Int. J. Morphol.,
44(3):1062-1070, 2026.

http://dx.doi.org/10.4067/s0717-95022026000301062

Sex Prediction with Machine Learning Algorithms Modeling on Brainstem Morphometric Features: An MRI Study

Predicción del Sexo Mediante Algoritmos de Aprendizaje Automático Basados en Características Morfométricas del Tronco Encefálico: Un Estudio de Resonancia Magnética

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RAY, G.; RAY, A.; AKÜNAL, C. & KÜRTÜL, I. Sex prediction with machine learning algorithms modeling on brainstem morphometric features: An MRI study. *Int. J. Morphol., 44(3)*:1062-1070, 2026.

SUMMARY: This study focuses on sex prediction by machine learning (ML) algorithms using brainstem data obtained from brain magnetic resonance images (MRIs) of a healthy adult Turkish population. In the study, midbrain thickness (TMT), pons thickness (TP), medulla thickness (TM), spinal cord thickness (TSC), mamillopontine distance (MPD), midbrain height (MBH), pontomesencephalic angle (PMA), tectum and tegmentum sagittal diameter, (TTSD) were measured from brain MR images of 200 women and 200 men, tectum and tegmentum transverse diameter (TTTD), right pedunculus cerebri sagittal diameter (RPCSD), left pedunculus cerebri sagittal diameter (LPCSD), right pedunculus cerebri transverse diameter (RPCTD), left pedunculus cerebri transverse diameter (LPCTD) variables were measured. Logistic Regression Classifier (LRC), Gradient Boosting Classifier (GBC), Decision Tree Classifier (DTC), K-Nearest Neighbors (KNN), Linear Discriminant Analysis (LDA), Random Forest Classifier (RFC), Naive Bayes Classifiers (NBC), XGBoost (XGB) ML algorithms were used. RStudio was used for statistical analysis. The RFC algorithm showed the highest ACC ratio of 0.79 and F1 score of 0.79. According to shap analysis, MPD made the greatest contribution to the performance of the classification models. The variables with statistically significant differences between sexes were TM, TSC, TTSD, RPCSD and RPCTD. The study shows that ML algorithms can predict sex with 79 % accuracy out of brainstem data. This result clearly shows the effect of sex on brainstem morphometry.

KEY WORDS: Brainstem; Brain morphology; Machine learning; Sex dimorphism; Magnetic resonance imaging.

INTRODUCTION

Several studies have been accumulating in the literature evaluating the processes related to normal development, maturation and aging of the brain, and the effects of diseases, in relation to various age groups and sexes (Giedd *et al*., 2012; Kariev *et al*., 2019; Reinard *et al*., 2015; Jahanshad *et al*., 2017; Rajagopal *et al*., 2021). These studies have concluded that aging and pathological processes cause certain changes in the anatomical and morphological structures of the brain. It has also been emphasized that the sex factor is effective in the morphometric structures of the brain and the prevalence of several diseases (Giedd *et al*., 2012; Jahanshad *et al*., 2017). MR imaging has, in recent years, been used to provide reliable morphometric data in research in which the brain is examined because it reflects soft tissues very well (Giedd *et al*., 2012; Reinard *et al*., 2015; Jahanshad *et al*., 2017; Kariev *et al*., 2019). Use of the brain MRIs in routine examinations, diagnosis and treatment follow-up processes of various diseases has become the gold standard in practice (Giedd *et al*., 2012; Rajagopal *et al*., 2021). Effects of neurodegenerative (Levit *et al*., 2020; Rajagopal *et al*., 2021; Jellinger, 2022) and psychiatric (Chen *et al*., 2023) diseases on critical structures of the brain such as the brainstem are reflected in brain MR images. Examples of such reflections include the use of the pontomesencephalic angle for intracranial hypotension (Shah *et al*., 2013) or the mamillopontine distance for the diagnosis of hydrocephalus (Kariev *et al*., 2019). The brain stem, which is located between the medulla spinalis and diencephalon (Koehler *et al*., 1985) is the part of the central nervous system consisting of the medulla oblangata, pons and mesencephalon, including many nuclei of the central nervous system and descending and ascending pathways.

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Received: 2025-12-18 Accepted: 2026-04-22

To the extent that literature has been reviewed, research in the field of sex estimation has been enriched by studies in various disciplines. The utilization of extensive data sets, bolstered by survey responses and medical histories, to estimate demographic parameters such as age, sex, and other characteristics is a common practice in the field of identification. The incorporation of such data has been found to expand the scope of applications of MLa. The estimation of sex necessitates a multidisciplinary approach incorporating the utilization of MLa. Research of this nature, which encompasses the entirety of an individual's anatomical structures, is poised to serve as a foundational reference point in the realm of forensic science, particularly in the context of natural disasters or armed conflicts (Tetiker & Gençer, 2020; Arslan & Tugutlu., 2023; Taskın *et al*., 2023).

Several literature reports have examined brainstem morphometry of healthy adults (Lee *et al*., 2009; Polat *et al*., 2020; Debnath *et al*., 2023; Demir *et al*., 2023). Such studies are of essential because they provide reference values in the diagnosis and treatment follow-up processes of pathological conditions. These studies have also been focusing on sex prediction through applying values of several variables of different organs. However, it has been observed that the number of studies evaluating the brainstem with a focus on healthy Turkish population is very limited (Polat *et al*., 2020; Demir *et al*., 2023). The present study therefore aims to acquire reference values of the certain brainstem variables on brain MRIs of the healthy participants aged between 25-55 years, and to predict the sex.

MATERIAL AND METHOD

In the cross-sectional retrospective study, healthy participants who came to Department of Neurology, BAI˙BÜ, with any complaint and were found to have no disease affecting the brain stem were evaluated. The study was approved by the Clinical Research Ethics Committee with decision number 2024/226 and was conducted in accordance with the Declaration of Helsinki. Brain MRIs of 200 healthy women and 200 healthy men aged 25-55 years between June 2023 and September 2024 were used in the study. MRIs were taken with 1.5 T Signa Explorer MRI Scanner (GE Medical Systems, Milwaukee, Wisconsin, USA. Images captured from Picture Archiving and Communication Systems (PACS) system BAIBÜ were transferred to MicroDicom Viewer 2024.1 (64 bit) personal workstation for morphometric analysis. Subjects with missing or insufficient images and those with a history of degenerative, cerebrovascular, neurologic or psychiatric diseases were excluded from the study.

Brain MRIs in the axial and sagittal planes were used for the variables in concern to be measured. For each participant, linear measurements were recorded in mm with electronic calipers on the current workstation and angle measurements were recorded in degrees on an excel sheet. Since inter-observer error was not desired, the measurements were made by an expert. The variables measured on the sagittal plane are TMT: midbrain thickness, TP: pons thickness, TM: medulla thickness, TSC: spinal cord thickness, MPD: mamillopontine distance, MBH: midbrain height, PMA: pontomesencephalic angle, TTSD: tectum and tegmentum sagittal diameter, TTTD: tectum and tegmentum transverse diameter, LPCSD: left pedunculus cerebri sagittal diameter, RPCSD: right pedunculus cerebri sagittal diameter, LPCTD: left pedunculus cerebri transverse diameter, RPCTD: right pedunculus cerebri transverse diameter. The measurement and reference points of the variables measured in the axial plane are shown in Figs. 1 and 2.

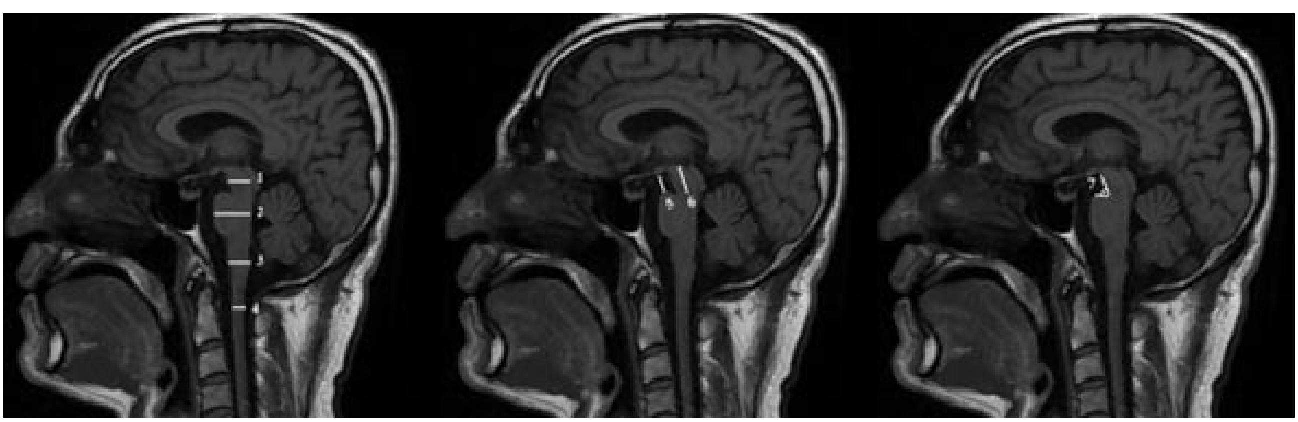

Fig. 1. 1- TMB, 2- TP, 3- TM, 4- TSC, 5- MPD, 6- MBH, 7- PMA (TMT: midbrain thickness, TP: pons thickness, TM: medulla thickness, TSC: spinal cord thickness, MPD: mamillopontine distance, MBH: midbrain height, PMA: pontomesencephalic angle).

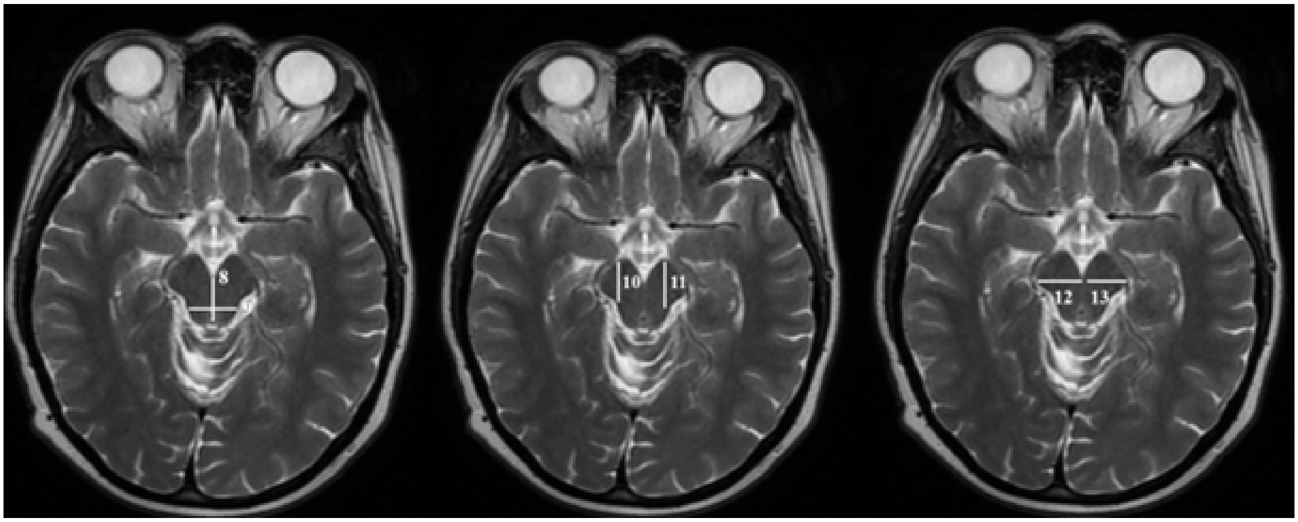

Fig. 2. 8- TTSD, 9- TTTD, 10- LPCSD, 11- RPCSD, 12- LPCTD, 13- RPCTD (TTSD: tectum and tegmentum sagittal diameter, TTTD: tectum and tegmentum transverse diameter, LPCSD: left pedunculus cerebri sagittal diameter, RPCSD: right pedunculus cerebri sagittal diameter, LPCTD: left pedunculus cerebri transverse diameter, RPCTD: right pedunculus cerebri transverse diameter).

Machine Learning Algorithms (ML)

The algorithms were written in Python software language through Spyder IDe. The specifications of the computer on which the algorithms were written and analyzed are shown in Table I.

Logistic Regression Classifier (LRC), Gradient Boosting Classifier (GBC), Decision Tree Classifier (DTC), K-Nearest Neighbors (KNN), Linear Discriminant Analysis (LDA), Random Forest Classifier (RFC), Naive Bayes Classifiers (NBC), XGBoost (XGB) were used as ML. Data were taken as 80 % training and 20 % testing (Random_state=4). Hyperparameters were chosen as “citerion=entropy, max_depth=8, random_state=0” in DTC algorithm; “metric=winskow, p=2, n_neighbors=7” in KNN algorithm; “citerion=entropy, n_estimators=61” in RFC algorithm. Performance evaluation in classification models is performed with confusion matrix (CM). CM consists of four labels: true positive (TP), true negative (TN), false positive (FP), false negative (FN). TP refers to the correctly predicted positive label. TN refers to a correctly predicted negative label. FP stands for falsely predicted positive values, while FN stands for falsely predicted negative values. Precision (pre), recall (rec), f1-score (F1), Accuracy (ACC) were used as evaluation criteria. The formulation of the evaluation criteria is shown in Formula 1.

$$ACC = \frac{TP + TN}{TP + TN + FP + FN}$$

$$PRE = \frac{TP}{TP + FP}$$

$$REC = \frac{TP}{TP + FN}$$

$$F1 = 2 * \frac{PRE * REC}{PRE + REC}$$

Formula 1. Precision (pre), recall (rec), f1-score (F1), Accuracy (ACC).

Statistical analysis

Statistical analyses were performed with RStudio open-source software program. One-factor analysis of variance (One-Way Anova) was applied to all variables. Anderson Darling Test was performed for the residual values revealed upon the analysis of variance, and then their conformity to the normal distribution was evaluated by drawing the QQplot and histogram graph. Logarithmic and square root transformation procedures were applied to the variables that did not fit the normal distribution. Parametric tests were applied to the variables that fit the normal distribution because of the transformation process. Following the independent sample t test for parametric variables and Mann Whitney U test for nonparametric variables; mean and standard deviation (std) values of parametric variables, median, minimum (min) and

Table I. Characteristics of the computer on which the algorithms are written and analyzed.

Processor	Intel Core i5-13400F 13th Generation
Video Card	Zotac GeForce RTX 4060 Ti Twin Edge 8 gb gddr 128 Bit Nvidia
Motherboard	MSI PRO H610M-E DDR4 Intel H610 3200 MHz (OC)
SSD	Crucial 1TB p3 Plut serisi 3D NVMe M.2
Ram	GS KILL 16 GB DDR4 3200Mhz CL16 1.35V

maximum (max) values of nonparametric variables were calculated. As a result of the transformation process, the mean and 95 % confidence intervals of the variables that fit the normal distribution are given.

RESULTS

The analysis revealed that the ACC ratio for LR, GBC, DTC, KNN, LDA, NBC, RFC, SVM, XGB algorithms were 0.75, 0.72, 0.70, 0.76, 0.75, 0.74, 0.79, 0.70 and 0.72, respectively (Table I). The F1 scores of the algorithms were 0.75, 0.73, 0.70, 0.76, 0.75, 0.75, 0.74, 0.79, 0.70 and 0.72 for LR, GBC, DT, KNN, LDA, NBC, RFC, SVM and XGB algorithms, respectively. The RFC algorithm had the highest ACC ratio of 0.79 and F1 score of 0.79 (Table II).

Table II. Algorithms evaluation criteria Precision, Recall, F1-score and Accuracy results (%).

Algorithm	Precision	Recall	f1-score	Accuracy
LR	0.75	0.75	0.75	0.75
GBC	0.73	0.72	0.73	0.72
DT	0.71	0.70	0.70	0.70
KNN	0.77	0.76	0.76	0.76
LDA	0.75	0.75	0.75	0.75
NBC	0.74	0.74	0.74	0.74
RFC	0.79	0.79	0.79	0.79
SVM	0.70	0.70	0.70	0.70
XGB	0.72	0.72	0.72	0.72

Logistic Regression Classifier (LRC), Gradient Boosting Classifier (GBC), Decision Tree Classifier (DTC), K-Nearest Neighbors (KNN), Linear Discriminant Analysis (LDA), Random Forest Classifier (RFC), Naive Bayes Classifiers (NBC), XGBoost (XGB).

Tenfold cross validation was performed as cross validation. The validation rates of LR, GBC, DT, KNN, LDA, NBC, RFC, SVM, XGB algorithms were 0.70±0.2, 0.67±0.1, 0.58±0.1, 0.68±0.1, 0.70±0.1, 0.71±0.1, 0.70±0.1, 0.70±0.1, 0.70±0.2, 0.68±0.1, respectively (Table III and IV).

Table IV. Descriptive statistics results of variables, Mann Whitney U and independent t test results.

Variables	M (n=200)		F (n=200)
Age	38 (25-55)		37 (25-55)
p-value		0.336[k]	
TMB	12.9±1.4		12.8±1.4
p-value		0.337[l]	
TP	22.8±1.5		22.0±1.8
p-value		1.000[l]	
TM	13.2±1.3		12.6±1.4
p-value		<.001[l]	
TSC	8.1±0.9		7.4±1.0
p-value		<.001[l]	
MPD	7.9±1.4		6.9±1.4
p-value		<.001[l]	
MBH	13.6 (13.3-13.8)		13.0 (12.7-13.3)
p-value		0.002[k]	
TTSD	15.2 (10.0-20.3)		14.7 (9.9-20.9)
p-value		0.038[k]	
TTTD	18.5 (14.6-23.7)		18.0 (10.7-22.2)
p-value		<.001[k]	
RPCSD	15.7±1.8		14.8±1.9
p-value		<.001[l]	
LPCSD	15.7±1.6		14.6±1.9
p-value		<.001[l]	
RPCTD	14.6 (14.4-14.9)		13.3 (13.1-13.5)
p-value		<.001[l]	
LPCTD	14.4±1.7		13.2±1.7
p-value		<.001[l]	

k: p value of Mann Whitney U test result. l: p value in the result of the independent test. Mean±std. Median (min-max). Mean (95 % confidence intervals). TMT: midbrain thickness, TP: pons thickness, TM: medulla thickness, TSC: spinal cord thickness, MPD: mamillopontine distance, MBH: midbrain height, PMA: pontomesencephalic angle, TTSD: tectum and tegmentum sagittal diameter, TTTD: tectum and tegmentum transverse diameter, LPCSD: left pedunculus cerebri sagittal diameter, RPCSD: right pedunculus cerebri sagittal diameter, LPCTD: left pedunculus cerebri transverse diameter, RPCTD: right pedunculus cerebri transverse diameter.

Table III. Tenfold results of LR, GBC, DT, KNN, LDA, NBC, RFC, SVM, XGB algorithms (%).

	LR	GBC	DT	KNN	LDA	NBC	RFC	SVM	XGB
1	0.58	0.58	0.40	0.63	0.58	0.53	0.55	0.55	0.55
2	0.40	0.45	0.45	0.65	0.43	0.48	0.43	0.40	0.45
3	0.63	0.70	0.60	0.75	0.63	0.73	0.73	0.68	0.63
4	0.75	0.75	0.60	0.65	0.73	0.75	0.78	0.75	0.60
5	0.58	0.70	0.55	0.63	0.60	0.65	0.70	0.68	0.73
6	0.75	0.60	0.68	0.70	0.75	0.75	0.68	0.65	0.68
7	0.75	0.68	0.63	0.63	0.75	0.70	0.78	0.80	0.78
8	0.73	0.68	0.58	0.65	0.73	0.78	0.75	0.75	0.73
9	0.93	0.73	0.48	0.70	0.90	0.85	0.75	0.90	0.83
10	0.88	0.88	0.85	0.80	0.88	0.88	0.90	0.93	0.93
	0.70±0.2	0.67±0.1	0.58±0.1	0.68±0.1	0.70±0.1	0.71±0.1	0.70±0.1	0.70±0.2	0.68±0.1

Logistic Regression Classifier (LRC), Gradient Boosting Classifier (GBC), Decision Tree Classifier (DTC), K-Nearest Neighbors (KNN), Linear Discriminant Analysis (LDA), Random Forest Classifier (RFC), Naive Bayes Classifiers (NBC), XGBoost (XGB)

Out of the algorithms, LRC 44 out of 23 men, 24 out of 36 women; GBC 44 out of 30 men, 28 out of 36 women; DTC 41 out of 16 men, 34 out of 39 women; KNN 41 out of 28 men, 33 out of 39 women; LDA 41 out of 32 men, 28 out of 39 women; NBC correctly predicted 28 of 41 men, 31 of 39 women; XGB correctly predicted 30 of 41 men, 28 of 39 women; RFC correctly predicted 33 of 41 men, 30 of 39 women; SVM correctly predicted 27 of 41 men, 29 of 39 women (Fig. 3).

The AUC value of the Roc curve, which analyzes the model performances, was 0.80 for LR, 0.81 for GBC, 0.72 for DTC, 0.84 for KNN, 0.80 for LDA, 0.78 for NBC, 0.79 for RFC, and 0.81 for XGB (Fig. 4).

Shap analysis was performed to determine the variable that is effective in the performance of the ML models. According to the Shap analysis, the MPD variable made the largest contribution to the performance of the classification models. The contributions of the variables were analyzed as MPD, RPCTD, TSC, LPCTD, PMA, TP, RPCSD, TM, MBH, TTTD, LPCSD, TTSD and TMB respectively (Fig. 5).

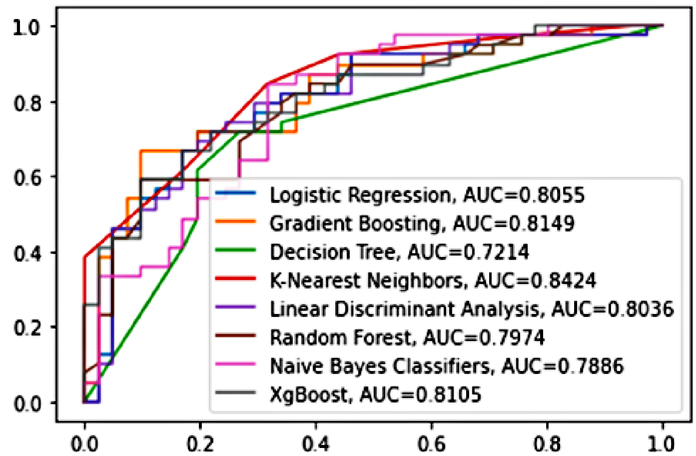

Fig. 4. ROC curve of LR, GBC, DT, KNN, LDA, NBC, RFC, SVM, XGB algorithms.

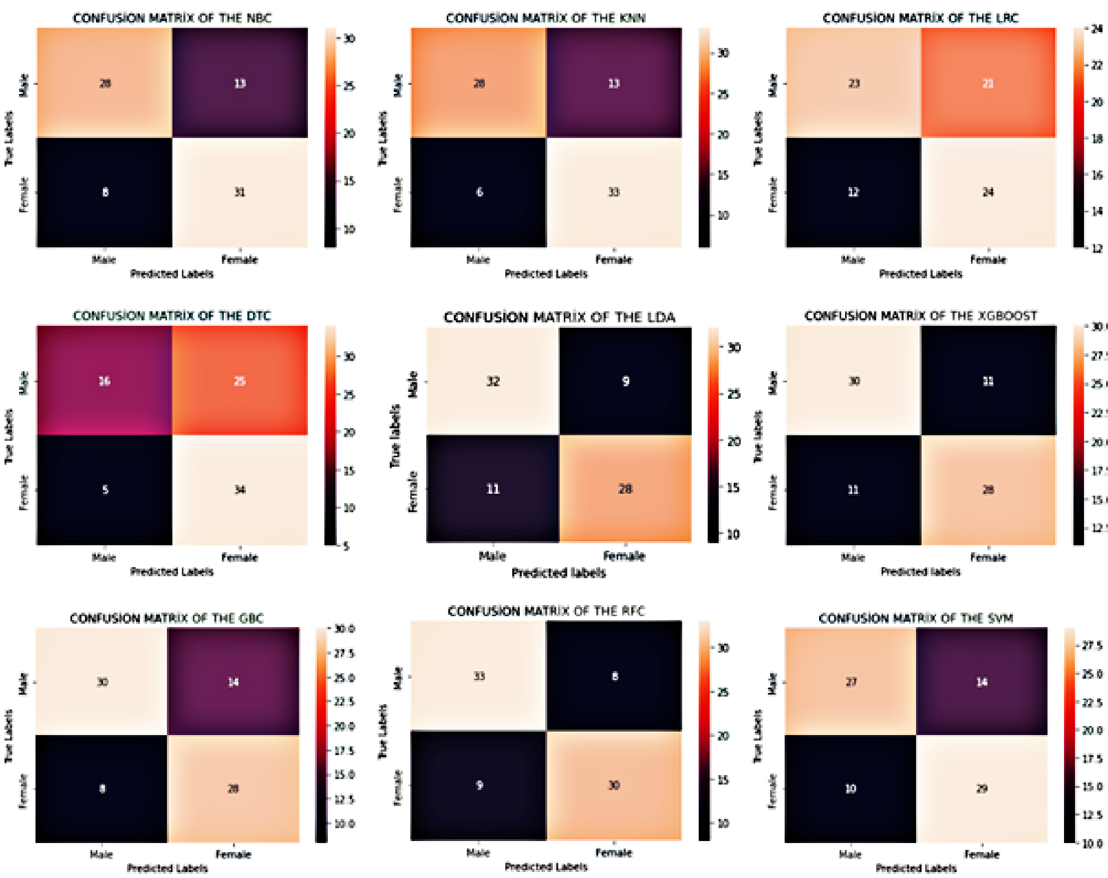

Fig. 3. CM table for LR, GBC, DT, KNN, LDA, NBC, RFC, SVM, and XGB algorithms. Logistic Regression Classifier (LRC), Gradient Boosting Classifier (GBC), Decision Tree Classifier (DTC), K-Nearest Neighbors (KNN), Linear Discriminant Analysis (LDA), Random Forest Classifier (RFC), Naive Bayes Classifiers (NBC), XGBoost (XGB), CM (confusion matrix)

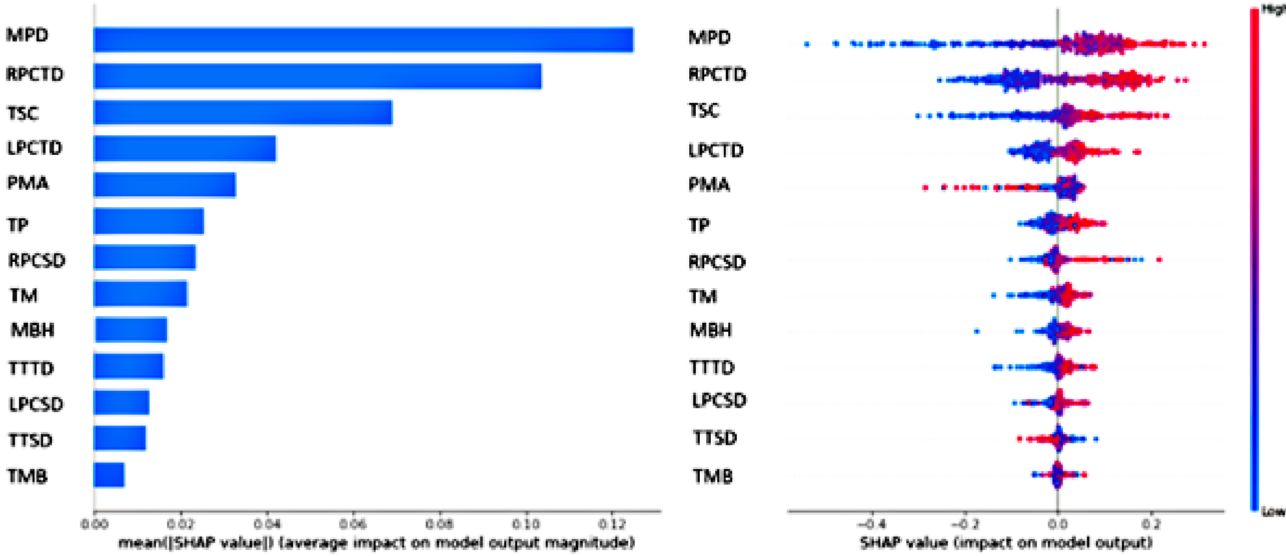

Fig. 5. SHAP analysis results showing the contribution of variables to model performance.Thickness of midbrain (TMB), thickness of pons (TP), thickness of medulla (TM), thickness of spinal cord (TSC), mamillopontine distance (MPD), midbrain height (MBH), pontomesencephalic angle (PMA), tectum and tegmentum sagittal diameter (TTSD), tectum and tegmentum transverse diameter (TTTD), right pedunculus cerebri sagittal diameter (RPCSD), left pedunculus cerebri sagittal diameter (LPCSD), right pedunculus cerebri transverse diameter (RPCTD), left pedunculus cerebri transverse diameter (LPCTD).

According to the statistical analysis, the median value of the age variable was found to be 38 in males and 37 in females (p=0.336). The mean and SD values of the TM variable were found to be 13.2±1.31 and 12.6±1.4 in men and women, respectively. As a result of the analysis for the TM variable, the difference between men and women was statistically significant (p<.001). As a result of the analysis for the TSC variable, it was found to be 8.1±0.9 in men and 7.4±1.0 in women. The difference between men and women for the TSC variable was statistically significant (p<.001). The mean and standard deviation for the MPD variable was 7.9±1.4 in men and 6.9±1.4 in women (p<.001). The median value of the MBR variable was found to be 13.6 in men and 13.0 in women (p=0.002). Another variable for which the difference between sexes was statistically significant (p=0038) was TTSD, with a median value of 15.2 in men and 14.7 in women. The median value for the TTTD variable was found to be 18.5 in men and 18.0 in women (p<.001). The difference between sexes was found to be statistically significant for the RPCSD variable, which was 15.7±1.8 in males and 14.8±1.9 in females (p<.001). LPCSD variable was found as 15.7±1.6 in males and 14.6±1.9 in females (p<.001). RPCTD variable with a mean value of 14.6 in males and 13.3 in females was found to be statistically different between sexes (p<.001). The LPCTD variable was found to be 14.4±1.7 in men and 13.2±1.7 in women (p<.001).

DISCUSSION

Sex-related differences are observed in the onset, prevalence and manifestations of neurological and neuropsychiatric disorders. Interest in these variations has led to an increasing number of studies examining the critical effects of sex on brain architecture. The brain stem, which is connected to the cerebrum, cerebellum and spinal cord, is an important structure involved in the regulation of autonomic and cognitive processes and the transmission of motor and sensory information. In this context, in this study which aims to predict sex with ML methods using normal brainstem reference values on brain MRIs of the healthy participants aged between 25-55 years, the RFC algorithm had the highest ACC ratio of 0.79 and F1 score of 0.79. In addition, the differences between the sexes were found to be significant in TM, TSC, TTSD, RPCSD and RPCTD variables.

A review of the literature has shown that most of the brainstem morphometric studies are retrospective and cross-sectional, as is the case in the present study. In these studies, measurements were made on brain MRIs. In this context, in a study examining the brainstem structure of healthy individuals to be used in the detection of neurodegenerative diseases (Rajagopal *et al*., 2021), the findings of TMD and TP variables were in relation to those of the current study. In another research investigating brainstem values in healthy and pathologic brains (Koehler *et al*., 1985), TMT, TP, TM and TSC variables of the control group were found to be parallel to the related data of the present study. Moreover, another paper on the brainstem-related values in healthy adults reported the correlation between brainstem findings and sex was not found to be an essential parameter that yielded statistically significant differences, while TM and TP variables were found to have similar mean values, as compared to those of the present study. Furthermore, in a study (Debnath *et al*., 2023) designed to provide reference values for the brainstem at all ages in a healthy Indian population, most of the findings were found to have higher mean values in males. Among the study findings, MPD, TM, TP, TMD and variables showed similar results with the current study, while RPCSD and LPSCD variables were lower. Likewise, another literature examining the effects of aging and sex on the total volume of the brain and the volume of the brainstem, lateral ventricle and cerebellum in healthy Koreans (Lee *et al*., 2009) showed a significant difference in the volume of the midbrain, cerebellum and lateral ventricle between the younger and older groups. Like the present study, the findings related to brainstem sections were higher in men. Parallel to the present study, in a study in which the morphometry of the mesencephalon was examined in a healthy adult Turkish population (Demir *et al*., 2023), it was emphasized that there was a significant difference between the variables and sex. When the findings of this literature were examined, it was observed that the TTSD, TTTD, RPCSD, LPCSD, RPCTD, LPCTD variables belonging to the mesencephalon were higher and the MPD variable was lower than the current study. It is thought to be because the unequal distribution of sexes in the study and the wider range of age groups compared to the current study are among the main causes of this difference.

A research study (Ranganath *et al*., 2022) using brain MR images to determine brainstem reference values and to examine the correlation between sex and age in a healthy Indian population, has found that the TP, TM and MBH variables are parallel to the present study whereas the TMB variable is higher. No significant correlation was observed between the study findings and sex. It is thought that this difference with the present study is due to the fact that different populations and different age groups have been studied. Another study evaluating the effect of age and sex on the development of the pons in the pediatric population (Bayar Kapıcı *et al*., 2022) has reported significantly larger results in males for most of the variables. These results, parallel with the present study, have suggested that brainstem segments show sexual dimorphism starting from the pediatric period. Another research (Hu *et al*., 2024) designed to evaluate age- and sex-related changes in the volumetric measurements of the brainstem and surface shape analysis in healthy adults, has revealed no differences between the sexes or in the correlation of sex and age. This might be due to the presence of a sample group between the ages of 18-70 living in different populations, the limited number of people studied, and different variables examined. It may also explain the differences in the findings between this report and the current study. Similarly, a report evaluating the differences in brain stem and cerebellum areas according to sex (Murshed *et al*., 2003), has documented the brain stem area larger in men, just as the data of the present study. Likewise, another research (Zhang *et al*., 2020), designed to examine the structural and functional effects of sex differences in the brain of healthy adults, has revealed sexual dimorphism in the brain lobes and cerebellum, emphasizing that the results of the study can explain sex-related behavioral differences. Another study (Mendes *et al*., 2021) has focused on predicting sex, age and any, if there is, psychiatric disorder out of the brain MRIs in children and adolescents using convolutional neural networks, which uses volume data of the gray and white matter of the central nervous system to train the neural network. This study has acquired a satisfactory result with sex accuracy between 85-89 %, just like the findings of the present study.

A literature report investigating whether personality is related to sex differences in brain structure (Nostro *et al*., 2017), has examined the correlation between personality traits and gray matter in a healthy sample group. The results of the study, in line with the present study, have underlined that sex has significantly influenced the outcome and this result has been attributed to the differences in brain organization and hormones. Another study searching for the changes in cortical morphometry and white matter structures of the brain in aging in reliance to the sex differences (Sang *et al*., 2021), has reported volume decrease and the slope of decrease affected by sex. Similarly, another study focusing on the sex-related changes in brain morphometry by calculating gray matter volume in chronic stress (Shang *et al*., 2024), has found statistically significant differences between male and female participants. Further research that has examined gray matter volumes regionally in middle-aged healthy individuals (Chen *et al*., 2007), after adjusting for age, years of education and total head volume, has reported larger brain volume and higher gray matter ratio in men. The results of this literature have emphasized that sex differences, independent of age, have an impact on certain cognitive functions and brain structure. Another literature (Brennan *et al*., 2021) has contributed to this topic profoundly, which was designed to map differences in the structure of the male and female brain during adolescence, aimed to predict sex with a large dataset. At the end of the study, the classifier has been able to correctly predict sex with a rate of 86 %, similar to the results of the current study.

On the other hand, unlike the findings of the present study, there have been literature reports indicating that the effect of sex on brain structures is not significant after certain ratios are made. It has been indicated that the indices obtained by expressing the brain size of subjects in question as a proportion of the brain size are not likely to be sexually dimorphic (Smith *et al*., 2007; Ranganath *et al*., 2022; Hu *et al*., 2024). A study has investigated the effect of sex, age and head/brain ratio by volumetric brain analysis in a healthy population living in Poland (Kijonka *et al*., 2020). The overall volume of the subcortical brain structures and brain has also been calculated in the study. Sex differences have been shown to be statistically insignificant, as far as the head and brain ratio is concerned. This result has emphasized that taking sex and age into account when evaluating brain structures is necessary for an accurate reference value. Similarly, in a further study examining the relationship between age and sex and brain volume change in healthy elderly people (Smith *et al*., 2007), it has been reported that volume decreases with age. The change in the data related to sex has been found to be significant after proportions have been made ($p<0.05$).

Consequently, this study has aimed to determine sex from brainstem variables in healthy brain MRI images with ML algorithms. Healthy geriatric age group was excluded from the study, and hormonal effects such as pregnancy and menopause in women were neglected since the study was designed retrospectively. The findings has shown the ability of ML algorithms to predict sex from brainstem variables derived from brain MRI images with 79 % accuracy. This suggests the existence of complex but clearly measurable markers of sex in brain morphometry. The study findings can also be considered as a reference for identifying neurodegenerative disorders.

RAY, G.; RAY, A.; AKÜNAL, C. & KÜRTÜL, I. Predicción del sexo mediante algoritmos de aprendizaje automático basados en características morfométricas del tronco encefálico: Un estudio de resonancia magnética. *Int. J. Morphol., 44(3)*:1062-1070, 2026.

RESUMEN: Este estudio se centra en la predicción del sexo mediante algoritmos de aprendizaje automático (AA) utilizando datos del tronco encefálico obtenidos a partir de imágenes de resonancia magnética (RM) cerebral de una población adulta turca sana. En el estudio, se midieron el grosor del mesencéfalo (TMT), el grosor del puente (TP), el grosor de la médula (TM), el grosor de la médula espinal (TSC), la distancia mamilopontina (MPD), la altura del mesencéfalo (MBH), el ángulo pontomesencefálico (PMA), el diámetro sagital del tectum y el tegmento (TTSD) a partir de imágenes de RM cerebral de 200 mujeres y 200 hombres, y se midieron las variables diámetro transversal del tectum y el tegmento (TTTD), diámetro sagital del pedúnculo cerebral derecho (RPCSD), diámetro sagital del pedúnculo cerebral izquierdo (LPCSD), diámetro transversal del pedúnculo cerebral derecho (RPCTD) y diámetro transversal del pedúnculo cerebral izquierdo (LPCTD). Se utilizaron los algoritmos de aprendizaje automático (ML) de regresión logística (LRC), potenciación de gradiente (GBC), árbol de decisión (DTC), k-vecinos más cercanos (KNN), análisis discriminante lineal (LDA), bosque aleatorio (RFC), clasificadores bayesianos ingenuos (NBC) y XGBoost (XGB). RStudio se utilizó para el análisis estadístico. El algoritmo RFC mostró la mayor precisión (ACC) de 0,79 y una puntuación F1 de 0,79. Según el análisis de forma, el dimorfismo sexual múltiple (MPD) fue el factor que más contribuyó al rendimiento de los modelos de clasificación. Las variables con diferencias estadísticamente significativas entre sexos fueron TM, TSC, TTSD, RPCSD y RPCTD. El estudio demuestra que los algoritmos de ML pueden predecir el sexo con una precisión del 79 % a partir de datos del tronco encefálico. Este resultado muestra claramente el efecto del sexo en la morfometría del tronco encefálico.

PALABRAS CLAVE: Tronco encefálico; Morfología cerebral; Aprendizaje automático; Dimorfismo sexual; Resonancia magnética.

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