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Artículo original

Can the isotropic imaging be used to locating the subthalamic nucleus?

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ABSTRACT

Background: the development of correlation methods for higher confidence in the location of the position of the STN are needed in Functional Neurosurgery. *Objectives:* To compare with the axial isotropic imaging *versus* the axial T2 weighted trace images, the position of the subthalamic nucleus with respect to the red nucleus. Thus in order to know the statistical significance among this two imaging methods. *Methods:* 30 patients were evaluated using the DTI asset protocol in a 3 Tesla MRI (General Electric) with the Functool Software that displays simultaneously the Isotropic and the T2-wieghted images. Measurements were performed using the geometric centers of the nucleus and fixed settings for the isotropic images. The values were compared using a paired T test. In order to verify a higher probability of a nucleus on the spot were the Isotropic and T2 –W indicated, a tractography was performed. *Results:* With a confidence of 95%, no statistical significance among the Isotropic and the T2-W data acquisition regarding the geometric centers of the STN with respect to the geometric center of the Rn was found. On average and based on the isotropic data, the lateral distance from the geometric center of the Rn to the geometric center of the STN was 4.82 mm (+- 1.24) and 4.90 mm (+- 1.25) for the right and left side respectively and the A-P distance was 6.82 mm (+-1.52) and 6.73 mm (+-1.74) for the right and left side respectively. *Conclusions:* The lack of statistically significant differences among the isotropic and the T2-W images for the detection of the geometric center of the STN can guide to the assumption that the isotropic imaging technology can be as reliable as the T2-weighted trace for the targeting of the STN.

Key words: subtalamic nucleus, location, isotropic imaging, functional neurosurgery.

¿PUEDE USARSE LA IMAGEN ISOTRÓPICA PARA LOCALIZAR LOS NUCLEOS SUBTÁLAMICOS?

RESUMEN

El desarrollo de métodos de correlación que permitan una mayor confianza en la exactitud de la localización del núcleo subtalámico ha sido una necesidad dentro de la neurocirugía funcional. *Objetivos:* el comparar la posición del núcleo subtalámico (STN) con relación al nucleo rojo obtenida en las imágenes axiales isotrópicas en relación con las imágenes T2 axiales, las cuales son consideradas como las más confiables para la visualización del STN. Lo anterior se lleva a cabo con el propósito de determinar la significancia estadística entre estos dos métodos de adquisición de imágenes. *Métodos:* treinta pacientes fueron evaluados utilizando el protocolo de difusión de tensor de imagen en un aparato de resonancia magnética de 3 teslas (General Electric) con el programa “Functool” el cual presenta en pantalla de forma simultánea las imágenes isotrópicas y las tipo T2. Las mediciones se realizaron utilizando el centro geométrico de los núcleos y con parámetros de adquisición fijos para las imágenes isotrópicas. Los valores fueron comparados utilizando el método *t* de student para muestras pareadas. Con el propósito de confirmar la localización adecuada del núcleo subtalámico en donde las imágenes isotrópicas y de T2 mostraban, se realizó una tractografía en cada caso. *Resultados:* con una confianza del 95%, no fue posible encontrar una

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diferencia estadísticamente significativa entre ambos tipos de imágenes (isotrópicas y T2) con respecto a la localización de los centros geométricos de los STN con respecto a los centros geométricos del núcleo rojo (Rn). En promedio, y basándonos en los datos de isotropía, la distancia lateral del centro geométrico del Rn con respecto al centro geométrico del STN fue de 4.82mm (+-1.24) y 4.90 mm (+-1.25) para los lados derecho e izquierdo respectivamente, siendo la distancia anteroposterior de 6.82mm (+-1.52) y 6.73mm (+-1.74) para el lado derecho e izquierdo respectivamente. *Conclusiones:* la ausencia de significancia estadística en la localización del STN entre ambos tipos de imágenes, permite asumir que la tecnología de imagenología basada en la isotropía es tan confiable como la que proveen las imágenes obtenidas mediante la tecnología T2.

Palabras claves: nucleo subtalámico, localización, imagen isotrópia, neurocirugía funcional.

The development of correlation methods for higher confidence in the location of the position of the STN are needed in Functional Neurosurgery since an accurate location of the target provides consequently a better performance in the correct placement of the DBS electrodes.

It is generally accepted that there is a strong relation between the microscopic morphology of tissue that governs the self-diffusion of water in tissue and the macroscopic results of the DWI[1].

The anatomical connectivity pattern of a brain region determines its function[2]. Although invasive tracer studies have produced a large body of evidence, concerning connectivity patterns in non-human animals[3,4], direct information concerning brain connections in humans is very limited. Injection of fluorescent dyes *post mortem* allows tracing of tracts, but only for distances of tens of millimeters[5]. Longer distance connections can be investigated by dissection of major tracts or histological studies of remote degeneration following focal lesion[6] but such work is based on a relatively small number of informative patients.

A specific, important focus for investigation is the Subthalamic Nuclei because it has been regarded as an important structure in modulation of activity of output of basal ganglia structures and has been implied in the pathology of Parkinson's disease[7]. Regarding the intrinsic organization of the STN, it is thought that the caudal third of the nucleus and the dorsolateral portion of the rostral two-thirds are related to motor circuits. The ventral portion of said rostral two-thirds is thought to belong to associative territory. The medial portion of said rostral two-thirds is thought to be devoted to be limbic and partly associative territory[8,9].

Diffusion imaging characterizes the apparent diffusion properties of water[10,11]. The diffusion tensor is an ellipsoidal approximation of directional anisotropy of diffusion, which shows distance covered in 3D space by molecules in a certain diffusion time[12,13]. In tissue with a high degree of directional organization the diffusion of water protons is different in different directions. In brain white matter, the principal diffusion direction corresponds well with orientation of major fibers in each voxel[12]. The developments of diffusion. Tensor Imaging (DTI) techniques have enabled tracing of large fiber tracts in the living human brain[14-22]. Not surprisingly, many clinical applications of anisotropism analysis are evident in the literature[8,15-19]. In contrast, clinical application of isotropism still remains to be fully explored. Although neural fibers such as axons are known to show significant anisotropism, the remaining structures, including neural and glial cell bodies are believed to essentially exhibit isotropism[22], specially the nucleus.

OBJETIVES

To compare with the axial isotropic imaging *versus* the Axial T2 weighted trace images, the position of the Subthalamic Nucleus with respect to the Red Nucleus. Thus in order to know the statistical significance among this two imaging methods.

MATERIAL AND METHODS

Eighty seven patients were randomly selected from a Magnetic Resonance Image (MRI) Diffusion Tensor Image (DTI) data bank. From those 87, since the MRI boundary between the STN and the SN has not clearly been defined in the literature[23,27], we reselected forty - seven patients for our study because their DTI asset was able to comprise a slice where the STN was visualized without the substantia nigra (SN) in the same image.

From each patient, the DTI asset comprised 780 images acquired with a 3T General Electric MR, using the Functool software to perform the functional DTI imaging in the isotropic mode in order to compare it with the T2 weighted images of the STN.

The parameters were: b value = 1000, T2 images = 2, threshold; noise = 300, Upper = 4095, Fibertrak-Maxsteeps = 160, Fibertrak-Min FA value = 0.18, Fibertrak Max ADC Value 0.01. After scrutiny, seventeen patients were also excluded in spite of the presence of tumors in the brain stem or with mass effect anywhere else, hydrocephalus or obvious malformations.

On those thirty remaining, 18 were females and 12 males, with age mean 36.7 years old, Std. Dev. 16.61. The diagnosis prior the MRI, were seizures in 12 patients, tumors in 7 patients and miscellaneous in 5 other patients (Parkinson's Disease 2, Trauma follow up 1, Intra cerebral hemorrhage 1, Multiple Sclerosis 1). Five patients remained undiagnosed at the time of the study with an MRIs reported as normal.

We developed an algorithm in order to compare the geometric center of the STN as identified in the isotropic image from the geometric center of the STN obtained with the T2 weighted images (Please refer to figure 1) assuring the position of the ROI on the STN by anatomy and by IRM landmarks as described elsewhere[24].

We also used a third method (please refer to figures 2 and 3) of checking the real correspondence of the ROI selection with the STN based in the coherence of the fiber tracks with known pathway studies of the STN[7,25-27]. As mentioned before, we only placed ROIs for tracking on images were *substantia nigra* (SN) was not present in the axial isotropic Images since the boundaries between the SN and the STN has not been well defined on IRM[23,27].

Measurements were performed using the geometric centers of the nucleus and fixed settings for the isotropic images. The values were compared using a paired T test. In order to verify a higher probability of a nucleus on the spot were the Isotropic and T2 –W indicated, a tractography was performed.

RESULTS

With a confidence of 95%, no statistical significance among the isotropic and the T2-W data acquisition regarding the geometric centers (GC) of the STN with respect to the GC of the Rn was found.

On average and based on paired T test for the lateral distance between RN and the STN in the right side. (Values in mm) the following location values were found. Distance was measured in cartesian coordinates from the GC of the red nucleus (RN) to the STN (Values in mm).

Scattered graphic that shows the distribution of the geometric center of the STN with respect to the geometric center of the Rn. (Spots at the left of the zero represent the left side and at the right of the zero the right side).

Using the Isotropic data, it was found that the lateral distance from the GC of the Rn to GC the geometric center of the STN was 4.82 mm (+- 1.24) and 4.90 mm (+- 1.25) for the right and left side respectively and the A-P distance was 6.82 mm (+- 1.52) and 6.73 mm (+-1.74) for the right and left side respectively.

Paired samples statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	X from RN to STN (right)	-4.8250	30	1.2442	.2272
	T2 X from RN to STN (right)	-4.8500	30	1.2519	.2286
Pair 2	Y from RN to STN (right)	6.8276	29	1.5267	.2835
	T2 Y from RN to STN (right)	6.8276	29	1.5267	.2835

Paired samples correlations

		N	Correlation	Sig.
Pair 1	X from RN to STN (right) & T2 X from RN to STN (right)	30	.997	.000

Paired samples test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	X from RN to STN (right) - T2 X from RN to STN (right)	2.500E-02	.1006	1.838E-02	-1.2581E-02	6.258E-02	1.361	29	.184

Paired samples statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	X from RN to STN (left)	4.9052	29	1.2525	.2326
	T2 X from RN to STN (left)	4.9138	29	1.2576	.2335
Pair 2	Y from RN to STN (left)	6.7328	29	1.7410	.3233
	T2 Y from RN to STN (left)	6.7328	29	1.7229	.3199

Paired samples correlations

		N	Correlation	Sig.
Pair 1	X from RN to STN (left) & T2 X from RN to STN (left)	29	.999	.000
Pair 2	Y from RN to STN (left) & T2 Y from RN to STN (left)	29	.999	.000

Paired samples test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	X from RN to STN (left) - T2 X from RN to STN (left)	-8.6207E-03	4.642E-02	8.621E-03	-2.6279E-02	9.038E-03	-1.000	28	.326
Pair 2	Y from RN to STN (left) - T2 Y from RN to STN (left)	.0000	9.449E-02	1.755E-02	-3.5942E-02	3.594E-02	.000	28	1.000

CONCLUSIONS

The lack of statistically significant differences among the Isotropic and the T2-W images for the detection of the geometric center of the STN can guide to the assumption that the Isotropic Imaging technology can be as reliable as the T2-weighted trace for the targeting of the STN.

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