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Morphology of Axon Initial Segments under Normal and Pathological Conditions

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Introduction & Objective

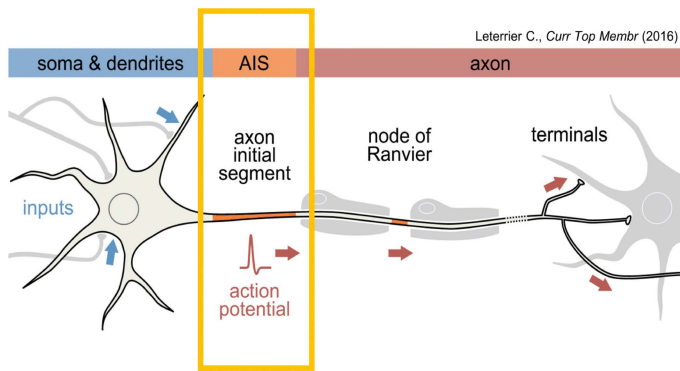
- Axon Initial Segment (AIS) plays major role in the initiation of action potentials
- Dense with voltage-gate ion channels and other proteins
- Majority of modeling studies consider AIS to have linear morphology
- Objective of research is to determine how AIS morphology differs among normal and pathological conditions

Methods

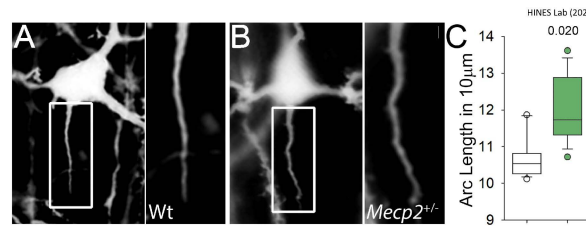
- AISs stained with immunofluorescent techniques for better viewing under confocal microscope
- Qualitatively categorized by shape and curvature, as well as by using ImageJ program to obtain numerical data (Cartesian coordinates) of curvatures

Preliminary Results & Conclusion

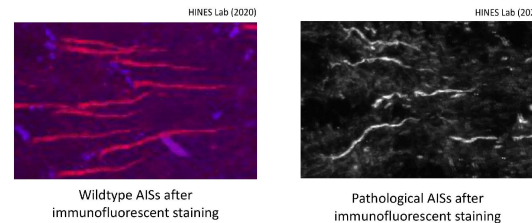
- AISs in cortical tissue from wildtype mice compared to those from the *Mecp2*^{+/-} model of Rett syndrome
- Cartesian data will be used to develop model that describes linear and non-linear morphology



Location of Axon Initial Segment (AIS) within neuron



Images of (A) wildtype AIS and (B) Rett syndrome AIS. (C) Graph describes tortuosity of both. Wildtype AIS (white box) is close to 10 μm in length indicating that they are nearly straight. *Mecp2*^{+/-} AIS (green box) is close to 12 μm in length indicating that they are more tortuous (p=0.020).



Wildtype AISs after immunofluorescent staining

Pathological AISs after immunofluorescent staining

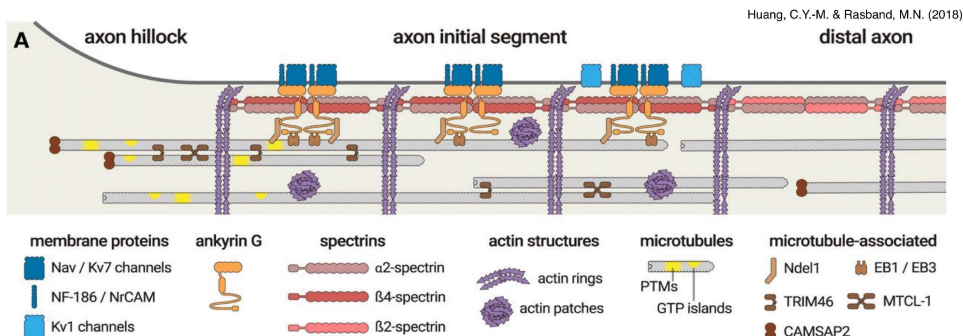
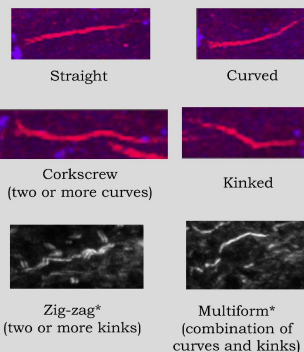


Diagram depicting organization of proteins within AIS

AIS Morphology Categories



*was not observed in wildtype, but rather in pathological phenotype

	Area	Mean	Min	Max	X	Y
1	0	89	89	89	104.833	74.500
2	0	101	101	101	109.167	74.833
3	0	94	94	94	113.167	75.500
4	0	133	133	133	117.167	75.167
5	0	87	87	87	121.167	74.167
6	0	108	108	108	125.167	73.167
7	0	92	92	92	129.167	72.167
8	0	147	147	147	133.167	71.167
9	0	143	143	143	137.833	70.500
10	0	90	90	90	141.500	71.167
11	0	72	72	72	145.833	70.833

Data obtained from ImageJ. X, Y coordinates helpful in determining curvature of AIS

Discussion & Future Directions

- Previous research showed that position, composition, and length important in neuronal excitability
- Not much research on relationship between AIS shape and pathology
- Will help gain deeper understanding of wildtype and pathological conditions
- May lead to practical applications such as new medicines and treatments