Computationally Predicting the Effects of Tau Protein Hyperphosphorylation on AMPA Receptors in a Single Neuron Model

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Introduction

- Tau proteins stabilize microtubules in neurons
- Various diseases (Alzheimer’s, Parkinson’s, CTE) associated with defective tau
- Previous studies show that hyperphosphorylated tau protein negatively affects AMPA receptor function
- Understanding its effects on AMPA receptors could help understand Alzheimer’s as well

Methods

- Used Saraga et. al model
- Reduced AMPA receptor conductance to simulate how tau protein hyperphosphorylation would affect the receptors in real life
- Stimulus of fixed value is applied to neuron, and voltage over time at preset locations on dendrites are measured
- Current = -0.05 nA, resting voltage = -70 mV

Results

- AMPA receptors farther from soma
  - Baseline graph
  - 500ms
  
- AMPA receptor conductivity 99.43% of baseline
  - 500ms

- AMPA receptors closer to soma
  - Baseline
  - 500ms

  - Conductivity 70.71% of baseline, 500ms

  - Conductivity 9.25% of baseline, 500ms

Discussion/Conclusions

- Reduced AMPA receptor conductivity results in fewer action potentials
- Effect magnified when AMPA closer to soma
- No AP when conductivity 8.61% of baseline in case when AMPAR farther from soma
- No AP when conductivity 9.25% of baseline in case when AMPAR closer to soma
- Results show that decreased number of viable AMPA receptors leads to decreased action potential strength and frequency
- Affected AMPA receptor closer to soma likely has more effects than compared to receptors farther from soma
- Results suggest that defective tau protein could contribute to memory loss by reducing frequency and strength of APs because AMPAR damage
- Since Alzheimer’s is very complicated, more complex studies with multiple neuron networks must be done

References

Active dendrites and spike propagation in a hippocampal interneuron (Saraga et al 2003).


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