

Public Abstract

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Title:Characterization of Dysphagia Onset in a Mouse Model of Amyotrophic Lateral Sclerosis (ALS)

The primary goal of this study was to characterize dysphagia onset and progression in the low copy number SOD1-G93A (LCN-SOD1) mouse model of ALS. A secondary goal was to determine the effect of serial radiation exposure throughout the lifespan on dysphagia severity. To accomplish this goal, we used our lab's established Videofluoroscopic Swallow Study (VFSS) assay to objectively assess swallow function in 54 mice, divided into serial versus single radiation exposure groups. The serial X-ray exposure group (n=24; 13 LCN-SOD1, 11 control) underwent VFSS testing once a month, starting at 2 months of age until disease end-stage. The single X-ray exposure group (n=30; 15 LCN-SOD1, 15 control) underwent VFSS testing only once at disease end-stage. VFSS videos from both groups were analyzed to quantify 8 swallow metrics. Results showed that all swallow metrics were similar within and between genotypes from 2 to 6 months of age, which coincided with the pre-clinical disease stage in LCN-SOD1 mice. At disease end-stage, LCN-SOD1 mice had significantly altered swallow function for 5 of the 8 VFSS metrics under investigation, compared to age-matched controls. Between disease onset and end-stage, LCN-SOD1 mice demonstrated highly variable disease phenotypes and survival durations, which rendered it impossible to characterize the onset and rate of dysphagia progression with the small sample size. However, two main findings emerged from this study. First, dysphagia onset in LCN-SOD1 mice did not occur until after 6 months of age. This finding suggests that treatments for dysphagia in this mouse model of ALS should begin after 6 months of age (i.e., after clinical disease onset) for optimal translational potential to humans with ALS. Our second novel finding was that dysphagia severity at disease end-stage was similar for single versus serial radiation exposure in LCN-SOD1 mice, which provides evidence that our lab can continue to perform longitudinal VFSS studies in this small animal without confounding outcomes relative to dysphagia. However, the majority of mice developed evidence of surface-level radiation toxicity (fur depigmentation and dry eyes) as the number of x-ray exposures increased, even though it did not affect swallow function. Therefore, we are taking proactive measures to reduce radiation exposure during VFSS and thereby prevent skin and eye morbidities for future longitudinal dysphagia investigations.