The Developing Canine Brain: Characterization by MRS and DTI

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Introduction

The beagle is a model of cognitive development and decline in humans[1]. Beagles are known to exhibit cognitive deficits similar to those observed in human dementia, such as memory, inhibitory control and attention deficits. In this study we sought to evaluate whether MRS and DTI could be used to characterize the developing beagle brain over the course of the first year of life.

Methods

A comprehensive MR exam was developed to assess the development of the beagle brain. Seventy-eight (78) beagles were examined at three time points: 6 weeks, 6 months and 1 year of age. The MR exam consisted of the following sequences: T1W scan (3D-FSPGR, TR=10.5ms, TE=4.7ms, TI=175ms, flip=30^o, 90-1mm slices, 16x10cm FoV, 256x160 acquisition matrix, 4 averages, time=9 min), T2W scan (2D-FSE, TR=4800ms, TE=102ms, ETL=15, 39-2mm slices, 16x10cm FoV, 256x160 acquisition matrix, 4 averages, time=8 min), DTI scan (SE-EPI, TR=10s, TE=111ms, b=1000, 6 directions, 26-3mm slices, 16cm FoV, 128x128 acquisition matrix, 8 averages, time=10 min) and MRS (probe-p, TR=1500ms, TE=30ms, 20mm^3 voxel centrally located in brain, 256 acquisitions, time=7 min). All data were collected on a 1.5T Signa scanner (GE Healthcare, Waukesha, WI, USA), software version 11, using a standard quadrature knee coil.

The MRS data were analyzed using LCModel[2], using the standard human basis set as a first approximation for the dog. The DTI data was processed using custom software developed in Matlab (Mathworks, Natick, MA, USA) to compute the diffusion tensor, eigenvectors and fractional anisotropy (FA). Three regions of interest encompassing the whole brain, frontal lobes and cerebellum were traced on the b=0 DTI images using NVM (Neuromorphometrics, Somerville, MA, USA). The ROI masks were applied to the FA maps and the mean FA computed for each ROI. ANOVA, followed by Duncan's test were used to test for statistically significant differences between the different time points for the main metabolites fit by LCModel and the mean FA.

Discussion

Sample MR spectra from the same dog at 6 weeks and 1 year are plotted in Figure 1. The MRS results are plotted in Figure 2 for metabolites with Cramer-Rao bounds less than 20%; a * indicates significance at $P < 0.05$ level. N-acetylaspartate (NAA), found only in neurons, increases significantly as the brain matures, as observed in human studies[3], as does creatine (Cr)[4,5]. Choline (GPC+PCh), essential in membrane and neurotransmitter synthesis, remains unchanged in the beagle, but decreases with age in humans[4,5]. Myo-inositol (mI), thought to be needed for cell growth and glucose storage dramatically increases with time, although it is reported to decrease in human brain over the first year of life[5]. The sum of the amino-acids glutamate (Glu) + glutamine (Gln) increases at 6 months, only to return to the 6 week level at 1 year. The mean FA for each time point is plotted in Figure 3. The FA increases significantly in all measures ($P<0.005$), except when comparing the 6 week to 6 month results in cerebellum. The mean FA, which included both gray and white matter in this study, is a measure of neuronal development. The greatest change in FA is observed in the frontal lobes, while the mean FA of the cerebellum at 6 weeks was roughly equivalent to that of the frontal lobes at 1 year.

Conclusions

Both DTI and MRS can measure significant changes in brain structure and metabolism during development. While some changes are analogous to that observed in human (NAA, Cr, FA increases), perhaps more interesting are the metabolites that differ from human development (Choline, mI).

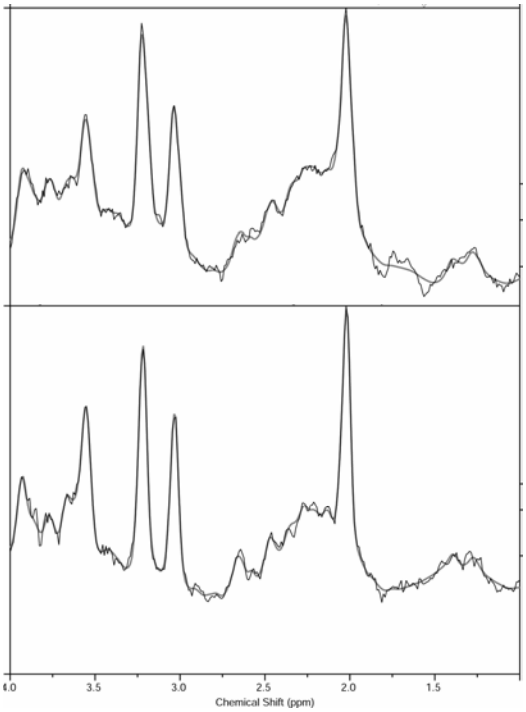

Figure 1. Sample MR spectra and LCModel fit at 6 weeks (top) and from same dog at 1 year (bottom).

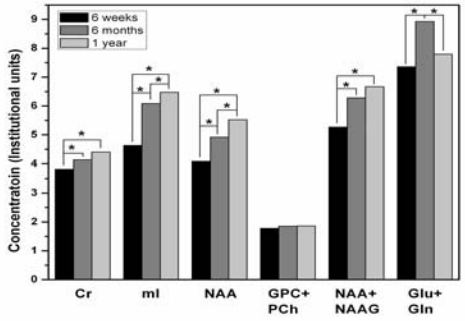

*Figure 2. Principal metabolites measured by MRS over time. P<0.005 indicated by *.*

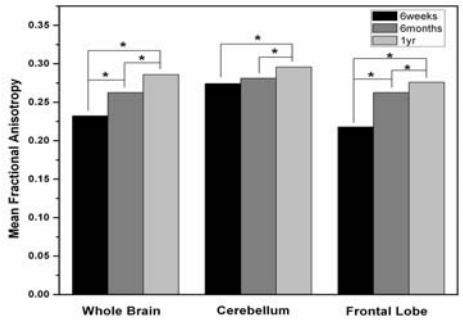

*Figure 3. Mean FA measured over time in three brain regions. P<0.005 indicated by *.*

References

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