On the neural dynamics role of excitation-inhibition balance in Parkinson's disease

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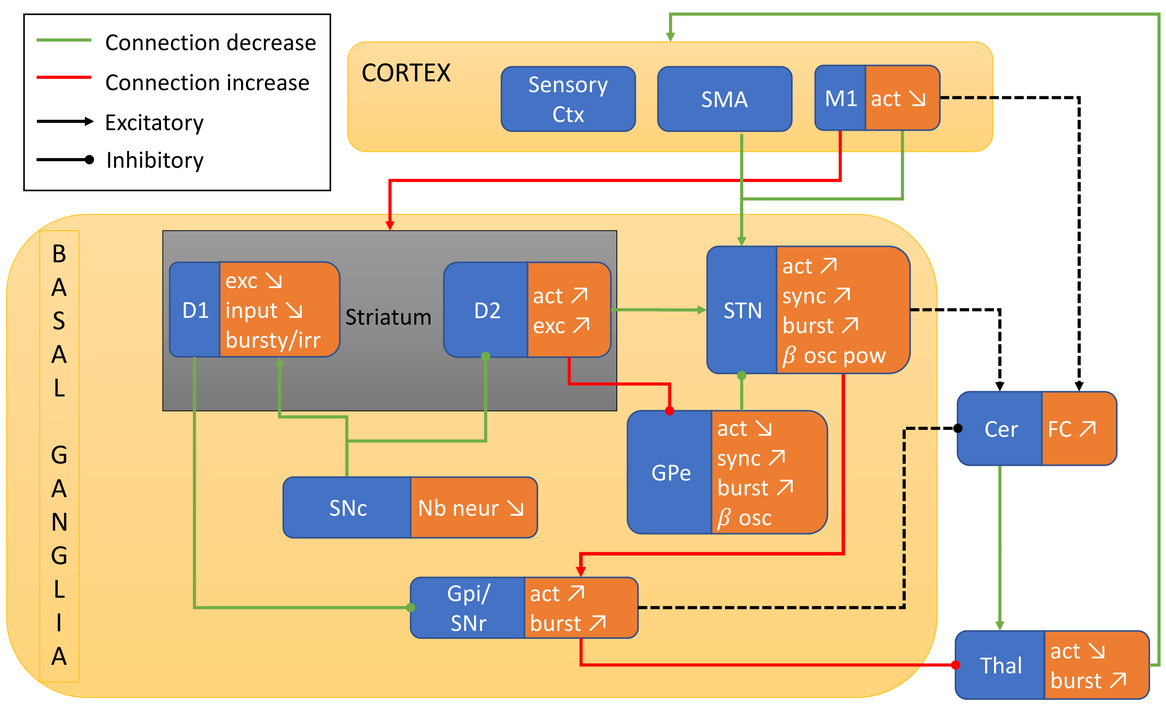
Summary

- Excitatory-Inhibitory (E-I) balance is here considered at the population level that can be measured by LFP, EEG or MEG
- E-I balance forms the basis of many important neural processes like balance amplification, asynchronous firing, contrast invariance, efficient coding ...
- E-I balance is altered in several brain diseases like epilepsy, schizophrenia, autism, Alzheimer's, Parkinson's disease (PD)[1,2]
- Even though usually not mentioned, neuromodulatory changes reported in PD lead to E-I ratio alteration from basal ganglia (BG) to the cortex
- We review neuronal changes occurring in PD, how they relate to E-I imbalance as well as the role of modelling in understanding them

PD cortico-basal ganglia-thalamic (CBT) circuit changes

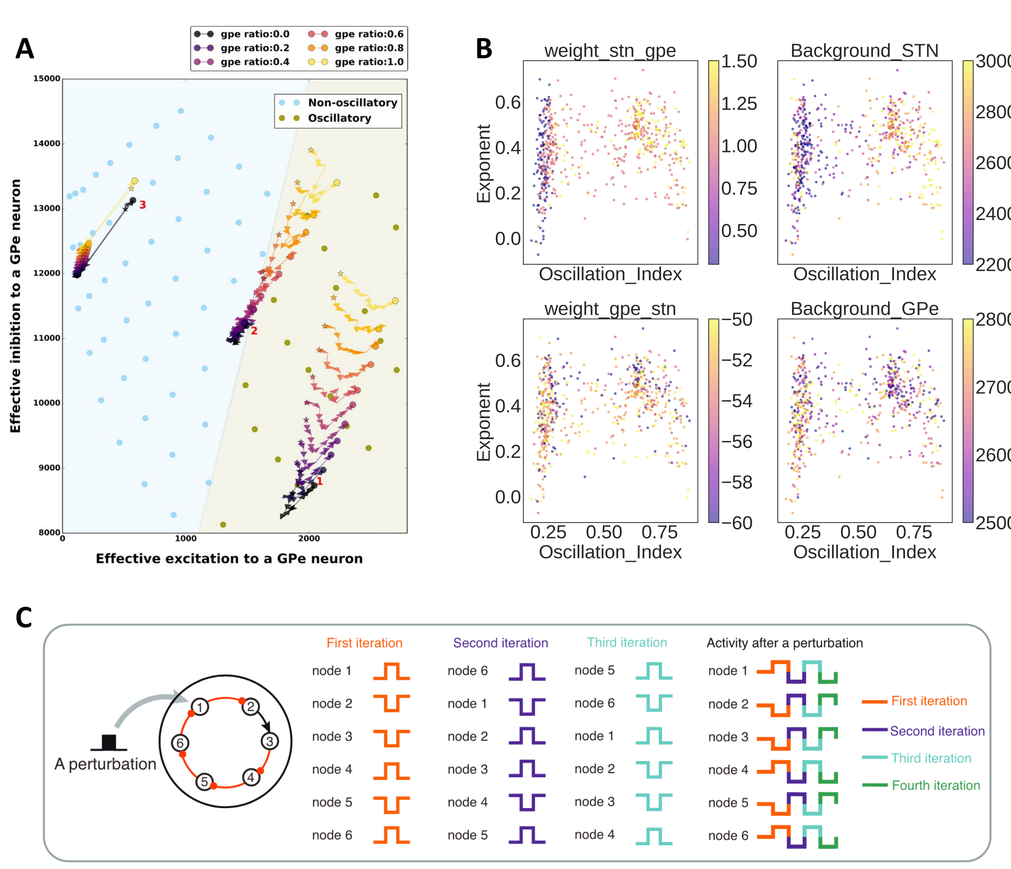
- Loss of Substantia Nigra compacta (SNc) dopaminergic neurons in PD
- Human patients and animal models of PD show BG activity alterations [3]
  - affecting factors such as neuronal excitability, synaptic strength and synaptic plasticity
- The most studied pathological activity in the BG network is the emergence of high power β oscillations (13-30Hz) in the Subthalamic Nucleus (STN) and Globus Pallidus external (GPe)
  - Even though many ways of generating such oscillations exist there is no consensus [4]
- Decrease in thalamic activity is the main consequence from BG alterations [3]
  - Lead to a suppression of movement
- Cerebellum has been recently put forward for its possible role in PD [5]



Schematic of how affected is CBT in PD.

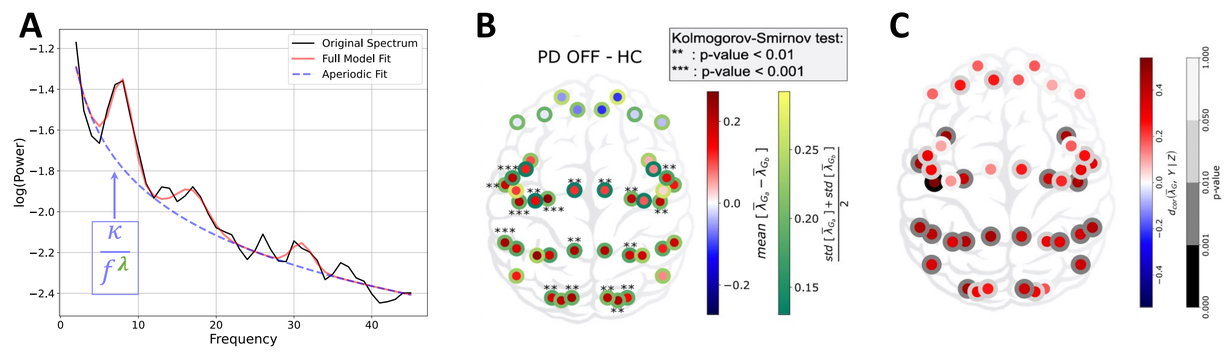
Patahological activity and altered E-I balance in PD

- Clear effects of most changes on the E-I balance but not for all:
  - Bursting activity, oscillations, functional connectivity, fluctuations
- Modelling can help understand their link with E-I balance
  - Bursting increase changes effective E-I balance [6]
  - E-I variations are not so trivial [7]
  - Oscillations emerge from cyclic network with an odd number of inhibitory nodes and can be quenched by changing synaptic weights [8]

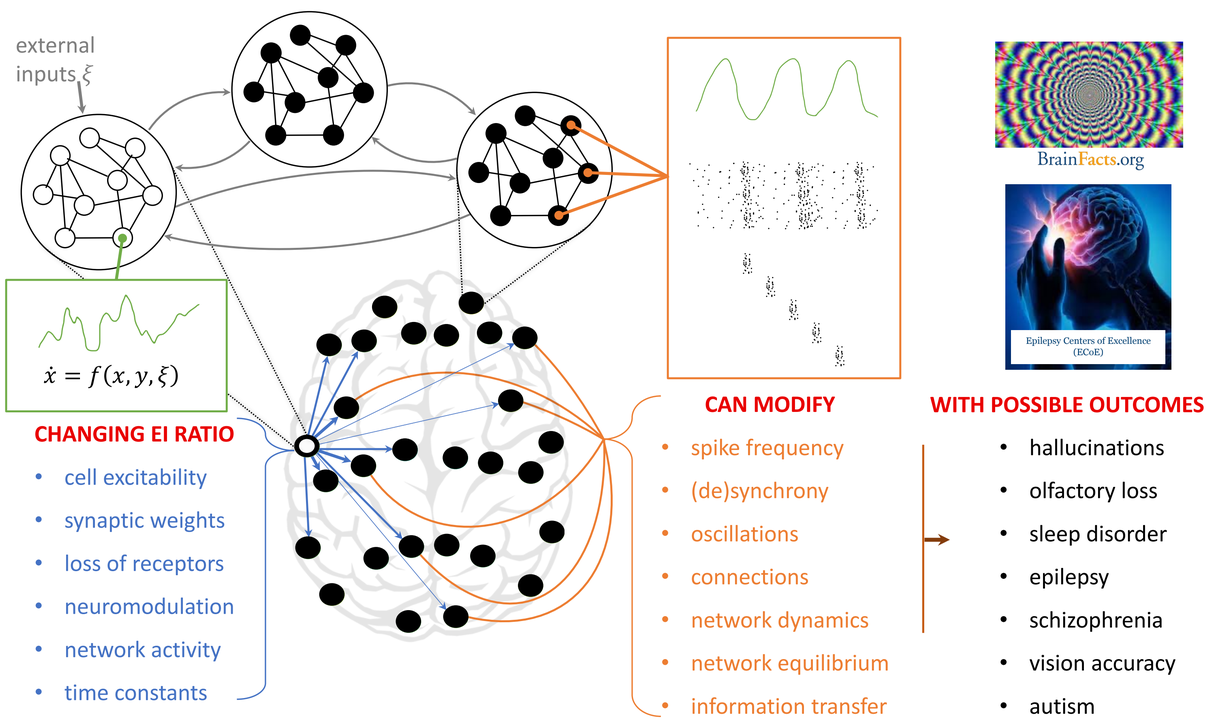


In the search of reliable E-I balance proxies

- Human brain data are mainly obtained from (non-)invasive imaging techniques
- Actual measures of E-I ratio have low spatio-temporal resolution (PET, MRS)
- Several tools to infer E-I balance from data with high temporal resolution
  - Using FOOOF [9] on MEG from PD patients and healthy controls (HC) suggests that PD involves major reorganisation of neo-cortex E-I balance [10,11]

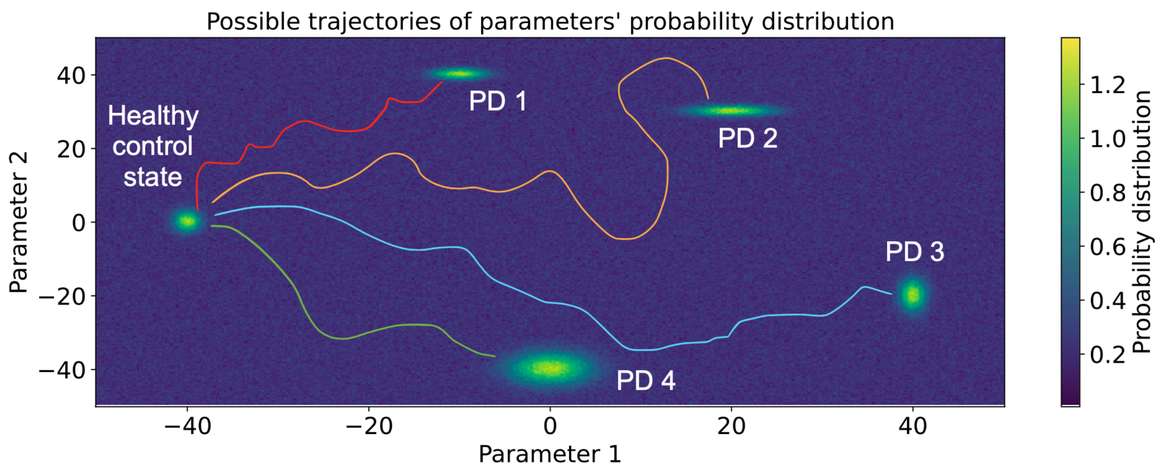


The next step, towards treatments



Using Bayesian inference with PD constraints

- **End goal** : following possible trajectories of parameter changes leading to 'Parkisionian like' brain activity states
  - Cortical rate model and spiking model for the BG [12]
  - Determine the right parameters (as a distribution) for a 'typical' healthy control using structural and functional connectivities, M/EEG knowledge as constraints (possibly use task responses)
  - Use the HC state as a prior state in the Simulation Based Inference algorithm whose objective is dictated by our knowledge on pathological neuronal activity [13]



Conclusion

A lot of knowledge has been accumulated on the brain activity statistical changes occurring in PD. Only a few of them (independently one to another) have been used in modelling studies. Understanding their link with E-I balance will help reduce the number of parameters to study as well as better constrain the statistics we want to reproduce.

References

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