Segmentation of Sensory Pathways in Human Trigeminal Ganglion and Brain Stem

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Introduction

Anatomical descriptions of brain stem axonal pathways that form the human trigeminal system and other related pain and sensory systems have in large part been identified by postmortem histological techniques or contrast-enhanced MRI (Paxinos and Huang, 1995; Williams et al, 2003). What these methods cannot easily facilitate is a more direct link between functional properties of neuronal structures defined by functional imaging during pain processing and mechanical sensation (Borsook et al., 2003) and the biophysical properties of the axonal pathways that connect the structures. An approach where structural connectivity could more easily be related to function would allow for a better understanding of the neurobiology of healthy and diseased states of processing networks, such as the human trigeminal system. Here we use diffusion tensor imaging (DTI) and probabilistic tractography to segment known sensory and pain pathways and assess the usefulness of DTI with regards to segmenting specific sensory and pain pathways of interest in the brain stem (Basser and Pierpaoli, 1996; Behrens et al., 2007). Our results indicated that this anatomic technique can not only be implemented to map the pain and sensory circuitry at the level of the brainstem, but may also provide a better means to comprehend the functionality of sensory and pain processing networks (i.e. human trigeminal systems).

Materials and Methods

Subjects: 8 healthy subjects were scanned for this study (6 males and 2 females; age range (32.2 ± 12.8)).

Data Acquisition: Scanner: 3 T Siemens Trio scanner with an 8 channel phased array head coil (Erlangen, Germany). DTI data were collected using a single shot-twice refocused echo planar pulse sequence at a 1.75 x 1.75 x 2.5 mm^3 resolution. A single non-diffusion weighted (b = 0 sec/mm^2) volume was collected, while 72 distinct diffusion-weighted volumes were collected at b = 1000 sec/mm^2 (TR = 7900 msec, TE = 92 msec). 50 axial slices were sufficient to cover the entire cerebral cortex and cerebellum. T_1-weighted structural images were acquired using a 3-D magnetization-prepared rapid gradient echo sequence (MPRAGE) at a resolution of 1.33 x 1.0 x 1.0 mm^3 (TR = 2100 msec, TE = 2.74 msec, TI = 1100 msec, Flip angle = 12°, 128 sagittal slices).

Data Analysis: Single subject data analysis was performed using FMRIB Software Library (FSL) (www.fmrib.ax.ac.uk/fsl). DTI datasets were corrected for eddy current distortion and head motion using an affine registration (Jenkinson and Smith, 2001; Jenkinson et al., 2002). Automated affine registration and manual registration amongst DTI and MPRAGE datasets were performed for each subject. Probabilistic diffusion tensor tractography was performed using the modeling technique proposed by Behrens and colleagues (Behrens et al., 2003; Behrens et al., 2007). To eliminate noise and threshold probabilistic tractography maps, the minimum probability threshold was set to at least 2% of the maximum probability calculated.

Seeding Masks: The following anatomical locations were used as seeding masks during probabilistic tractography to segment the brain stem pain and sensory pathways: 1) Trigeminal nerve root (TNR) lying between the trigeminal ganglion (TG) and pons (**Figure 1**); 2) TNR and spinal trigeminal tract (STr) at the level of the pons (**Figure 2**). 3) STr in superior medullary regions and spinal thalamic tract (STh), trigeminal thalamic tract (TTh) and medial lemniscus (ML) at the level of midbrain (**Figure 3**). A differentiation between STh, TTh and ML was not possible at the current DTI voxel resolution. Brain stem histological atlases were used to define all seeding masks. (http://www.msu.edu/~brains/index.html).

Results and Discussion

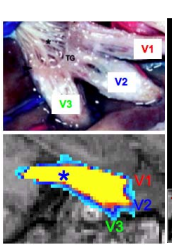

Figure 1A

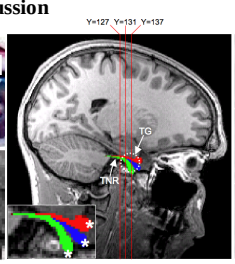

Figure 1B

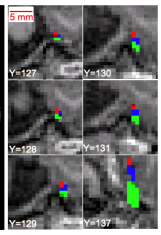

Figure 1C

It is known that all sensory and pain information of the face enters the brain stem via the TNR. Thus, as an initial step to characterizing pain and sensory pathways, the peripheral trigeminal system circuitry was first mapped. The top image in **Figure 1A** shows the anatomy of the TNR, TG and peripheral trigeminal nerve branches (**V1**, **V2** and **V3**) (Adapted from Williams et al., 2003), while the bottom image in **Figure 1A** was obtained by placing a seeding mask in the TNR (blue asterisk) and performing probabilistic tractography. The TG was identified along with the division of **V1**, **V2** and **V3** pathways within the TG. Using the initial tractography results shown in **Figure 1A**, three seeding masks (white asterisks) were placed in the general regions of **V1**, **V2** and **V3** (**Figure 1B**). The latter probabilistic tractography results depicted a clear division of the three trigeminal nerve branches at the level of the TG (Y=130 to Y=137), but not in the TNR (Y=127 to Y=129) (**Figure 1C**).

Figure 2 shows the TNR projecting towards caudal pontine regions in six consecutive sagittal slices. The TNR is depicted in yellow and light blue, while the two seeding masks used are represented as white asterisks. In sagittal slices, X=52 to X=54, the pathway defined by using only the STr mask is shown. The latter probabilistic tractography procedure segmented the STr, STh, middle longitudinal fasciculus (MLF) and tegmental tract (TT). A projection to cerebellar lobules 4 and 5 was also observed across all subjects. Brain stem to thalamus pathways were segmented next (**Figure 3**). In **Figure 3**, seeding masks are shown as white asterisks in the medulla and midbrain. Given the in-plane resolution of DTI data, a distinction between spinal thalamic and trigeminal thalamic pathways was not always possible as a result of the close proximity of the two pathways. The trigeminal thalamic and spinal thalamic pathways each convey both sensory and pain information from the face and body, respectively. The following pathways were observed at various levels of the brain stem; 1) *Medulla* → STr and STh, 2) *Medulla-Pons* → STr and STh, 3) *Pons* → STh, ventral TTh and mesencephalic tract, 4) *Midbrain* → STh, ventral TTh and ML. Coronal slices through the brain stem where the trigeminal and spinal thalamic system pathways are present are shown in **Figure 3**. Red lines in each coronal slice represent the location of the axial slices shown in the middle row of **Figure 3**. In the bottom row, histological cross sections of the brain stem correspond to the general location of the axial slices shown above. Yellow circles indicate location of the spinal thalamic and trigeminal system pathways in each cross section. The location of the above mentioned brain stem pathways as determined by DTI and probabilistic tractography are in good agreement with histological description of tract location of various brain stem pathways.

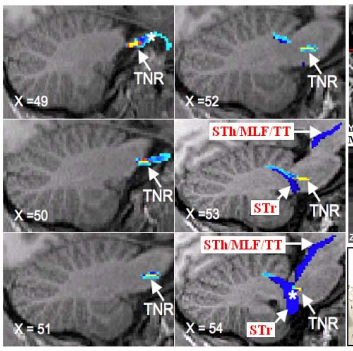

Figure 2

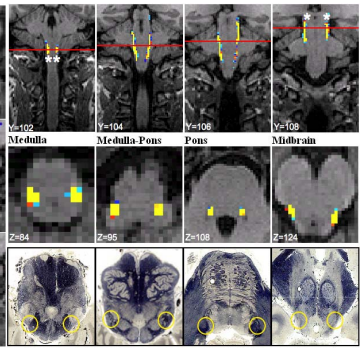

Figure 3

Conclusion

The results of this study indicate that DTI can be implemented to segment peripheral and brain stem pathways relevant to processing pain and sensory information. Previously, identifying the anatomical location of these pathways was only possible via postmortem histological methods or contrast-enhanced MRI. The present DTI findings, such as the segmentation of trigeminal nerve branched within the TG, further explain the previously observed functional properties of the TG (Borsook et al., 2003). Future studies where functional imaging of pain and sensory processing is performed in conjunction to DTI will better characterize the trigeminal and other related systems.

References: 1. Paxinos and Huang, Atlas of the Brainstem; 1995. 2. Williams et al., AJNR; 2003. 3. Borsook et al., J of Neurosci; 2003. 4. Basser and Pierpaoli, MRM; 1996. 5. Behrens et al., MRM ; 2003. 6. Behrens et al., Neuroimage; 2007. 7. Jenkinson and Smith, Med Image Anal; 2001. 8. Jenkinson et al., Neuroimage; 2002.