
CORTICOSTRIATAL PLASTICITY AFTER MIDDLE CEREBRAL ARTERY OCCLUSION

NAOMI COHEN

ADVISOR: DR. THERESA JONES

GRADUATE STUDENT ADVISOR: KRYSTAL SCHAAR VALENZUELA



BACKGROUND

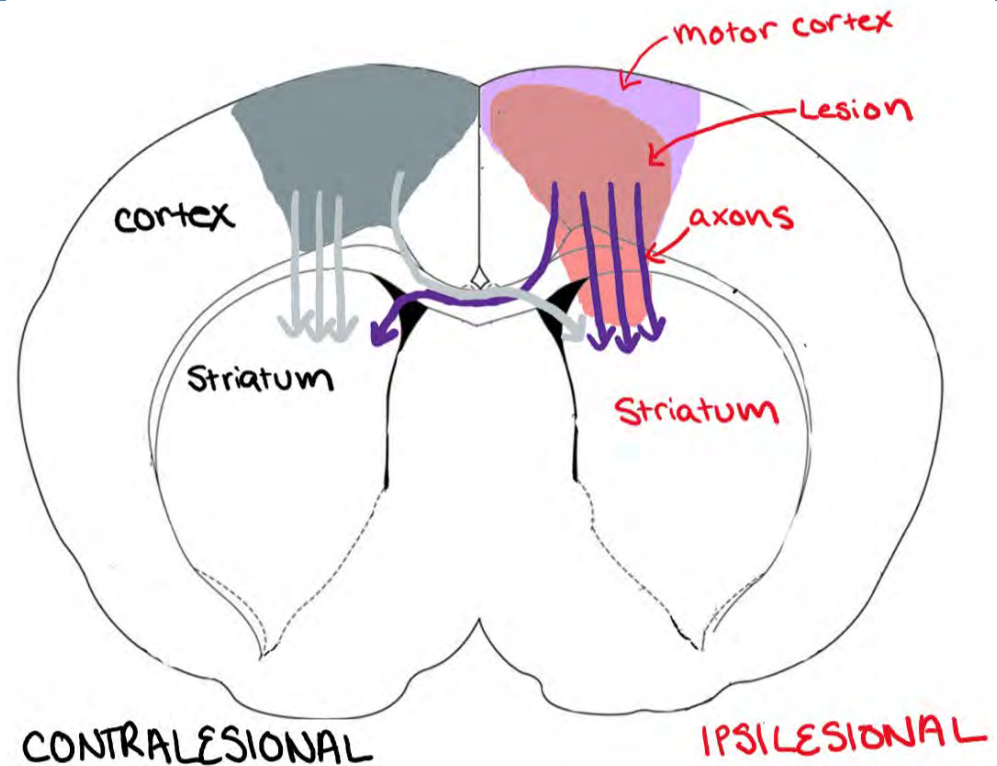
- Stroke is 5th leading cause of death (American Heart Association, 2017)
- A leading cause of long term disability (Yang et al., 2017)
- What is a stroke? (American Heart Association, 2017)
 - Ischemic 85%
 - Cause by a clot
 - Hemorrhagic 15%
 - Caused by a bleed

BACKGROUND

- Physical rehabilitation is primary treatment in humans
 - Produces neuroplastic changes in rat models
- Rehabilitation affects functional outcome
 - Timeline- too early, too late
 - Lateralization
 - “good” (non-paretic) vs. “bad”(paretic) limb
 - Training with the non-paretic limb impairs functional recovery of paretic limb
(Nudo et al. 1996, Adkins, Bury, & Jones, 2002)

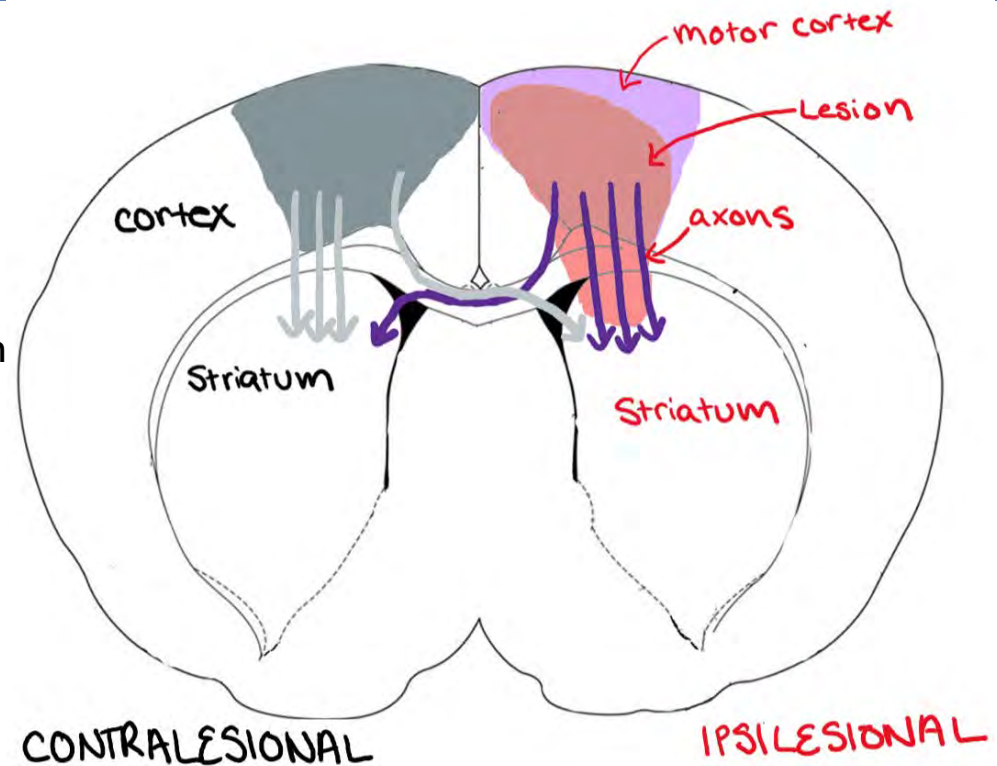
BACKGROUND

- Motor Cortex-essential for planning, control and execution of motor functions
- Striatum- input from motor cortex to basal ganglia
- Corticostriatal projections
- Lateralized damage



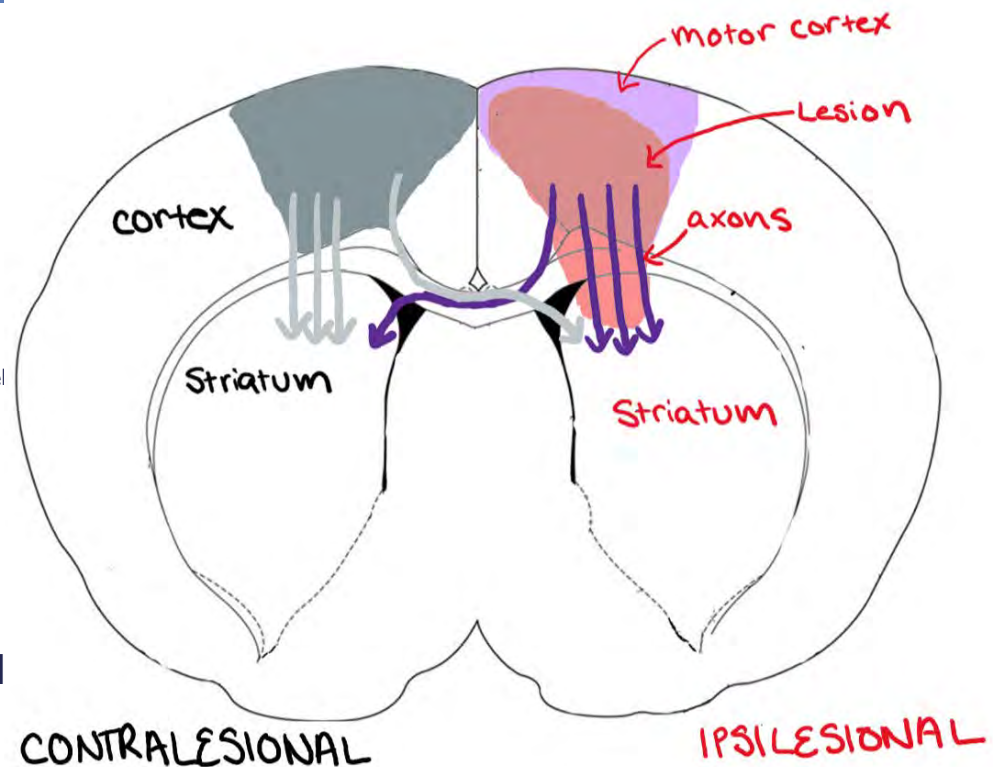
BACKGROUND

- Middle cerebral artery occlusion (MCAo)
 - Large lesions = bigger functional change
 - Most common type of ischemia in humans
- Corticostriatal connections
 - Damaged by stroke
 - Striatum denervated (no longer receives information from motor cortex)



BACKGROUND

- Stroke results in corticostriatal axonal regeneration (Napieralski et al. 1996, Carmichael and Chesselet 2002)
 - Found in ipsilesional striatum after stroke, originated in contralesional cortex
 - One study correlated function with behavioral measures (Rosenzweig and Carmichael 2013)
 - Damage to corticostriatal axons positively correlated with motor impairment
- What is not known
 - Above study has not been replicated
 - Effects of rehabilitative training?



STUDY OVERVIEW

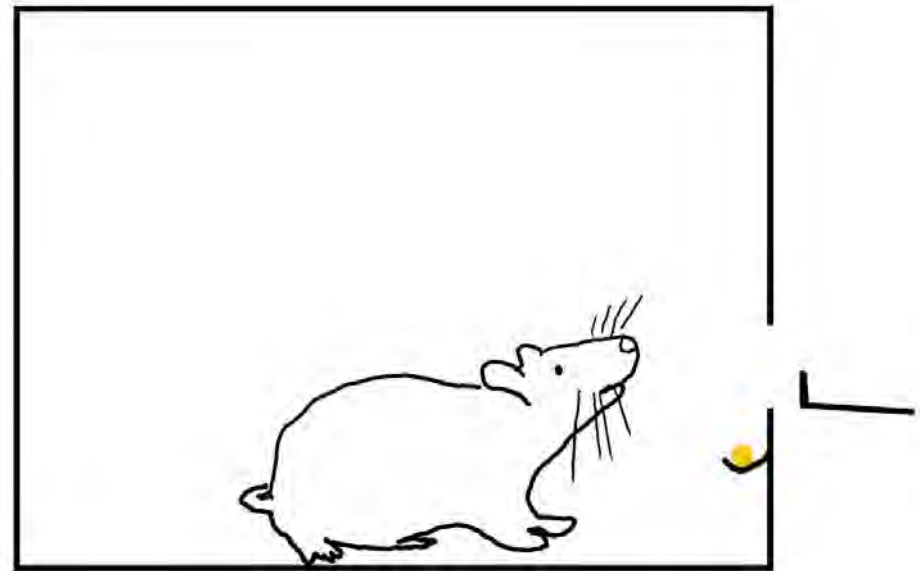
- Induce MCAo
- Rehabilitative training
- Tracer
- Quantify axons



METHODS

Behavioral Methods:

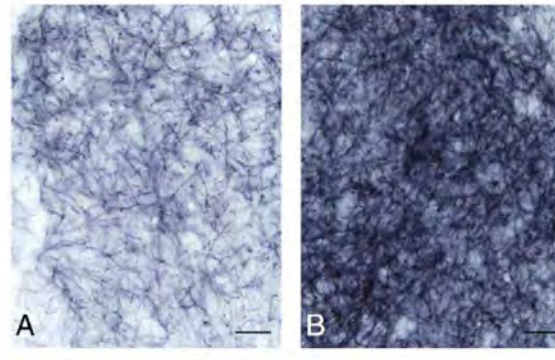
- Male Long Evans Rats (3-12 months)
- Rats learn reach task (3-4wks)
- Induce stroke
 - Occlude middle cerebral artery for 60 minutes
- Rehab groups
 - Standard, control, non-paretic, delayed
- Tracer



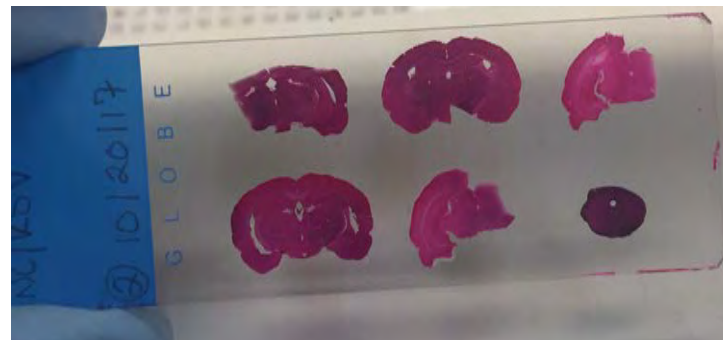
METHODS

Histology Methods

- Sections
- Immunohistochemistry
- Slides
- Microscopy and axon quantification

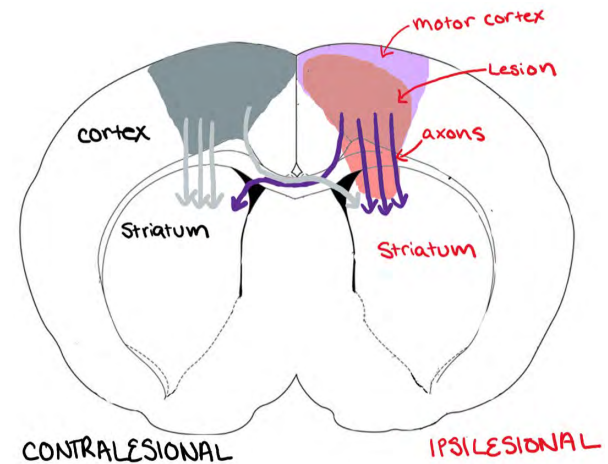


(Riban and Chesselet, 2006)



DATA ANALYSIS

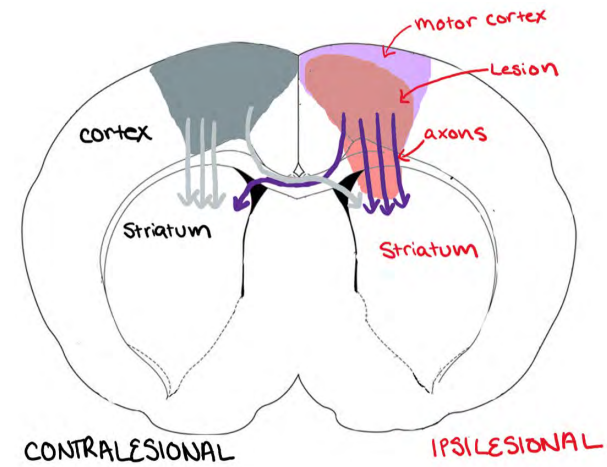
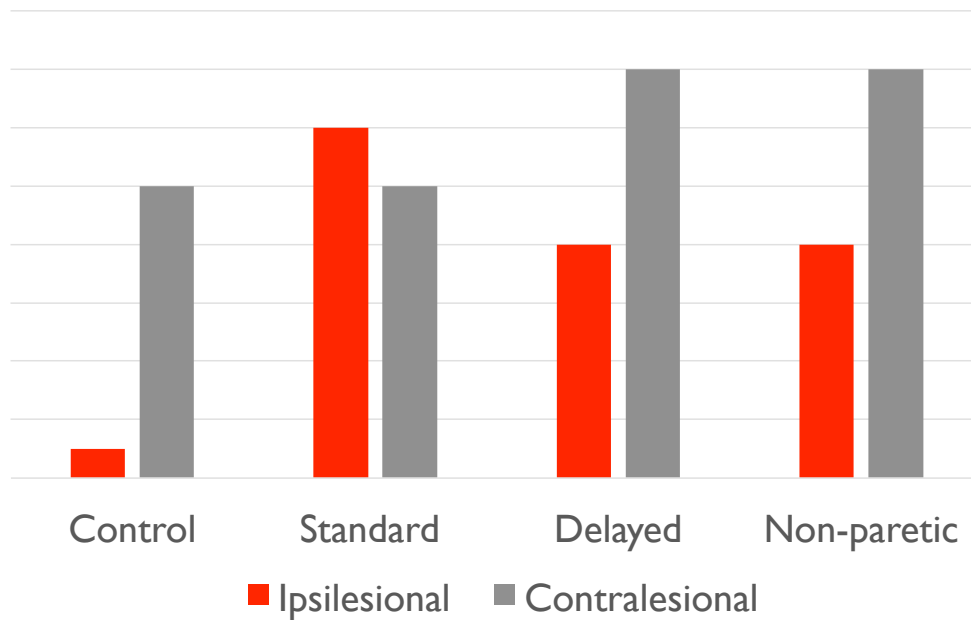
- Two options for data analysis.
 - Compare standard rehab to control and non-paretic rehab to delayed rehab, treating the two as separate experiments
 - Compare all four groups using an ANOVA test.



Paretic limb- “bad” or affected limb
Non-paretic limb- “good” or unaffected limb
MCAo- middle cerebral artery occlusion (type of stroke)
Ipsilesional- side of the lesion
Contralesional- opposite from the lesion

EXPECTATIONS

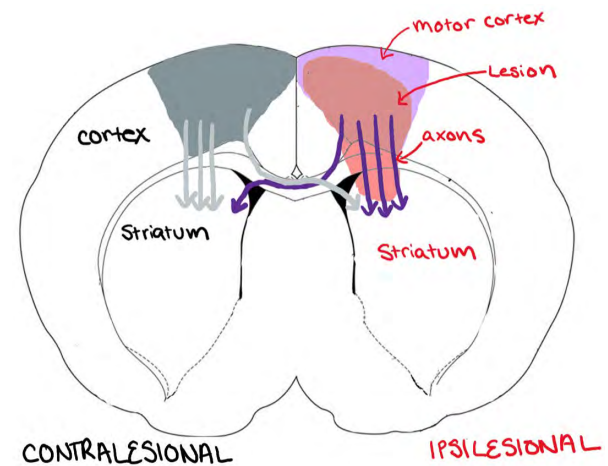
Expectations



Paretic limb- “bad” or affected limb
Non-paretic limb- “good” or unaffected limb
MCAo- middle cerebral artery occlusion (type of stroke)
Ipsilesional- side of the lesion
Contralesional- opposite from the lesion

ALTERNATIVES

- Standard rehab group- no increase in ipsilesional or contralesional projections
- Non-paretic rehab group and delayed rehab group- no increase in ipsilesional or contralesional projections
- Control- no increase in contralesional projections



Paretic limb- “bad” or affected limb
Non-paretic limb- “good” or unaffected limb
MCAo- middle cerebral artery occlusion (type of stroke)
Ipsilesional- side of the lesion
Contralesional- opposite from the lesion

REFERENCES

- Adkins, D. L., Bury, S. D., & Jones, T. a. (2002). Laminar-dependent dendritic spine alterations in the motor cortex of adult rats following callosal transection and forced forelimb use. *Neurobiology of Learning and Memory*, 78, 35–52. <https://doi.org/10.1006/nlme.2001.4045>
- Carmichael, S., & Chesselet, M. (2002). Synchronous Neuronal Activity Is a Signal for Axonal Sprouting after Cortical Lesions in the Adult. *The Journal of Neuroscience*, 22(14), 6062-6070.
- A. (2017). Heart Disease and Stroke Statistics 2017 . Retrieved from www.heart.org/idc/groups/ahamah-public/@wcm/@sop/@smd/documents/downloadable/ucm_491265.pdf.
- Napieralski, J., Butler, A., & Chesselet, M. (1996). Anatomical and functional evidence for lesion-specific sprouting of corticostriatal input in the adult rat. *The Journal of Comparative Neurology*, 373(4), 484-497. doi:10.1002/(sici)1096-9861(19960930)373:4<484::aid-cne2>3.0.co;2-y
- Nudo, R. J., Wise, B. M., Sifuentes, F., & Milliken, G. W. (1996). Neural Substrates for the Effects of Rehabilitative Training on Motor Recovery After Ischemic Infarct. *Science*, 272(5269), 1791-1794. doi:10.1126/science.272.5269.1791
- Riban, V., & Chesselet, M. (2006). Region-specific sprouting of crossed corticofugal fibers after unilateral cortical lesions in adult mice. *Experimental Neurology*, 197(2), 451-457. doi:10.1016/j.expneurol.2005.10.026
- Rosenzweig, S., & Carmichael, S. T. (2013). Age-Dependent Exacerbation of White Matter Stroke Outcomes. *Stroke*, 44(9), 2579-2586. doi:10.1161/strokeaha.113.001796
- Yang, Q., Tong, X., Schieb, L., Vaughan, A., Gillespie, C., Wiltz, J. L., . . . George, M. G. (2017). Vital Signs: Recent Trends in Stroke Death Rates — United States, 2000–2015. *MMWR. Morbidity and Mortality Weekly Report*, 66(35), 933-939. doi:10.15585/mmwr.mm6635e1