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Research Article

Diffusion Tensor Tractography of the Corticospinal and Medial Lemniscus Pathways in Healthy Adults

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Objective: This study aims to visualize major brainstem white matter pathways in vivo through MR tractography, with a specific focus on the corticospinal tract (CST) and medial lemniscus (ML), which are essential motor and sensory tracts in healthy individuals.

Methods: Twenty right-handed healthy adults (10 females, 10 males; mean age: 29.95 ± 8.77 years) with normal brain MRI findings were included. DTI was acquired using a 3T MRI scanner. For each participant, CST and ML tracts were reconstructed bilaterally by placing regions of interest (ROIs) at anatomically defined points within the internal capsule and brainstem. Tracts fractional anisotropy (FA) values were calculated for quantitative assessment, and tract visual quality was scored independently by two observers using a 5-point scale.

Results: Tract reconstruction was successful in all participants. CSTs demonstrated consistently higher FA values and clearer anatomical delineation compared to ML tracts. Visual quality was independently rated by two experts using a 5-point scale. Mean CST scores were significantly higher than ML scores ($p < 0.001$), and inter-observer consistency was strong.

Conclusion: This study demonstrated that the CST and ML pathways can be reliably and anatomically accurately visualized in healthy individuals using ROI-based tractography. Establishing normative data for these vital brainstem tracts may serve as a valuable reference, particularly for neurological disorders or neurosurgical planning in which these pathways are likely to be affected.

Keywords: Diffusion tensor imaging (DTI), Tractography, Corticospinal tract (CST), Medial lemniscus (ML)

1. INTRODUCTION

Diffusion tensor imaging (DTI) is an advanced magnetic resonance imaging (MRI) technique that enables the in vivo examination of white matter microstructure by capturing the directional diffusion of water molecules.[1] Through this property, DTI provides information about fiber integrity and organization across the brain's white matter networks.[2] One of the major strengths of DTI is its ability to support tractography, a technique that reconstructs three-dimensional representations of neural pathways, offering both qualitative and quantitative assessments of connectivity.[3,4] As such, DTI-based tractography has become an essential tool in neuroscience and clinical neuroimaging, aiding in the mapping of normal white matter anatomy and the detection of subtle structural abnormalities in various disease states.[5]

Among the numerous white matter pathways, the corticospinal tract (CST) and medial lemniscus (ML) stand out due to their fundamental roles in motor and sensory processing, respectively.[6] The CST is a principal descending tract that conveys voluntary motor commands from the cerebral cortex to the spinal cord, enabling conscious movement control.[7] In contrast, the ML is a major ascending somatosensory pathway that transmits proprioceptive and fine tactile information from the periphery to the thalamus and then to the sensory cortex.[6] Both tracts pass through the brainstem, a structurally dense and functionally vital region, rendering them particularly vulnerable to disruption and critically important in surgical navigation and diagnostic imaging.[8]

Clinically, CST and ML integrity is frequently compromised in a range of neurological disorders. CST degeneration is a hallmark of motor neuron diseases such as amyotrophic lateral sclerosis

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(ALS) and primary lateral sclerosis, while ML abnormalities have been observed in conditions affecting sensory pathways, including multiple sclerosis, brainstem infarcts, and central pain syndromes.[9-11] Tractography of these pathways is also gaining relevance in preoperative assessment of brainstem tumors, cavernomas, and demyelinating lesions, where understanding the displacement or infiltration of these tracts can directly influence surgical planning and risk stratification.[12-15]

In neurosurgical cases involving brainstem tumors or vascular malformations precise localization of white matter tracts is critical for planning safe resection margins.[12,16] Tractography enables preoperative visualization of lesion–tract relationships, helping preserve healthy tissue and reduce surgery-related damage.[12,17] Despite its growing use and the variability in tract localization caused by lesions, standardized approaches for ROI placement and tract delineation, particularly for brainstem pathways, remain limited in the literature, and reference data from healthy individuals are essential to interpret patient-specific findings meaningfully.[18]

In addition to their diagnostic and surgical implications, the CST and ML are increasingly recognized for their role in differential diagnosis and disease monitoring. For instance, distinguishing between upper and lower motor neuron involvement in neurodegenerative conditions often hinges on CST integrity.[19-21] Likewise, ML tract alterations may support the identification of central versus peripheral sensory deficits. However, accurate reconstruction of these tracts remains technically challenging due to crossing fibers, low spatial resolution in deep brain regions, and variation in individual anatomy. Manual ROI placement, though anatomically informed, may be affected by lesion-induced distortion or operator variability. Therefore, understanding the typical appearance and variability of these tracts in healthy individuals is essential for interpreting pathological findings in clinical settings. Therefore, reliable tract reconstruction techniques that capture the integrity and spatial trajectory of CST and ML fibers in the healthy brain are essential for enhancing our understanding of disease mechanisms and for guiding safe and effective therapeutic interventions.[21]

This study focuses on the reconstruction and evaluation of the CST and ML in a healthy population using an ROI-based tractography method. We aimed to visualize these tracts in three orthogonal planes and extract quantitative metrics such as fractional anisotropy (FA) to assess tract integrity. Additionally, we incorporated a visual scoring system performed by expert raters to qualitatively evaluate tract clarity and reproducibility. Particular emphasis was placed on the methodological relevance of ROI placement in capturing the trajectory of brainstem tracts, given their anatomical complexity and surgical importance. By establishing normative tractography patterns and visual benchmarks for CST and ML pathways, this work intends to provide a foundational reference for future clinical applications, especially in cases involving brainstem lesions where functional preservation is paramount.

2. MATERIAL AND METHODS

2.1. Participants

A total of 20 healthy individuals were included in the study. All participants were right handed, neurologically healthy adults with no history of neuropsychiatric or neurosurgical conditions. The dataset was balanced in terms of sex and age distribution to ensure representativeness in assessing white matter tract integrity and visualization quality. Written informed consent was obtained from all participants prior to data inclusion. The study protocol was approved by the Institutional ethics committee and conducted in accordance with the Declaration of Helsinki.

2.2. MRI

All participants underwent imaging on a 3T MRI (Ingenia, Philips Medical Systems, Netherlands) system using a 48-channel head coil. In addition to routine brain MRI sequences, including a DTI sequence was acquired with the following parameters: TR = 6000 ms, TE = 55 ms, slice thickness = 2.5 mm, and no interslice gap. The DTI protocol included two b-values (b = 0 and b = 800

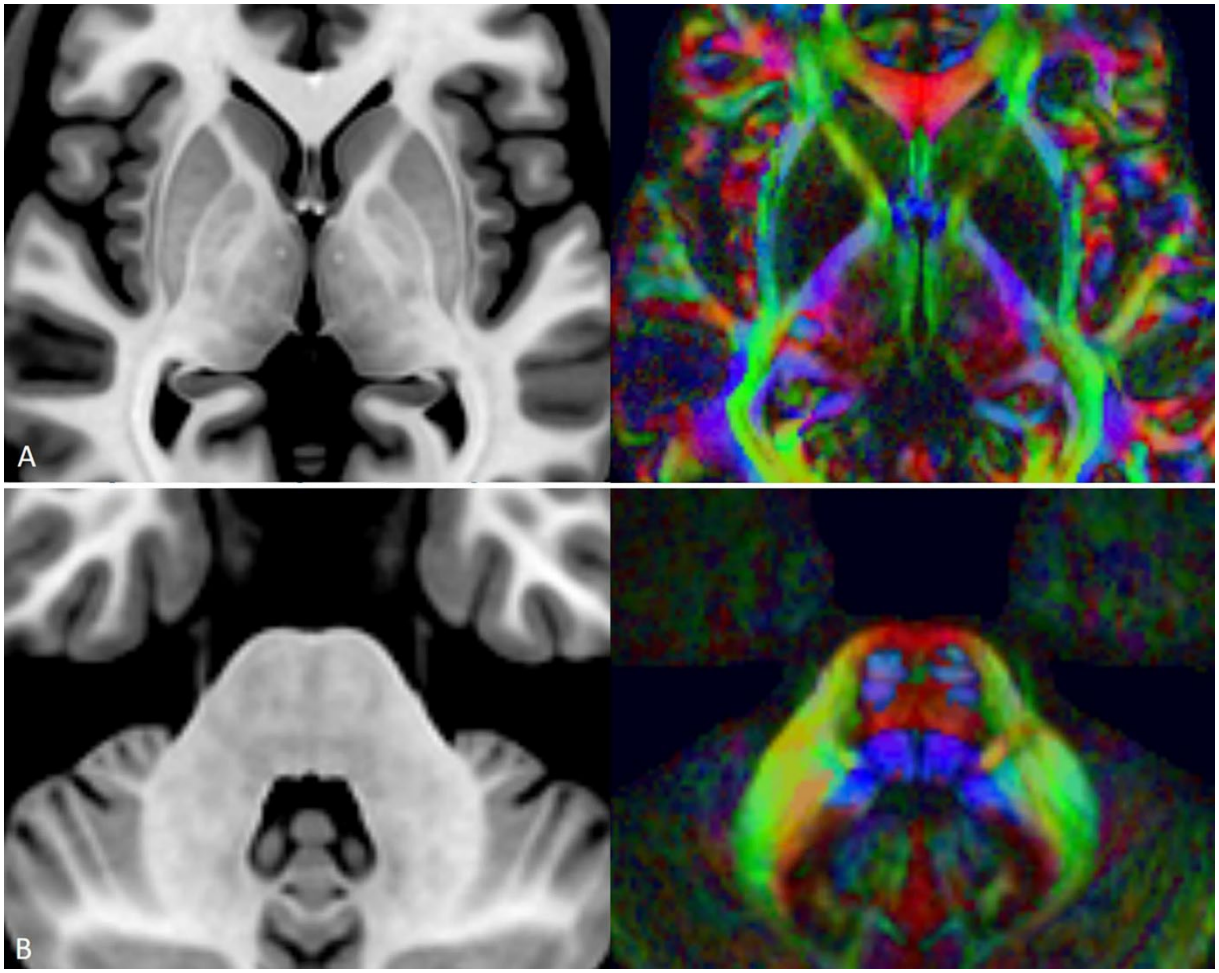
s/mm^2) and diffusion encoding in 32 directions. The total acquisition time for the DTI sequence was approximately 4 minutes.

2.3. DTI analysis

DTI data from all participants were transferred to the Extended MR Workspace R2.6.3.1 platform (Philips Medical Systems, Hamburg, Germany) for post-processing. This platform was used to generate directionally encoded color coded FA maps and perform 3D fiber tractography (Figure 1).

Figure 1.

Axial T1-weighted anatomical images (left) and their corresponding directionally encoded FA maps (right) displayed at two representative levels: (A) through the posterior limb of the internal capsule and (B) at the level of the brainstem. Color-coded FA maps illustrate dominant diffusion directions (red: mediolateral, green: anteroposterior, blue: craniocaudal). Both the CST and ML tracts appear predominantly blue due to their superior–inferior orientation along the brainstem

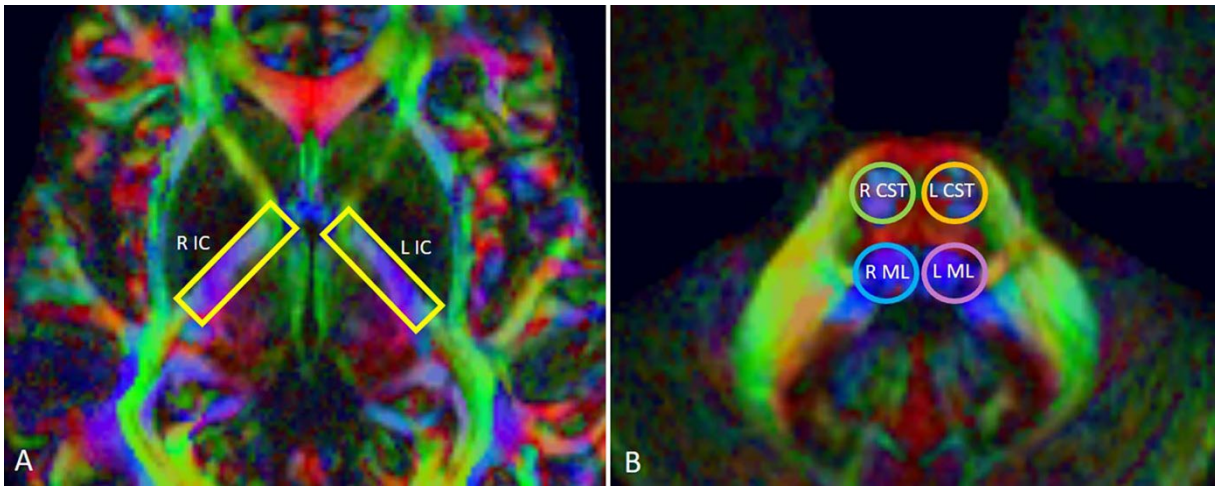


2.4. Tractography analysis and ROI placement

For each subject, bilateral CST and ML pathways were analyzed. Tract reconstructions were conducted using standardized anatomical landmarks and established protocols to ensure consistent visualization across participants Regions of interest (ROIs) were manually defined to enable tract reconstruction of the CST and ML using anatomically guided landmarks (Figure 2).

Figure 2.

These sections highlight key white matter regions relevant to CST and ML tractography and served as anatomical references for regions of interest (ROIs) placement. A color-coded FA map shows the ROI positioned at the level of the posterior limb of the internal capsule (A) and ROI localization at the level of the brainstem (B). For right CST reconstruction, ROIs were placed in the right internal capsule (R IC) and right CST region; for left CST, ROIs were placed in the left internal capsule (L IC) and left CST region. Similarly, for right ML reconstruction, ROIs were placed in the right internal capsule and right ML region; and for left ML, in the left internal capsule and left ML region



ROI placement was performed in accordance with established tractography protocols and white matter anatomy as outlined in previous studies.[6,22] For the CST, ROIs were placed in segments known to encompass motor fibers, specifically, the posterior limb of the internal capsule and the anterior brainstem on the right side for the right CST, and the corresponding left-sided structures for the left CST. For the ML, ROIs were positioned in regions associated with somatosensory signal transmission. These included the posterior limb of the internal capsule and the dorsomedial brainstem on the right for the right ML, and the anatomically equivalent locations on the left for the left ML.

This dual-ROI strategy facilitated anatomically constrained fiber tracking, minimizing the inclusion of false-positive fibers and improving the specificity and reproducibility of tract delineation across all participants. Following ROI placement, deterministic tractography was performed, and the resulting fiber pathways were visualized in three orthogonal planes (axial, coronal, and sagittal) and rendered in three-dimensional space. For each tract, FA mean ± SD was computed within the tract defined by streamlines traversing the ROIs, excluding the ROI voxels themselves.

2.5. Tract quality assessment

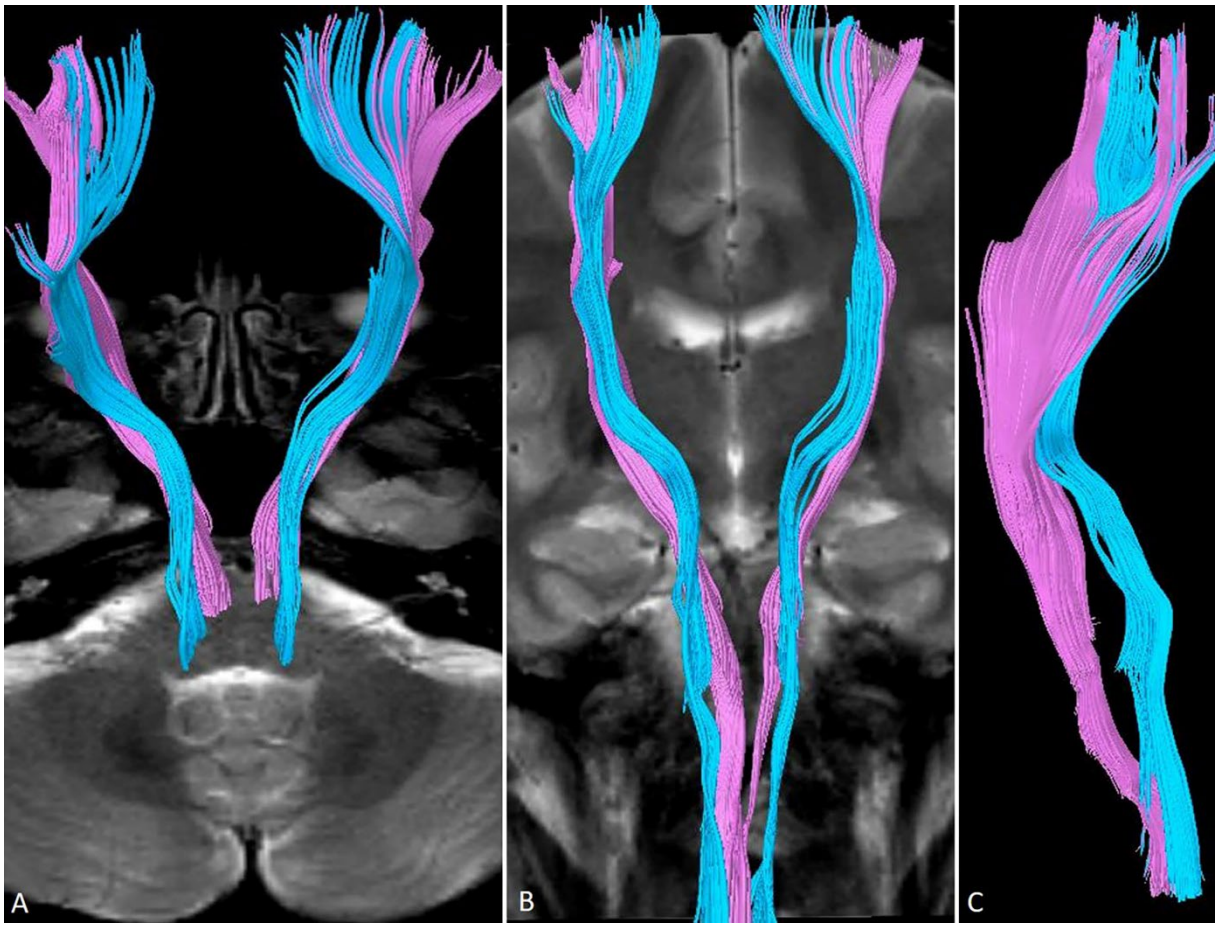
In addition to quantitative analysis, a qualitative evaluation was performed. Each tract was visually rated by two experienced observers using a standardized 5-point ordinal scale (1 = Very Poor, 2 = Poor, 3 = Decent, 4 = Good, 5 = Very Good), assessing overall tract clarity, anatomical fidelity, and continuity. These visual scores served as a complementary measure of tract quality and inter-subject consistency.

2.6. Statistical analysis

All analyses were performed using IBM SPSS Statistics (v26.0). Independent t-tests assessed sex differences in FA values, while paired t-tests evaluated hemispheric lateralization and visual scoring differences. Age-related associations were examined using Pearson and Spearman correlations, along with linear regression. A p-value < 0.05 was considered statistically significant. Descriptive statistics were reported as mean and standard deviation. Inter-observer consistency in visual scores was reviewed by comparing average ratings across observers.

Figure 3.

Representative tractography from a healthy right-handed 23-year-old female: reconstruction of the bilateral corticospinal tract (CST, pink) and medial lemniscus (ML, blue), visualized in axial oblique (A), coronal (B) and sagittal (C) planes. The CST is positioned anteriorly and the ML posteriorly within the brainstem, each showing a continuous trajectory extending toward the motor cortex and somatosensory regions, respectively. The tractography demonstrates clear anatomical separation and directionality of motor and sensory pathways in healthy individuals



3. RESULTS

3.1. Tract FA

Twenty right-handed healthy adults (10 females, 10 males; mean age = 29.95 ± 8.77 years) were included. Mean FA in the corticospinal tract was hemispherically symmetric (L CST: 0.55 ± 0.05; R CST: 0.54 ± 0.04), whereas the medial lemniscus showed a modest rightward elevation (L ML: 0.54 ± 0.03; R ML: 0.56 ± 0.04) (Table 1).

Table 1.

Participant Characteristics and Tracts FA Values

n	Sex (F / M)	Handedness	Age	Tract FA (mean±std)			
			(mean±std)	Left CST	Right CST	Left ML	Right ML
20	10F - 10M	Right	29.95±8.77	0.55±0.05	0.54±0.04	0.54±0.03	0.56±0.04

3.2. Age-related associations with tract FA

Correlation analyses were performed to assess the relationship between participant age and FA values in the corticospinal tract (CST) and medial lemniscus (ML) (Table 2). Both Pearson and Spearman correlation coefficients indicated no statistically significant associations between age and FA in any of the examined tracts. For the left

CST, Pearson r = –0.022 (p = 0.926) and Spearman ρ = –0.083 (p = 0.729); for the right CST, r = 0.074 (p = 0.757) and ρ = 0.028 (p = 0.907); for the left ML, r = 0.037 (p = 0.877) and ρ = 0.026 (p = 0.912); and for the right ML, r = 0.103 (p = 0.664) and ρ = 0.074 (p = 0.758).

Table 2.

Age-Related Associations With FA in CST and ML Tracts

Tracts	Pearson r (p)	Spearman ρ (p)
Left Corticospinal Tract	-0.022 (0.926)	-0.083 (0.729)
Right Corticospinal Tract	-0.074 (0.757)	0.028 (0.907)
Left Medial Lemniscus	0.037 (0.877)	0.026(0.912)
Right Medial Lemniscus	0.103 (0.664)	0.074 (0.758)

3.3. Sex-related associations with tract FA

No statistically significant differences were observed in the FA values of the CST and ML tracts between female and male (Table 3). Independent samples t-tests revealed comparable mean FA values across sexes for all examined pathways, including the left CST (t = 0.046, p = 0.964), right CST (t = -0.372, p = 0.714), left ML (t = -0.204, p = 0.840), and right ML (t = -0.107, p = 0.916).

Table 3.

Sex-Related Associations With FA in CST and ML Tracts

Tracts	t-statistic	p-value
Left Corticospinal Tract	0.046	0.964
Right Corticospinal Tract	-0.372	0.714
Left Medial Lemniscus	-0.204	0.840
Right Medial Lemniscus	-0.107	0.916

Group-level analysis revealed no significant differences in FA values of the CST and ML between sexes. Mean FA values were also not significantly associated with age. Linear regression models showed no meaningful effect of age or sex on either CST (p = 0.75 and p = 0.82, respectively) or ML (p = 0.67 and p = 0.87, respectively) tract integrity.

3.4. Lateralization of tract FA values

Paired t-tests were performed to evaluate potential lateralization in CST and ML tracts (Table 4). The comparison between left and right CST revealed no significant difference (t = 0.348, p = 0.732), indicating symmetric FA values across hemispheres. In contrast, a significant lateralization was found in the ML tract, with the right ML showing higher FA values than the left (t = -2.157, p = 0.044).

Table 4.

Hemispheric Asymmetry in Tract-Specific FA Metrics

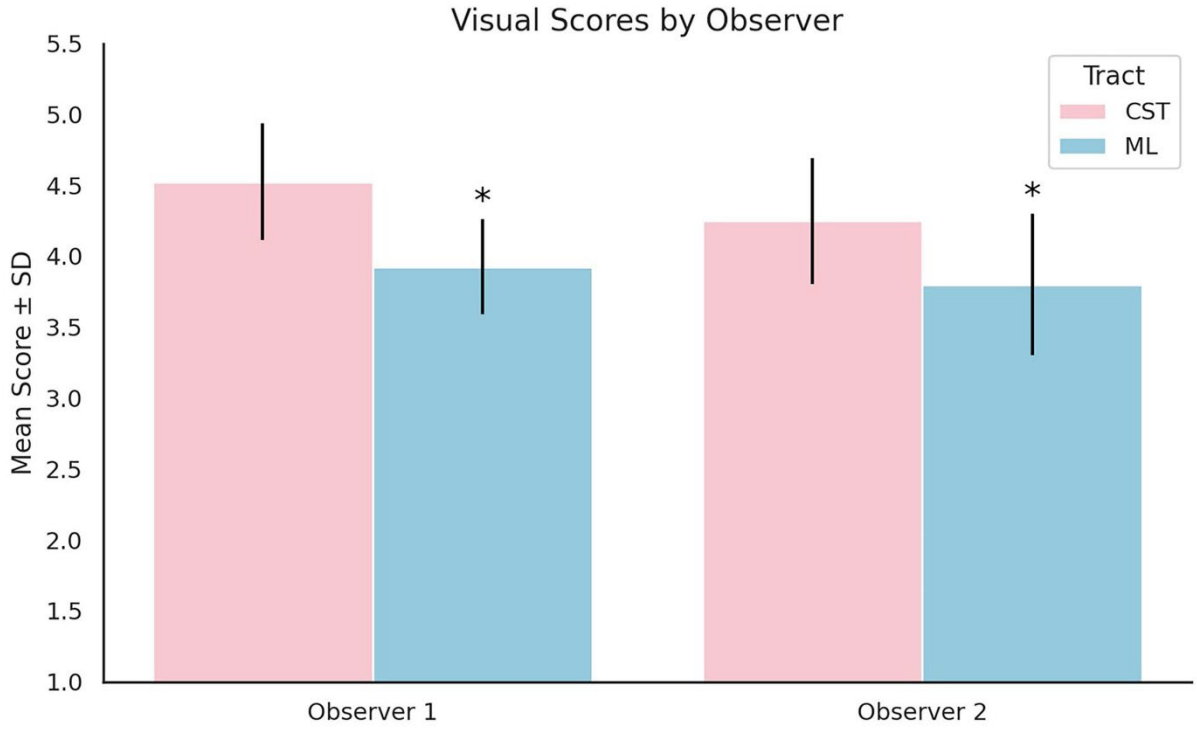
Correlation	t-statistic	p-value
Left Corticospinal Tract vs Right Corticospinal Tract	0.348	0.732
Left Medial Lemniscus vs Right Medial Lemniscus	-2.157	**0.044**

3.5. Qualitative evaluation of tractography: Visual scoring of CST and ML

Visual scoring of the CST and ML was independently conducted by two trained observers, as illustrated in Figure 4, using a standardized 5-point ordinal scale (1 = Very Poor, 5 = Very Good). This qualitative evaluation aimed to assess the overall anatomical clarity and tract delineation quality of the reconstructed fiber bundles. Each tract was scored based on well-established neuroanatomical criteria, including the accuracy of its anatomical trajectory, the consistency of its extension toward the cortex, the absence of misalignment or overlap with adjacent tracts, and the overall continuity and coherence of its pathway. These parameters reflect widely accepted standards in white matter tractography evaluation and ensure reliability in observer based ratings.[6,23]

Figure 4.

*Bar plot showing mean visual scores (±SD) for the corticospinal tract (CST) and medial lemniscus (ML) as rated by two independent observers. CST tracts received significantly higher scores than ML tracts (*p < *0.001), indicated by asterisks*



Across all tract evaluations, the CST received significantly higher mean visual scores compared to the ML, indicating superior anatomical clarity and tract reconstruction quality. A paired-sample t-test confirmed this difference as statistically significant ($t(39) = 7.12$, $p < 0.000001$). Both observers independently demonstrated this pattern, with CST tracts being rated more favorably than ML tracts across nearly all subjects. This consistent trend suggests that CST pathways are generally more robustly visualized and easier to identify using tractography techniques, potentially due to their larger caliber, higher fiber coherence, and more distinct anatomical trajectory.

4. DISCUSSION

This study presents a comprehensive evaluation of the CST and ML pathways in healthy individuals using ROI based tractography. By combining quantitative measurements of FA and expert based visual scoring, we aimed to establish normative tractography benchmarks that could inform both clinical and research applications, particularly in cases involving the brainstem. Our findings demonstrate that CST and ML tracts can be consistently reconstructed in healthy subjects,

but they differ in terms of FA values, lateralization tendencies, and visual clarity.

Despite age-related microstructural decline being well-documented in the literature,[24] particularly in frontal and association fibers,[25] our correlation analyses did not demonstrate any significant associations between age and FA values in either the CST or ML. This likely reflects the restricted age range of our sample (18–49 years), which consisted primarily of younger adults. Linear regression models further supported these findings, showing no meaningful predictive effect of age or sex on tract integrity. These findings support the notion that in early to mid-adulthood, the CST and ML maintain relatively stable microstructural features and more resistant to age-related microstructural degeneration, making them suitable targets for early disease detection in patient populations.

Contrary to earlier studies that reported potential sex-related differences in white matter microstructure in specific brain regions,[26,27] our findings revealed no statistically significant FA differences in the CST or ML tracts between male and female participants. Independent samples t-tests yielded comparable mean FA values across sexes for both left and right hemispheric pathways. This suggests that the examined projection fibers, particularly those involved in sensorimotor function, may not be substantially influenced by biological sex in healthy young adults. These results align with prior DTI studies that found negligible sex-based FA differences in motor pathways,[28] underscoring the stability of these tracts across demographic variables.

Hemispheric asymmetry in white matter tracts has long been a topic of neuroscientific interest.[29] Our paired-sample comparisons between left and right hemispheric tracts revealed no significant lateralization in CST FA, suggesting a bilateral structural symmetry that is consistent with the known bilateral organization of the pyramidal motor system. However, a small but statistically significant lateralization was observed in the ML tract, with the right ML showing higher FA values. This asymmetry may reflect underlying differences in axonal density or myelination patterns, potentially linked to lateralized sensory processing.[30] While the clinical relevance of this finding in healthy subjects remains limited, it raises the possibility that ML lateralization may become more pronounced in neurological populations, such as those with sensory integration deficits.

In addition to quantitative analysis, this study employed qualitative visual scoring to assess the anatomical clarity and coherence of reconstructed white matter tracts. The results revealed a consistent and statistically significant distinction between the CST and ML pathways, with the CST receiving higher visual quality ratings from both observers. This finding suggests that the CST is more reliably visualized using tractography techniques in healthy individuals.

The observed superiority of CST visualization over ML can be attributed to both anatomical and technical factors. The CST is a larger, well-organized motor pathway with coherent fiber alignment, which enhances its compatibility with DTI-based tractography.[22,31] In contrast, the ML courses through the brainstem, a region known for complex fiber crossings, decussations, and dense neural structures, all of which can impair tracking algorithms and reduce visual clarity.[17,32] These findings are consistent with previous studies suggesting that motor tracts, such as the CST, are more reliably reconstructed than sensory pathways like the ML due to their higher anisotropy and clearer anatomical definition.

In this study, the integration of a standardized 5-point ordinal visual rating scale alongside quantitative FA analysis provided complementary insight into white matter tract integrity. Visual scoring consistently favored the CST over the ML, a finding that may be attributed to the CST's larger diameter, clearer anatomical boundaries, and greater fiber coherence, which facilitate more robust tract reconstruction.[33] In contrast, the ML's smaller size and diffuse organization within the complex architecture of the brainstem likely contributed to lower visual ratings, despite standardized ROI placement. Importantly, visual assessment holds particular clinical relevance in scenarios where anatomical distortion or suboptimal image quality may limit the reliability of quantitative metrics alone. These results

highlight the value of combining objective diffusion-based measures with observer-based qualitative evaluation to achieve a more comprehensive understanding of tract quality.

Clinically, the reliable reconstruction of CST and ML tracts holds significant implications for preoperative planning, particularly in brainstem pathologies where direct intraoperative visualization of white matter pathways is not feasible. DTI-based tractography has emerged as a valuable adjunct in neurosurgical workflows, enabling clinicians to anticipate tract displacement, infiltration, or disruption in patients with tumors, demyelinating conditions, or vascular malformations.[13,16] Establishing normative references for tract reconstruction in healthy subjects, as done in this study, contributes to improved interpretation accuracy when evaluating pathologic cases, particularly given the tractography's sensitivity to algorithm selection, ROI placement, and image resolution.

The small sample size may limit detection of subtle demographic effects. Tractography algorithms have known limitations, particularly in brainstem regions with complex fiber architecture. FA-only characterization may miss microstructural nuances; future work should incorporate complementary diffusion metrics such as mean, radial, and axial diffusivity, as well as model-based indices, to strengthen inference. Observer-based scoring, though informative, is subjective. Future studies should include larger cohorts and explore automated or machine learning based segmentation methods[18,34] to support clinical use, especially in brainstem pathologies. Notwithstanding these limitations, our dual ROI protocol and expert quality control provided anatomically credible localization of the brainstem CST and ML pathways at their expected levels, which we consider sufficient for the aims of this study.

5. CONCLUSION

This study shows that ROI-guided DTI tractography enables reliable reconstruction and evaluation of both the CST and ML in healthy individuals, despite their anatomical differences. The CST demonstrated high structural symmetry and superior visual clarity, while a mild rightward lateralization was noted in the ML tract. Age and sex were not significant contributors to FA variability across subjects. Observer based visual scoring further supported the robustness of CST reconstruction. Importantly, establishing normative tractography profiles for these critical brainstem pathways is essential for standardizing DTI analysis and provides a valuable reference for preoperative white matter mapping, especially in neurosurgical cases involving the brainstem.

Article Information Form

Authors' Contribution

ZF collected the data, performed the statistical analyses, and drafted the manuscript. GE supervised the study and critically revised the manuscript. Both authors served as observers and approved the final version of the manuscript.

The Declaration of Conflict of Interest/ Common Interest

No conflict of interest or common interest has been declared by authors.

The Declaration of Ethics Committee Approval

This study involved only human data; no animal experiments were conducted. Written informed consent was obtained from all participants prior to their inclusion. The study protocol was approved by the Yeditepe University Non-Interventional Clinical Research Ethics Committee (Approval No: 202507Y0883) and conducted in accordance with the principles outlined in the Declaration of Helsinki.

Artificial Intelligence Statement

No artificial intelligence tools were used while writing this article.

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