Supplementary Figure Legends

Supplementary Figure 1: Experimental time line of the olesoxime treatment study.

Olesoxime levels and the effects of olesoxime treatment on Huntington disease-like disease phenotypes were investigated in the BACHD rat. *In vivo* screening covered the major pathologies of BACHD rats, reminiscent of symptoms found in Huntington disease patients: motor impairments, mood disturbances, cognitive deficits and brain atrophy. *Ex vivo* analyses addressed the effects of olesoxime on further important Huntington disease-related pathologies, such as mHTT aggregation and fragmentation, protease activation as well brain mitochondria dysfunction. In the main cohort (cohort I), olesoxime was administered continuously from 1–13 months of age via the food. Olesoxime safety parameters were assessed longitudinally, and behavioral tests were performed at different ages during the study. All neuropathological examinations were carried out after the MRI and subsequent tissue sampling at 13 months of age. A second cohort (cohort II) was fed olesoxime for 2 weeks at 4 months of age to analyze olesoxime brain concentration. EPM: elevated plus maze, SST: simple swim test.