Modeling chronic stress-induced LTD on the CA1hippocampal microcircuit

Sofia Alvazzi[1,6], Fiona Bean[2,6], Antonia Duffey[3,6], Caroline Fore[4,6], Amy Tian[5,6], Karla Montejo[6]

International School of Zug and Luzern, Walterswil 1, 6340 Baar, Switzerland[1]; Niskayuna High School, 1626 Balltown Rd, Niskayuna, NY 12309[2]; Bronx HS of Science, 75 W 205th St, Bronx, NY 10468[3]; Model Laboratory High School, 521 Lancaster Avenue, Richmond, Kentucky 40475[4]; The John Cooper School, 1 John Cooper Dr, The Woodlands, TX 77381[5], Boston University, Boston, MA 022156[6]

INTRODUCTION

- Previous research[1] has shown that **chronic stress** leads to **Long Term Depression (LTD)**
  - LTD is the weakening of synaptic connections

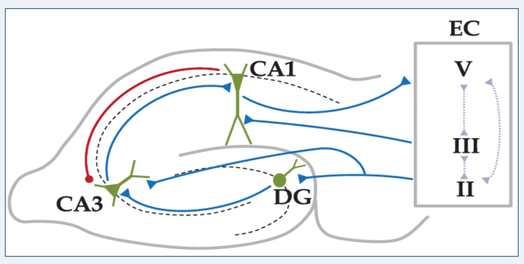

Figure 1 Diagram of the hippocampus[2]

  - The hippocampus plays a significant role in memory encoding and retrieval[3]
  - By introducing LTD to the CA1 hippocampal region, the process of memory retrieval is affected and may lead to the development of **anterograde amnesia**
  - This study induced different levels of LTD into a model of the **CA1microcircuit** and compared the resulting **memory recall rates**

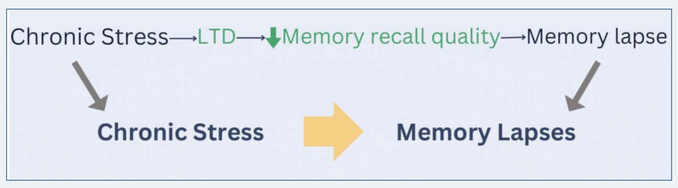

Figure 2. Schematic representation of our project aims

RESULTS

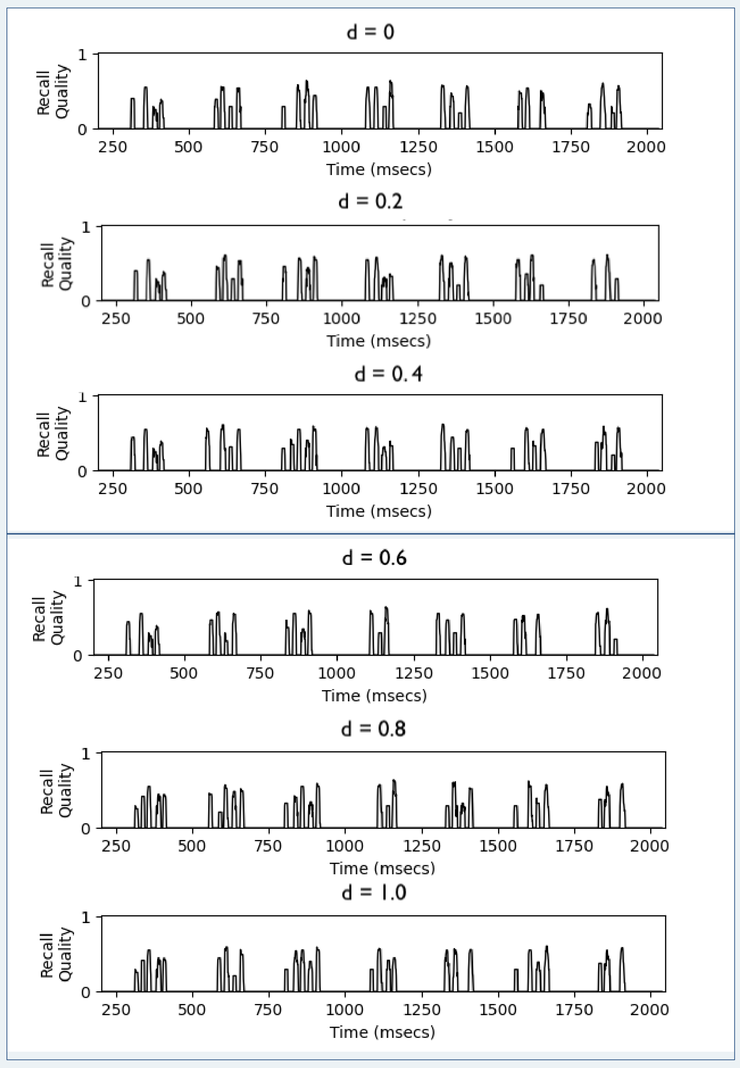

Figure 6. Recall quality over time (msecs) at different spike-time dependent plasticity (STDP) depression rates (d)

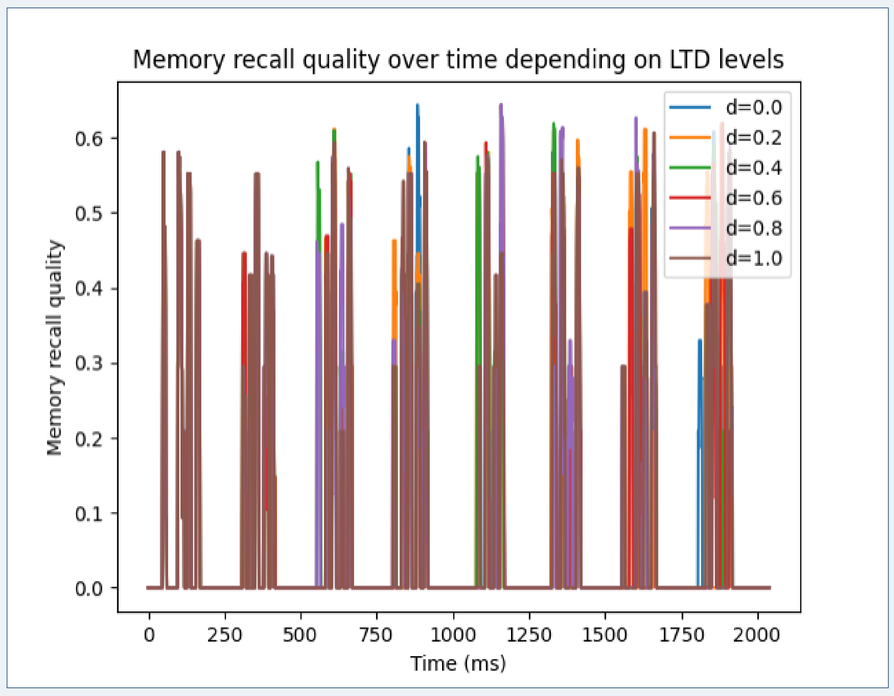

Figure 7. Graph of memory recall over time with spikes representing how this varies across LTD levels. The different LTD levels are color-coded above.

Graph Process

These models were both generated using the matplot library extension in Python. Figure 7 was created by layering arrays of our data on top of each other for comparison.

METHODS

- We altered a pre-existing Python NEURON model[4] of CA1pyramidal (P) cells receiving inputs from the entorhinal cortex (EC), CA3 region and medial septum (MS)

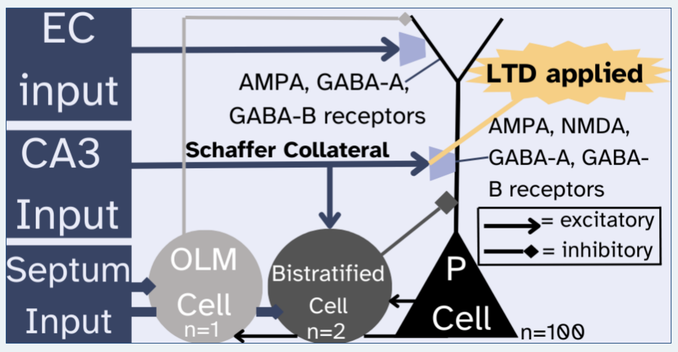

Figure 3. Diagram of the recall cycle of the model

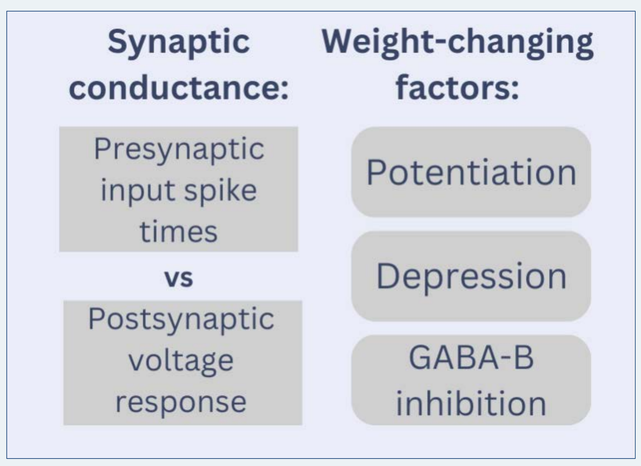

Figure 4. STDP learning rule

- Introducing LTD:
  - The "depression factor" in the learning rule that scales **synaptic conductance** was altered to values of 0.0, 0.2, 0.4, 0.6. 0.8 and 1.0

DISCUSSION

- Conclusions:
  - There does **not** appear to be a significant difference between the memory recall qualities produced by differing LTD values
    - the spikes in our graph comparing the memory recall qualities produced by the various LTD levels were very homogenous
  - The memory recall firing rates change
    - We hypothesize that this difference corresponds to the amount of memories recalled

- Limitations:
  - Our learning rule ignores molecular properties like calcium influx that influence synaptic plasticity and activity patterns[6]
  - The model simplifies synaptic plasticity into a two-step process, when it occurs continuously over time
  - GABAergic input to the CA1pyramidal cells was only considered at one step, but it continuously affects spike timing

- Further Research:
  - Explore the significance of our different memory recall firing rates experimentally and in the NEURON model
  - Research the possible relationship between our findings and the autoassociative memory recall process[7]
  - Investigate possible therapeutics that could regulate the NMDA receptors that mediate calcium influxes

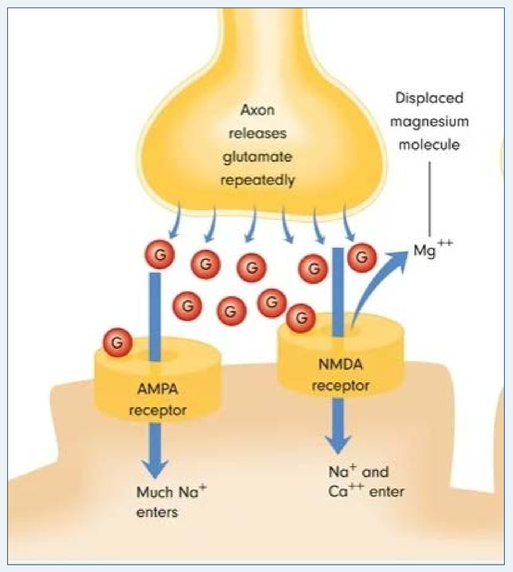

Figure 5. Diagram of a NMDA receptor[5]

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