1. Intro
2. Methods
   1. Experimental setup & Data acquisition
      1. Fig1: experiment & data collect. Use dong’s slide from 2014
      2. Data quantities: 6 rats, 120 sessions.
   2. MVAR model
      1. Fig 2: MVAR model config
   3. Input selection & MonteCarlo methods
   4. Global PDMs
   5. FCT selection
   6. Statistical analysis
3. Results
   1. Behavioral impairement
      1. Fig3: behavioral results for cann & THC & mean impairement over delay
   2. Signals analysis
      1. No reduction in MFR during SP
      2. Reduction in trial type cells pretty equally in both CA3 & CA1
         1. Example of FCT – find a cell that was FCT in Con sesh but not in THC!
      3. Reduction in FFT in both CA3, CA1
   3. System analysis
      1. Amount significant
         1. No difference in #/strength of significant models as measured by rho
         2. Also no difference in kernel area
      2. Fig 4a all kernels & Fig.5:examplesystem
      3. Table1&Fig6-
         1. AR kerns show huge reduction in theta, slight increase in delta
         2. FF kernels show very slight decline in theta
         3. THC AR kernels are more inhibitory
      4. Fig 4B,C PDMs T&F
         1. Table1: no diff in AR PDMs. FF PDM 2 shows decline
      5. Fig 7: Signif PDMs affect behavior
         1. Only 2 PDMs modulate behavioral performance: FF PDM1 & AR PDM3. Both are indicative of theta power
      6. Fig 8: Inhib index
         1. As THC makes FB kernels become more excitatory, performance decreases
         2. \*\*In THC, FF kernels more excitatory (P>.05). As FF kernels get more inhibitory, performance decreases (P=.0485)
4. Discussion
   1. Results Summary
      1. No change in predictive power
      2. No change in MFR (contrary to prior work???)
      3. Theta declines in THC
         1. This is apparent both in signals & systems (ie transfer funcs)
      4. Excitatory changes
         1. As FF & FB kernels get more inhibitory w/ THC, performance decreases. This is seen despite MFR being the same, why???
   2. Theory
      1. Hodgepodge of facts. Start w/ the dual ideas of increased FF inhib & FB excit & MFR stays the same.
      2. This suggests we dealing with 2 competing influences which in this case seem to balance each other out
      3. Our theory is that the 2 effects are: 1) decreased Glut🡪PV IN. this inhibits FF kernels & lowers CA1 excit. 2) decreased GABA from CA1 CCK INs. This causes excit in CA1 FB kernel & net excit. These two effects balanced out to create net MFR contant
         1. Further proved since predictive power doesn’t decline – i.e. SC connection just as strong
         2. If dose increased like in Goon2011, then MFR goes down since now FF decrease stronger.
         3. This is directly relevant to THC anticonvulsant shit where these two forces are in different balance
         4. Furthermore this breakup of IN dynamics will f\*\*\* up theta which we see both in FF& FB!
      4. NMDA also reduced so LTP reduced and thus we see behavioral changes\* (may not be so important to add)
   3. Misc
      1. No previous qualitative work on THC
      2. Very little point-process work, mostly EEG
      3. No differences in FFT/MFR/freq in CA3/CA1 cells?
         1. QUESTION: is this the same w/ place cells?
      4. Relevance to anticonvulsants
   4. PDM methodology
      1. Signal vs system analysis
         1. Signals showed decreased theta, but only very slightly. Systems much more efficient as capturing these changes
         2. Furthermore, system analysis can lead to analysis of predictive power, inhibition, connectivity, and most importantly dynamics!
         3. Saw inhibitory changes, even though MFR was same. This requires systems analysis
      2. Global PDMs
         1. Global PDMs extracted from large dataset & shown to have significant statistical power. 1st time this has been demonstrated in neuroscience
         2. Global PDMs shown to be correlated with behavioral performance. First time this is used
         3. Why we chose linear?
            1. Data analysis much easier due to lack of ANFs & no 2nd order kernel
         4. PDM improvements
            1. Nonlinear & ANFs

Theory:

Discrepancy between fig1e (CA1 theta declines) & AR PDM increases

Caveat abt systemic injection making changes upstream

Cann AHP effects not noted – could be intracellular of network (Ins) – must check this out….

Katona, István, et al. "Presynaptically located CB1 cannabinoid receptors regulate GABA release from axon terminals of specific hippocampal interneurons." *The Journal of neuroscience* 19.11 (1999): 4544-4558. – Says that CB1 receptors 96% on CCK Ins, not PV Ins. This is big since CA1 projects mostly to PVs, while CCKs mostly activately via feedback connections

Decline in FF excit could be due to THC reducing glut release. However, this theory complicated by fact that most CB1 receptors on Ins (and they more suscept to THC see Ozaita s94) thus u would expect more excitation since IN decreases and take brake off the oyrs. …

Still no theory for why indigenous CA1 activity more excitatory – could be due to THC f\*\*\*in w/ CA1 Ins – this breaks indigenous CA1 theta &&&& makes MFR go up

TODO:

1. Make behavioral impairement graphs clearer/ ask marm
2. Add letters to figures
3. Research anticonvulsant effects of THC

NOTES:

1. eCBs released from post-syn terminal in response to calcium influx (during AP) and target both pre-&post syn terminal! Thus affect AR & FF. However, it appears AR more effected!
2. Inhibit LTP by lowering glutamate release levels below those needed to activate NMDA [102]. This explains more inhibition in FF kernels
3. Hampson,98 reports delay-dependant decline in DNMS task. But I don’t?
4. See [104] pg996-997 for summary on THC effect on membrane channels (which make PDMs). They are extremely complex & thus it nessecitates nonparametric modeling
5. See [104] pg997: THC worsens GABA reuptake which will lead to higher inhibition & our observed effects!
6. [102] says that GABA INs shape oscillatory activity & thus their suppression would lower it see pg2
7. Several biphasic effects of CBs reported. Thus, dynamics may be strongly influenced by dosage
8. Mention why PDMs better than CrossCorr used in Goon11, Robbe06
9. Reduces paired-pulse depression. Thus needs 2nd order kernel
10. In Pouille,2001 there is a lot of talk of how EPSP is shaped by Pyr🡪Pyr and then slower Pyr🡪IN🡪Pyr. This is direct example of how THC, which fucks w/ IN dynamics, will f\*\*\* w/ the FF kernel

Outline

Para1: Key Findings

1. The current study uses novel system dynamics modeling tools to study the effects of THC on the Schaffer Collateral synapse in rodents.
2. The chief contributions of the study can be summarized as:
   1. THC induced little or no change in traditional signal analysis metrics such as MFR and theta power.
   2. THC altered the CA1 EIB by reducing feedforward excitation from CA3 while increasing feedback excitation from CA1.
   3. THC reduced theta information flow through the Schaffer collateral synapse.
   4. The magnitudes of both of the previous effects were directly correlated with the severity of behavioral deficits induced by THC
3. From a computational perspective, this study advances the use of global PDMs to analyze neuronal circuit dynamics in neuroscience and for the first time directly correlated changes in global PDMs with behavior.
4. Furthermore, while most in-vivo studies on THC analyses macro level signals such as ECoG and EEG, this work adds to a relatively small body of work which analyzes the effects of THC on neuronal population spiking activity.
5. Finally, to our knowledge, this is the first work which examines the effect of THC on neuronal systems dynamics, or the causal interactions between signals, rather than on neuronal signals themselves.

Para2: Theory

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