Received: 11 March 2024 | Accepted: 30 May 2024 Nig J Neurosci 15(2):62-67.2024

Nigerian Journal of Neuroscience

https://njn.nsn.org.ng

DOI: 10.47081/njn2024.15.2/003

Original Article Open Access

Thalamic Nuclei Morphometry and Handedness: Assessing Grey Matter Volume Differences in Left- and Right-Dominant Individuals

Eberechi Wogu[1] **and Patrick Filima**[1]

[1]Department of Anatomy, Faculty of Basic Medical Science, University of Port Harcourt, Port Harcourt, Nigeria

ABSTRACT

The connection between thalamic structure and handedness has important implications for understanding the neural basis of lateralization, and this may shed light on the underlying mechanisms of motor control and cognitive processes. This study investigated the relationship between thalamic nuclei morphometry and handedness, aiming to elucidate the neuroanatomical basis of manual preference. Utilising neuroimaging data from a test-retest functional magnetic resonance imaging (MRI) dataset, T1-weighted volumes were acquired and processed using automated segmentation methods. Thalamic nuclei were parcellated into 25 regions, and grey matter volumes were analysed using the Freesurfer software tool. Statistical comparisons of the interhemispheric volume of the four thalamic nuclei between left- and right-dominant individuals were conducted using independent sample t-tests. This study identified interhemispheric differences in specific thalamic nuclei (the ventral anterior thalamic nucleus and the ventral posterolateral thalamic nuclei) in the left- and right-dominant individuals, suggesting structural variability within the thalamus associated with handedness. The findings underscore the importance of considering subcortical structures in understanding the neural basis of manual preference and highlight avenues for further research in thalamic morphology and its relationship with handedness.

Keywords
Thalamic nuclei, Handedness, Grey matter volume, Freesurfer, Cortical morphology, Functional asymmetry

Correspondence: Eberechi Wogu, PhD; Department of Anatomy, Faculty of Basic Medical Science, University of Port Harcourt, Port Harcourt, Nigeria. E-mail: eberechi.wogu@uniport.edu.ng; Phone Number: +2347033098930; ORCID: 0000-0002-2708-2945
Patrick Filima - 0000-0001-9976-5609, patrick_filima@uniport.edu.ng

Cite as: *Wogu, E. and Filima, P. (2024). Thalamic nuclei morphometry and handedness: Assessing grey matter volume differences in left- and right-dominant individuals. Nig. J. Neurosci. 15(2):62-67. https://doi.org/10.47081/njn2024.15.2/003*

INTRODUCTION

A person's inclination to use one hand exclusively for unimanual tasks and their capacity to do these tasks more efficiently while using one hand is termed handedness. Handedness, a seemingly innocuous marker of functional asymmetry, harbours deep-seated mysteries regarding its origins and implications for human evolution. While theories abound, consensus on the aetiological factors remains elusive (Witelson *et al*., 1991).

The human brain exhibits remarkable asymmetry, with distinct functional and anatomical differences between the left and right hemispheres. Handedness, or manual preference, is one of the most overt manifestations of cerebral lateralization. Understanding the neural correlates of handedness is essential for unravelling the complex interplay between genetics, environment, and brain structure. In exploring the intersection of anatomical brain asymmetries and hand preference, previous research has uncovered significant links between brain morphology and handedness (Amunts *et al*., 2000).

There have been many studies about the relationship between handedness and brain morphology using magnetic resonance imaging (MRI) data. However, many of them were focused only on cortical morphology. Areas investigated include whole grey matter (Good *et al*., 2001; Ocklenburg *et al.*, 2016), and individual areas of the cortex such as the central sulcus (Amunts *et al.,* 2000), pars triangularis (Foundas *et al*., 1995*), planum temporale (*Foundas *et al*., 1995*;* Herve *et al*., 2006), inferior frontal sulcus, precentral sulcus (Herve *et al*., 2006), and insula (Keller *et al*., 2011; Biduła and Króliczak, 2015). Cortical thickness analysis and sulcal depth measurements have unveiled subtle yet significant differences in brain structure between left- and right-dominant individuals (Geschwind and Levitsky, 1968; Luders *et al*., 2006). However, because the cortex is well connected with various subcortical structures and exchanges information with them, morphological investigation of subcortical structures is also important. One of the subcortical structures connected to the cerebral cortex is the thalamus.

The thalamus is one of the key relay stations in the brain. It plays a crucial role in sensorimotor processing and may contribute to handedness preferences (Fama and Sullivan, 2015). However, the specific relationship between thalamic nuclei morphometry and handedness remains understudied. The present research study aimed to address this gap by examining the interhemispheric disparities in the thalamic nuclei grey matter volume of left- and right-dominant individuals, shedding light on the neuroanatomical basis of handedness. By examining key topological properties such as normalised clustering coefficient and global efficiency, we aim to unravel the interhemispheric- and handedness-related differences in the organisational patterns of hemispheric structural networks (Bassett *et al*., 2008).

MATERIALS AND METHODS

The Original Purpose of the Data Acquisition

A test-retest functional magnetic resonance imaging (fMRI) dataset on motor, linguistic, and spatial attention functions provided the neuroimaging data utilised in this investigation. It is open-access data and can be accessed at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC361991/.

Other data used for this research and its metadata are open source and obtained from the GigaScience Database (Gorgolewski *et al.,* 2013).

Study Participants

The 10 subjects (median age 52.5 years, min = 50, max = 58) included four males and six females, of which three were left-handed and seven right-handed. Each subject was scanned twice, either two (eight subjects) or three (two subjects) days apart. All subjects were informed that the data collected during this study may be shared with other researchers, given that the data would be anonymized, and they all gave their consent. Ethical approval for the present study was obtained from the University of Port Harcourt Research Ethics Board with ethical approval number UPH/CERMAD/REC/MM84/05.

The selection criteria for study participants include that participants be left or right-handed, aged 50 years and older, and healthy with no neurological disorders. Subjects with neurological disorders or a history of such disorders were excluded from the study.

Data Acquisition

Data were acquired on a GE Signa HDxt 1.5 T scanner with an 8-channel phased-array head coil at the Brain Research Imaging Centre, University of Edinburgh, UK. T1-weighted volumes were acquired in the coronal plane with a FOV of 256 × 256 mm, a slice thickness of 1.3 mm, 156 slices, an acquisition matrix of 256 × 256, TR = 10 s, TE = 4 s, and an inversion time (TI) of 500 ms. High-resolution whole brain DTI scans were acquired with 64 directions (b = 1000 s/mm² [6]) plus seven T2-weighted (b = 0 s/mm^2) single-shot spin-echo echo-planar imaging volumes with a FOV = 256 × 256 mm, slice thickness of 2 mm, 72 axial slices, an acquisition matrix of 128 × 128, TR = 16.5 s, and TE = 98 ms.

Anatomical Data Pre-processing (T1w)

Each subject was assigned a random, unique identifier using the Digital Imaging and Communications in Medicine (DICOM) confidential de-identification toolkit (http://sourceforge.net/projects/privacyguard/). This toolkit replaced their names and any other medical identification information. For each scanning sequence, the DICOM files were anonymized according to the Health Insurance Portability and Accountability Act guidelines. DICOM to Neuroimaging Informatics Technology Initiative (NIfTI) data format conversion was performed using the dcm2niix tool (http://www.mccauslandcenter.sc.edu/mricro/mricron/dcm2nii.html).

To prevent visual identification of study participants, the 3D T1-weighted images were defaced using mri_deface (http://www.na-mic.org/Wiki/index.php/Mbirn:_Defacer_for_structural_MR) (Gorgolewski *et al.*, 2013). The defaced T1w datasets were imputed into the brainlife.io platform (defaced_datasets).

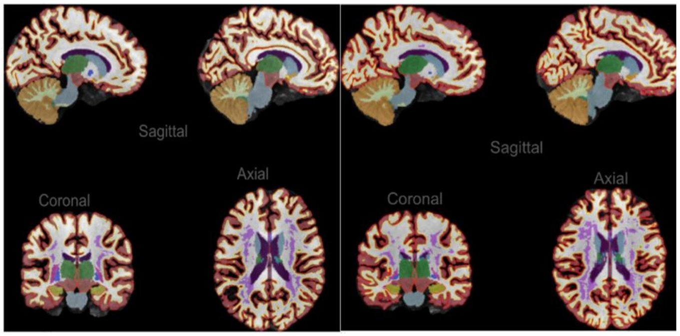
To crop, reorient, and debiase the images to match the orientation of the MNI152 template, the fsl_anat (T1) process on Brainlife was staged and executed. The cropped and reoriented images were then linearly aligned using FMRIB's Linear Image Registration Tool (FLIRT) (Jenkinson and Smith, 2001; Jenkinson, 2003) and subsequently aligned non-linearly to the MNI152 1mm template using FNIRT (Greve and Fischl, 2009). The linearly aligned images will hereafter be referred to as the 'acpc aligned' anatomical (T1w) images. The non-linearly aligned image, often referred to as the "warped" image, underwent a more complex transformation compared to the linear alignment process. This transformation involves adjusting the image to better match the intricate anatomical features of a standard template, such as the MNI152 1mm template mentioned. This involved techniques like nonlinear registration or deformation-based morphometry. These techniques allow for more flexible adjustments to align the individual anatomical features of the subject's brain with those of the template.

After the non-linear alignment process, the resulting image is usually referred to as the "registered" or "warped" image. This image represents the subject's anatomical data in a standardised space, allowing for more accurate comparisons and analyses across different subjects.

Morphometric Analysis

Following alignment, the 'acpc aligned' anatomical (T1w) images were processed via the Freesurfer 7.3.2 function to generate a parcellation of the thalamus into 25 different nuclei using a probabilistic atlas built with histological data.

The parcellation is based on structural MRI, either the main T1 scan or recon-all [http://freesurfer.net/fswiki/ThalamicNuclei].



A **B**

Fig. 1: Thalamic nuclei morphometry for left- and right- handed individuals showing different views (sagittal, coronal, and axial) of study participants using Freesurfer software. A. Left-handed individual; B. Right-handed individual

Subsequently, Freesurfer Statistics was used to convert important parcellation statistics, including volume, to a.csv file for each hemisphere. The output data for the respective thalamic nucleus for each hemisphere was used for the statistical analysis.

Statistical Analysis

A statistical analysis was performed on this data. Assumptions of normality were tested for continuous variables using the Shapiro-Wilk test for normality and Levene's test for homogeneity of variances. All of these showed a normal distribution. An independent sample t-test was used to assess interhemispheric differences in thalamic nuclei volumes between left- and right-handed subjects. A p-value of <0.05 was used for defining statistical significance.

RESULTS

Demographic Information of Participants

The 10 subjects were between the ages of 50 and 58. (median age 52.5 years, min = 50, max = 58) included four males and six females, of which three were left-handed and seven right-handed (Table 1).

Table 1: Demographic information of left- and right-handed study participants

Category	Description
Participants	10 healthy volunteers over 50 years of age
Age range	50-58 years
Gender	4 males and 6 females
Handedness	3 left-handed and 7 right-handed
Scanning	Each subject was scanned twice, either 2 or 3 days apart

Differences Between the Left and Right Hemispheric Thalamic Nuclei Volumes in the Left- and Right-Handed Subjects

Thalamic Nuclei Variation: The mean grey matter volume for different thalamic nuclei, such as ventral anterior magnocellular nucleus (VAmc), ventral lateral anterior nucleus (VLA), ventral lateral posterior nucleus (VLP), and ventral posterolateral nucleus (VPL) are clearly delineated. Each nucleus exhibited distinct mean grey matter volumes, indicating structural variability within the thalamus. VAmc showed a lower mean grey matter volume compared to VLP and VPL. This variation suggests that different nuclei serve unique functional roles or have differential contributions to cognitive and motor processes (Table 2).

Differences Between the Volumes of the Ventral Anterior Thalamic Nuclei (Magnocellular Part) in the Left and Right Hemispheres of the Light and Left-Handed Subjects

In right-handed subjects, there was no statistically significant difference ($p = 0.888$) in the VAmc thalamic nuclei volume between the left hemisphere and the right hemisphere. In left-handed subjects, there was also no significant difference ($p = 0.105$) in the VAmc thalamic volume between the left hemisphere and the right hemisphere . This shows that there were no interhemispheric disparities in VAmc thalamic volume, both in the right-handed subjects and the left-handed subjects (Table 2).

Differences Between the Volumes of the Ventral Lateral Anterior (VLA) Thalamic Nuclei in the Left and Right Hemispheres of the Right and Left-Handed Subjects

In right-handed subjects, there was a significant difference ($p < 0.05$) in the VLA thalamic nuclei volume between the left hemisphere and right hemispheres, with a mean volume reduction of approximately 242.87 mm³ in the right hemisphere compared to the left. In the left-handed subjects, there was no significant difference in VLA thalamic nuclei volume between the left and right hemispheres (Table 2).

Differences Between the Volumes of the Ventral Lateral Anterior Posterior (VLP) Nuclei in the Left and Right Hemispheres of the Left and Right-Handed Subjects

In right-handed subjects and left-handed subjects, there was no significant difference in VLP thalamic nuclei volume between the left and right hemispheres (Table 2).

Differences Between the Volumes of the Ventral Posterolateral (VPL) Nuclei in the Left and Right Hemispheres of the Right and Left-Handed Subjects

In right-handed subjects, there was a significant difference ($p < 0.05$) in grey matter volume between the left and right hemispheres, with a mean volume increase of approximately 55.19 mm³ in the left hemisphere compared to the right. In left-handed subjects, no significant difference in grey matter volume between the left and right hemispheres was observed (Table 2).

Table 2: The thalamic nuclei volumes between the left and right hemispheres of right handed and left-handed individuals

Subjects	Hemisphere	Grey Matter Volume (mm³)			
		VAmc	VLA	VLP	VPL
		Mean ± SD (mm^3)	Mean ± SD (mm^3)	Mean ± SD (mm^3)	Mean ± SD (mm^3)
RH	Left	38.15±6.89	756.95±66.70	942.70±85.35	1098.82± 234.077
	Right	38.38±5.02	738.48±86.41	994.82±100.71	954.06±154.51
LH	Left	44.64±3.21	883.71±21.47	1142.43±36.54	1201.41±44.42
	Right	45.29±3.32	881.23±39.97	637.30±467.76	1281.12±1.528

P<0.05 is significant. LH - left hemisphere; RH - right hemisphere; VAmc - ventral anterior nucleus, magnocellular part; VLA - ventral lateral anterior nucleus; VLP - ventral lateral posterior nucleus; VPL - ventral posterolateral nucleus

DISCUSSION

This study investigated the relationship between thalamic nuclei morphometry and handedness, aimed to show the neuroanatomical basis of manual preference. This study has identified interhemispheric differences in specific thalamic nuclei (the ventral posterolateral nuclei) in left- and right-dominant individuals, providing insights into the structural variability within the thalamus associated with handedness.

Thalamic nuclei play a crucial role in sensorimotor processing and are intricately connected with various cortical regions involved in motor control and cognitive functions (Wolff *et al*., 2021*)*. Our study's focus on thalamic morphology expands upon previous research primarily centred on cortical morphology, emphasising the importance of investigating subcortical structures in understanding manual preference (Boelens *et al*., 2021). By utilising advanced neuroimaging techniques and automated segmentation methods, thalamic nuclei and their grey matter volumes analysis were accurately delineate.

The observed differences in grey matter volume between left- and right-dominant individuals suggest structural variability within the thalamus associated with handedness: This is in tandem with the work of Chibaatar *et al.* (2023). Specifically, thalamic nuclei such as VAmc, VLa, VLp, and VPL exhibited distinct mean grey matter volumes, indicating potential functional specialisation or differential contributions to cognitive and motor processes. For instance, VAmc displayed a lower mean grey matter volume compared to other nuclei, suggesting potential differences in its functional role or connectivity patterns.

The nonsignificant differences in VAmc grey matter volume between hemispheres suggest balanced structural development in both hemispheres, irrespective of handedness. This finding may indicate that manual preference does not strongly influence the asymmetry of this thalamic nucleus. This finding is in line with a previous study (Chibaatar *et al.,* 2023).

The significant reduction in grey matter volume of VLa in the right hemisphere of right-handed individuals suggests a potential link between manual preference and structural asymmetry in this thalamic nucleus. This finding suggests that there may be differences in the neural architecture related to motor planning and execution between the left and right hemispheres, which could be linked to the preference for using the right hand in manual tasks among right-handed individuals. It also suggests a reduction in the density or size of neurons and their associated structures within this thalamic nucleus. This may indicate a decreased number of neurons, dendrites, or synapses, potentially affecting the processing and transmission of motor-related signals and sensory information.

The decreased grey matter volume in the VLa of the right hemisphere in right-handed individuals could indicate less efficiency or reduced structural complexity in this region. Since the left hemisphere typically controls motor functions in right-handed individuals, a decrease in grey matter volume in the right hemisphere, particularly in regions associated with motor planning and execution like the VLa, may reflect a lesser degree of neural specialisation or structural development compared to the left hemisphere.

This interpretation aligns with the idea that handedness is associated with hemispheric specialisation, where the dominant hemisphere, typically the left hemisphere in right-handed individuals, exhibits greater structural and functional specialisation for motor tasks (Annett, 1985). Therefore, the observed reduction in grey matter volume in the VLa of the right hemisphere in right-handed individuals may reflect the asymmetrical distribution of neural resources related to motor control and manual preference (Ghaderi *et al*., 2012).

In right-handed subjects, there was no significant difference in grey matter volume between the left and right hemispheres. The absence of significant interhemispheric differences in VLP grey matter volume between hemispheres in right-handed individuals suggests bilateral structural symmetry in this thalamic nucleus.

The ventral posterolateral nucleus (VPL) of the thalamus is primarily involved in somatosensory processing, particularly the relay of sensory information from the body to the cerebral cortex. It receives input from the dorsal column-medial lemniscal pathway, carrying tactile and proprioceptive information from the body, and projects this information to the primary somatosensory cortex (Hirato *et al*., 2021). A decrease in grey matter volume in the VPL could suggest alterations in the density or size of neurons and their connections within this nucleus. This may influence the processing and transmission of somatosensory signals, potentially affecting tactile perception and proprioceptive awareness.

In the context of right-handed individuals, a significant increase in grey matter volume in the ventral posterolateral nucleus (VPL) of the left hemisphere suggests asymmetrical structural development related to somatosensory processing. As the left hemisphere typically processes sensory information from the right side of the body, an increase in VPL grey matter volume may indicate enhanced neural resources dedicated to somatosensory processing for the dominant hand, which is often the right hand in right-handed individuals.

This finding suggests that manual preference may influence the structural development of specific thalamic nuclei associated with sensorimotor processing.

Conclusion

In conclusion, the study sheds light on the neuroanatomical basis of manual preference by investigating the relationship between thalamic nuclei morphometry and handedness. Through detailed analysis of gray matter volumes in specific thalamic nuclei, notable differences between left- and right-dominant individuals was identified, offering insights into the structural variability within the thalamus associated with handedness.

Our findings reveal distinct gray matter volume differences in specific thalamic nuclei, such as the ventral anterior nucleus, magnocellular part (VAmc), ventral lateral anterior nucleus (VLa), ventral lateral posterior nucleus (VLP), and ventral posterolateral nucleus (VPL), suggesting potential functional specialization or differential contributions to cognitive and motor processes..

Our study contributes to a deeper understanding of the intricate neural mechanisms underlying manual preference and emphasizes the relevance of thalamic morphology in elucidating the structural basis of manual dexterity and function.

Data availability

The raw datasets analysed in the current study are publicly available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3641991/. The data used for this research and its metadata is open source and obtained from the GigaScience Database (Gorgolewski *et al*., 2013). The pre-processed data and software metadata from the present study is available at Brainlife.io.

Acknowledgements

We acknowledge the African Brain Data Network, the Kavli Foundation, and Brainlife.io for all their support in this research study.

Grants and Financial Support

The African Brain Data Network (ABDN) provided financial support for this research paper through the Kavli funded African Brain Data Science (ABDS) Academy, 2024 at Lagos, Nigeria

Conflict of Interest

None declared.

Authors' Contribution

EW conceptualized the study, wrote and revised the manuscript. PF contributed to the analysis and also wrote the manuscript.

REFERENCES

Amunts, K., Jancke, L., Mohlberg, H., Steinmetz, H. and Zilles, K. (2000) Interhemispheric asymmetry of the human motor cortex related to handedness and gender. Neuropsychologia. 38:304-312.

Annett, M. (1985) Left, Right, Hand and Brain: The Right Shift Theory. London: Erlbaum.

Bassett, D.S., Bullmore, E.T., Meyer-Lindenberg, A., Apud, J.A., Weinberger, D.R. and Coppola, R. (2008) Cognitive fitness of cost-efficient brain functional networks. Proc Natl Acad Sci. 105(4):1081–1086. https://doi.org/10.1073/pnas.0703874105

Biduła, S.P. and Króliczak, G. (2015) Structural asymmetry of the insula is linked to the lateralization of gesture and language. Eur J Neurosci. 41:1438–1447.

Boelens, J.T., van Heese, E.M., Laansma, M.A., Weeland, C.J., de Joode, N.T., van den Heuvel, O.A., et al. (2021) Structural assessment of thalamus morphology in brain disorders: A review and recommendation of thalamic nucleus segmentation and shape analysis. Neurosci Biobehav Rev. 131:466-478. https://doi.org/10.1016/j.neubiorev.2021.09.044

Chibaatar, E., Watanabe, K., Okamoto, N., Orkhonselenge, N., Natsuyama, T., Hayakawa, G. et al. (2023) Volumetric assessment of individual thalamic nuclei in patients with drug-naïve, first-episode major depressive disorder. Front Psychiatry. 14:1151551.

Fama, R. and Sullivan, E.V. (2015) Thalamic structures and associated cognitive functions: Relations with age and aging. Neurosci Biobehav Rev. 54:29-37.

Foundas, A.L., Leonard, C.M. and Heilman, K.M. (1995) Structural hemispheric asymmetries in the human precentral gyrus hand representation. Neuropsychologia. 33(10): 1327-1338.

Geschwind, N. and Levitsky, W. (1968) Human brain: left-right asymmetries in temporal speech region. Science. 161(3837):186-187.

Ghaderi, H., Sadikot, A., Campbell, J. and Pike, G. B. (2012) Automatic, rapid, non-invasive and precise localization of thalamic nuclei for deep brain stimulation (DBS) surgery using a combination of diffusion and functional MRI. In Proceedings of the International Society for Magnetic Resonance in Medicine: Oral presentation at ISMRM 0th Scientific Meeting and Exhibition, Melbourne, Australia 2, page 652.

Good, C.D., Sherrill, J.T., Barnes, L.L., Fox, P.T. and Lancaster, J.L. (2001) A comparison of voxel-based morphometry and manual region-of-interest analysis for measuring cortical gray matter volume. Neuroimage. 14(6): 1276-1282. https://www.sciencedirect.com/science/article/abs/pii/S1053811901910671

Gorgolewski, K.J, Storkey, A., Bastin, M.E., Whittle, I.R., Wardlaw, J.M. and Pernet, C.R. (2013) A test-retest functional MRI dataset for motor, language and spatial attention functions. GigaScience Database. http://dx.doi.org/10.5524/100051.

Greve, D.N. and Fischl, B. (2009) Nonlinear registration of structural MR images to a standard atlas: Automated subcortical segmentation of the human brain. NeuroImage. 47(1):27-37.

Herve, H., Crivello, F., Perchey, G., Mazoyer, B. and Tzourio-Mazoyer, N. (2006) Hemispheric lateralization of language and handedness in the human brain: a meta-analysis of functional neuroimaging studies. Hum Brain Mapp. 27(6):467-482.

Hirato, M., Miyagishima, T., Takahashi, A. and Yoshimoto, Y. (2021) Thalamic anterior part of the ventral posterolateral nucleus and central lateral nucleus in the genesis of central post-stroke pain. Acta Neurochir. 163(8):2121-2133.

Jenkinson, M. (2003) Fast, automated, N-dimensional phase-unwrapping algorithm. Magn Reson Med. 49(1): 193-197.

Jenkinson, M. and Smith, S. (2001) A global optimization method for robust affine registration of brain images. Med Image Anal. 5(2):143-156.

Keller, S.S., Roberts, N., García-Fiñana, M., Mohammadi, S., Ringelstein, E.B., Knecht, S. et al. (2011) Can the language-dominant hemisphere be predicted by brain anatomy? J Cogn Neurosci. 23:2013–2029.

Luders, E., Narr, K.L., Thompson, P.M., Rex, D.E., Woods, R.P., DeLuca, H., et al. (2006) Gender effects on cortical thickness and the influence of scaling. Hum Brain Mapp. 27(4):314–324. https://doi.org/10.1002/hbm.20188

Ocklenburg, S., Friedrich, A., Gunturkun, O. and Genc, Y. (2016) The influence of sex and handedness on the asymmetry of the planum temporale in the human brain. Brain Behav. 6(11):e00517. https://onlinelibrary.wiley.com/doi/abs/10.1002/brb3.517

Witelson, S.F. and Goldsmith, C H. (1991) The relationship of hand preference to anatomy of the corpus callosum in men. Brain Res. 545:175–182.

Wolff, M., Morceau, S., Folkard, R., Martin-Cortecero, J. and Groh, A. (2021) A thalamic bridge from sensory perception to cognition. Neurosci Biobehav Rev. 120:222-235.

Published by Neuroscience Society of Nigeria