dm.* dorsomedial nucleus; *fm,* fasciculus mamillo-thalamicus; *f,* fornix; *hg,* hypothalamic gray; *v,* infundibular nucleus; *in,* intermediate nucleus; *oc,* optic chiasm; *of,* optic tract; *pe,* periventricular nucleus; ph, posterior hypothalamic nucleus; *pm,* posteromedial nucleus; *pv,* paraventricular nucleus; *re,* retrochiasmatic nucleus; *sc,* suprachiasmatic nucleus; *so,* supraoptic nucleus; *st,* nucleus of the stria terminalis; *su,* subthalamic nucleus; *fh,* thalamus; *tl,* lateral tuberal nucleus; *fm,* tuberomamillary nucleus; *un,* uncinate nucleus; *vm,* ventromedial nucleus (Source: Reprinted from Prog Brain Res, 93, Braak H, Braak E. 1992. Anatomy of the human hypothalamus (chiasmatic and tuberal regions). :3–16. Copyright (1992) with permission from Elsevier)

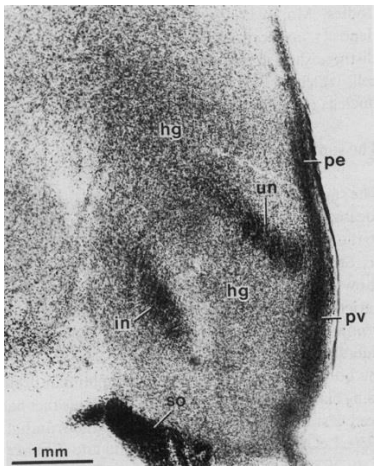

Figure 4: Coronal section through anterior portions of the chiasmatic region of the human hypothalamus (aldehydefuchsin Darrow red, 400 gm). Note the well delineated intermediate nucleus halfway between the supraoptic nucleus and the paraventricular nucleus. (For abbreviations see legend to Fig. 4.) (Reprinted from Prog Brain Res, 93, Braak H, Braak E. 1992. Anatomy of the human hypothalamus (chiasmatic and tuberal regions). :3–16. Copyright 1992, with permission from Elsevier)

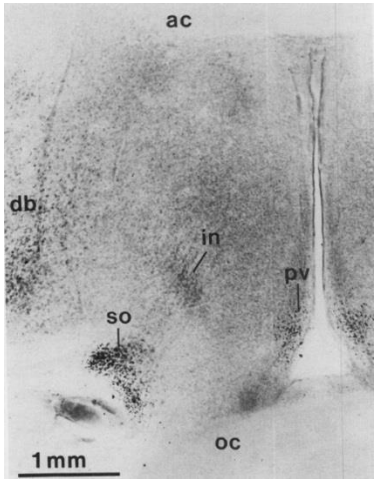

Figure 5: Coronal section through the chiasmatic region of the rhesus monkey (aldehydefuchsin, Darrow red, 400 em). The intermediate nucleus is seen as a basophilic structure at about the same position as in the human brain. (For abbreviations see legend to Figure. 4.) (Reprinted from Prog Brain Res, 93, Braak H, Braak E. 1992. Anatomy of the human hypothalamus (chiasmatic and tuberal regions). :3–16. Copyright 1992, with permission from Elsevier)

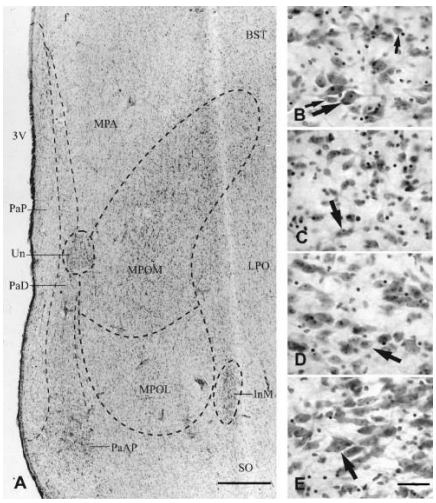

Figure 6: Photomicrographs of cresyl violet-stained section of the human hypothalamus at the level of the anterior commissure, showing the variations in cell concentration, shape, and topographic position among different subnuclei of the human MPO; **A:** For abbreviations in this see list. Neuronal types in different subdivisions of the human MPO are demonstrated in photomicrographs at right; **B:** MPOM mostly large, densely packed neurons (large arrow), but also some small cells (small arrows); **C:** MPOL medium-sized, dispersed, bipolar neurons (arrow) and few small, round cells; **D:** Un mostly medium-sized, tightly packed, round neurons (arrow). E: InM large, tightly packed, spindle-shaped neurons (arrow). Scale bars =1.0 mm in A; 50 µm in E (applies to B–E). (Koutcherov Y, Paxinos G, Mai JK. Organization of the human medial preoptic nucleus. J Comp Neurol. 2007;503(3):392-406. Wiley doi: 10.1002/cne.21355. PMID: 17503490.)

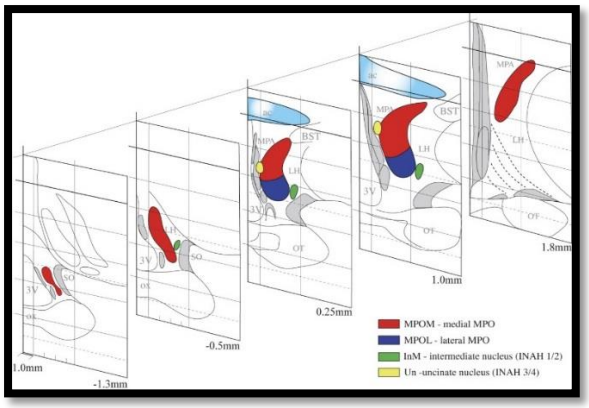

Figure 7: Model of the human medial preoptic nucleus showing the subnuclei delineations based on the distribution of six histochemical markers (AChE, SMI32, Cb, NPY, CART, and MCH For abbreviations in this see list.) and cytoarchitectonic characteristics. Individual subnuclei are illustrated by different colors. The stereotaxic coordinates were borrowed from Mai et al. (1997). The third ventricle wall lies to the left. (Koutcherov Y, Paxinos G, Mai JK. Organization of the human medial preoptic nucleus. J Comp Neurol. 2007 Jul 20;503(3):392-406. Wiley doi: 10.1002/cne.21355. PMID: 17503490)

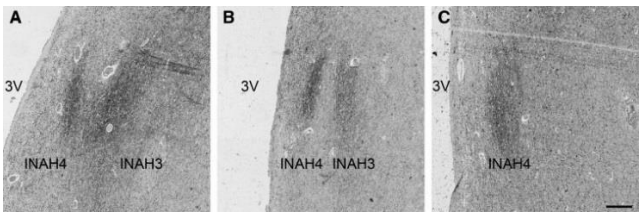

Figure 8: Representative immunocytochemical staining of the NPY innervation of the uncinate nucleus showing the three different types; **A:** typical horse-shoe shape, in which fornix fibers do not completely bisect the nucleus; **B:** the two subdivisions of the Un clearly divided by fornix fibers, originally called INAH3 and INAH4 and; **C:** the nucleus as just one part, considered to be the INAH4 (A NBB # 98031man 33 years old, B NBB # 98006 man 50 years old, C NBB # 91009 woman 36 years old. INAH3 and 4: interstitial nuclei of the anterior hypothalamus 3 and 4, 3V: third ventricle. Scale bar=250 mm. (Garcia-Falgueras A, Swaab DF. A sex difference in the hypothalamic uncinate nucleus: relationship to gender identity. Brain. 2008; 131:3132-3146 by permission of Oxford University Press)

As mentioned earlier (section 1), studies conducted by Hofman and Swaab, on 30 human brains (13 males, and 17 female subjects) documented various morphometric aspects of SDN-POA. Prior to comparing the SDN-POA morphology between sexes, different factors, like age, autopsy delay, fixation time, brain size, time and date of death were also documented and analysed. The reason for the prior analysis of different factors was to minimise their influence on the SDN-POA measurement. No factors showed significant differences between the groups (males and females) except for the brain size (volume), which showed an evident dimorphism with male brain weighing 1440±24.4g and

females around 1226±35.3g. The shape of SDN-POA in general appeared circular in males and females it was elongated. It was the volume of the nucleus in adults that showed striking evidence of sexual dimorphism. In males, mean volume of this nucleus was 2.2 times larger in comparison to females. The total cell number within SDN-POA in males was 2.1 times higher than in females. No statistically significant sex difference was observed in cell nuclear size or cell density (**Table 2**). Swaab and colleagues explain the volume difference of SDN-POA in sexes could be attributed to the sexual dimorphism in the entire brain size. Their results showed evident sexual dimorphic changes in cell morphology, size, and shape of the human SDN-POA of hypothalamus and documented reduction in cell number in males aged between 50-60 years. These results align with the similar results shown by Swaab and fliers, 1985 (8). Therefore, authors hypothesized that the areas of the brain with sexual dimorphism have its own sex-based pattern of growth and degeneration. Would these changes seen in SDN-POA with aging be a result of age-related modifications in gonadal functions, remains unclear.[6]

4. Conclusion

SDN-POA is among the fewer areas of the brain that has displayed remarkable sexual dimorphism in human and non-human species. Experimental lesion of SDN in rats and other species have satisfactorily uncovered the sexual functions regulated by this nucleus. Even with a strong backing of studies highlighting the influence of steroidal hormones like testosterone on masculinization of developing brain, particularly the sexually dimorphic regions. As well as emphasizing the importance of prenatal over the postnatal factors in influencing and establishing gender identity and sexual orientation. We would like to conclude that it has become increasingly difficult to construct a clear outline of the region and establish its connection with gender identity or orientation. Ambiguity still persists with regards to its nomenclature, location and its function. As the present review does not encompass the neural circuits, or the pathway involved in sexual orientation nor the causative factors for gender dysphoria, it would be unjust to solely allocate SDN-POA the status of the key area of the brain that orchestrates sexual orientation or gender identity. This definitely invites the need of more research in this particular field of neuroscience, that would help understand the gender dysphoria and probably assist psycho-sexologists, neuropsychologists and neurobehavior experts in combating it.

5. Source of Funding

No funding was received for the review.

6. Conflict of Interest

None.

References

1. Balthazart J, Ball GF. Topography in the preoptic region: Differential regulation of appetitive and consummatory male sexual behaviors. *Front Neuroendocrinol*. 2007;28(4):161–78.
2. Larsen CS. The past 12,000 years of behavior, adaptation, population, and evolution shaped who we are today. Vol. 120, Proceedings of the National Academy of Sciences of the United States of America. *Natl Acad Sci*. 2023;120(4):e2209613120.
3. Sih A, Ferrari MCO, Harris DJ. Evolution and behavioural responses to human-induced rapid environmental change. *Evol Appl*. 2011;4(2):367–87.
4. American Psychological Association. Understanding sexual orientation and homosexuality [Internet]. 2008 [cited 2024 Aug 21]. Available from: https://www.apa.org/topics/lgbtq/orientation
5. Brown JL. Sexual Behavior. In: Gellman MD, Turner JR, editors. Encyclopedia of Behavioral Medicine [Internet]. New York, NY: Springer New York; 2013. p. 1773–4. Available from: https://doi.org/10.1007/978-1-4419-1005-9_667
6. Hofman MA, Swaab DF. The sexually dimorphic nucleus of the preoptic area in the human brain: a comparative morphometric study. *J Anat*. 1989;164:55–72.
7. Purves Dale, Augustine JG, Fitzpatrick D, Hall CW, LaMantia Samuel A, Mooney DR, et al. Neuroscience. 6th ed. Purves D, Augustine JG, Fitzpatrick D, Hall CW, LaMantia Samuel A, Mooney DR, et al., editors. New York: Oxford University Press; 2018.
8. Swaab DF, E Fliers. A Sexually dimorphic nucleus in the human brain. *Science*. 1985;228(4703):1112–5.
9. Allen LS, Hines M, Shryne JE, Gorski RA. Two Sexually Dimorphic Cell Groups in the Human Brain. *J Neurosci*. 1989;9(2):497–506.
10. Koutcherov Y, Paxinos G, Mai JK. Organization of the human medial preoptic nucleus. *J Comp Neurol*. 2007;503(3):392–406.
11. Simerly RB, Swanson LW. The organization of neural inputs to the medial preoptic nucleus of the rat. *J Comp Neurol [Internet]*. 1986;246(3):312–42.
12. Braak H, Braak E. Anatomy of the human hypothalamus (chiasmatic and tuberal region). *Prog Brain Res*. 1992;93:3–16.
13. Garcia-Falgueras A, Swaab DF. A sex difference in the hypothalamic uncinate nucleus: Relationship to gender identity. *Brain*. 2008;131(12):3132–46.
14. Mai JK, Majtanik M, Paxinos G. Atlas of the human brain. Academic Press; 2015.
15. Byne W. The medial preoptic and anterior hypothalamic regions of the rhesus monkey: cytoarchitectonic comparison with the human and evidence for sexual dimorphism. *Brain Res [Internet]*. 1998;793(1-2):346–50.
16. Viglietti-Panzica C, Panzica GC, Fiori MG, Calcagni M, Anselmetti GC, Balthazart J. A sexually dimorphic nucleus in the quail preoptic area. *Neurosci Lett [Internet]*. 1986;64(2):129–34.
17. Roselli CE, Larkin K, Resko JA, Stellflug JN, Stormshak F. The volume of a sexually dimorphic nucleus in the ovine medial preoptic area/anterior hypothalamus varies with sexual partner preference. *Endocrinology [Internet]*. 2004;145(2):478–83.
18. Gorski RA, Harlan RE, Jacobson CD, Southam AM. Evidence for the existence of a sexually dimorphic nucleus in the preoptic area of the rat. *J Comp Neurol*. 1980;193(2):529–39.
19. He Z, Ferguson SA, Cui L, Greenfield LJ, Paule MG. Development of the sexually dimorphic nucleus of the preoptic area and the influence of estrogen-like compounds. *Neural Regen Res [Internet]*. 2013;8(29):2763–74.
20. LeVay S. A difference in hypothalamic structure between heterosexual and homosexual men. *Science*. 1991;253(5023):1034–7.

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