**Longitudinally evaluation of brain volumetric changes by structural MRI in Preclinical studies of Huntington’s Disease**

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Huntington’s disease (HD) is characterized by striatal atrophy that begins long before the onset of motor symptoms. Clinical diagnosis of HD is based on the unequivocal presence of otherwise unexplained extrapyramidal movement disorder. However, structural MRI imaging studies of HD patients found that striatal volumes begin to atrophy at least 11-12 years prior to expected onset, and then continue to shrink. In symptomatic HD, striatal volumes decline predictably with disease course. Previous studies suggest volumetric structural imaging measures could be considered as biomarkers for presymptomatic as well as symptomatic clinical trials of HD. HD mouse models show some behavioral and neuropathological features related to HD, and are widely used in preclinical therapeutic trials. However, there has been relatively little study of *in vivo* longitudinal brain atrophy in relation to other phenotypes and in response to experimental treatments in HD mouse models. We used micro MRI technology T2-weighted images combined with automated morphological analysesto monitor brain volume change longitudinally in mouse models of HD. We found that there are significant and progressive brain atrophy in the striatum, cortex and several other brain regions in fragment mouse models including both R6/2 mice and N171-82Q mice. The progressive regional brain atrophy is positively correlated with motor behavioral deficit and response to experimental treatment significantly. This is the first longitudinally study to show structural MRI measures can detect therapeutic effect in HD mouse models, suggesting that MRI could be considered as a potential biomarker to evaluate therapeutics in HD clinical trials.

Finance support: CHDI foundation Inc (WD) and NINDS (WD, CAR, JZ, SM).