What is psychosis?

What is schizophrenia?

What else causes psychosis?

- Full blown mania in Bipolar Disorder - Type I
- Drugs
- Alzheimer's and other types of dementia

Circuits in the brain

Some circuits in the brain are well understood.

What circuit have I showed you before?

Hint: It involved one region sending axons to a second region and releasing a specific neurotransmitter to send a certain message.

Key

Increases/causes OR excitatory (synapse)

Note: An arrow from one brain region to another is glutamate, unless otherwise noted

Decreases/blocks OR inhibitory (synapse)

Note: A T-headed arrow from one brain region to another is GABA, unless otherwise noted

Modulates

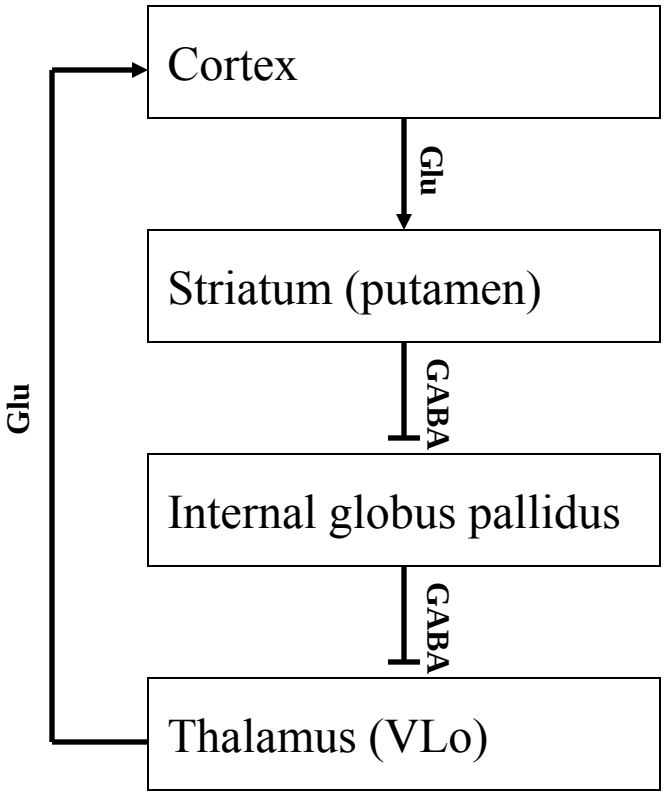
The relationship may be complex and/or poorly understood

Entity	A brain region, cell, protein, or other entity
Entity	Hypoactive, decreased, or dead
Entity	Hyperactive, increased

Movement and Parkinson’s

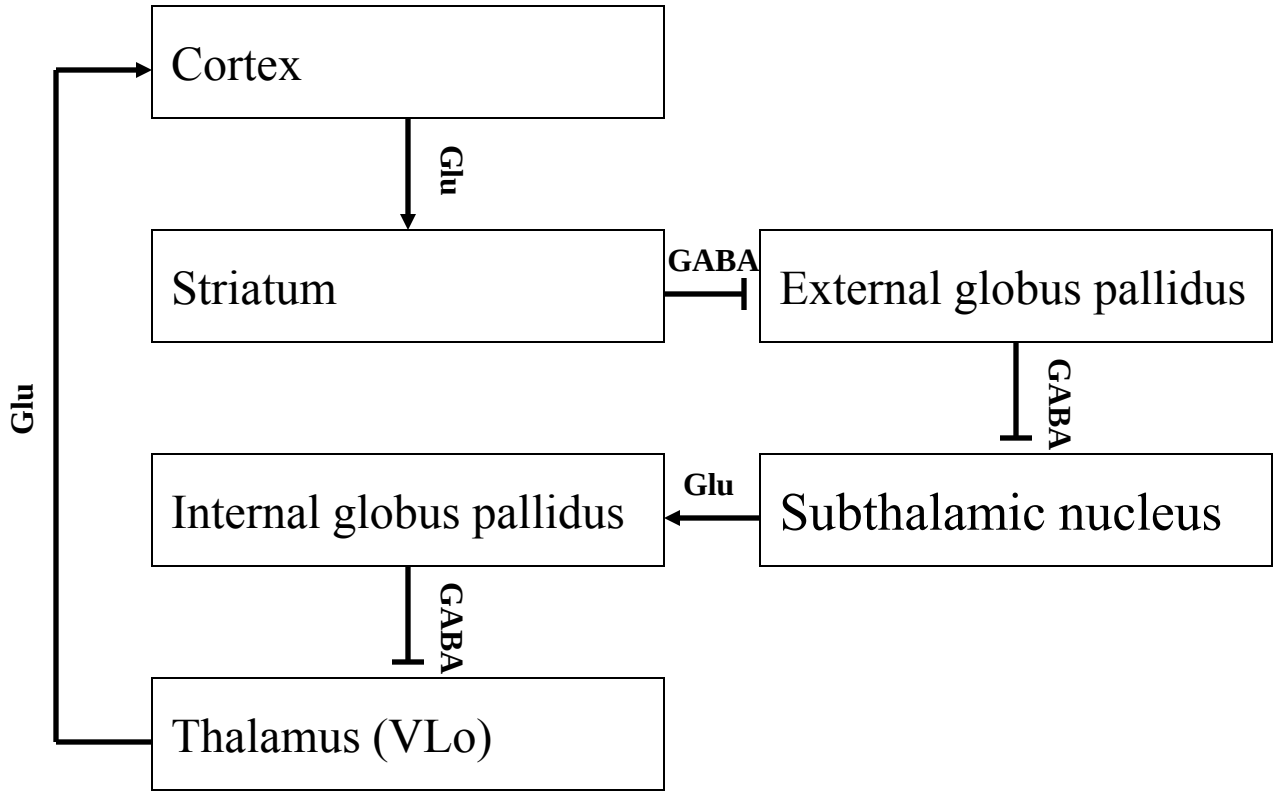
The direct pathway

Amplifies activity in the cortex. It is thought that a plan for movement is a small flurry of activity in the cortex, and that neural activity (plan) is amplified by going through this loop several times until finally enough activity builds up and the movement is performed.



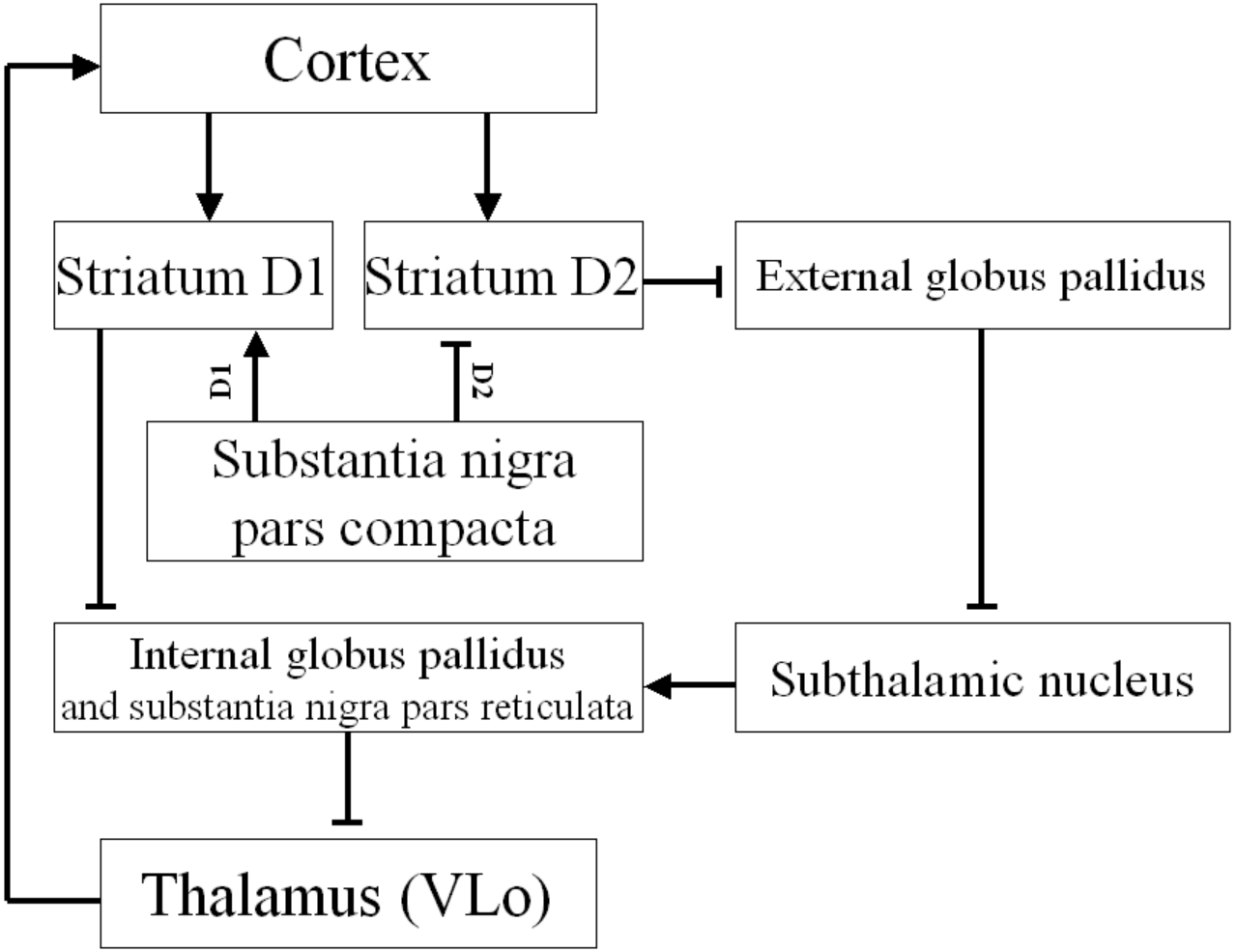
The indirect pathway

This inhibits activity in the cortex, rather than amplifying it like the direct pathway. This inhibitory loop may be important for eliminating plans that we do not carry out, so that only certain movements are chosen and executed.



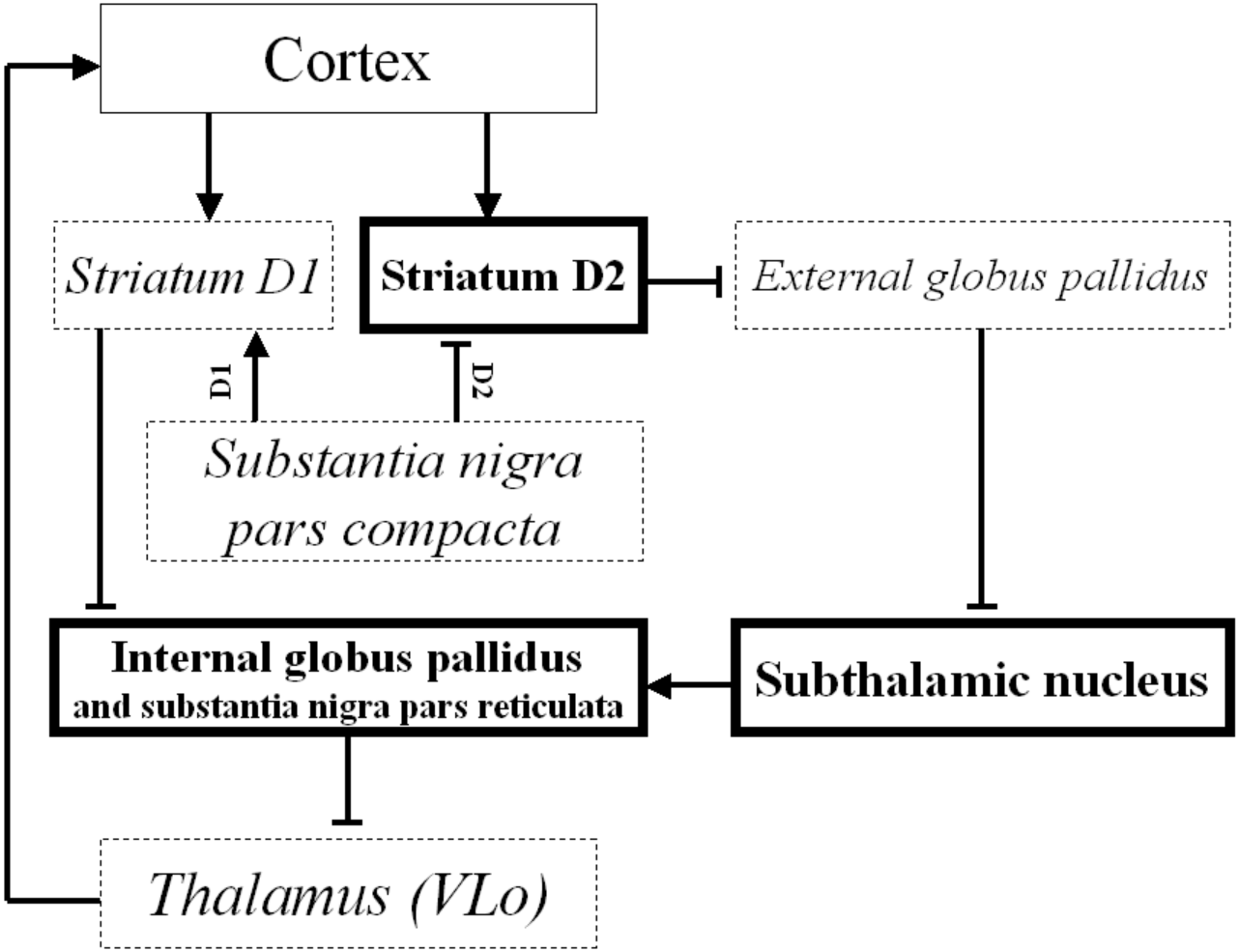
Adding the substantia nigra

Dopamine from the substantia nigra pars compacta activates the direct pathway and inhibits the indirect pathway, both of which have the net result of reinforcing cortical activity.



Parkinson's Disease

The substantia nigra pars compacta dopaminergic neurons die, leading to the pattern of hyper- and hypoactivity shown here, which ultimately leads to decreased activity in the areas of cortex necessary to initiate movement.



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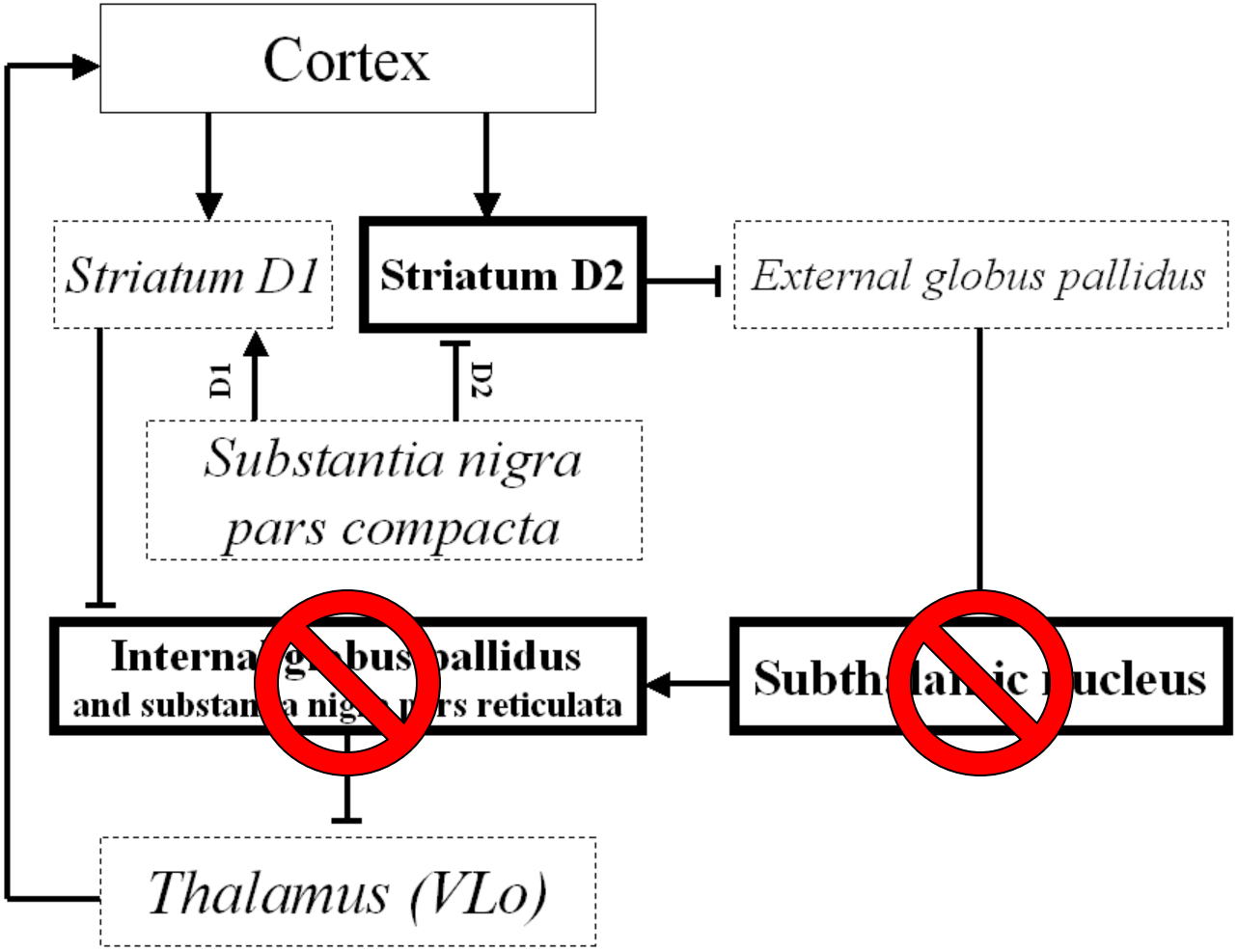

Synaptic structure

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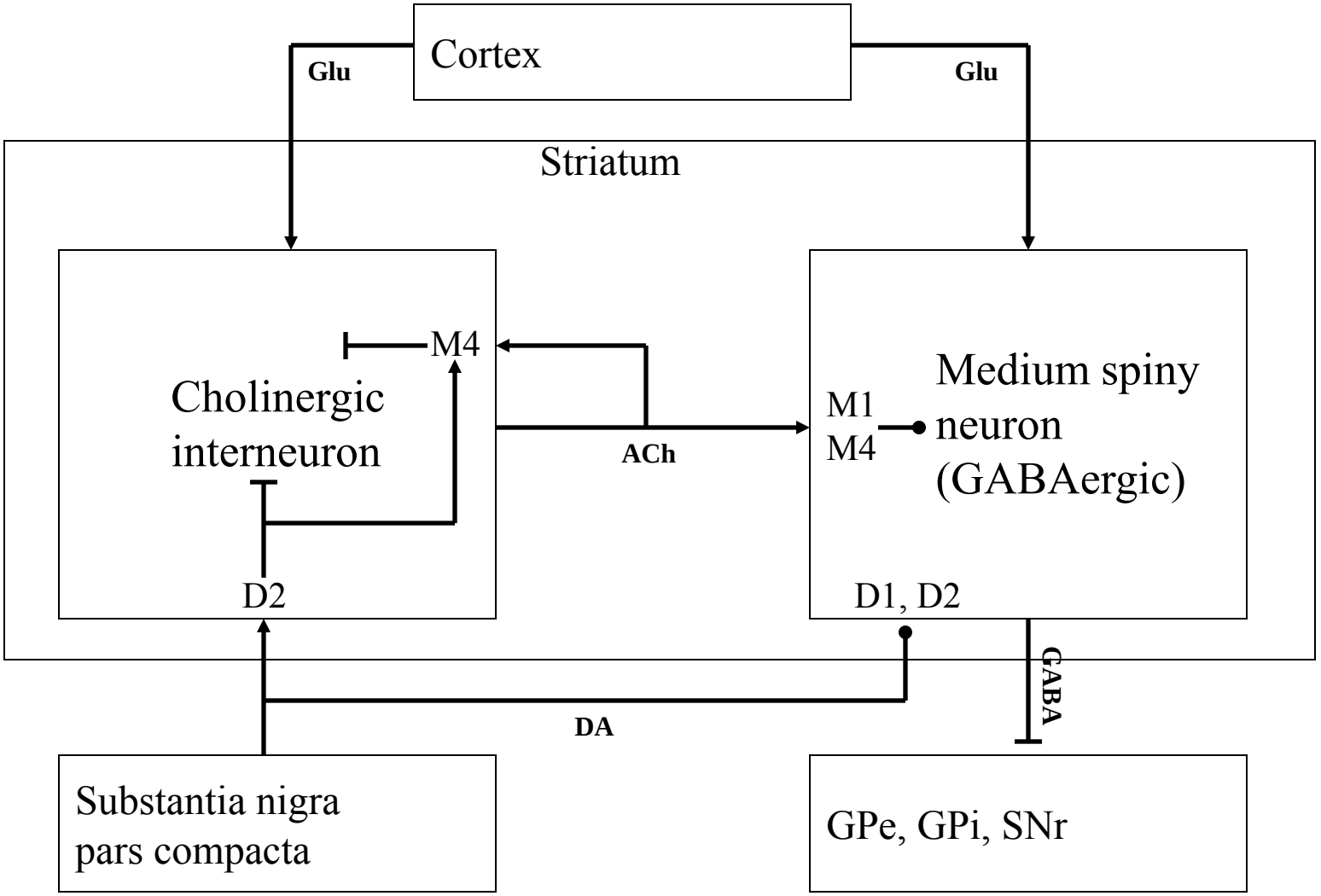
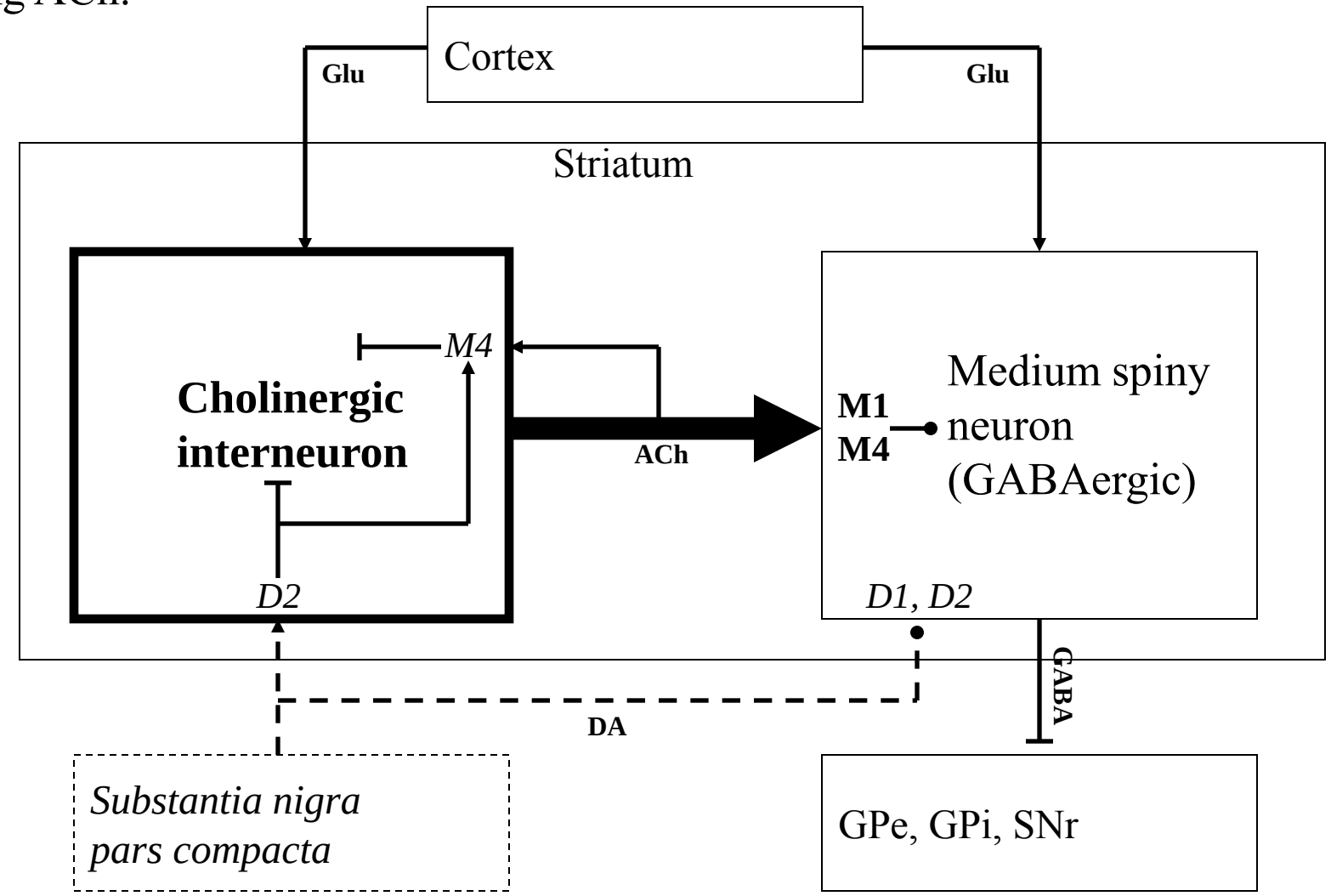


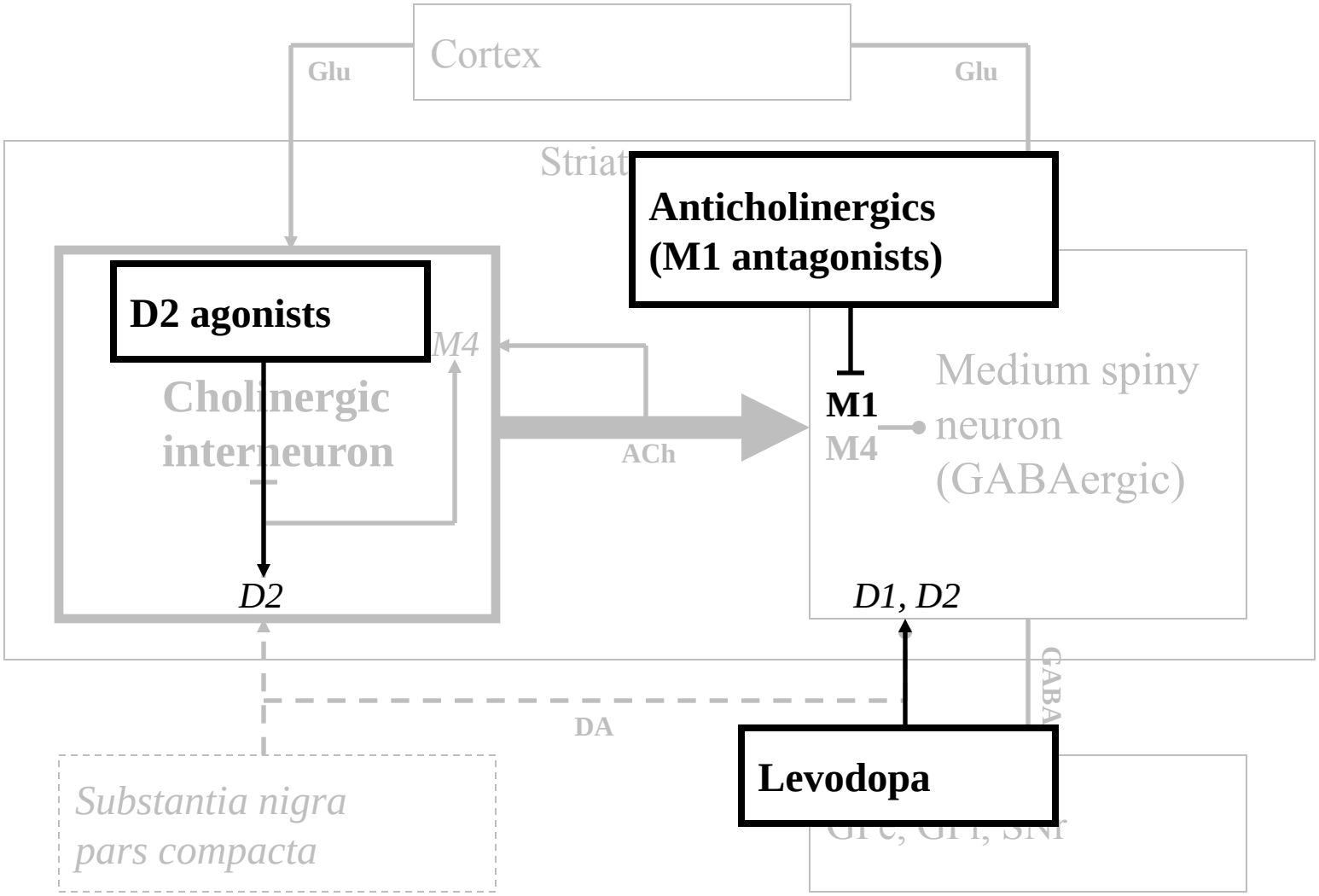
ACh/DA balance in PD

There is too little DA in Parkinson's Disease (PD). This causes symptoms directly through D1 and D2 receptors on the MSNs, but it also causes symptoms indirectly by elevating ACh.



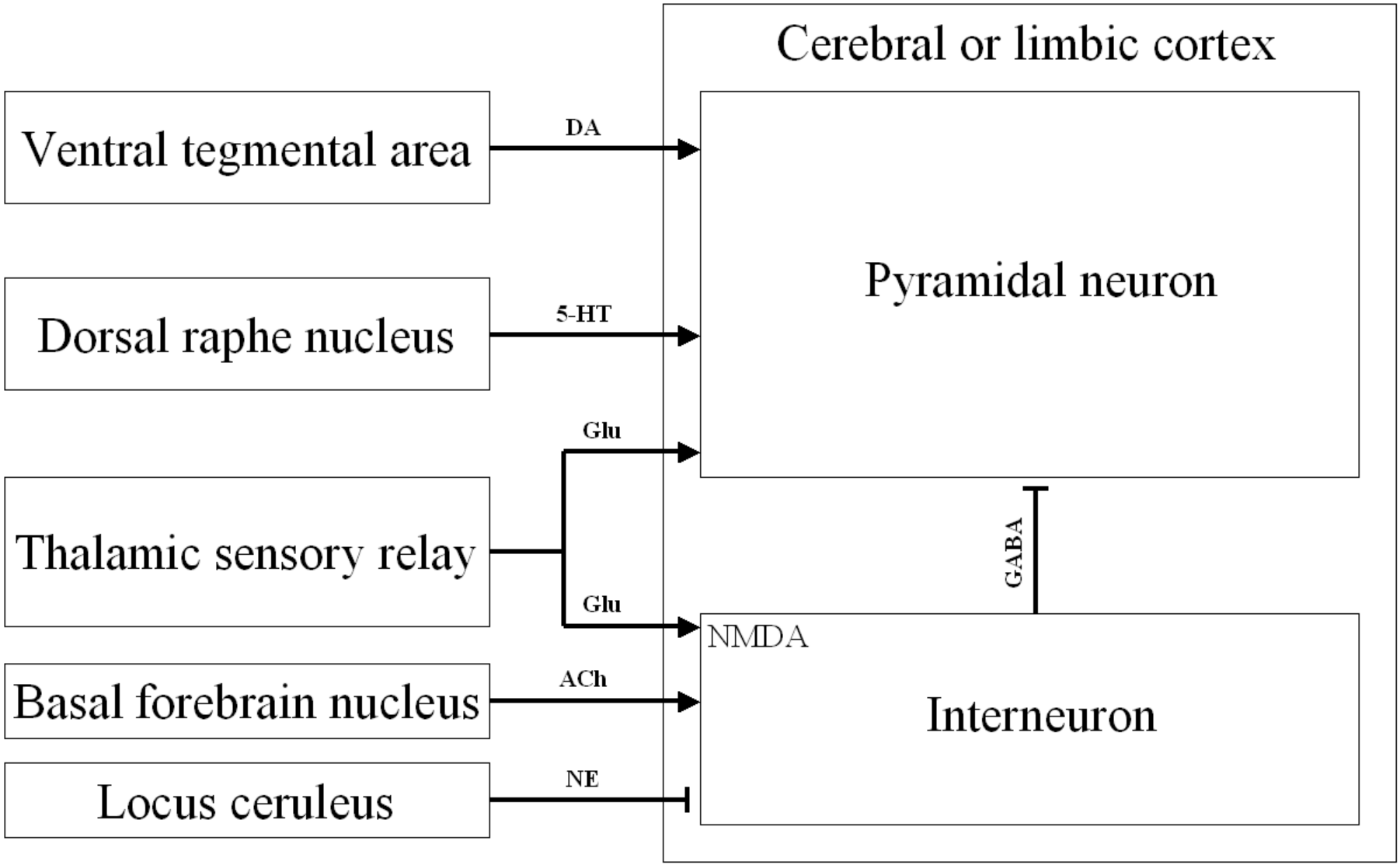
ACh and DA drugs for PD

Drugs that increase DA or decrease ACh can help alleviate the symptoms of PD.



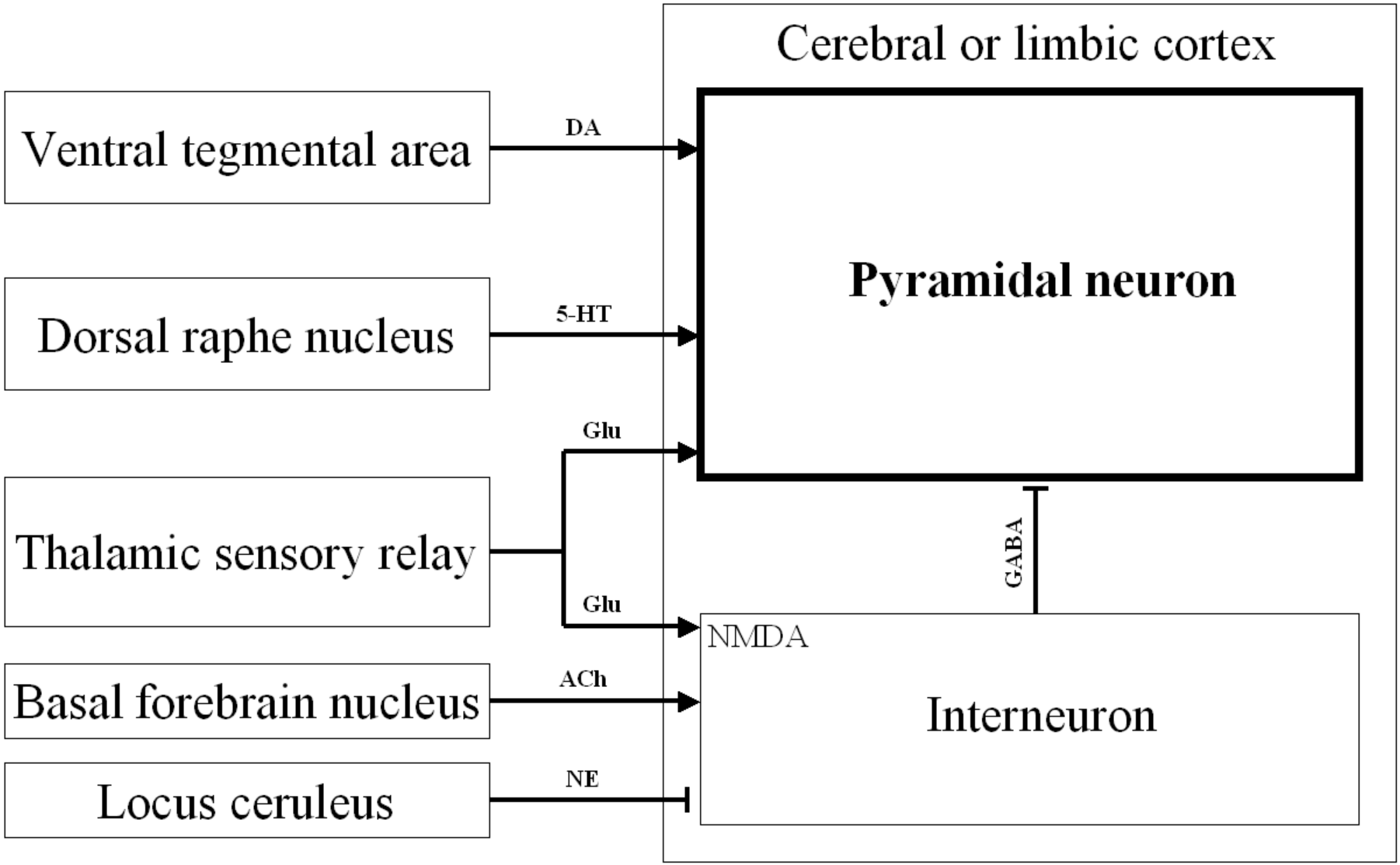
Schizophrenia

This diagram shows the pathways that may be involved in schizophrenia.



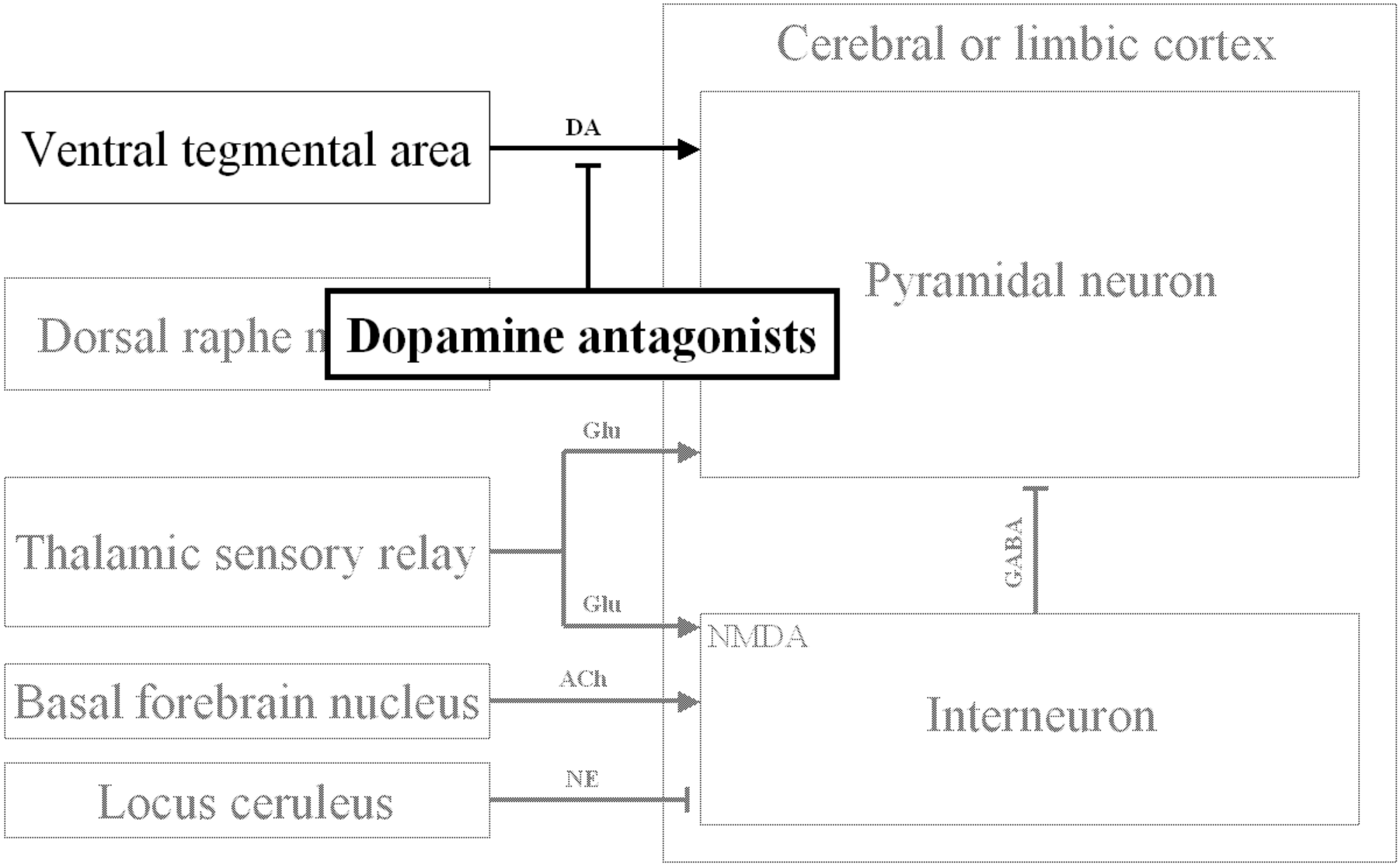
Schizophrenia

Psychosis results when the pyramidal neurons are overly excited and fire too often.



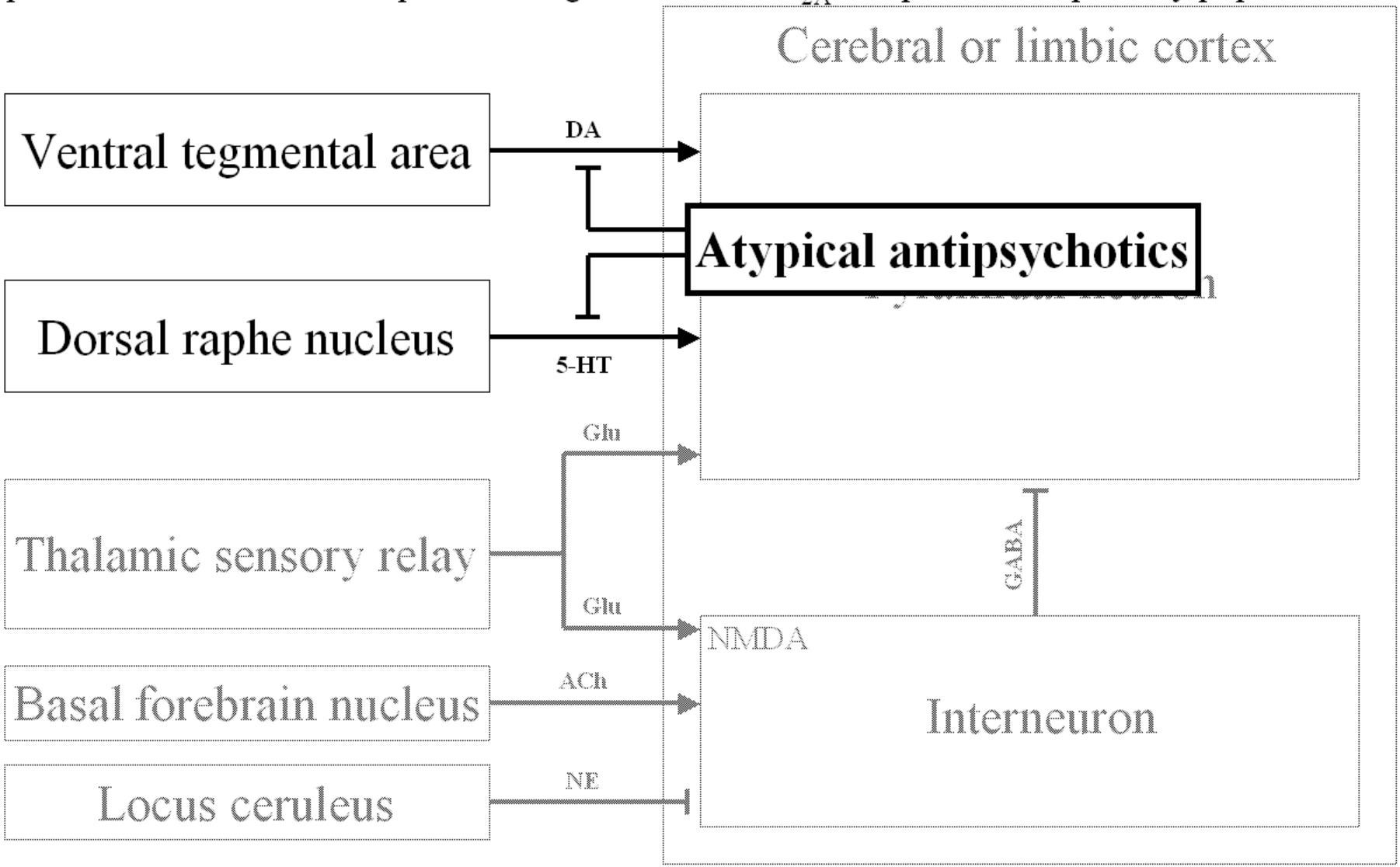
Antipsychotics

Typical antipsychotics, also called neuroleptics, are antagonists at dopamine receptors



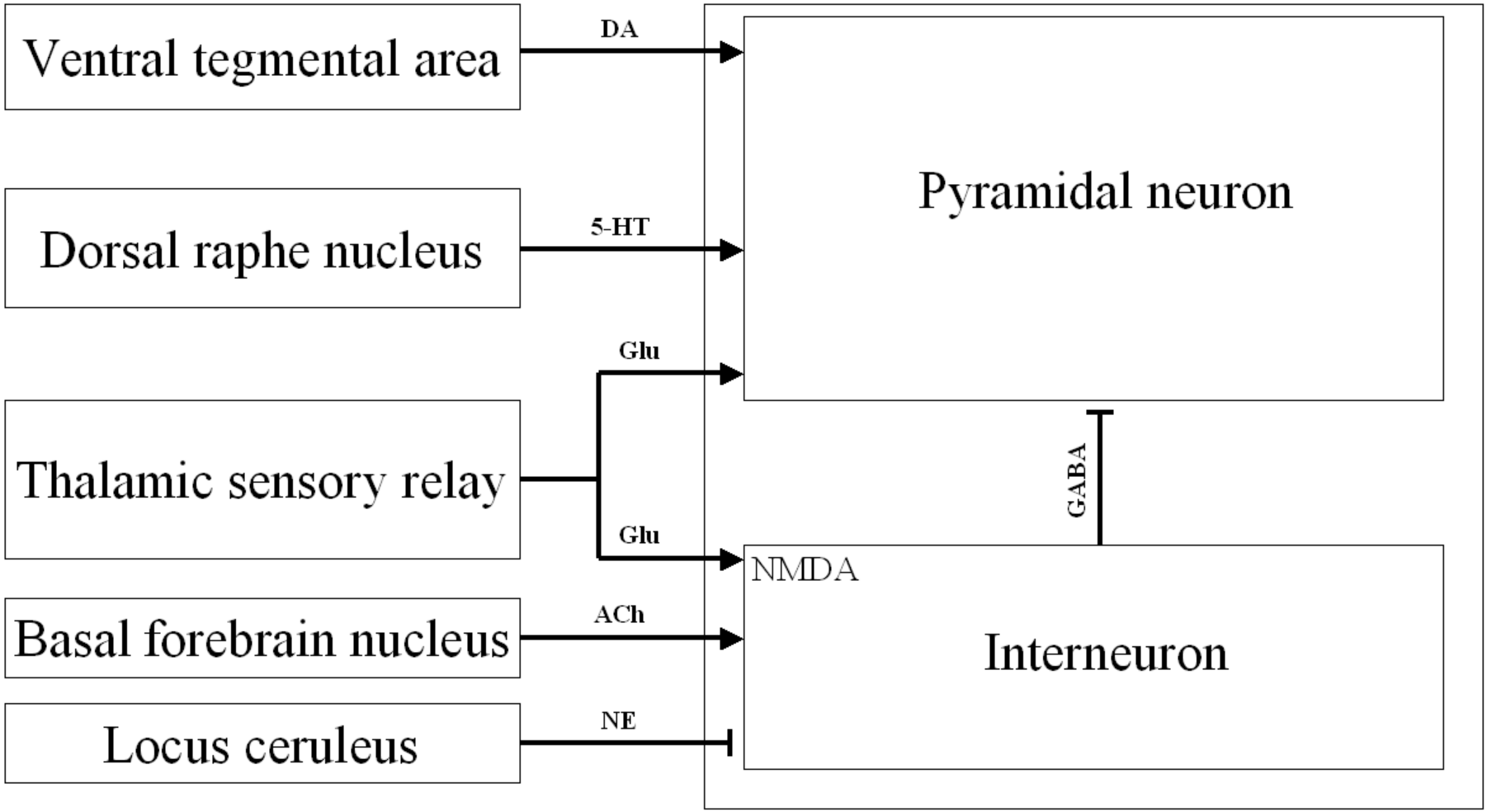
Atypical antipsychotics

Atypical antipsychotics (second-generation antipsychotics) are often antagonists at both dopamine and serotonin receptors. Antagonists of 5-HT_{2A} receptors are especially popular.



Psychotomimetics

Psychotomimetics are drugs that cause psychosis. Drugs that increase 5-HT, DA, and/or NE are all psychotomimetics (amphetamine, cocaine, psychedelics). Drugs that block NMDA receptors (ketamine, PCP, dextromethorphan) and drugs that block muscarinic ACh receptors (anticholinergics) are also psychotomimetic.



Other psychosis treatments

- Benzodiazepines, which boost the inhibitory effect of GABA, can effectively suppress psychosis. (This was predicted by the diagram.)
- Clozapine increases ACh release, which helps alleviate psychosis (as predicted).
- Many antipsychotics block NE, which further helps treat psychosis.

Nicotine Mitigates Psychosis

Nicotine is an agonist at nicotinic ACh receptors, meaning nicotine mimics ACh. As expected, nicotine helps mitigate psychotic symptoms. Many psychotic patients smoke.

Dr. A: “All my schizophrenic patients smoke, and they’re still batshit insane.”

Dr. B: “Maybe you should prescribe something in addition to the cigarettes.”

Other Psychotomimetics

κ opioid agonists such as **salvinorin A** (found in *Salvia divinorum*)

THC, found in marijuana.

Over the past 50 years, the THC content of marijuana has increased while the CBD (cannabidiol) content has stayed the same or decreased. CBD suppresses the anxiogenic and psychotomimetic effects of THC, so modern marijuana is more likely to cause psychosis and panic.

ES.S10 Drugs and the Brain

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