

The Changes of FLAIR and DTI Images of the Brain and Upper Spinal Cord in Rabid Dogs: Voxel-wise Group Comparisons

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Introduction: Rabies is caused by virus in Rhabdovirus family in the genus Lyssavirus genotype 1. It can manifest as paralytic and furious forms [1]. Paralytic rabies is characterized by delayed viral neuroinvasion and more intense inflammation in the brain than its furious counterpart (with more viruses and less inflammation [2]). BBB leakage is demonstrated only during late phase [3]. Conventional MR imaging of early rabies infected brain showed only subtle changes. New technique is required for early detection and for giving accurate anatomical localization of the abnormalities. Diffusion tensor imaging (DTI) technique is considered a molecular imaging technique in studying water (H₂O) molecules motion in vivo and is sensitive in detecting architectural change of the neurons and adjacent environment [4]. Whole brain probabilistic map, a voxel-wise group comparison is an MR quantitative method considered to be sensitive in detecting subtle brain abnormality by comparing this to normal brain data [5].

Purpose: To compare between conventional magnetic resonance imaging (MRI) and FLAIR/ DTI (MD and FA) probabilistic maps in the study of the brain and spinal cord of furious and paralytic rabies infected dogs

Materials and Methods: MRI studies of the brain, brainstem and upper spinal cord of normal (8), early furious (2) and early paralytic (4) dogs were performed using 3-Tesla MRI scanner (Achieva, Philips Healthcare, Best, the Netherlands) with T1-weighted, T1-weighted with gadolinium, T2-weighted, T2 FLAIR and a whole brain diffusion tensor imaging (DTI) using a single shot echo planar imaging (EPI) pulse sequence (8-element phased array RF coil, TR=10.3s, 128x128 matrix, 30 contiguous slices at 2-mm thick, one b=0s/mm² and 16 isotropic gradient directions with b=800s/mm², NEX=2 at voxel size of 1.41x1.41x2.00 mm³). Comparison was made based on the abnormalities detected between conventional MRI and voxel-wise group comparisons of normalized FLAIR and DTI images. The normalization was performed using a new whole brain probabilistic diffusion tensor imaging tractography normalization method presented elsewhere. Briefly, individual whole brain probabilistic diffusion tensor imaging tractography map (as well as Fractional anisotropy (FA), Mean diffusivity (MD), and FLAIR images) was computed, and then normalized to a new custom whole brain probabilistic diffusion tensor imaging tractography template.

Results and Discussion: Conventional MRI abnormalities in paralytic rabid dogs were seen as nonenhancing moderate hypersignal T2 in the upper spinal cord and brain stem and as mild degree at the temporal lobes compared to the poorly demonstrated mild hypersignal T2 change seen in furious dogs at the same regions. Additional more diffuse subtle hypersignal T2 was seen in the frontal and parietal lobes in furious dogs compared to more localized abnormality in the temporal lobes in paralytic dogs (Figures 1 and 2). FLAIR and DTI (MD and FA) probabilistic maps of the paralytic and furious dogs demonstrated the abnormality much better with $p < 0.05$ and also clearly demonstrated the intensity and areas of abnormalities at different regions between these 2 forms (Figures 3 and 4).

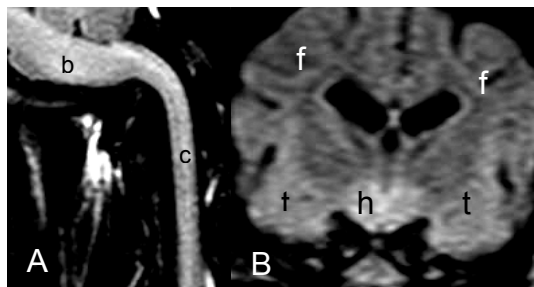


Figure 1: Sagittal FLAIR MR images of the early paralytic dog demonstrating moderate hyperintense T2 change at the brain stem (b) and upper spinal cord (c), hypothalamus (h) and less hyperintense T2 at bilateral temporal lobes (t) without signal abnormality detected at bilateral frontal lobes (f).

Figure 2: Sagittal FLAIR MR images of the early furious dog demonstrating mild hyperintense T2 change at the brain stem (b) and upper spinal cord (c), hypothalamus (h), bilateral temporal lobes (t) and bilateral frontal lobes (f).

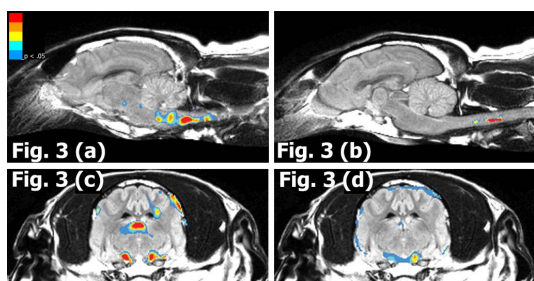
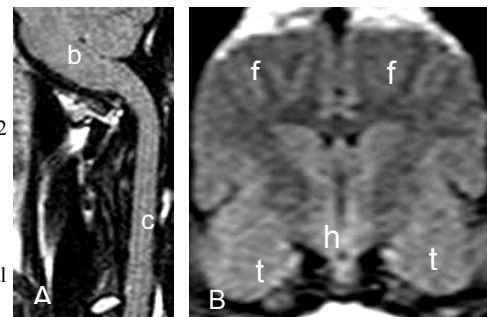


Figure 3: Probabilistic DTI (FA, MD) maps, voxel-wise group analysis of early paralytic and furious dogs compared with the normal dog group.

- (a) and (c) FA and MD probabilistic maps in early paralytic dogs
 - (b) and (d) FA and MD probabilistic maps in early encephalitic dogs
 - (a) decreased FA at the brain stem and upper spinal cord in early paralytic rabid dogs
 - (b) decreased FA with much less intensity at the spinal cord in encephalitic rabid dogs,
 - (c) decreased MD more intense at the brain stem in paralytic rabid dogs
 - (d) decreased MD more prominent at the cerebral hemisphere in early encephalitic rabid dogs
- Every difference map is superimposed on co-registered structural FLAIR images.

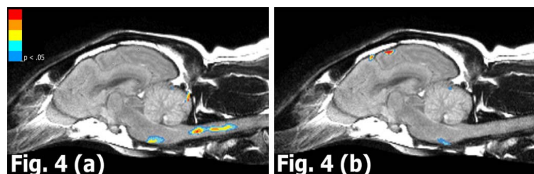


Figure 4: Probabilistic FLAIR maps, voxel-wise group analysis of early paralytic and encephalitic dogs compared with the normal dog group

- (a) increased FLAIR signals more intense at the brain stem in early paralytic rabid dogs
- (b) increased FLAIR signals more intense at the cerebral cortex in early furious rabid dogs

The more hyperintense T2 seen in paralytic dogs represent changes caused by more intense inflammation localized in the spinal cord, brain stem and temporal lobes due to immune response with less viral load [2]. While in encephalitic rabies, there was less intense and subtle hypersignal T2 change of more widely spread of the signal over the frontal and parietal lobes due to more virus load and less immune response. These similar findings were demonstrated in FLAIR voxel-wise group analysis maps. In MD probabilistic maps, preserved BBB was demonstrated as no increased MD in both forms, cytotoxic edema as decreased MD was found more in paralytic than the encephalitic form. Impaired FA was more evident at the brain stem of the paralytic dogs (Figure 3 (a)) and more in cerebral hemispheres of the furious form (Figure 3 (b)).

Conclusions: FLAIR and DTI (MD and FA) probabilistic maps are more sensitive and better detected and localized the abnormality in the brain and upper spinal cord of the paralytic and encephalitic dogs compared to conventional MR imaging. This technique should be useful in detecting abnormality in the patients clinically suspected of encephalitis with normal or subtle conventional MRI findings.

References: [1] Hemachudha et al., Lancet Neurol 2002;1(2):101-9; [2] Laothamatas et al., J. of Neurovirology 2008;14(2):119-29; [3] Laothamatas et al., AJNR Am J Neuroradiol 2003;24(6):1102-9; [4] Thomas et al., Neuroimaging Clinics of North America 2006;16(4):619-32; [5] Mechelli et al., Current Medical Imaging Reviews 2005;1(2):105-113