Laterality of the corticospinal tract and variation with handedness: the findings of a DTI study

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Target audience: Clinicians and scientists who are involved in interpretation and application of the major diffusion tensor imaging (DTI) indices of the brain and the spinal cord

Background and Purpose: Controversies exist on laterality in the absolute values of the DTI indices of the corticospinal tract (CST) of the brain[1, 2]. The influence of handedness on the DTI characteristics of the major white matter tracts of the brain including the CST is also a subject of debate[2]. The existence of laterality in the absolute values of the DTI indices of the CST of the spinal cord and their variation with handedness are not known. This study aimed to evaluate laterality in the absolute values of the major DTI indices of the CST of the brain and the cervical spinal cord and their variation with handedness.

Methods: DTI of the brain and the cervical spinal cord was performed in 8 left-handed (4 men and 4 women; mean age = 34 ± 6.7 years, age range = 21 – 42 years) and 8 age and gender-matched right-handed (4 men and 4 women; mean age = 35 ± 6.0 years, age range = 23 – 42 years) healthy subjects. The absolute values of the major DTI indices ─ longitudinal ($\lambda_{//}$), transverse ($\lambda_{\perp}$), and mean (MD) diffusivities, and fractional anisotropy (FA), were measured by using circular regions-of-interest. Measurement was made at bilateral precentral gyri (PrCG), posterior limbs of internal capsule (PLIC), the either sides of the basis pontis, and bilateral lateral columns (LC) of the cervical spinal cord from the second cervical vertebral body (C2) through the intervertebral disc between the sixth and seventh cervical vertebrae (C6/7). For each handedness group, the absolute values of the major DTI indices were compared between the two sides. Between-group comparison of the absolute values of major DTI indices was also performed. Paired and two-sample t-tests were used to determine significance at $P<0.05$. Repeatability of the measurements was tested in one subject; and the scanner-related factors which might influence on laterality of the results were excluded through a phantom experiment involving two asparagus stems.

Results: For both handedness groups, the left LC had significantly lower $\lambda_{\perp}$ and MD, and higher FA values than the right *(Table)*. The left PrCG and PLIC of the left handers had significantly lower $\lambda_{\perp}$ and MD, and higher FA values than the right side. The left side of basis pontis tended to have lower $\lambda_{\perp}$ than the right side. In the right handers, the left PrCG had significantly lower MD values than the right. There were tendencies toward lower $\lambda_{\perp}$and higher FA of the left PrCG, higher FA of the left PLIC, and lower $\lambda_{\perp}$ and MD and higher FA of the left side of basis pontis, compared to the right side. The left handers had lower $\lambda_{\perp}$ and higher FA values of the left PrCG, higher $\lambda_{\perp}$ and MD values of the right PLIC, higher $\lambda_{//}$ of the right side of basis pontis, and lower MD and higher FA of the left LC than the right handers. Repeatability assessment revealed Cronbach's α values >0.80 for all areas, suggestive of repeatability of measurements in all areas.

Discussion: The results suggest lower $\lambda_{\perp}$ and MD, and higher FA values of the left CST for both the brain and the cervical spinal cord. The observation of similar pattern of laterality of the major DTI indices between the brain and the spinal cord is contradictory to the expectation of reversed pattern of laterality between the brain and spinal cord due to the decussation of the CST at the medulla oblongata. Dominancy of the CST of the left cerebral hemisphere (relative increase in the axonal number and myelin thickness) together with increased branching of nerve fibers from the right side of the spinal cord[3, 4] *(Fig. 1)*, dominancy of the CST of the left cerebral hemisphere and decussation of large number of fibers of the CST at each spinal level[5] *(Fig. 2)*, and the development of the ipsilateral lateral CST[6] *(Fig. 3)*, are considered as the possible mechanisms for the observation. Variation in the axonal number or myelin thickness between the two handedness groups is thought to be attributable for the variation of DTI indices between the two handedness groups.

Conclusion: The results suggest a similar pattern of laterality in the absolute values of the major DTI indices of the CST between the brain and the cervical spinal cord. The values may vary with handedness. The knowledge of laterality of the major DTI indices and their variation with handedness is important in the interpretation of the major DTI indices of the CST in diseased states. This is the first report which evaluated laterality of the major DTI indices of the CST from the PrCG to the cervical spinal cord and compared the indices between the left and right handers.

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Figure legends: Fig. 1; Scheme illustrating a proposal for the observation of symmetrical pattern of laterality between the CST of the brain and the cervical spinal cord. The coronal (above) and axial (below) sections of the LC at two different levels are shown. Despite entry of larger number of fibers to the right LC (A), larger number of fibers branched from the right LC can result in lesser number of residual longitudinally-aligned fibers running along the right LC at the lower levels (C) ─ to give rise to lower anisotropy[3, 4]. Fig. 2; Scheme illustrating another proposal. The course of the CST fibers at the level of the medulla oblongata and LC is shown in the oblique coronal (above) and axial (below) sections. This proposal is based on documentation of the presence of decussation of the CST axons at each spinal level[5]. If a larger number of the CST fibers decussate from the right (dominant side)(A) to the left LC at each spinal level, the number of fibers running along the left LC (D) as well as the degree of anisotropy might increase. Fig. 3; Scheme illustrating another proposal. The course of the CST fibers at the level of the medulla oblongata and LC is shown in the oblique coronal (above) and axial (below) sections. This proposal is based on documentation of the presence of ipsilateral (uncrossed) lateral CST axons in human[6]. Persistence of these CST fibers might induce an increase in the number of fibers running along the left LC as well as the degree of anisotropy.

Table: The mean (± standard deviation) values of the major DTI indices of the CST at various levels.

Indices	Handedness	PrCG		PLIC		Basis pontis		LC	
		Right	Left	Right	Left	Right	Left	Right	Left
$\lambda_{//}$ ($mm^2\ s^{-1}$)	Right	1.14 ± 0.12	1.11 ± 0.12	1.44 ± 0.11	1.46 ± 0.09	1.17 ± 0.06	1.18 ± 0.09	1.60 ± 0.15	1.55 ± 0.14
	Left	1.16 ± 0.11	1.15 ± 0.12	1.48 ± 0.09	1.47 ± 0.10	1.24 ± 0.15	1.23 ± 0.12	1.59 ± 0.14	1.57 ± 0.14
$\lambda_{\perp}$ ($mm^2\ s^{-1}$)	Right	0.52 ± 0.07	0.50 ± 0.06	0.38 ± 0.04	0.38 ± 0.07	0.56 ± 0.05	0.54 ± 0.07	0.43 ± 0.08	0.35 ± 0.09
	Left	0.52 ± 0.05	0.48 ± 0.05	0.42 ± 0.03	0.37 ± 0.05	0.55 ± 0.07	0.52 ± 0.06	0.39 ± 0.08	0.33 ± 0.08
MD ($mm^2\ s^{-1}$)	Right	0.73 ± 0.04	0.71 ± 0.05	0.73 ± 0.04	0.74 ± 0.05	0.78 ± 0.04	0.76 ± 0.05	0.82 ± 0.08	0.75 ± 0.08
	Left	0.74 ± 0.04	0.70 ± 0.04	0.77 ± 0.03	0.74 ± 0.03	0.72 ± 0.05	0.78 ± 0.06	0.79 ± 0.07	0.75 ± 0.07
FA (a.u.)	Right	0.47 ± 0.10	0.48 ± 0.09	0.68 ± 0.05	0.70 ± 0.06	0.49 ± 0.07	0.51 ± 0,07	0.70 ± 0,05	0.75 ± 0.06
	Left	0.49 ± 0.08	0.52 ± 0.08	0.68 ± 0.04	0.71 ± 0.06	0.53 ± 0.07	0.53 ± 0.06	0.72 ± 0.07	0.75 ± 0.07

Adjacent pairs with statistical significance (P<0.05) between the right and left sides

Adjacent pairs with statistical significance (P<0.05) between the right and left handers