Introduction

ALS-PDC is a progressive human neurological disease linked to the consumption of seeds from the cycad palm tree (Cycas micronesica K.D. Hill), particularly in the populace of Guam (1). Recently, Wilson et al. (2) developed an animal model of ALS-PDC through cycad feeding, in which specific cortical and subcortical cell losses were measured with histologically stained, two-dimensional sections and were correlated with behavioral testing. We implemented the non-destructive technique of MR microscopy on intact, excised brains and spinal cords at resolutions of at least 50 µm through the use of optimally constructed RF coils and a 17.6-T magnet.

Experimental

Mice were fed washed cycad for two months and showed progressive motor deficits resembling human ALS-PDC. After sacrifice, CNS tissues (brain and lumbar-sacral spinal cords) were extracted and fixed. Using a homebuilt split ring resonator, samples were imaged at 17.6 T using a three-dimensional gradient-echo pulse sequence to achieve a 41-µm isotropic resolution.

Results and Discussion

Figure 1 shows an example of segmented brain regions from the microimages. The high resolution images facilitate accurate segmentation of these features. Cycad-fed mice showed significantly decreased volumes in lumbar spinal cord gray matter, substantia nigra (example data shown in Fig. 2), striatum, basal nucleus/internal capsule and olfactory bulbs compared to flour-fed controls. In fact, MR microscopy was successful in identifying changes in the basal nucleus/internal capsule that were previously unseen in histological studies. Additionally, these alterations in MR neuroanatomy correlated well with behavioral deficits and with the expected areas of neurodegeneration related to the ALS-PDC pathology.

Conclusions

These results show that MR microscopy is sensitive enough to measure degeneration in this early stage model of a progressive neurological disease. Recently, this volumetric work has been published (3). Current efforts are focused on (a) comparing cycad-induced ALS-PDC with genetic models of ALS (e.g. SOD1 knockouts) and (b) assessing ALS-PDC neuronal alterations through diffusion tensor imaging. Ideally, similar analysis may be used in the future as a diagnostic aid in tracking the early progression of neurological disorders in pre-clinical human subjects.

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References