Comparison of Published Calbindin D 28k Immunohistochemical Staining of the Substantia Nigra to 8 Tesla Human Gradient Echo Images

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Synopsis Calbindin D $_{28k}$ immunohistochemical staining of the brainstem has demonstrated the anatomy of the substantia nigra (SN) with greater detail than in the past (1). The calbindin stains show a different distribution of the SN than standard histological techniques. Our goal was to compare high-resolution axial ultra high field 8 Tesla (T) gradient echo (GE) phase and magnitude images of normal human upper brainstem- SN images to published axial calbindin stain brain sections. The SN was seen as a low signal region with complex margins between the low intensity red nuclei and the high intensity cerebral peduncles on the magnitude and phase images. The phase images best correlated with the published calbindin stains demonstrating that high field imaging generates unique anatomy display of the SN not visible using other MRI techniques.

Methods We studied 6 normal human subjects. All subjects signed informed consent approved by an Investigational Review Board. The studies were performed on an 80 cm bore Magnex- General Electric (Abingdon, U.K.) 8 T magnet system with a water-cooled asymmetric gradient controlled by a Bruker Avance (Billerica, MA, U.S.A.) console and a 21 cm long transverse electromagnetic head coil. GE MR images were acquired with imaging parameters of TR 600, TE 12, slice thickness of 2 mm, scan gap 2 mm, field of view of 18 cm, flip-angle approximated 20 ^{o}, bandwidth 50 kHz, acquisition time approximately 8 minutes, and a matrix size of 1024 x 768. Images were acquired for 24 total slices in two separate interleaved overlapping acquisitions. The second acquisition covered the gap in the first series. In addition to the magnitude images, phase images were calculated after subtracting the slow varying phase due to the static field (2). The images were displayed as either routine magnitude images or pure phase images (Figure 1). We correlated the 8 T images to the published axial calbindin stain images.

Results Only one exam failed for technical reasons. Overall the image quality of the brain stem region was good and consistent. The imaging findings between all of the subjects were similar. On the magnitude images the red nuclei and the SN demonstrated similar homogeneous smooth margined low signal. The margins of the SN were not well defined particularly facing the cerebral peduncle. On the phase images the SN demonstrated low intensity, but the phase intensity findings were less homogenous. The phase differentiation of the medial lemniscus and the SN was much better than the magnitude images. The medial margin of the SN was straight, but the lateral margin had multiple "flame" like irregularities. The red nuclei were also inhomogenous as depicted in the phase images. The SN was visible on approximately ten different sections for each subject. There was a clear similarity between the published caldindin stained axial brain sections of the SN and the phase images.

Discussion Parkinson's disease is associated with massive degeneration of the dopamine containing neurons of the midbrain. Individual cell vulnerability is heterogeneous in part based on location within the SN. The SN is the dominant, but not the sole location for dopamine containing neurons. The global dimensions of the SN correlate poorly with Parkinson's symptoms. Cabindin stains for the neuropil of striatonigral afferent fibers and is independent of neurons. Therefore it is a more accurate marker for the SN than neuron distribution in disease because the landmarks are lost. There are five different "poor" staining calbindin regions called nigrosomes in the SN. These regions are consistent between individuals. In Parkinson's disease there is severe focal loss of neurons in the nigrosomes. Progression of the clinical findings corresponds to focal cell loss in these specific regions. Therefore if imaging is to play a significant role in evaluating Parkinson's disease it is essential to be able to evaluation specific small subdivisions of the SN with great accuracy, particularly in the evaluation of early disease. The 8 T phase imaging suggests that there is a close relationship of the low signal phase regions of the SN and the calbindin staining regions. The phase images in general demonstrate greater contrast to the contiguous structures. Also the SN demonstrated "flame" margins laterally on the phase images that correlate very well with the calbindin staining. Also there were many available 8 T images to evaluate the microscopic SN at 1 mm steps. Therefore 8 T imaging appears to generate excellent and unique information about the SN. If Since 8 T images can demonstrate image changes of the sub segments of the SN that correlate specifically with nigrosome pathology then this may be a very important new means of evaluating patients with Parkinson's disease.

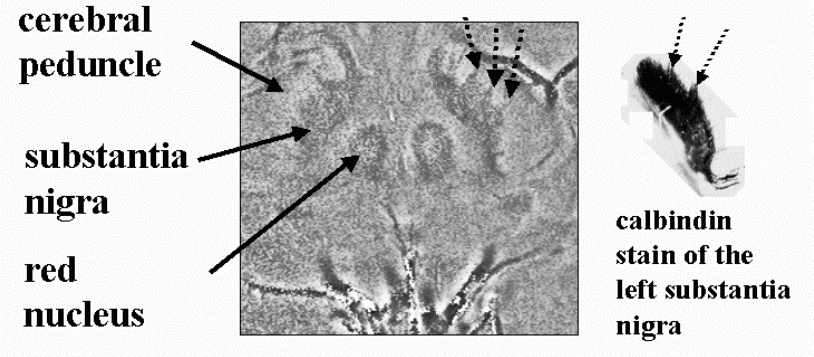

Figure 1. This is an axial GE phase image (to the left) through the upper SN. The right cerebral peduncle, substantia nigra, and the red nucleus are all labled with solid arrows. The image to right is an inverted calbindin stain from reference (1). Note the close correlation of the "flame" like margins (dotted arrows) of the SN facing the cerebral peduncle. These details were not as well seen on the magnitude images.

References

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