

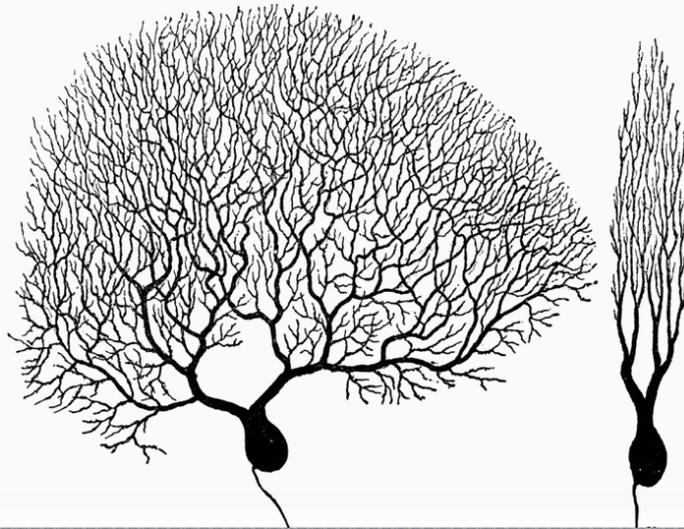
The Story of **AUTISM**

PART 16:

**PURKINJE
CELL FIRING:
TIMING IS
EVERYTHING**

THE STORY OF AUTISM: Purkinje Cell Firing Timing

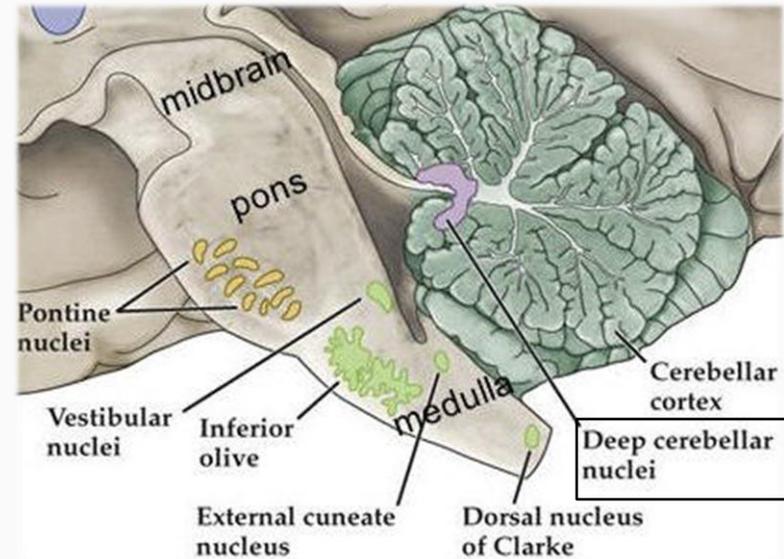
Purkinje cells (PCs) have long been thought to have a causal connection to autism – and with good reason. Not only are they **the primary neurons of the cerebellum**, but they are the ones that **control its output**.



THE STORY OF AUTISM: Purkinje Cell Firing Timing

The **Deep Cerebellar Nuclei (DCN)** are the sole source of output from the Cerebellum as a whole. But **their output is 100% influenced and determined by the PCs.**

So...the PCs tell the DCNs what data to output to the brain and body.



THE STORY OF AUTISM: Purkinje Cell Firing Timing

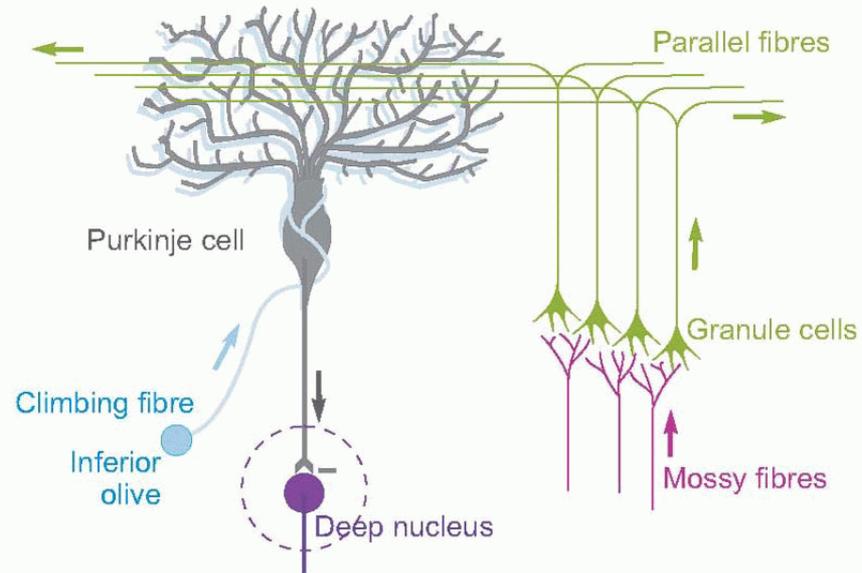
But what influences the PCs in this decision-making process?

Actually, a bunch of neural cells and fibers, the most prominent of which are the **climbing fibers and mossy fibers sent out from the brainstem.**

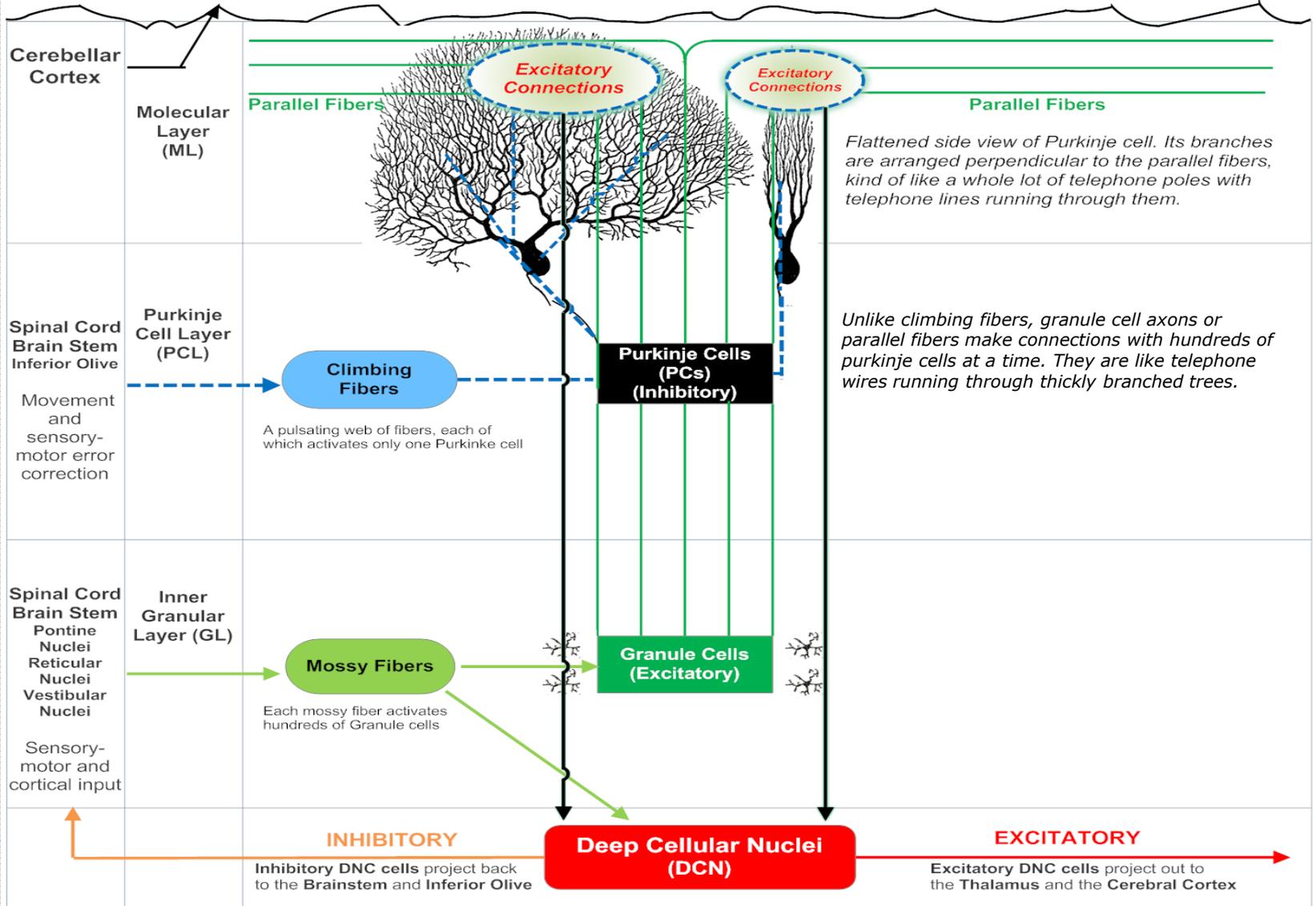


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Mossy fibers carry sensory input and innervate **granule cells** in the cerebellum that sprout **parallel fibers**. These fibers make connections with hundreds of PCs at a time.



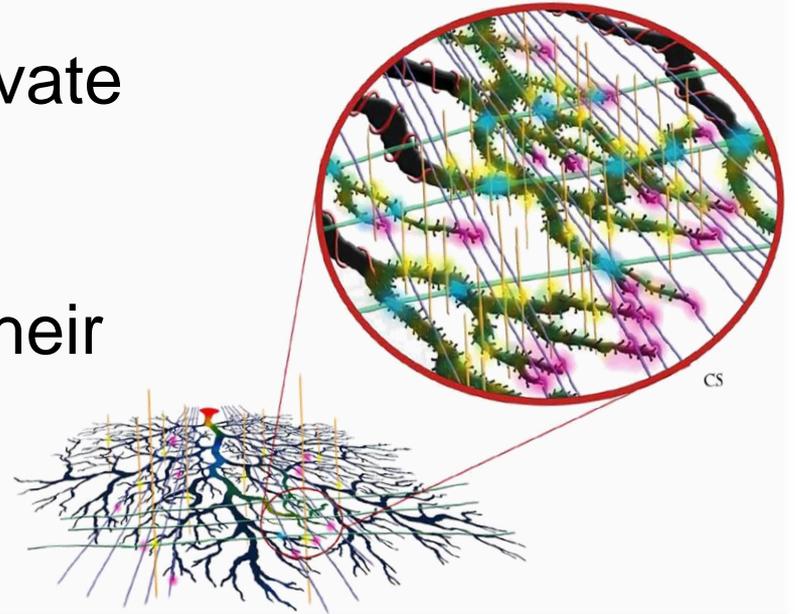
Cerebellum Layers



THE STORY OF AUTISM: Purkinje Cell Firing Timing

Climbing fibers carry sensory motor feedback and error correction information.

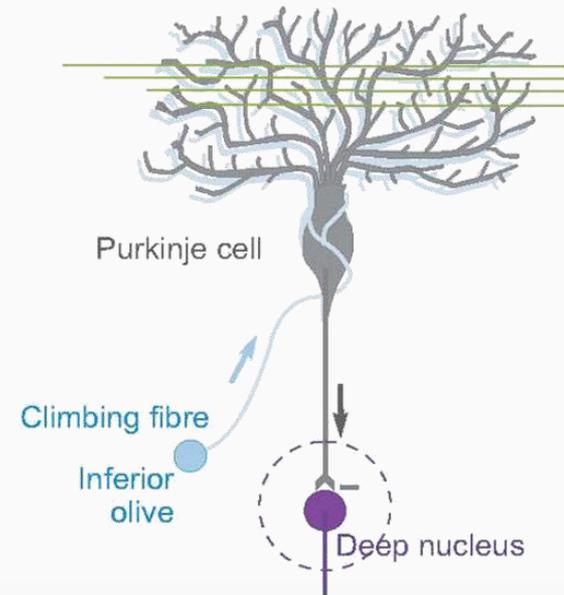
Each CF is supposed to activate only one PC, but they wrap themselves entirely around the branched dendrites, so their input is extremely powerful.



THE STORY OF AUTISM: Purkinje Cell Firing Timing

Early on in development, PCs are activated by multiple climbing fibers, but as the cerebellum matures, these inputs gradually reduce until there is only a single CF input per PC.

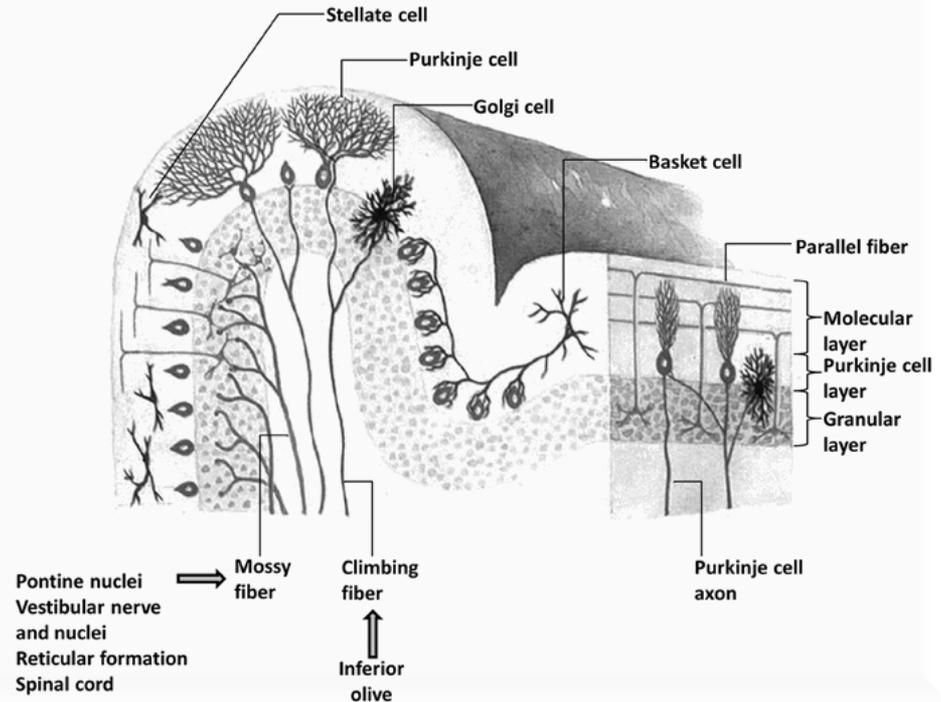
At least this is what is supposed to happen. If there is no pruning problem.



THE STORY OF AUTISM: Purkinje Cell Firing Timing

There are two other types of cells that impact the PCs output – **basket cells** and **stellate cells**.

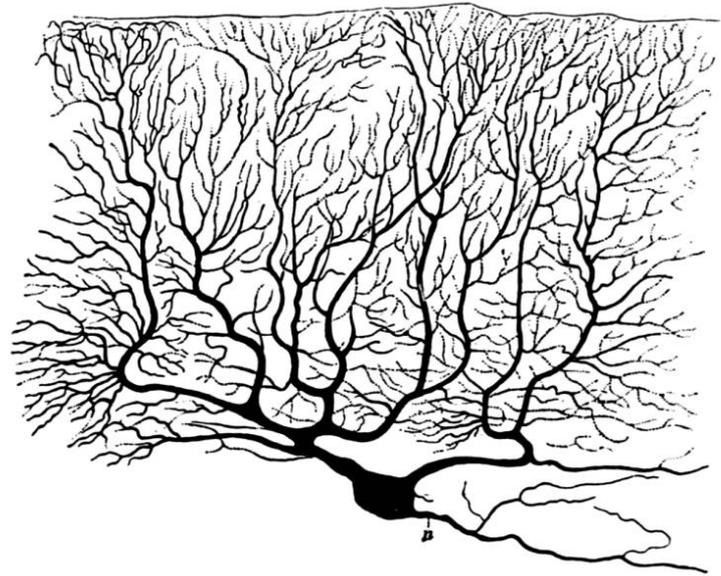
Like the PCs, they are **GABAergic**, which means that they release the neurotransmitter GABA and are inhibitory.



THE STORY OF AUTISM: Purkinje Cell Firing Timing

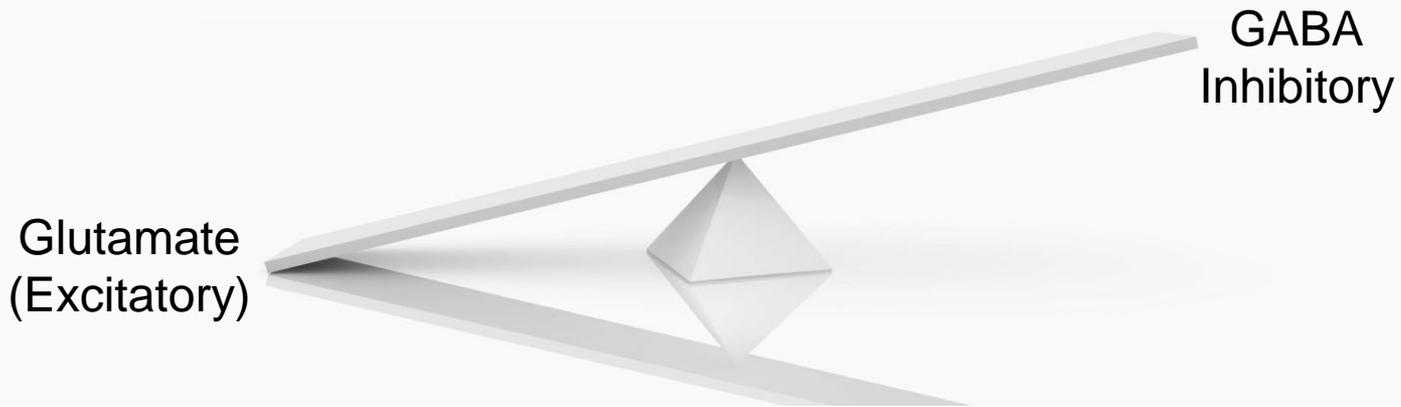
Climbing fibers and parallel fibers are GLUTAgenic and excitatory.

GABA, along with Glutamate, modulates the outgrowth and branching of PC dendrites (or fibers).



THE STORY OF AUTISM: Purkinje Cell Firing Timing

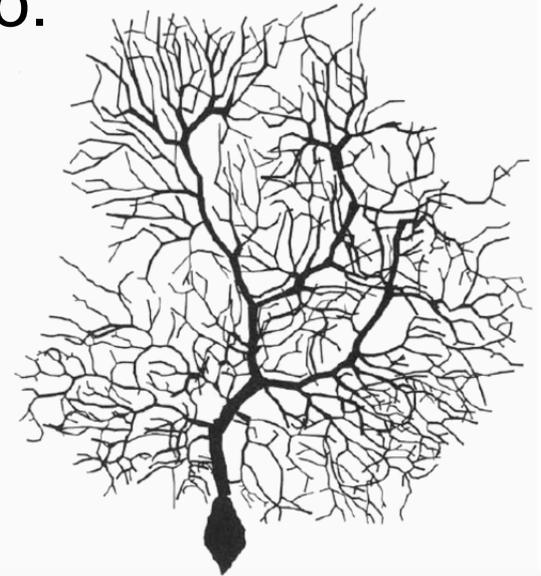
PCs in postmortem autistic brains have been found to be smaller in size, which could mean that they have fewer and/or shorter branches, indicating an imbalance of GABA and Glutamate modulatory input, with the latter predominating.



THE STORY OF AUTISM: Purkinje Cell Firing Timing

If our **failure to prune** premise holds true, then the early developmental pattern of multiple climbing fibers innervating multiple PCs might not mature to the typical one-on-one 'fire and wire' ratio.

This would account for excess glutamate and smaller PCs.



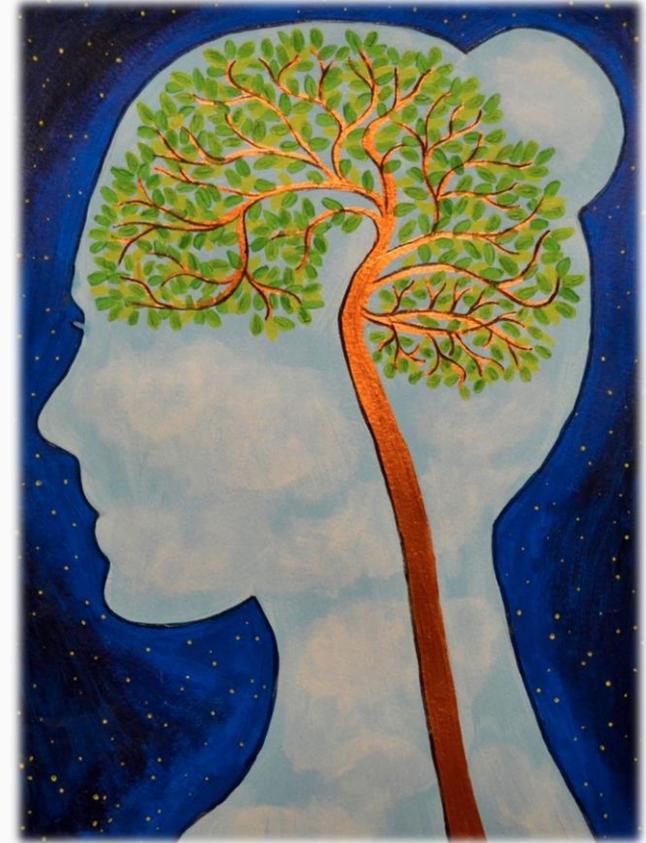
THE STORY OF AUTISM: Purkinje Cell Firing Timing

Tests with autistic model mice show they possess an over-abundance of climbing fibers, which means that these fibers are not getting pruned as they should.⁸



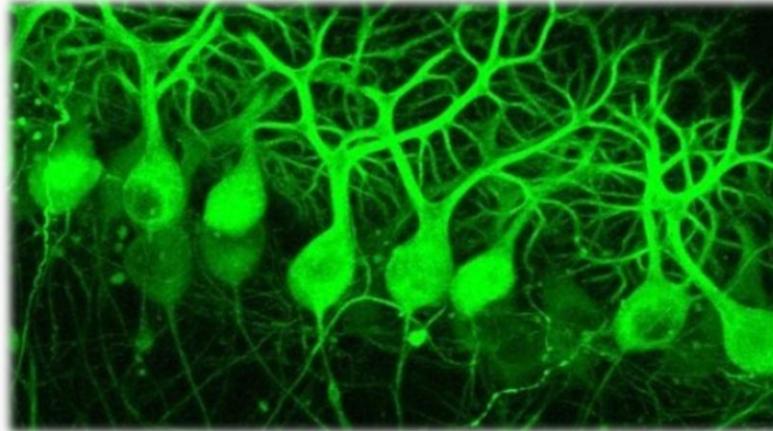
THE STORY OF AUTISM: Purkinje Cell Firing Timing

According to Christian Hansel, professor of neurobiology at the University of Chicago, “Inefficient synaptic pruning seems to be a common motif in autism.”⁹



THE STORY OF AUTISM: Purkinje Cell Firing Timing

But the real determining factor in how smooth our motor and cognitive processing will be is the rate of PC firing.

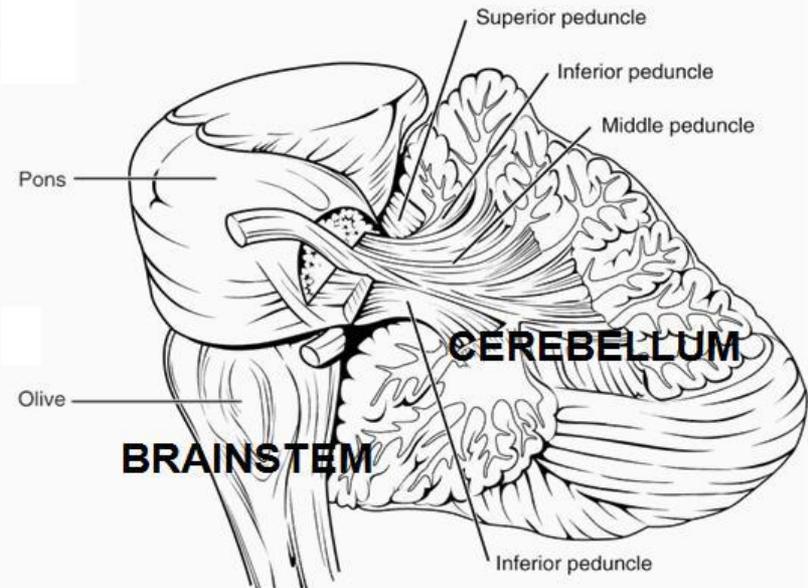


Climbing fibers regulate the timing for PC firing activity.

THE STORY OF AUTISM: Purkinje Cell Firing Timing

Climbing Fibers (CFs) originate in the **inferior olive** of the **brainstem**. They pick up movement and sensory-motor error correction information there and carry it to the PCs in the cerebellum.

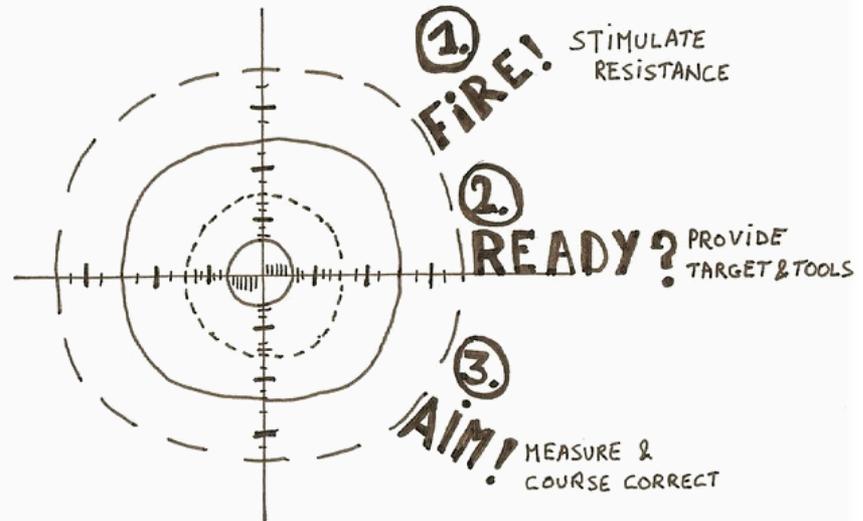
CFs are **excitatory**.



THE STORY OF AUTISM: Purkinje Cell Firing Timing

When excitatory fibers innervate PCs, they cause them to FIRE.

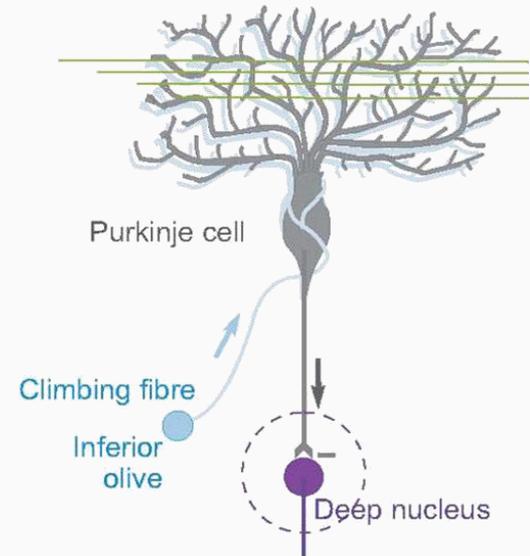
Inhibitory cell/PC synapses cause the firing to PAUSE.



THE STORY OF AUTISM: Purkinje Cell Firing Timing

It is the finely-tuned balance between FIRING and PAUSING, between the excitatory and inhibitory input the PCs relay down to the DCN, that keeps us on an even keel.

More firing of the inhibitory PCs would cause more inhibition of the DNC output.



THE STORY OF AUTISM: Purkinje Cell Firing Timing

Unfortunately, what gets inhibited in the climbing fiber – purkinje cell feedback loop **is essential error checking and correction!**

What gets inhibited is the very information that would prevent all the sensory motor problems that cause autism.

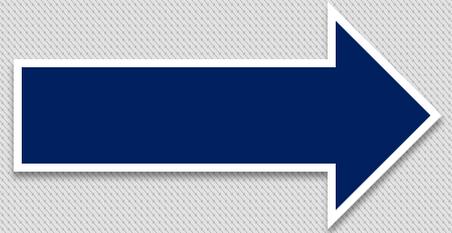


THE STORY OF AUTISM: Purkinje Cell Firing Timing

FOOTNOTES:

8. <https://www.psychologytoday.com/us/blog/the-athletes-way/201411/how-are-purkinje-cells-in-the-cerebellum-linked-autism>
9. <https://www.psychologytoday.com/us/blog/the-athletes-way/201411/how-are-purkinje-cells-in-the-cerebellum-linked-autism>

GO ON TO THE NEXT PRESENTATION



The Story of
AUTISM

PART 17:
DYSMETRIA
OF THOUGHT
AND
MOVEMENT

