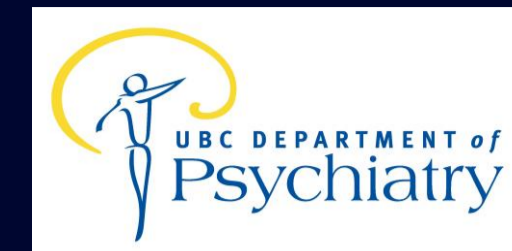




Age-specific motor and cognitive deficits in the Q175/B6 mouse model of Huntington's disease

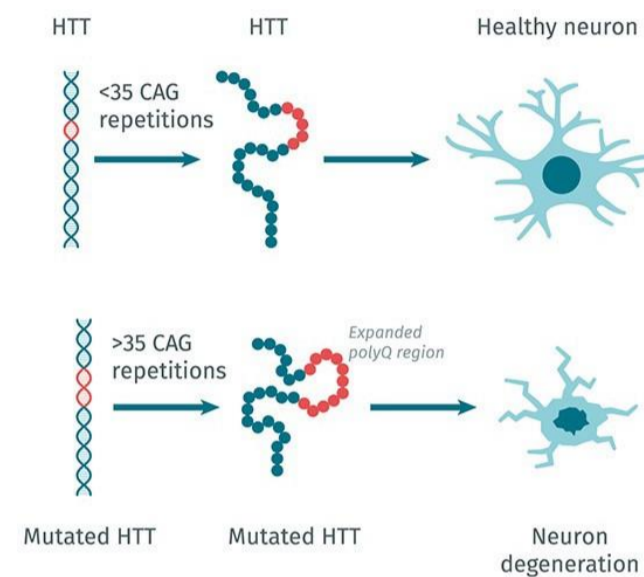
Judy Cheng¹, Ellen T. Koch¹, Lynn Raymond^{1,2}

1. Neuroscience Program, Department of Psychiatry, Faculty of Medicine, University of British Columbia
2. Djavad Mowafaghian Centre for Brain Health, University of British Columbia



Introduction

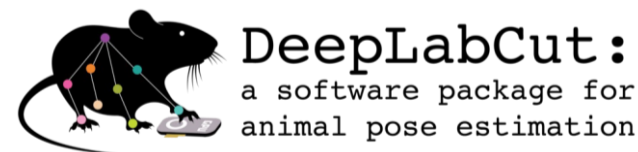
Huntington's Disease is a neurodegenerative disorder characterized by loss of motor control, mood changes and cognitive deficits and is associated with degeneration of the striatum, important for motor learning¹



Q175/B6 is a knock-in mouse model with a CAG repeat expansion mutation in the murine Huntingtin gene, similar to that in HD patients²

HD mice have shown motor abnormalities and cognitive deficits in the open field, rotarod and water T-maze tasks from 10 months of age^{2,3}

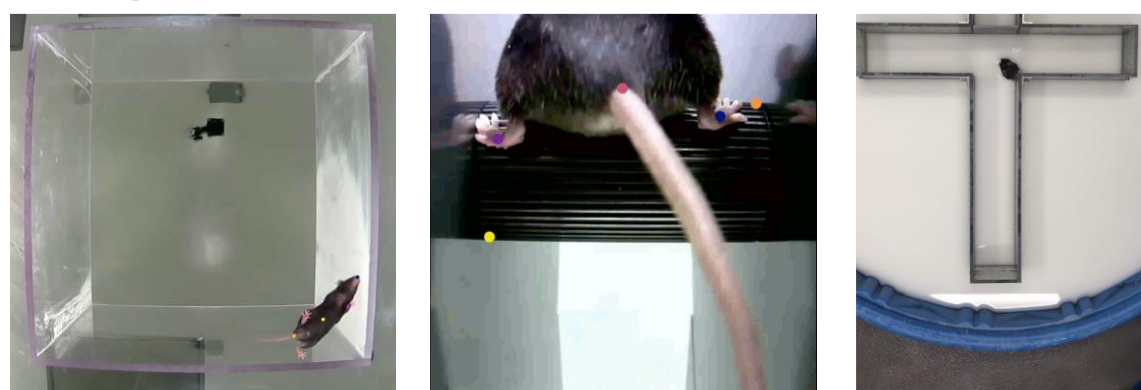
We used the Behavioral Segmentation of Open Field in DeepLabCut (B-SOiD) clustering algorithm⁴ to observe more specific behavioural patterns in the open field and used other more sensitive analyses to characterize the Q175 model



Methods

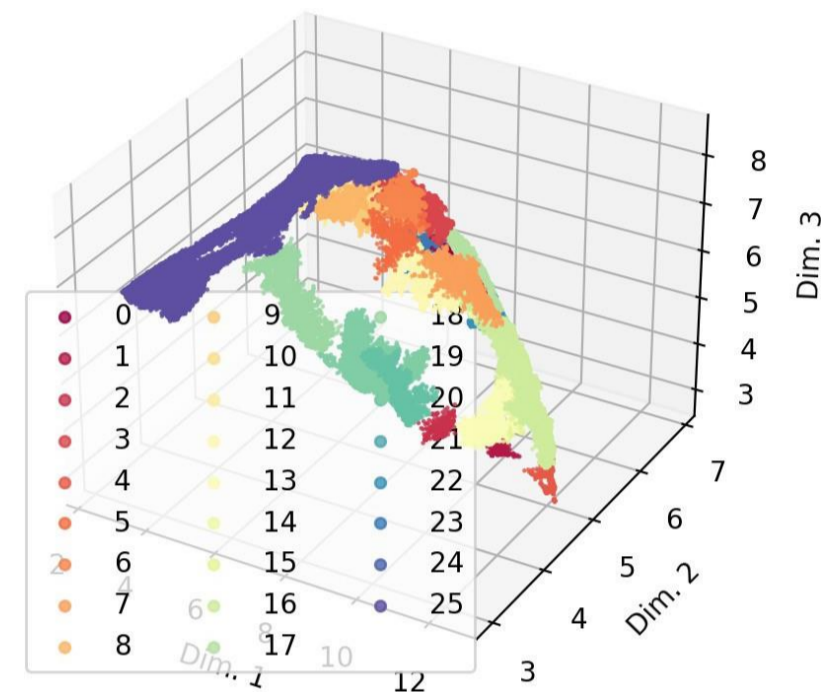
Male and female Q175 and wild-type (WT) mice at pre-symptomatic (younger; 2-3 months) and symptomatic (older; 9-11 months) disease stages

Open Field Rotarod Water T-Maze

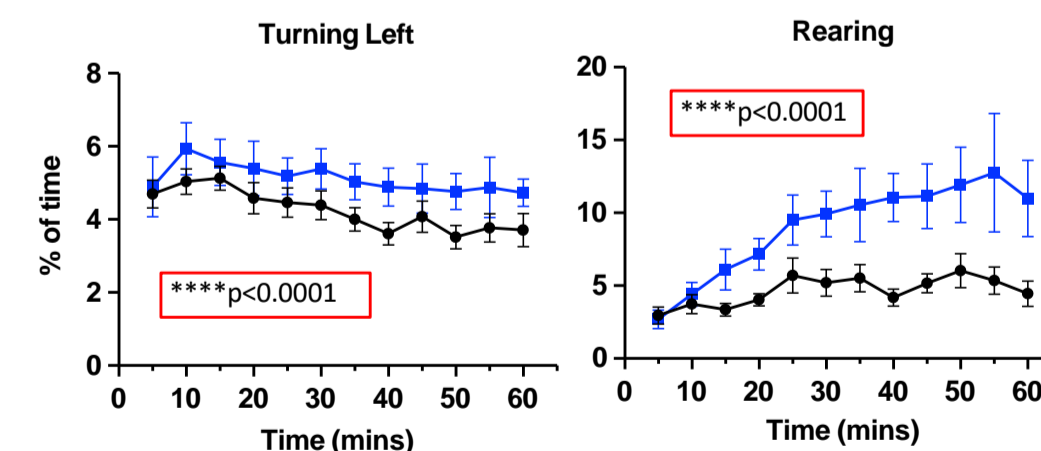
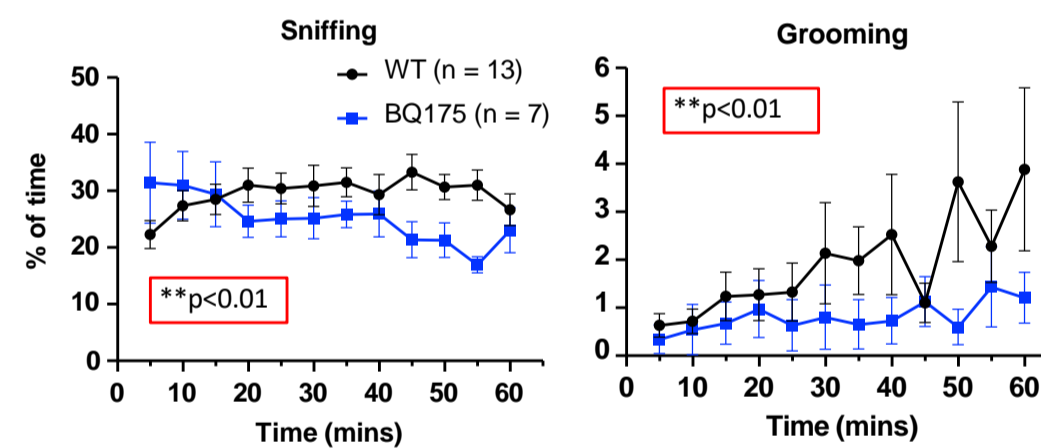


Results

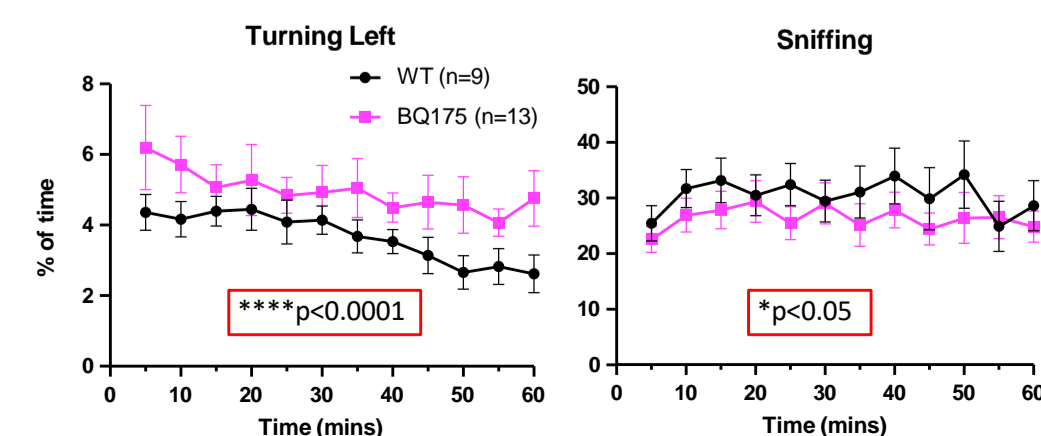
Open Field



Older Males

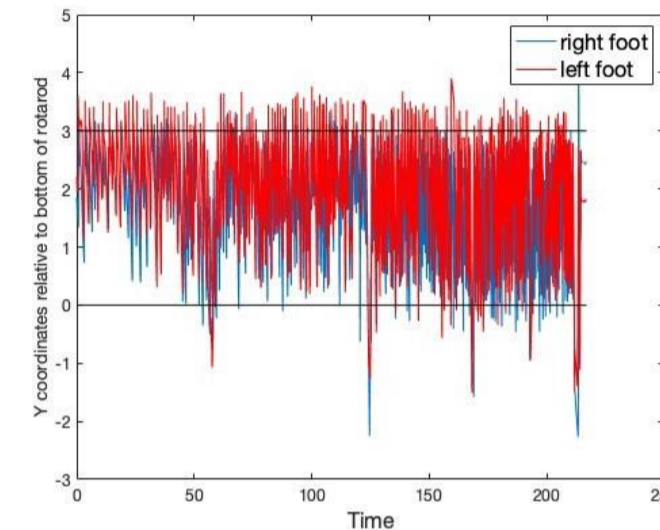


Older Females

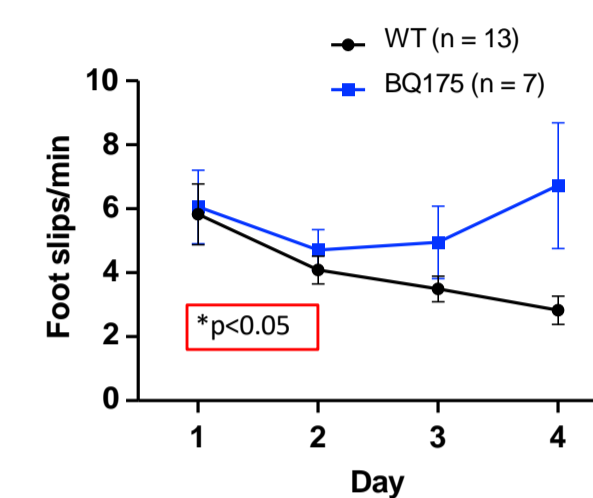


Accelerating Rotarod

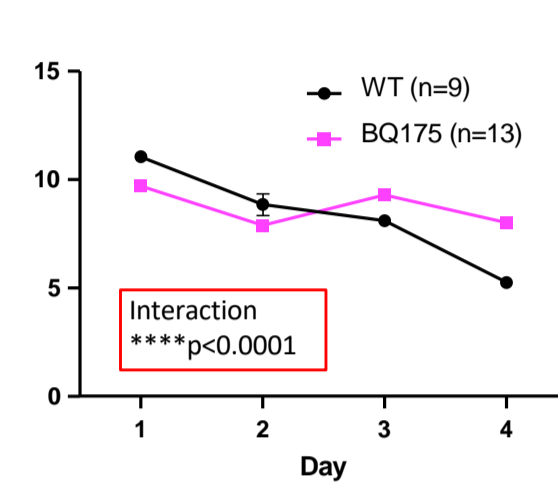
Foot slip analysis - example graph



Older Males



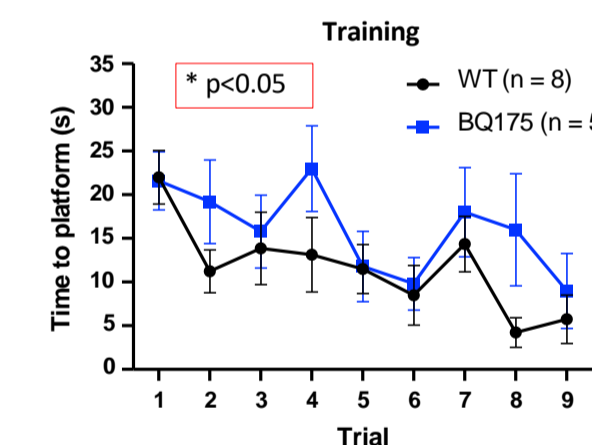
Older Females



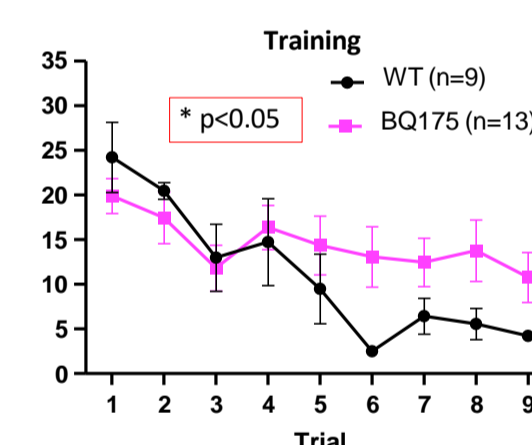
Water T-Maze

- Training phase:** Response learning strategy (striatum-dependent)
Place learning strategy (hippocampus-dependent)
- Reversal phase:** probes cognitive flexibility

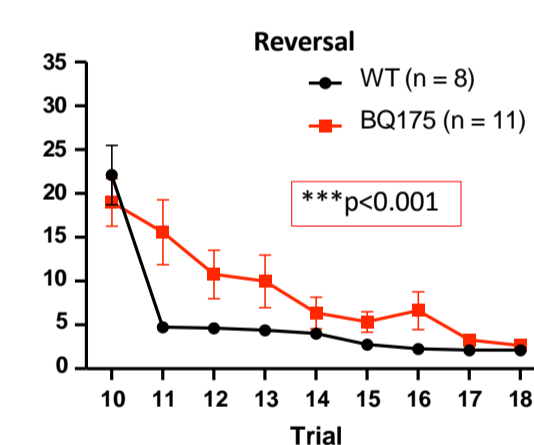
Older Males - response learning



Older Females



Younger Males



Conclusion

- Older Q175 males showed more stereotypical rearing and less exploratory and grooming behaviours than WT in the open field; older females showed the same genotype differences for turning left and sniffing
- Older Q175 males showed more foot slips than WT on the rotarod; older Q175 females only showed more foot slips in the last two days of testing
- Motor learning deficits revealed during water T-maze training in older male Q175 response learning group - learning strategy could be more relevant at the older age
- Younger Q175 males showed impaired water T-maze reversal learning - potential deficit in cognitive flexibility at the early age
- Older Q175 females showed motor learning deficits during training, potential sex difference in learning strategies used to learn water T-maze task

References

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