



Using Divalent siRNA for Targeted Post-Transcriptional Silencing in Huntington's Disease

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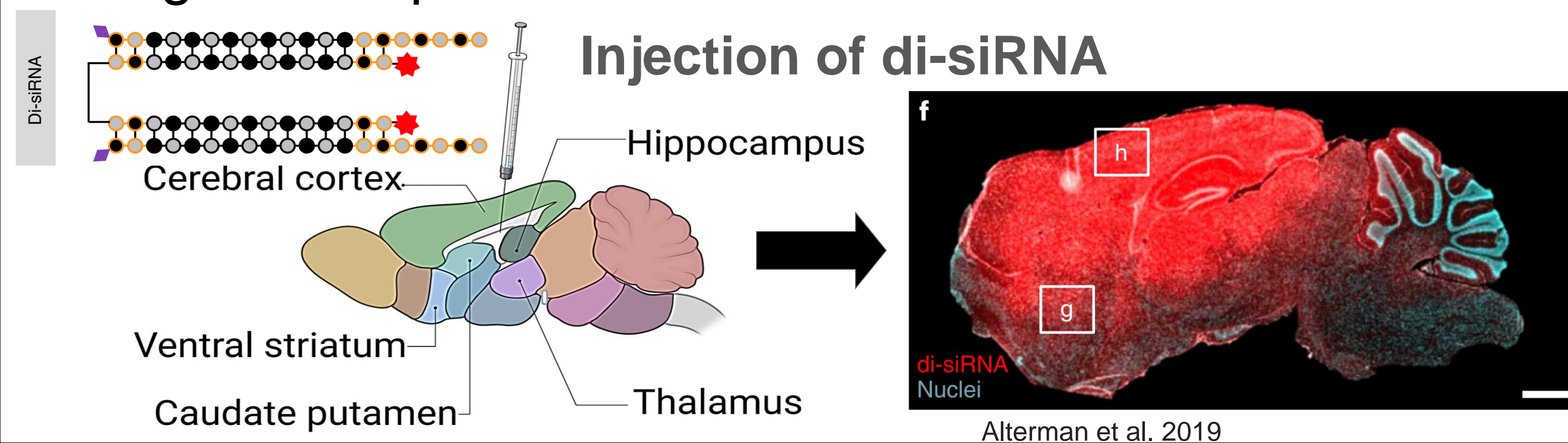


Huntington's Disease

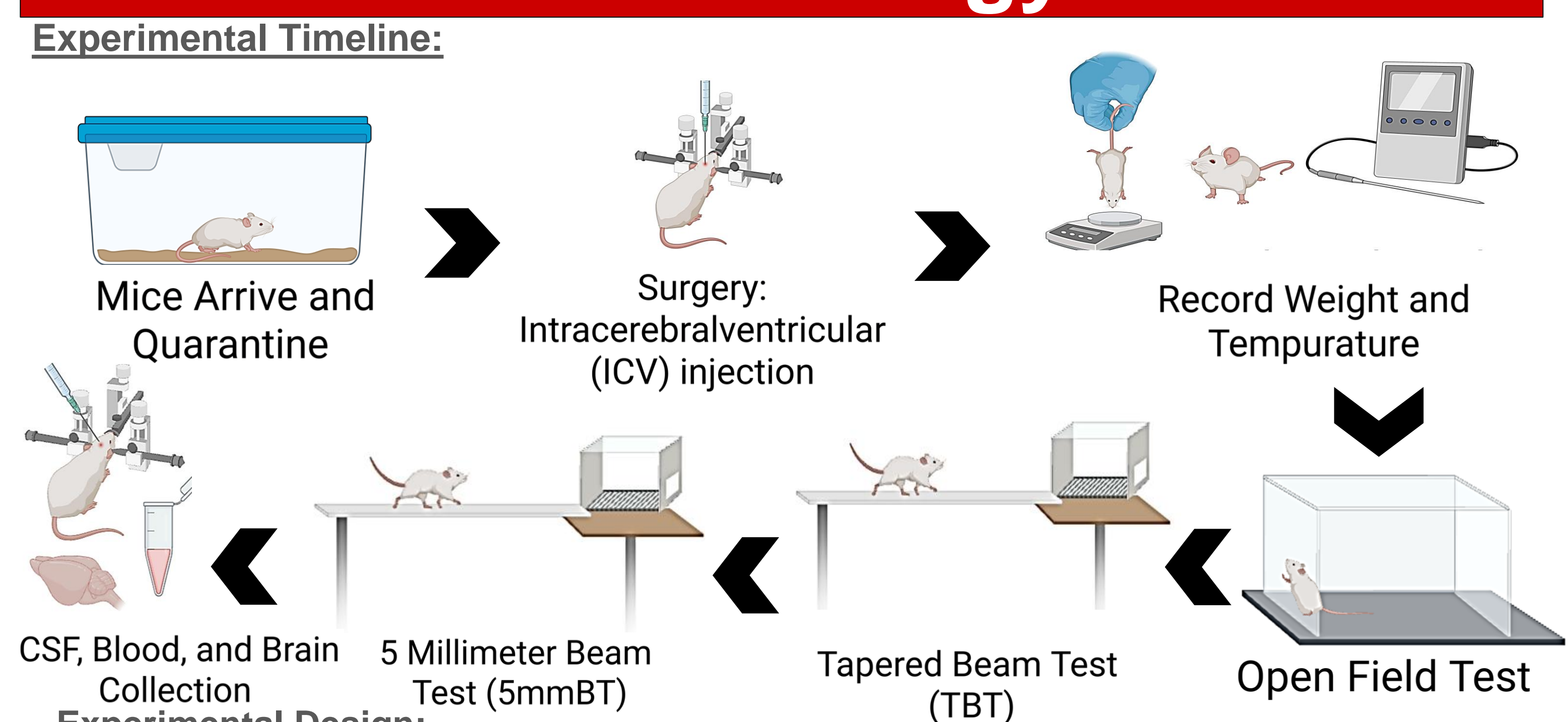
- Huntington's Disease (HD) is a progressive, autosomal disorder affecting psychiatric, motor and cognitive function. HD is ultimately fatal.
- Caused by a CAG repeat expansion increasing production of mutant Huntingtin protein (mHTT).

Divalent siRNA as a Gene Therapy

Aim: evaluate the effect of di-siRNA lowering mHTT protein through motor performance in a HD mouse model



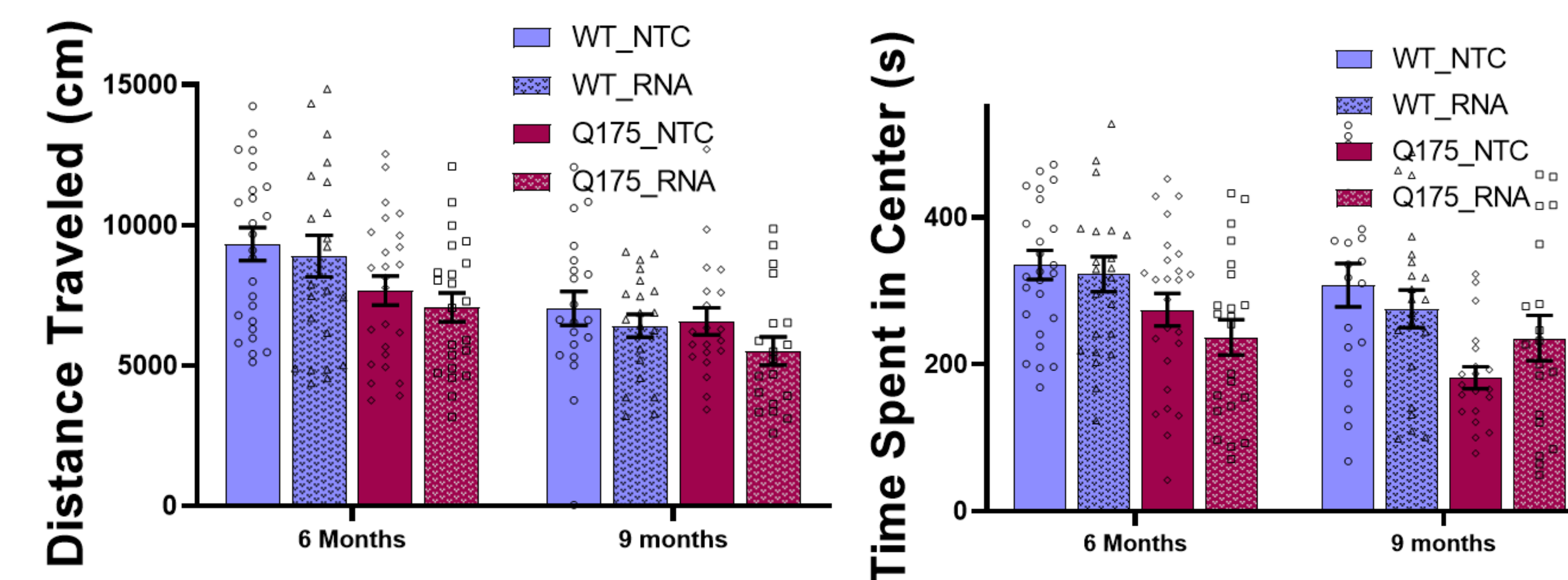
Methodology



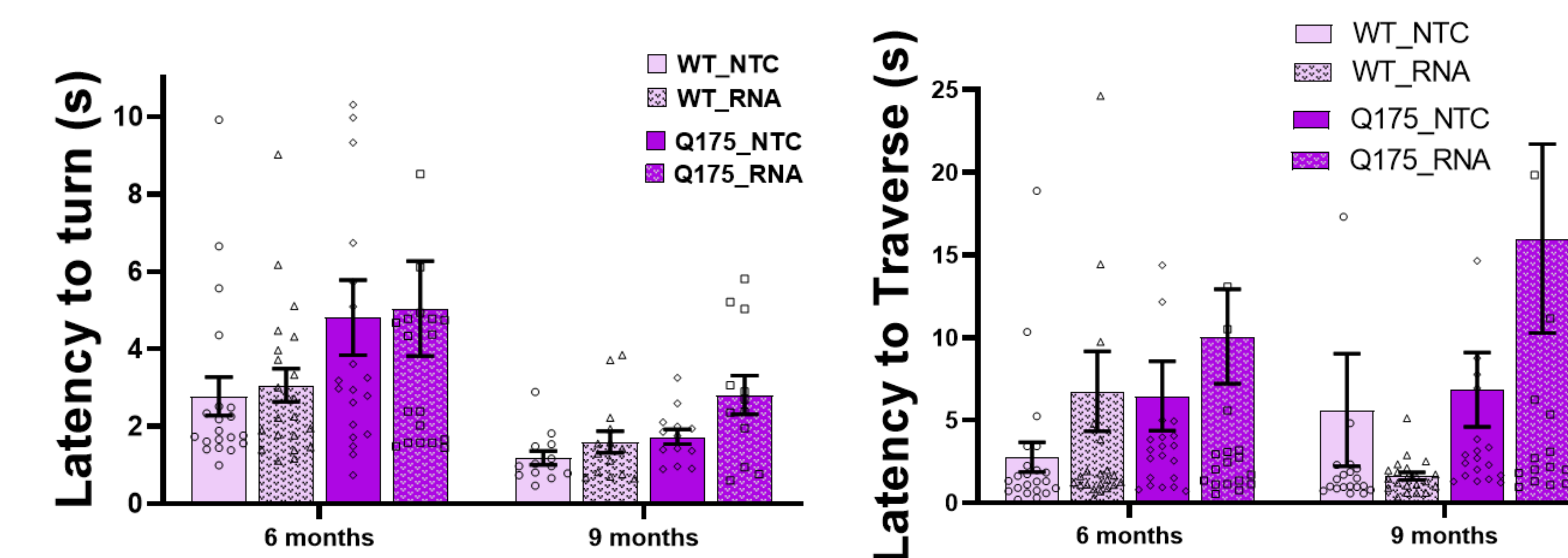
Males		Females	
di-siRNA ^{NTC}	di-siRNA ^{HTT}	di-siRNA ^{NTC}	di-siRNA ^{HTT}
Wild type (WT)	WT_NTC	WT_NTC	WT_RNA
Q175	Q175_NTC	Q175_NTC	Q175_RNA

Results

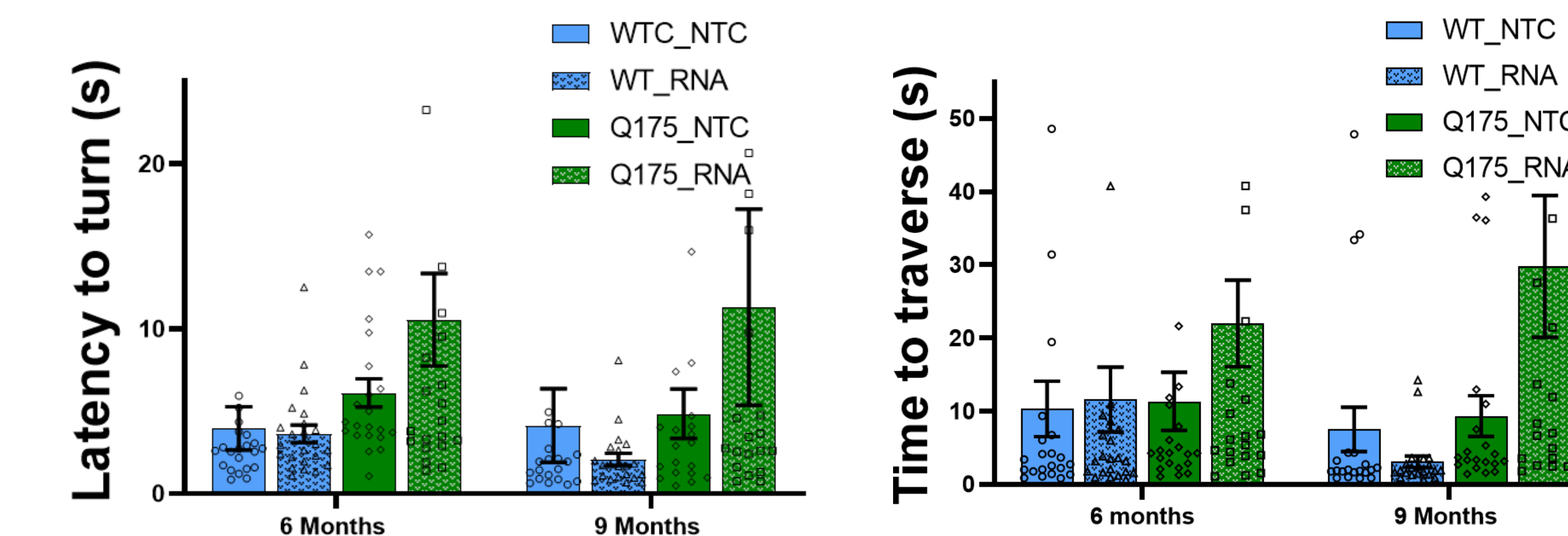
Open Field (OF) Test:



Tapered Beam Test (TBT):



5 mm Beam Test (5mmBT):

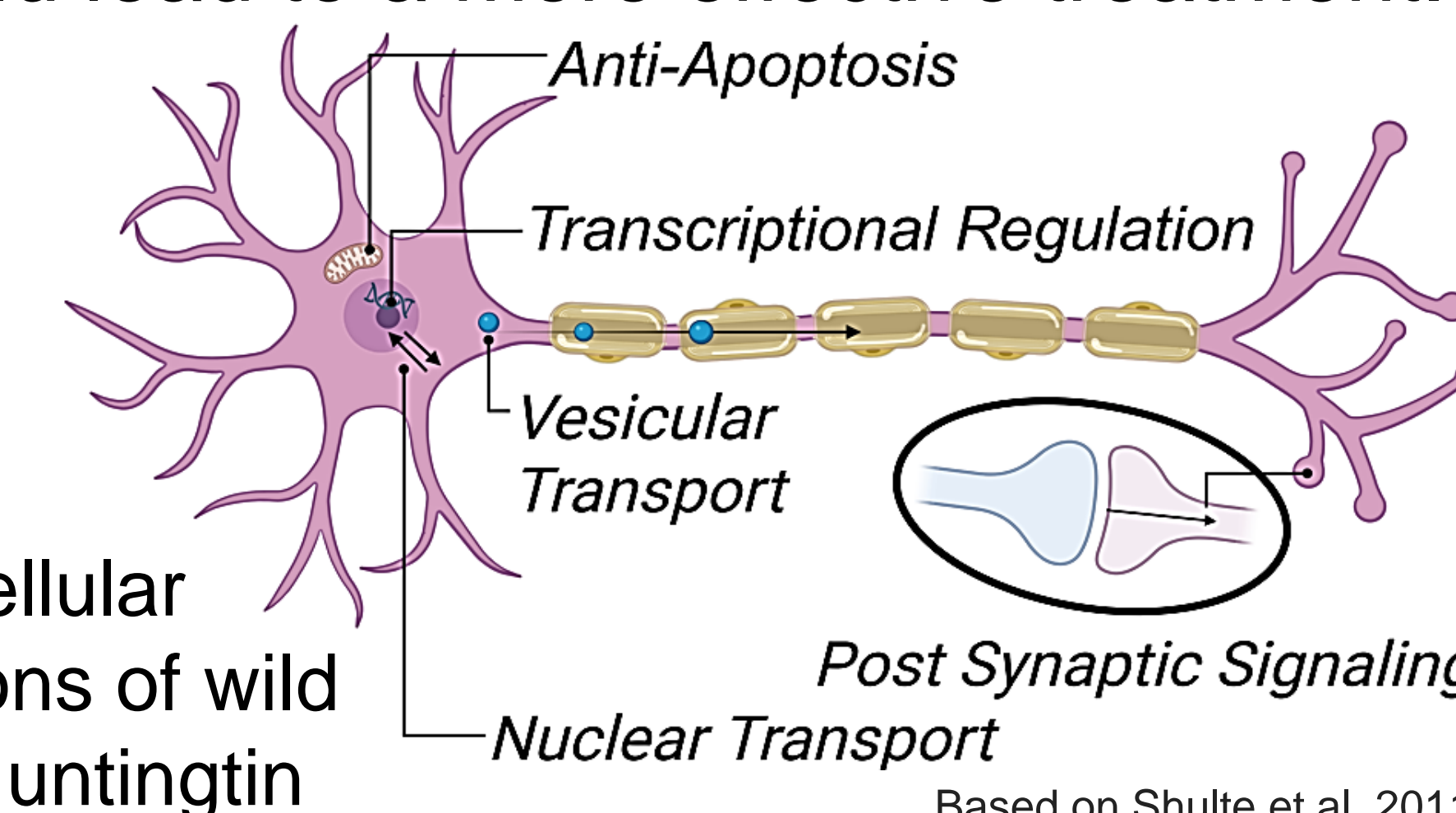


Conclusion/Discussion

- The di-siRNA^{HTT} treatment showed increased latency to action in the beam tests and decreased traveled distance in the open field test.
- Overall, the wild type mice performed better than the Q175 mice.

Future Work

- In future research, we could run an experiment where the di-siRNA is specific to only the mutant Huntingtin protein.
 - The di-siRNA targets both the normal and the mutant huntingtin protein.
- Investigations into the process of Base-Excision Repair on the CAG repeats could lead to a more effective treatment.



The cellular functions of wild type Huntingtin

References & Acknowledgements

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