Turk Neurosurg 32(6):960-967, 2022

Original Investigation

DOI: 10.5137/1019-5149.JTN.36551-21.2

Received: 11.09.2021
Accepted: 25.01.2022

Published Online: 18.07.2022

The Morphology and Morphometry of the Human Interthalamic Adhesion Using Cadaveric Brains and Magnetic Resonance Images and Their Clinical Significance

Apurba PATRA[1], Satish Ravi KUMAR[2], R Shane TUBBS[3], Khanak NANDOLIA[4], Adil ASGHAR[5]

[1]All India Institute of Medical Sciences, Department of Anatomy, Bathinda, India
[2]All India Institute of Medical Sciences, Department of Anatomy, Rishikesh, India
[3]Tulane University School of Medicine, Director of Surgical Anatomy, Program Director of Anatomical Research, Clinical Neuroscience Research Center Professor, Departments of Neurosurgery, Neurology, Surgery, and Structural and Cellular Biology Tulane, New Orleans, LA 70112, USA
[4]All India Institute of Medical Sciences, Department of Radiodiagnosis, Rishikesh, India
[5]All India Institute of Medical Sciences, Department of Anatomy, Patna, India

Corresponding author: Kumar Satish RAVI ✉ drksravi.jipmer@gmail.com

ABSTRACT

AIM: To determine the prevalence, location, and dimensions of interthalamic adhesions (ITAs) in Indian brains.

MATERIAL and METHODS: We examined 100 human brains [50 cadaveric and 50 magnetic resonance (MR) images] in the midsagittal plane for the presence or absence of ITAs, their location in the lateral wall of the third ventricle and dimensions.

RESULTS: ITA was found in 87 brains (87%), four showed duplication (4%). Both its duplication and absence were more frequent among males than in females. It was most commonly located in the anterosuperior quadrant with posterosuperior extension. The mean horizontal diameter (7.13 ± 4.31 mm) was longer than the vertical (5.13 ± 3.17) in all the brains. Its average area (37.98 ± 41.47 mm^2) showed tremendous variation (ranges between 4.40 mm^2 to 203 mm^2) and was significantly higher in females (61.23 ± 56.22 mm^2) than males (36.44 ± 43.21 mm^2) (p=0.026). No correlation was found between the surface area of the ITA and the length of the third ventricle.

CONCLUSION: Absence and duplication of ITA are fairly common in Indian brains with significant male predominance. Morphometric data are robust to advocate for sex differences in the ITA size, although not associated with surrounding thalamic or third ventricle anatomy.

KEYWORDS: Brain, Cadaver, Histological Techniques, Neuroanatomy, Schizophrenia, Thalamus, Third Ventricle

ABBREVIATIONS: ITA: Interthalamic adhesion, **MI:** Massa intermedia, **CC:** Corpus callossum **CA:** Anterior commissure, **CP:** Posterior commissure, **SA:** Cross-sectional area, **HD:** Horizontal diameter, **VD:** Vertical diameter, **T2W:** Midsagittal T2 weighted, **MRI:** Magnetic resonance images, **CSF:** Cerebro-spinal fluid, **DM:** Dorsomedial thalamic nucleus, **SSD:** Schizophrenia spectrum disorders, **CA-GP:** Anterior commissure-pineal gland.

Apurba PATRA : 0000-0002-1107-4481
Satish Ravi KUMAR : 0000-0003-0527-2825
R Shane TUBBS : 0000-0003-1317-1047
Khanak NANDOLIA : 0000-0002-8627-2992
Adil ASGHAR : 0000-0002-1404-1298

INTRODUCTION

An interthalamic adhesion (ITA) is a neuroanatomical structure that acts as a bridge of tissue joining the medial surfaces of the two thalami (11). It is also known as massa intermedia (MI), a mass of neural tissue containing commissural fibers (5). It crosses over the third ventricle behind the interventricular foramen of Monro (29). In most mammals, it is fully developed and contains many nuclei, but it is comparatively more minor and less developed in humans and includes only the nucleus reuniens and part of the nucleus rhomboideus (30). It can be absent or, on rare occasions, even double (22,40). During the early embryonic stage, the ITA appears concurrently with the thalami. As the thalami grow, they gradually approach each other, and around the end of the first trimester, they meet over a variable area. The area of this connection is the ITA. It elongates as a bar of neural tissue because of cerebrospinal fluid pressure accumulated within the third ventricle cavity (9).

The functional importance of the ITA in humans and the symptoms consequent on its presence or absence are unknown. Knowledge of its morphology, topographical location, and size is essential for neurosurgery, neuroanatomy, and neuroradiology. In humans, the ITA is variable (30); it is noteworthy since it has been linked to dopaminergic modulation of the limbic system in the substantia nigra and caudate nucleus of cats (5). In people with schizophrenia, the probability of its absence is more in males than in females (5). ITAs have been observed to be more frequent and prominent in healthy females, and their size disparities have recently been linked to neuropsychological measures of attention functioning in them (5). Most researchers agree that the ITA is an interhemispheric commissural route that connects limbic and cognitive processing networks with sexual dimorphism in size and prevalence. Understanding its anatomical connections is aided by *in vivo* neuroimaging methods (5,11). However, identifying the ITA in gained images remains a crucial challenge, particularly in younger subjects with narrow third ventricles and "kissing" thalami (5). Cadaveric studies can help establish the prevalence, location, and size of this tiny structure. Recently, probabilistic tractography has offered the advantage of studying the connectivity patterns of fibers crossing the ITA. The primary aim of the present study was to determine the prevalence, location, and size of the ITA in brains of South Asian origin. The secondary aim was to identify any relationship between the ITA size, sex and the size of the third ventricle.

MATERIAL and METHODS

The study was conducted on 100 human brains [50 cadaveric and 50 magnetic resonance images (MRI)]. Cadaveric brains (38 male and 12 female) aged approximately 45–65 years at death were fixed in a basic suspension of formalin. Brains with a history of intracranial lesions, head injuries, pathologies, and obvious abnormalities were all excluded from the study. Immediately, they were removed from the cranial cavities, and the brains were fixed in 10% formalin for four weeks, so all the anatomical structures were fully and uniformly fixed and exhibited their standard form. Formalin fixation is considered to cause brain shrinkage (18). To mitigate this, we employed a 10% formol solution for four weeks (the actual quantity of dissolved formaldehyde in 10% formalin is just 3.7–4.0%), which is a typical fixation technique. The brains were then meticulously sectioned in the midsagittal plane using a brain knife through the body of the corpus callossum (CC), the interhemispheric fissure, the septum pellucidum, the third ventricle chamber, and the cerebral aqueduct. The ITA between the two thalami's medial surfaces was therefore severed. On these midsagittal slices, its many characteristics were identified and documented.

First, we determined the presence or absence of the ITA. Then the medial surfaces of all the sagittal sections were photographed, and the shapes of the ITAs were noted. Sections with no ITA or a duplicated one were excluded from further procedures.

Second, a coordinate system was established on the lateral side of the third ventricle to more accurately pinpoint the topographic placement of the ITA (viewed from its medial aspect). A straight line from the superior most point of the anterior commissure (CA) to the inferior most end of the posterior commissure was established as the X-axis (abscissa) (CP). The midpoint of this CA-CP line was intercepted by the Y-axis (ordinate). This coordinate system divided the lateral wall of the third ventricle into four quadrants. The position of the ITA was described according to the location of its center in one of those quadrants (Figure 1).

The size (midsagittal cross-sectional area, SA) of the ITA was computed by measuring its horizontal (HD) and vertical (VD) diameters on the midsagittal sections using digital calipers (Mitutoyo12"/300 mm, 0.01 mm resolution). The HD was calculated by measuring the ITA's anteroposterior length at the level of the interventricular foramen's posterior point (of Monro). The VD was measured as the vertical tangential length of the ITA passing through its center. The SA determined using this approach was compared to the distance between the anterior and posterior commissures (CA-CP interval) to see if it was affected by the third ventricle's length.

Similarly, 50 (32 males and 16 females) midsagittal T2 weighted (T2W) MRI with no abnormality, aged between 18–86 years, were retrospectively evaluated for the presence or absence of ITA, their duplication, location and size (midsagittal cross-sectional area)

RESULTS

Findings from Cadaveric Brains

Prevalence: An interthalamic adhesion (ITA) was present in 43 of the 50 brains studied (86%). It was absent in seven brains (14%) (Figure 2), four males and three females. The prevalence of the ITA had no significant relationship with gender ($p>0.05$). Among the 43 cases, the ITA was single in 42 (96.97%) and doubled in one (male) (3.03%) (Figure 3).

Shape: ITAs of different shapes were found: oval (primary diameter or length was anteroposterior) in 19 (45.23%), circular in 17 (40.47%), and triangular in six (14.28%).

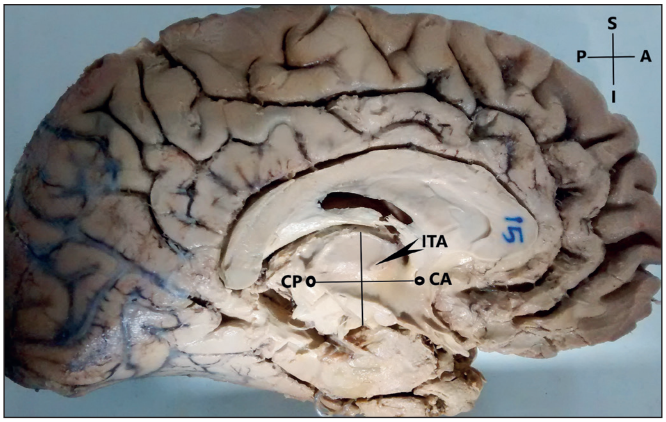

Figure 1: The medial surface of the sagittal section of brain. A coordinate system was framed on the lateral wall of the third ventricle to determine the topographic location of ITA. The X-axis of the system was defined as a straight line connecting the superior most point of the anterior commissure (CA) and the inferior most point of the posterior commissure (CP). The Y-axis or the ordinate intercepted the midpoint of the CA-CP line (X-axis). This coordinate system divides the lateral wall of the third ventricle into four quadrants. The position of the inter thalamic adhesion (ITA) was described according to the location of the center of the ITA in any one of these four quadrants. **A:** Anterior, **P:** Posterior, **S:** Superior, **I:** Inferior.

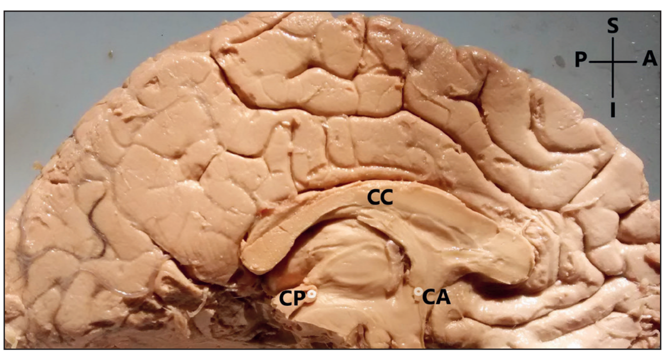

Figure 2: Brain without interthalamic adhesion (ITA). **CA:** Anterior commissure; **CP:** Posterior commissure: **A:** Anterior; **P:** Posterior; **S:** Superior; **I:** Inferior.

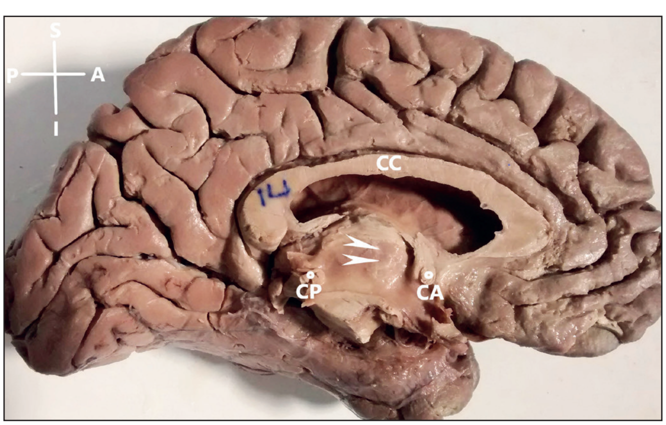

Figure 3: Brain with duplication of the interthalamic adhesion (ITA). **CA:** Anterior commissure; **CP:** Posterior commissure: **A:** anterior; **P:** Posterior; **S:** Superior; **I:** Inferior.

Location: The anterosuperior quadrant with posterosuperior extension (76.74%) was the most common location for ITA, followed by the central section of the lateral wall of the third ventricle (23.25%). In the specimen with double ITAs, both were located entirely within the anterosuperior compartment.

Dimensions: The HD of the ITA was between 2.34 mm and 7.10 mm (average 4.61 ± 1.17 mm), and the VD was between 1.88 mm and 5.30 mm (average 3.10 ± 0.78 mm). In all cases, the HD was longer than the VD.

The SA of the ITA ranged from 4.40 mm^2 to 27.00 mm^2 (mean 14.46 ± 5.42 mm^2). The mean SA was significantly greater in females (17.56 ± 5.26 mm^2) than males (13.62 ± 5.22 mm^2) ($p=0.025$).

The mean interval between CA and CP was 18.22 ± 4.54 mm. There was no significant correlation between SA and the CA-CP distance ($r=0.28$, $p>0.05$).

Findings from MRI Brains

Prevalence: ITA was present in 44 of the 50 brains studied (88%). It was absent in six brains (12%) (Figure 4), five males (10.52%), and one female (25.00%). There was no significant relationship between the prevalence of the ITA and sex ($p>0.05$). Among the 44 cases, the ITA was single in 41 (93.18%) and doubled in three (6.81%) (Figure 5).

Shapes: ITAs of different shapes were found: oval or elliptical (primary diameter or length was anteroposterior) in 23 (48.93%), circular in 15 (31.91%), pin-headed in seven (14.89%), spindle and semilunar shaped in one each (2.12%). Cases with duplication showed pin-headed small ITA.

Location: In 19 cases, ITA was extending into all the quadrants of the CA-CP coordinate system, in 16 cases located both

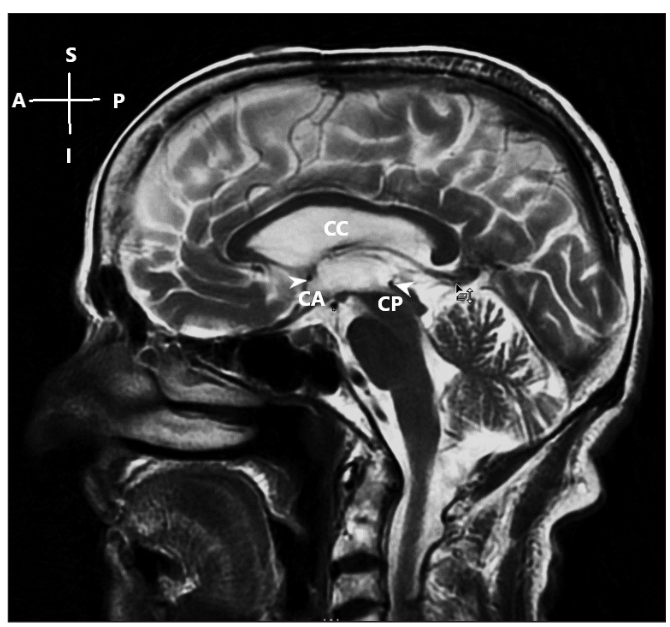

Figure 4: T2W MR image of left cerebral hemisphere without interthalamic adhesion. **CA:** Anterior commissure; **CP:** Posterior commissure; **CC:** Corpus callossum; **A:** Anterior; **P:** Posterior; **S:** superior; **I:** Inferior.

in the anterosuperior and posterosuperior quadrant, five cases in the anterosuperior quadrant, in one located centrally. Among the three cases with duplication, both the ITAs were positioned in a different quadrant.

Dimensions: The HD of the ITA was between 2.90 mm and 22.00 mm (average 8.21 ± 4.75 mm), and the VD was between 1.50 mm and 12.50 mm (average 5.77 ± 3.38 mm). In all cases, the HD was longer than the VD.

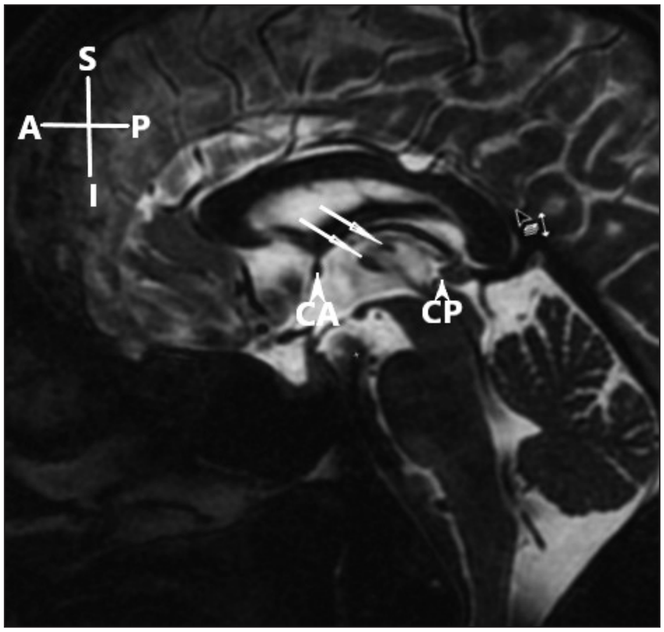

Figure 5: T2W MR image of left cerebral hemisphere with duplication of the interthalamic adhesion (double white arrows). **CA:** Anterior commissure; **CP:** Posterior commissure: **A:** Anterior; **P:** Posterior; **S:** Superior; **I:** Inferior.

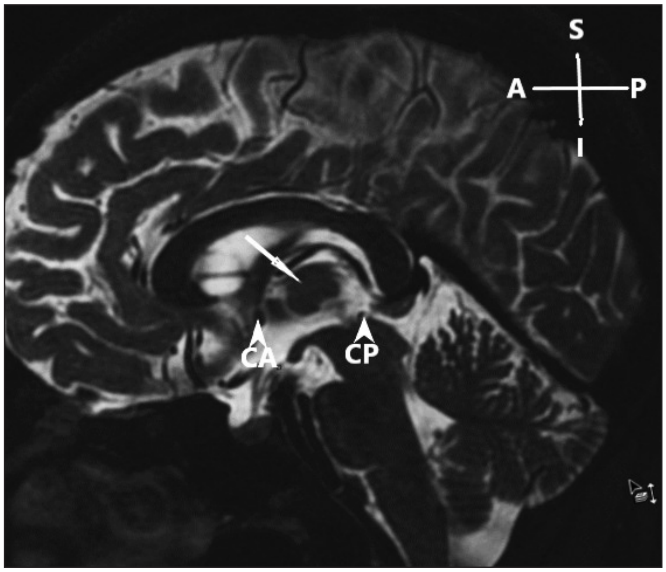

Figure 6: T2W MR image of left cerebral hemisphere with very large interthalamic adhesion (white arrow). **CA:** Anterior commissure; **CP:** Posterior commissure: **A:** Anterior; **P:** Posterior; **S:** Superior; **I:** Inferior.

The SA of the ITA ranged from 4.90 mm^2 to 203 mm^2 (mean 41.61 ± 37.72 mm^2). The mean SA was significantly higher in females (84.35 ± 55.60 mm^2) than males (44.70 ± 37.47 mm^2) (p=0.005). The one with a surface area of 203 mm^2 was extensive, blocking most of the third ventricular cavity (Figure 6).

The mean interval between CA and CP was 26.22 ± 4.42 mm. There was no significant correlation between SA and the CA-CP distance (r=0.35, p>0.05).

DISCUSSION

The interthalamic adhesion (ITA) is a tiny mass of neural tissue that connects the two thalami on their medial surfaces. Its morphology, function, and clinical importance have received little attention in anatomy textbooks and the published literature. According to Laslo et al., the particular circular network of neurons incorporated in the ITA can be regarded as an *in vivo* match-up of neurospheres (19). These neurons have a highly variable Golgi morphology, although their fusiform shape is unique (22). The ITA appears along with the ventricular system around the 13th to 14th week of development and becomes apparent about the second trimester of gestation and several features of the ventricular system (27,32). Its specific function is yet to be established, but it is assumed to affect cerebrospinal fluid (CSF) flow and pressure distribution within the third ventricle cavity (8). As the capacity of the third ventricle increases with advancing age, the ITA shrinks concomitantly (32). The ITA, along with other midline structures, helps construct the central neuronal circuits that process attention and information (36). However, recent functional anatomy studies of attention distribution processing did not depict the ITA as a structure determining the human brain's dorsal and ventral attention systems (13).

It also regulates electrocortical activities over the cerebral hemispheres, significant in the distribution of epileptiform discharges to the temporal and limbic regions of the cerebrum, and this can be more obvious in males than females (15,38).

Research (cadaveric and *in vivo* magnetic resonance imaging) has shown contradictory data regarding sex differences in the ITA's presence (11,24,26). Allen and Gorski studied 100 healthy cadavers and reported that it was more frequent in females (78.00%) than males (68.00%) (2). On the other hand, we found it slightly more often in males (87.14%) than females (86.67%). Such sex differences could be associated with aberrant neurodevelopmental growth processes, which are more common among males (31).

The actual incidence of the ITA in the general population and its absence during certain decades of life, are still debated. In previous studies, ITA was absent in 2.30–30% of normal human brains. However, it was missing in 4.70% of 233 normal brains scanned in recent research employing high-resolution coronal MRI sequences, which is lower than our result of 12.00% in MR pictures (11).

In contrast, a large cadaveric investigation of 921 cases revealed a 31.70% lack of ITA in various age groups (30). Another cadaveric study by Park et al. on Korean brains reported ITA absence in 11.60% (28). Even fewer Japanese brains lacked an ITA (5.80%) (35). According to the meta-analysis by Trzesniak et al. (38), the lack of the ITA varies from 2.30 % to 22.30%. The literature includes several explanations for this inconsistency. The wide variation could be attributed to differences in the type of study (cadaveric or neuroimaging), the ethnicity of the populations under study, and sample size. A wider age range is used for neuroimaging investigations, whereas cadaveric studies are skewed toward an older group (5). Previous studies have found no evidence of an increase in the prevalence of ITA as people become old. However, these studies were all limited by the age range of the individuals. We examined MR scans of adults in the current study and found no discernible trend in ITA occurrence as people become older (5,11). Rabl and Rosales et al. found that ITA decreased as people got older (30,32). Rosales et al. hypothesized a mechanism for this age-related “ITA involution” (32). It, therefore, remains plausible that age is an important determinant of ITA prevalence. A comprehensive longitudinal study across all decades of life is required to identify its true prevalence in human brains (5).

According to Wright et al., the lack of ITA is connected to the neurodevelopmental differences in the formation of structures around it during early embryogenesis (43). Erbagci et al. reported ITA missing more frequently in patients with schizophrenia than in healthy participants. According to them, those without ITA have less antagonism between the lateralized functions of the two hemispheres and are more resistant to neurological damage and cognitive deficiencies (12). However, no definitive clinical evidence for such a link has been found.

Most previous studies have reported sexual dimorphism in the ITA’s absence in various populations. Pavlovic et al. reported fewer females (18.18%) than males (21.05%) with no ITA, but this difference was not significant (29). Ceyhan et al. and Nopoulos et al. found more definite sexual dimorphisms in the ITA’s absence (6.00% vs 23.10%; 13.56% vs 32.08% respectively) (7,26). Allen and Gorski also revealed that men were less likely to have an ITA than women (2), suggesting an important sex difference in the structure of interhemispheric connections, potentially underlying sex differences in cognitive function (14,20). Most recently, Borghei et al. conducted the largest study on human ITA and reported its absence to be significantly more prevalent in males than in females (4). In the present study, males also lacked ITA more frequently than females in the cadaveric brains and MR images. This could be attributed to examining fewer female than male brains, or to the race and ethnicity of the specimens. Additionally, Erbagci et al. and Haghir et al. studied the brains of patients with schizophrenia by MRI but found no association between the absence of the ITA and schizophrenia (12,14).

A few researchers have also noted connections between the absence of the ITA and other midline brain deformities, such as cavum average, cavum septum pellucidum, corpus callosum agenesis, third ventricular hypertrophy. Even though the specific role of the ITA in humans is uncertain, animal studies have proven its role in regulating dopamine release from the basal ganglia (37,39). Patients with schizophrenia exhibit more dramatic surges of dopaminergic inactivity in the mesolimbic circuit, whereas they show less activity in the mesocortical pathway. As a result, these two routes might be responsible for the varied symptoms of schizophrenia (16). In addition, the disturbance of brain circuits that mediate attention and information processing may cause schizophrenia spectrum disorders (SSD) (10). Suggesting that a lack of the ITA might be a precursor to the development of schizophrenia in the future (12).

The literature has widely reported associations between ITA absence and mental disorders, notably SSD (5). Compared with 13.46% of healthy controls, 34.15% of hospitalized patients with the first episode of schizophrenia-associated psychosis had a missing ITA (5). Takahashi et al. discovered that patients with schizophrenia with no ITA had smaller amygdala than those with an ITA (37). These initial findings point to the ITA’s key involvement in linking interhemispheric limbic networks. Implying that the lack of ITA is a separate risk factor for limbic-mediated mental disorders (5). Crippa et al. on the other hand, reported similar incidence of missing ITA in patients and controls; however, it was more prevalent in male than female patients with schizophrenia (10). MRI studies by Cataltepe, Nayak and Soumya, and Shimizu et al. and revealed no difference in the ITA’s absence between people with schizophrenia and healthy controls (6,25,35). Such conflicts among findings could be attributed to the ITA being too small for MRI to identify or differences in sample size or ethnicity (35).

In the literature, there are just a few instances of ITA duplication. In 2/20 individuals who had an MRI for a Chiari II malformation, accessory ITAs were discovered (18,42). Tubbs et al. discovered the first case of ITA duplication in an infant with the Dandy-Walker variant (40). Later on, Whitehead reported another such finding during routine brain MR performed for dysmorphic facial features (42).

In some brains with double ITAs, it is not clear whether the duplication is actual or a single fenestrated ITA (3). Malobabic et al. reported duplication of ITA in 2% of Serbian brains studied (22). Pavlovic et al. studied 43 Serbian brains and reported duplication of the ITA in 3% (29). Samra and Cooper studied 32 brains and reported duplication in four cases (33). We found four brains with duplication of ITA, one in cadaveric brains (2%) and three (6%) in MR images. Although sexual dimorphism in the occurrence of duplication is not reported yet, we found only male brains to have duplication. ITA duplication is a congenital abnormality that does not require any intervention routinely. The long-term prognosis for such a case is unknown because there are just a few case reports in the literature. It might be a neurological component of some congenital disorders, although identified as a suspected accidental variant (42).

Variability in the location and size of the ITA is well known to neurosurgeons performing endoscopic ventriculostomy.

Patients with neural tube abnormalities have bigger ITA in particular (e.g., myelomeningocele). An enlarged ITA can prevent the third ventricle's floor visualization during the third ventriculostomy. Thus, it is critical to understand the ITA's specific location. Although there have been very few studies that have documented the location of ITA on the lateral wall of the third ventricle in midsagittal slices of the brain, further data like those reported in this study might help surgeons plan their operations.

Samra and Cooper studied 860 ventriculograms. They discovered the ITA at the middle of the third ventricle's lateral wall in more than half of the cases, followed by posterior quadrant in 8%, the anteroinferior quadrant in 4.2%, the anterosuperior quadrant in 3.8%, and the posteroinferior region in 0.8%. The coordinate line (CA-CP line) systems we used in the present study differ slightly from the CA-GP (anterior commissure-pineal gland) line used by Samra and Cooper, and we never found the ITA in the posteroinferior quadrant (33). The ITA, according to Kandel, is in the middle of the lateral wall of the third ventricle, which is significant since the nucleus ventralis lateralis thalami is immediately behind the ITA's ventrocaudal pole (17).

Pavlovic et al. used the CA-CP line technique to find the ITA in 43 Serbian brains. Most brains had it in the anterosuperior quadrant, but only two instances (5.13%) had it totally in that quadrant; the rest had it encroaching on other quadrants. It was mostly seen in the anterosuperior quadrant with caudal extension into the posterosuperior quadrant in 16 (41.02 %). Evenly distributed in the anterosuperior and posterosuperior quadrants in 11 (28.21%) and nearly in the middle of the third ventricle's lateral wall in 10 (25.64%) cases (29). We also located the ITA by constructing a coordinate system on the lateral wall of the third ventricle using the CA-CP line. In cadaveric specimens, the ITA was predominantly in the anterosuperior quadrant with posterosuperior extension (76.74%), consistent with the findings of Malobabic et al. (22). Whereas in MR images, they were extending into all the quadrants of the coordinate system. Such differences in the location of ITA among cadaveric brain and MR images might be because of the difference in the size of ITA. As ITAs were larger in MR images, they intended to spread in most quadrants. However, in the specimen with double ITAs, both were in entirely different quadrants.

The dimensions of the ITA vary widely, depending upon the type of study (cadaveric/neuroimaging), age, and ethnicity of the population. The dimensions of the ITA in MR images were almost double the value of the cadaveric brain specimens. In all cases, the HD was longer than the VD. An even larger ITA was found by Nayak and Soumya, with an HD of 30.00 mm; the longest we found was only 22 mm in the MR brain (25). According to Damle et al. males have a larger ITA transverse diameter than females, whereas females have a larger vertical and anteroposterior diameter (11).

The surface area of the ITA also showed tremendous variation, ranging from merely dotted with 4.40 mm^2 area in the cadaveric brain to unusually large with 203 mm^2 in MR images. An extremely big ITA might obstruct CSF circulation in the third ventricle. It is also possible to be misdiagnosed as a midline diencephalon tumor obstructing the third ventricle. Hence, any radiological findings in which the third ventricle's chamber seems to be obstructed in its entirety, the existence of an enlarged ITA must be considered (25).

The volume shrinkage property of formaldehyde might be the reason for such a lower surface area of cadaveric ITA. Malobabic et al. who measured ITA sizes in 50 cadaveric brains, recorded an average SA of 13.1 mm^2 (range 1.50 mm^2 to 34.00 mm^2), similar to our study results (22). In a similar study by Pavlovic et al. on 41 Serbian brains, the average SA was 29.81 ± 12.49 mm^2 (range 3.53 mm^2 to 56.50 mm^2). Pavlovic et al. found most SAs between 20.00 and 40.00 mm^2, while we found them mostly between 10.00 and 20.00 mm^2 (29). Most researchers have found larger SAs in females than male ITAs (34), even though the female brain is smaller (21). A larger ITA could enable females to counterbalance the overall brain size differences (2). We also reported significantly larger ITA in females than in males, both in the cadaveric brains and MR images. Although a sex difference in the SA is well established, there is no literature describing the timing at which this differentiation originates. It is believed that differences in ITA morphology can account for sexual dimorphism in cognitive functions and cerebral lateralization.

Damle et al. recently found that ITA size disparities in healthy females moderated outcomes in age-related measures of attention functioning (11). Showing that the ITA's role in anterior thalamic radiation and cognition might be independent of the dorsomedial (DM) thalamus (5). Females had a stronger connection between the ITA and the lateral orbitofrontal cortex, which might be because of their bigger ITA and right orbitofrontal cortices on average (41). In addition, Borghei et al. and Damle et al. found that females with an ITA had higher attention scores (5,11).

No correlation between the SA of the ITA and third ventricle size has been reported, nor did we find one. A few researchers have tried to correlate the development of the ITA with thalamus size or brain weight, but again, no relationship has been found (1,4,20,29). Furthermore, there is no difference in third ventricle volume between healthy individuals and patients with schizophrenia (12).

Researchers have rarely discussed the effects of age on the ITA. In one instance, Tubbs et al. (40) quoted Rolases et al. (30) reporting that ITA is prone to senile atrophy with advancing age (23). It becomes thinner and more prolonged with increasing age and is at its longest after 60 years (11,34).

The function of the ITA (MI) in the human brain has yet to be determined. Recent research has linked it to normal human brain function, whereas prior research has linked its lack to mental illnesses (11,36). Similar to other midline commissures, there is emerging evidence that it is a white matter conduit responsible for interhemispheric connection (5). The fibers that travel through the ITA serve as a link between the frontal cortex and the dorsomedial (DM) thalamic nucleus. As a result, it appears that the ITA serves as a conduit for interhemispheric connection in the wide frontal lobe, implying that its major function is to link limbic networks. Borghei et al. unearthed a wide network of connections between the ITA and the limbic, frontal, and temporal lobes, as well as the insula and pericalcarine cortices, using probabilistic tractography (5). Furthermore, women's ITA connections were stronger than men's The ITA's position as a midline commissure with substantial connections to the amygdala, hippocampus, and entorhinal cortex is supported by probabilistic tractography studies. Therefore, knowing its morphology, variability in topographic location, and SA/linear dimensions is of interest in neurosurgery (6). Although modern imaging techniques have enabled us to explore the anatomy and morphology of the ITA, a combination of morphological and histopathological examination postmortem is still considered the best way to attain more detailed knowledge about this tiny neuroanatomical structure.

CONCLUSION

Absence and duplication of ITA are fairly common in Indian brains with significant male predominance. Morphometric data are robust to advocate for the presence of sex differences in the ITA size, although not correlated with surrounding thalamic or third ventricle anatomy.

AUTHORSHIP CONTRIBUTION

Study conception and design: AP, KSR

Data collection: AP, KSR, KN

Analysis and interpretation of results: AP, KSR, KN, AA

Draft manuscript preparation: AP, KSR, RST, AA

Critical revision of the article: RST

All authors (AP, KSR, RST, KN, AA) reviewed the results and approved the final version of the manuscript.

REFERENCES

1. Agarwal N, Rambaldelli G, Perlini C, Dusi N, Kitis O, Bellani M, Cerini R, Isola M, Versace A, Balestrieri M, Gasparini A, Mucelli RP, Tansella M, Brambilla P: Microstructural thalamic changes in schizophrenia: A combined anatomic and diffusion weighted magnetic resonance imaging study. J Psychiatry Neurosci 33:440-448, 2008
2. Allen LS, Gorski RA: Sexual dimorphism of the anterior commissure and massa intermedia of the human brain. J Comp Neurol 312:97-104, 1991
3. Baydin S, Gungor A, Baran O, Tanriover N, Rhoton A: The double massa intermedia. Surg Neurol Int 7:30, 2016
4. Borghei A, Cothran T, Brahimaj B, Sani S: Role of massa intermedia in human neurocognitive processing. Brain Struct Funct 225:985-993, 2020
5. Borghei A, Kapucu I, Dawe R, Kocak M, Sani S: Structural connectivity of the human massa intermedia: A probabilistic tractography study. Hum Brain Mapp 42:1794-1804, 2021
6. Cataltepe O: Endoscopic third ventriculostomy: Indications, surgical technique, and potential problems. Turk Neurosurg 12:65-73, 2002
7. Ceyhan M, Adapinar B, Aksaray G, Ozdemir F, Colak E: Absence and size of massa intermedia in patients with schizophrenia and bipolar disorder. Acta Neuropsychiatr 20: 193-198, 2008
8. Cheng S, Tan K, Bilston LE: The effects of the interthalamic adhesion position on cerebrospinal fluid dynamics in the cerebral ventricles. J Biomech 43:579-582, 2010
9. Chéramy A, Romo R, Godeheu G, Glowinski J: Effects of electrical stimulation of various midline thalamic nuclei on the bilateral release of dopamine from dendrites and nerve terminals of neurons in the nigro-striatal dopaminergic pathways. Neuroscience Letters 44:193-198, 1984
10. Crippa JA de S, Zuardi AW, Busatto GF, Sanches RF, Santos AC, Araújo D, Amaro E, Hallak JEC, Ng V, McGuire PK: Cavum septum pellucidum and adhesio interthalamica in schizophrenia: An MRI study. Eur Psychiatr 21:291-299, 2006
11. Damle NR, Ikuta T, John M, Peters BD, DeRosse P, Malhotra AK, Szeszko PR: Relationship among interthalamic adhesion size, thalamic anatomy and neuropsychological functions in healthy volunteers. Brain Struct Funct 222:2183-2192, 2017
12. Erbagci H, Yildirim H, Herken H, Gumusburun E: A magnetic resonance imaging study of the adhesio interthalamica in schizophrenia. Schizophr Res 55:89-92, 2002
13. Fox MD, Corbetta M, Snyder AZ, Vincent JL, Raichle ME: Spontaneous neuronal activity distinguishes human dorsal and ventral attention systems. Proc Natl Acad Sci U S A 103:10046-10051, 2006
14. Haghir H, Mokhber N, Azarpazhooh MR, Haghighi M, Radmard M: A magnetic resonance imaging study of adhesio interthalamica in clinical subtypes of schizophrenia. Indian J Psychiatry 55:135-139, 2013
15. Hirayasu Y, Wada JA: N-Methyl-d-Aspartate injection into the massa intermedia facilitates development of limbic kindling in rats. Epilepsia 33:965-970, 1992
16. Juárez Olguín H, Calderón Guzmán D, Hernández García E, Barragán Mejía G: The role of dopamine and its dysfunction as a consequence of oxidative stress. Oxid Med Cell Longev 2016:9730467, 2016
17. Kandel EI: Functional and Stereotactic Neurosurgery. Springer Science & Business Media, 2012:1-724
18. Kochanski RB, Dawe R, Kocak M, Sani S: Identification of stria medullaris fibers in the massa intermedia using diffusion tensor imaging. World Neurosurg 112:e497-e504, 2018
19. Laslo P, Slobodan M, Nela P, Miloŝ M, Rade P, Tatjana I: Specific circular organization of the neurons of human interthalamic adhesion and of periventricular thalamic region. Int J Neurosci 115:669-679, 2005
20. Ligier Y, Ratib O, Logean M, Girard C: Osiris: A medical image-manipulation system. MD Comput 11:212-218, 1994
21. Luders E, Gaser C, Narr KL, Toga AW: Why sex matters: Brain size independent differences in gray matter distributions between men and women. J Neurosci 29:14265-14270, 2009

22. Malobabić S, Puskas L, Blagotić M: Size and position of the human adhaesio interthalamica. Gegenbaurs Morphol Jahrb 133:175-180, 1987
23. Meisenzahl EM, Frodl T, Zetzsche T, Leinsinger G, Heiss D, Maag K, Hegerl U, Hahn K, Möller HJ: Adhesio interthalamica in male patients with schizophrenia. Am J Psychiatry 157:823-825, 2000
24. Mohammadi MR, Hosseini SH, Golalipour MJ: Morphometric measurements of the thalamus and interthalamic adhesion by MRI in the South-East of the Caspian Sea border. Neurosciences (Riyadh) 13:272-275, 2008
25. Nayak SB, Soumya KV: Unusually large interthalamic adhesion and its clinical importance. Int J Anat Var 3:174-175, 2010
26. Nopoulos P, Swayze V, Flaum M, Ehrhardt JC, Yuh WTC, Andreasen NC: Cavum septi pellucidi in normals and patients with schizophrenia as detected by magnetic resonance imaging. Biol Psychiatry 41:1102-1108, 1997
27. O'Rahilly R, Müller F: Ventricular system and choroid plexuses of the human brain during the embryonic period proper: Human embryonic ventricular system. Am J Anat 189:285-302, 1990
28. Park KA, Lee HY, Chung IH, Han YP, Shin TS: A morphologic study of interthalamic adhesions in Korean brains. Clin Anat 6: 33-36, 1993
29. Pavlović MN, Jovanović ID, Ugrenović SZ, Kostić AV, Kundalić BK, Stojanović VR, Vlajković S, Trandafilović MM, Čukuranović-Kokoris JR, Antić MM: Position and size of massa intermedia in Serbian brains. Folia Morphol (Warsz) 79: 21-27, 2020
30. Rabl R: Studies on the structure of the massa intermedia of the thalamus opticus. J Hirnforsch 4:78-112, 1958
31. Raz S, Goldstein R, Hopkins TL, Lauterbach MD, Shah F, Porter CL, Riggs WW, Magill LH, Sander CJ: Sex differences in early vulnerability to cerebral injury and their neurodevelopmental implications. Psychobiology 22:244-253, 1994
32. Rosales RK, Lemay MJ, Yakovley PI: The development and involution of massa intermedia with regard to age and sex. J Neuropathol Exp Neurol 27:166, 1968
33. Samra KA, Cooper IS: Radiology of the massa intermedia. Radiology 91:1124-1128, 1968
34. Sen F, Ulubay H, Ozeksi P, Sargon MF, Tascioglu AB: Morphometric measurements of the thalamus and interthalamic adhesion by MR imaging. Neuroanatomy 4:10-12, 2005
35. Shimizu M, Fujiwara H, Hirao K, Namiki C, Fukuyama H, Hayashi T, Murai T: Structural abnormalities of the adhesio interthalamica and mediodorsal nuclei of the thalamus in schizophrenia. Schizophr Res 101:331-338, 2008
36. Snyder PJ, Bogerts B, Wu H, Bilder RM, Deoras KS, Lieberman JA: Absence of the adhesio interthalamica as a marker of early developmental neuropathology in schizophrenia: An mri and postmortem histologic study. J Neuroimaging 8:159-163, 1998
37. Takahashi T, Suzuki M, Zhou S-Y, Nakamura K, Tanino R, Kawasaki Y, Seal ML, Seto H, Kurachi M: Prevalence and length of the adhesio interthalamica in schizophrenia spectrum disorders. Psychiatry Res 164:90-94, 2008
38. Trzesniak C, Kempton MJ, Busatto GF, Oliveira IR de, Galvão-de Almeida A, Kambeitz J, Ferrari MCF, Filho AS, Chagas MHN, Zuardi AW, Hallak JEC, McGuire PK, Crippa JAS: Adhesio interthalamica alterations in schizophrenia spectrum disorders: A systematic review and meta-analysis. Prog Neuropsychopharmacol Biol Psychiatry 35:877-886, 2011
39. Trzesniak C, Linares IM, Coimbra ÉR, Júnior AV, Velasco TR, Santos AC, Hallak JE, Sakamoto AC, Busatto GF, Crippa JA: Adhesio interthalamica and cavum septum pellucidum in mesial temporal lobe epilepsy. Brain Imaging Behav 10:849-856, 2016
40. Tubbs RS, Smyth MD, Oakes WJ, Blount JP: Duplication of the massa intermedia in a child. Pediatr Neurosurg 40:42-43, 2004
41. Welborn BL, Papademetris X, Reis DL, Rajeevan N, Bloise SM, Gray JR: Variation in orbitofrontal cortex volume: Relation to sex, emotion regulation and affect. Soc Cogn Affect Neurosci 4:328-339, 2009
42. Whitehead MT: Thalamic massa intermedia duplication in a dysmorphic 14-month-old toddler. J Radiol Case Rep 9:1-5, 2015
43. Wright P, Takei N, Rifkin L, Murray RM: Maternal influenza, obstetric complications, and schizophrenia. Am J Psychiatry 152:1714-1720, 1995