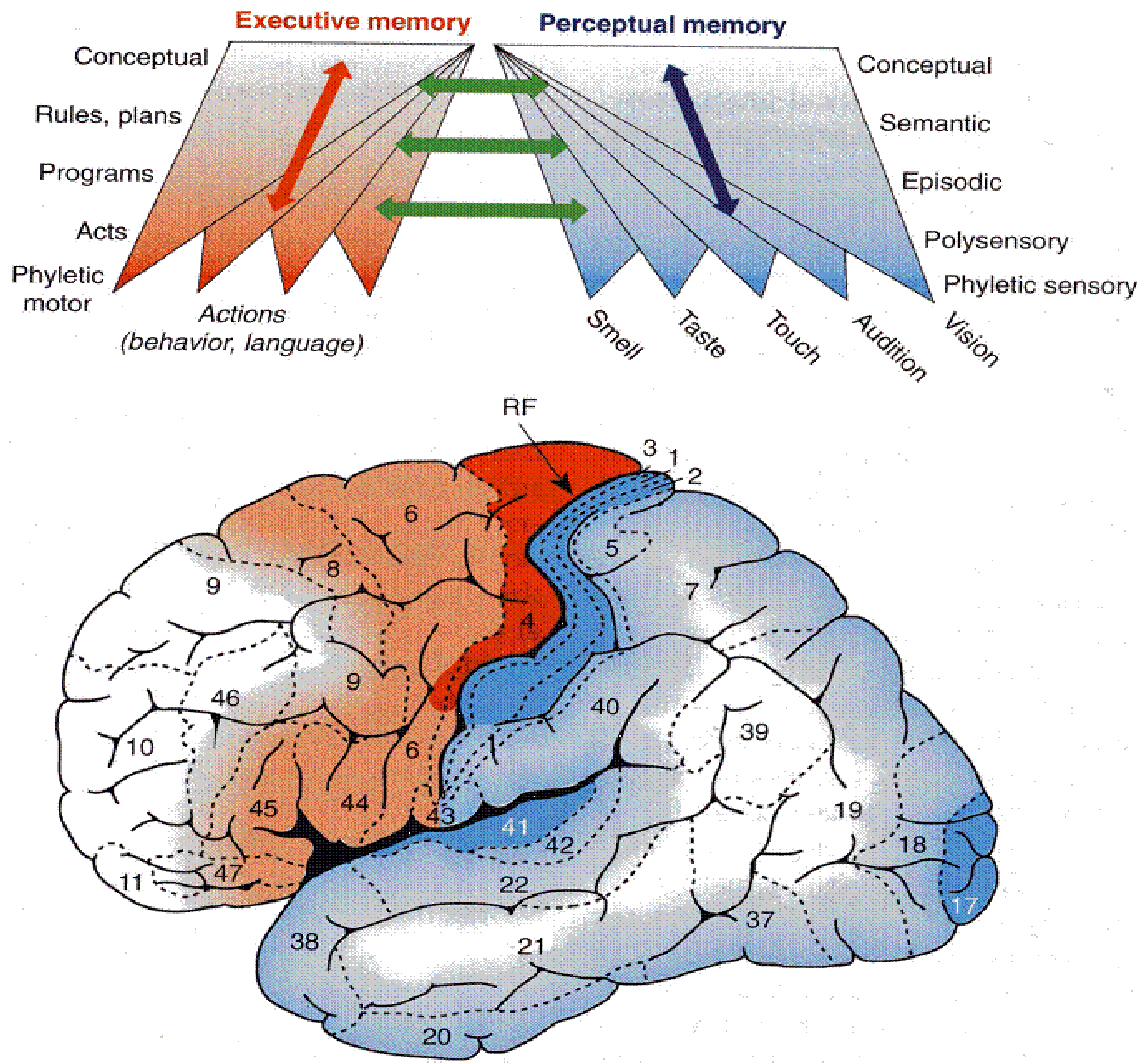
Computational cognitive neuroscience: 10. Prefrontal Cortex (PFC)

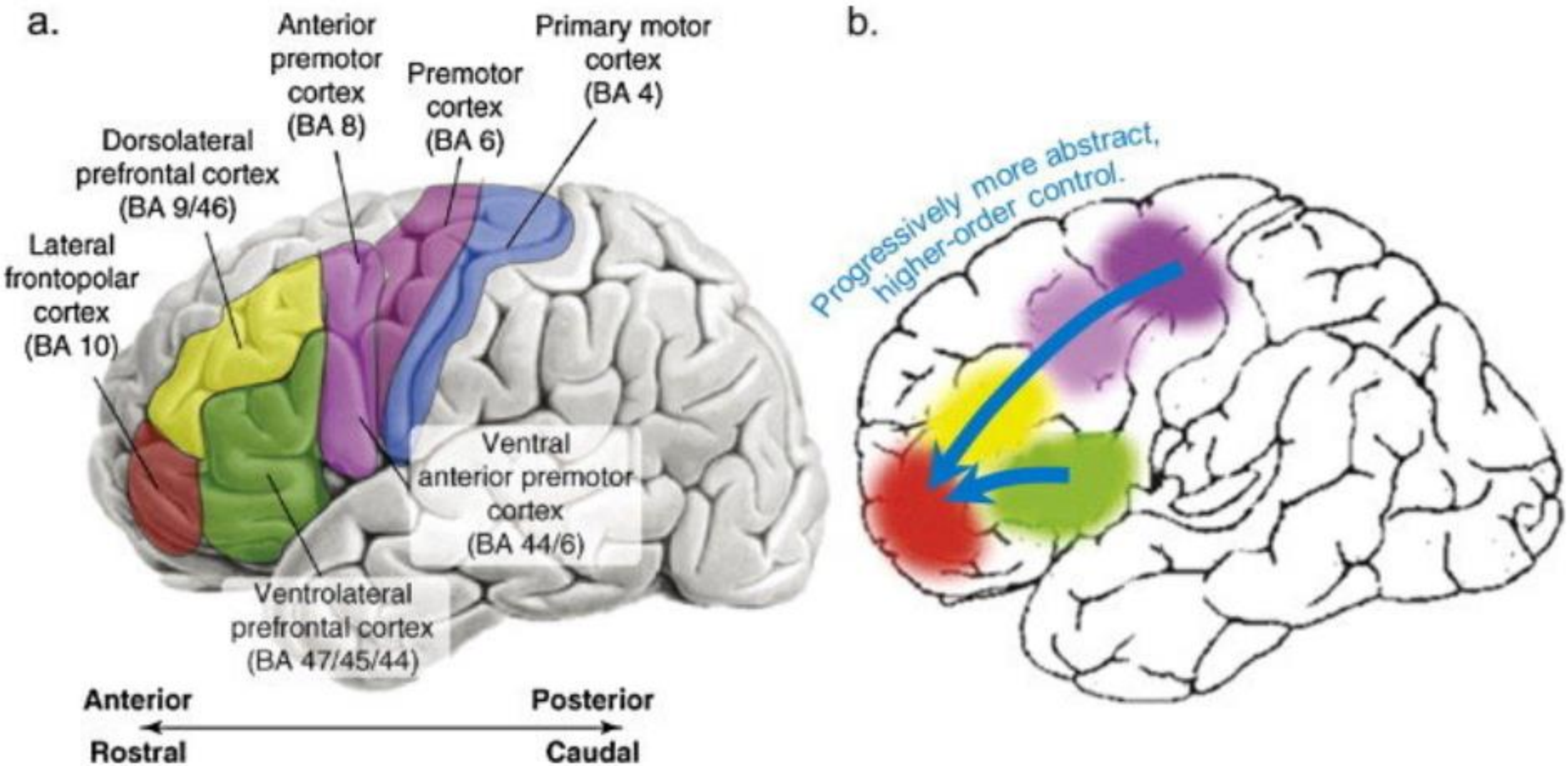
Lubica Beňušková
Centre for Cognitive Science, FMFI
Comenius University in Bratislava

“division of labour in the brain”



Prefrontal Cortex (PFC)

- Progressively more anterior PFC regions support cognitive control of progressively more abstract and temporally extended representations (Dumontheim, Dev. Cogn. Neurosci., 2014, doi 10.1016/j.dcn.2014.07.009)



PFC connectivity with sensory and motor areas

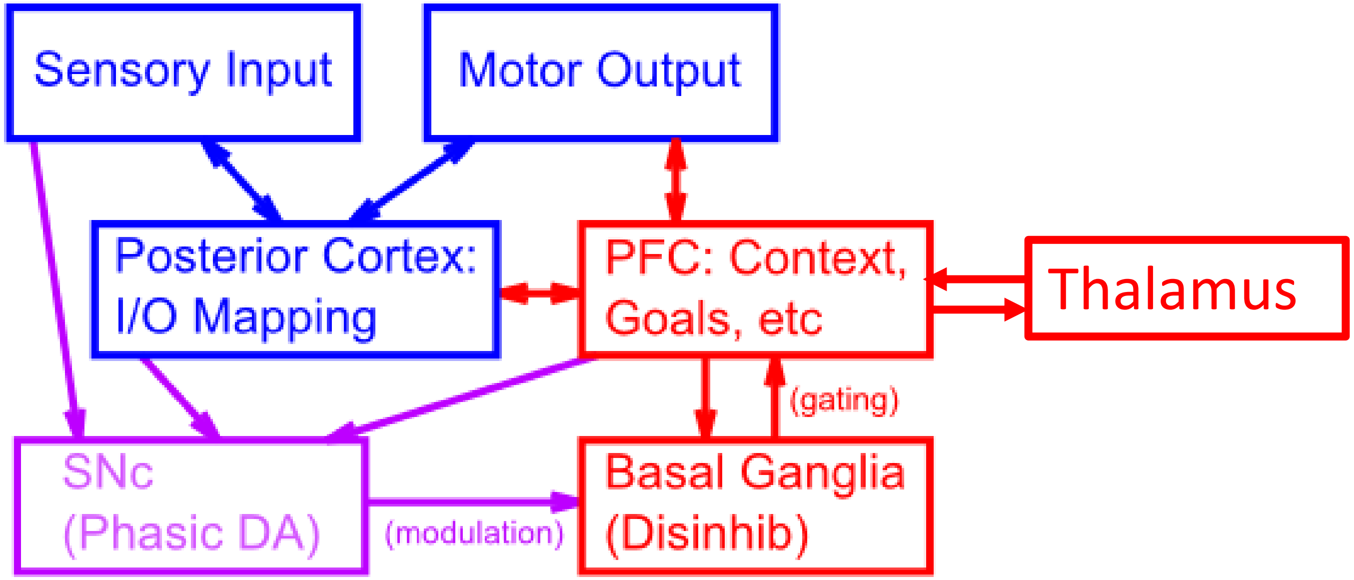
- The overall connectivity of the areas that are particularly important for executive function in relation to the sensory and motor processing

- The PFC is interconnected with higher-level association cortical areas in posterior cortex where highly processed and abstracted information about the sensory world is encoded.

- It also interconnects with higher-level motor control areas (premotor cortex, supplementary motor areas), which coordinate lower-level motor control to execute sequences of coordinated motor outputs.

- With this pattern of connectivity, PFC is in a position to both receive from, and exert influence over, the processing going on in posterior and motor cortex.

Connectivity schematics



- **PFC** also provides the **top-down** control over posterior cortical processing to ensure that interpretation of data is context appropriate.
- The **SNc** (substantia nigra pars compacta) exhibits **phasic dopamine** (DA) release that modulates the BG circuits thereby training the BG gating signals in response to external reward signals.
- The **BG** exert a **disinhibitory** gating over the excitatory loop between PFC and the thalamus, which controls updating of info in the PFC.

Maintenance and updating of info in the PFC

- The whole PFC has some special biological properties that enable it to *hold onto information in the face of distraction*, e.g., from incoming sensory signals or distracting thoughts.

- We refer to this ability as a **robust active maintenance** because it depends on the ability to keep a population of neurons actively firing over some duration needed to maintain a goal.

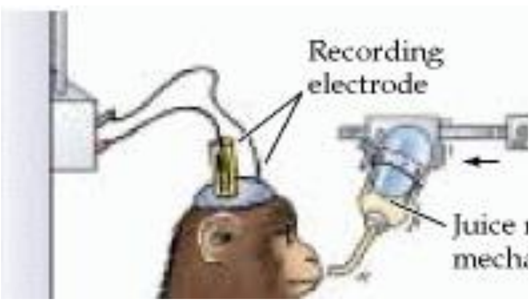
- Another important executive function is the *ability to rapidly shift behaviour or thought in a strategic manner* (often referred to as cognitive flexibility).

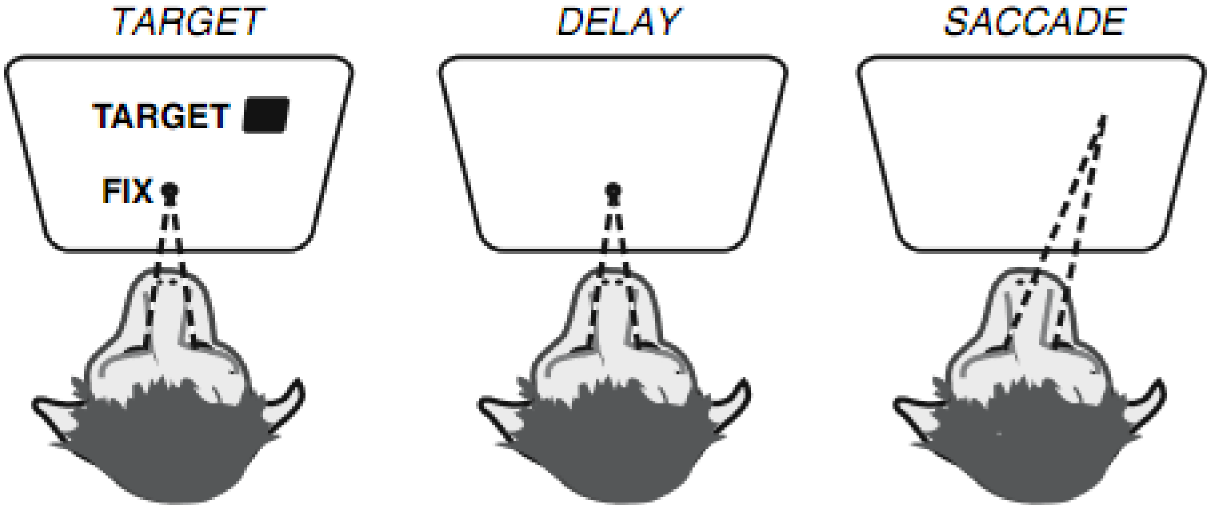
- The ability to **rapidly update what is being actively maintained** in the PFC is what enables the PFC to rapidly change behaviour or thought by updating the pattern of active neural firings in the PFC.

Robust active maintenance: experiment (1971)

- Oculomotor delayed or delayed saccade (i.e. voluntary eye movement) response task:

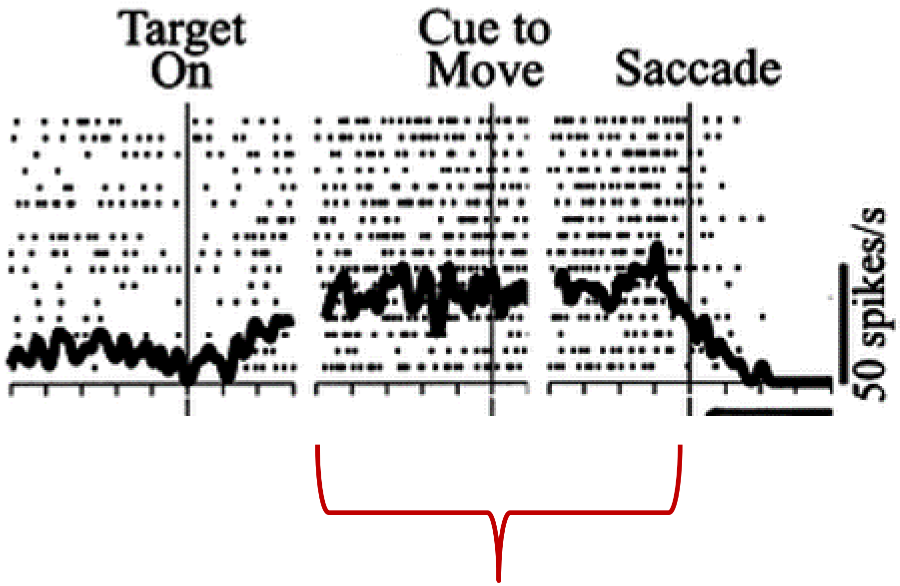
1) A target stimulus is flashed in a particular location of a video display.
2) The monkey is trained to maintain its eyes focused on a central fixation point until that point goes off (i.e. disappears).
3) At that point, the monkey must move its eyes to the previously flashed location in order to receive a juice reward.





Robust active maintenance: neurons

- Spikes (background dots) and curve of activity rate for an individual cell recorded in the frontal eye fields (FEF) during a delayed saccade task.



- Neurons in the FEF show robust delay-period firing and this activity terminates just after the monkey correctly moves its eyes after the delay.

- *This cell maintained its activity during the delay* so as to enable other cells to generate a correct saccade at the end of the trial.

Robust active maintenance: mechanisms

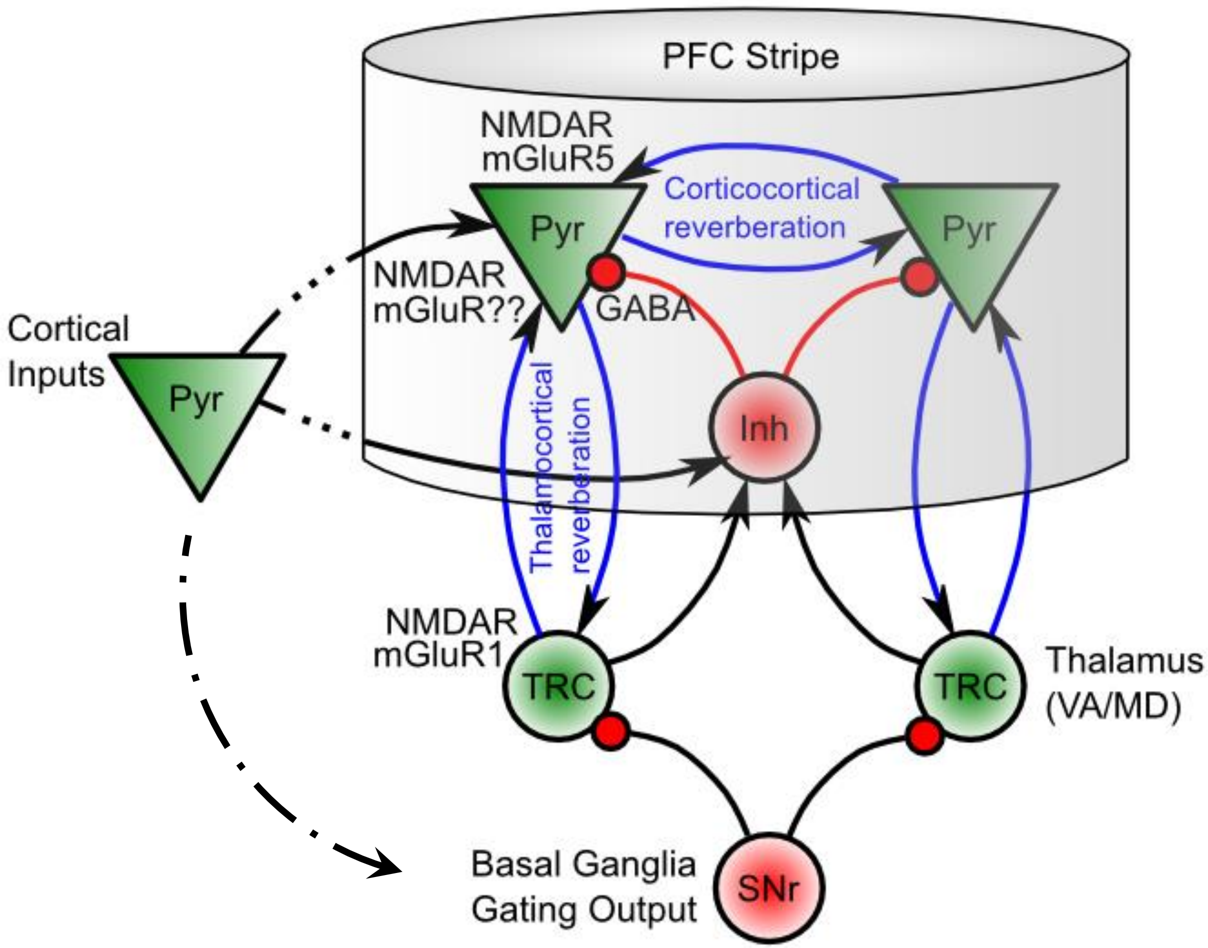
- There are two primary biological mechanisms that enable PFC neurons to exhibit sustained active firing over time:

- **Recurrent excitatory connectivity:** Populations of PFC neurons have strong excitatory interconnections, such that neural firing reverberates back-and-forth among these interconnected neurons, resulting in sustained active firing.

- There are two types of such connections:
  - 1) a **corticocortical loop** among pyramidal cells in the same PFC stripe, and;
  - 2) a **corticothalamocortical** loop between lamina VI pyramidal cells in PFC and the thalamic relay cells that project to that particular group of cells.

Recurrent excitatory connectivity

- Both, corticocortical and thalamocortical interconnections, use mutually supportive **recurrent excitation** plus **intrinsic maintenance currents** (mediated by the postsynaptic receptors NMDARs and mGluRs).



Intrinsic excitatory maintenance currents

- At the synapses formed by both of the recurrent excitatory loops there are **NMDA and metabotropic (mGluR)** receptors that, once opened by high frequency activity, provide for reverberant activity going.

- NMDA channel requires the neuron to be sufficiently depolarized to remove the Mg^{+} (magnesium) ions that otherwise block the channel. This activity-dependent nature is ideally suited to provide for only those neurons that have already been sufficiently activated will benefit from the increased excitation provided by these NMDA channels.

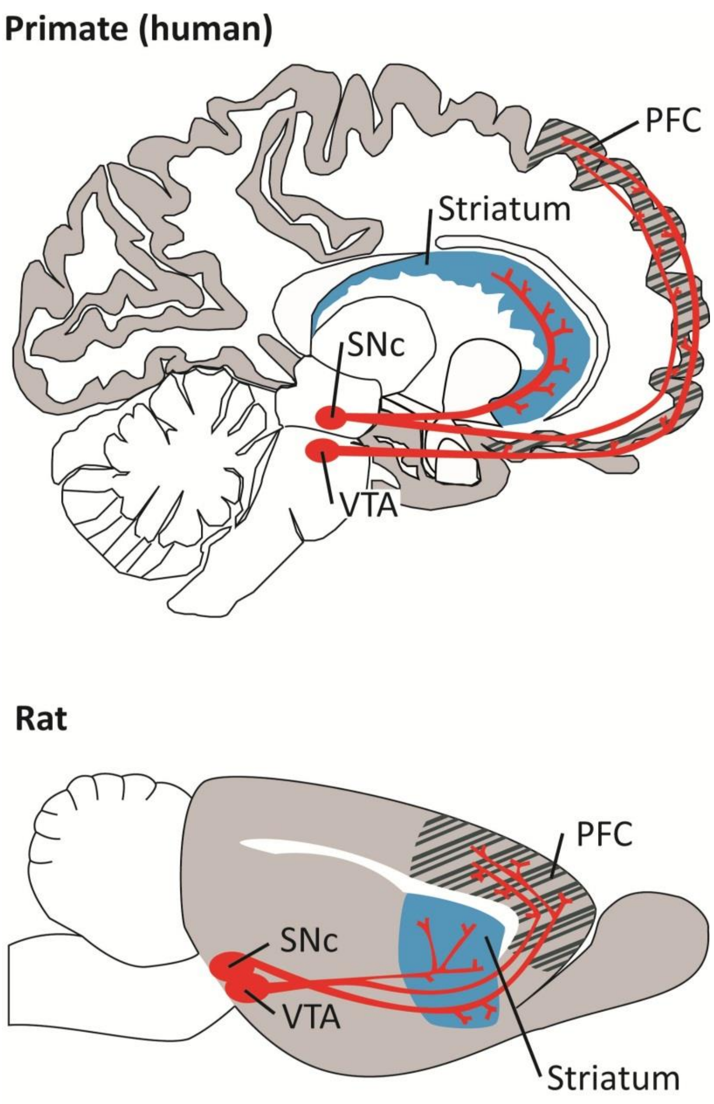
- This provides a "hook" for the **basal ganglia system to control active maintenance**: when the thalamic neurons are disinhibited via a BG gating action, the ensuing burst of activity enables a subset of PFC neurons to get over their NMDA Mg+ block thresholds, and thereby continue to fire robustly over time.

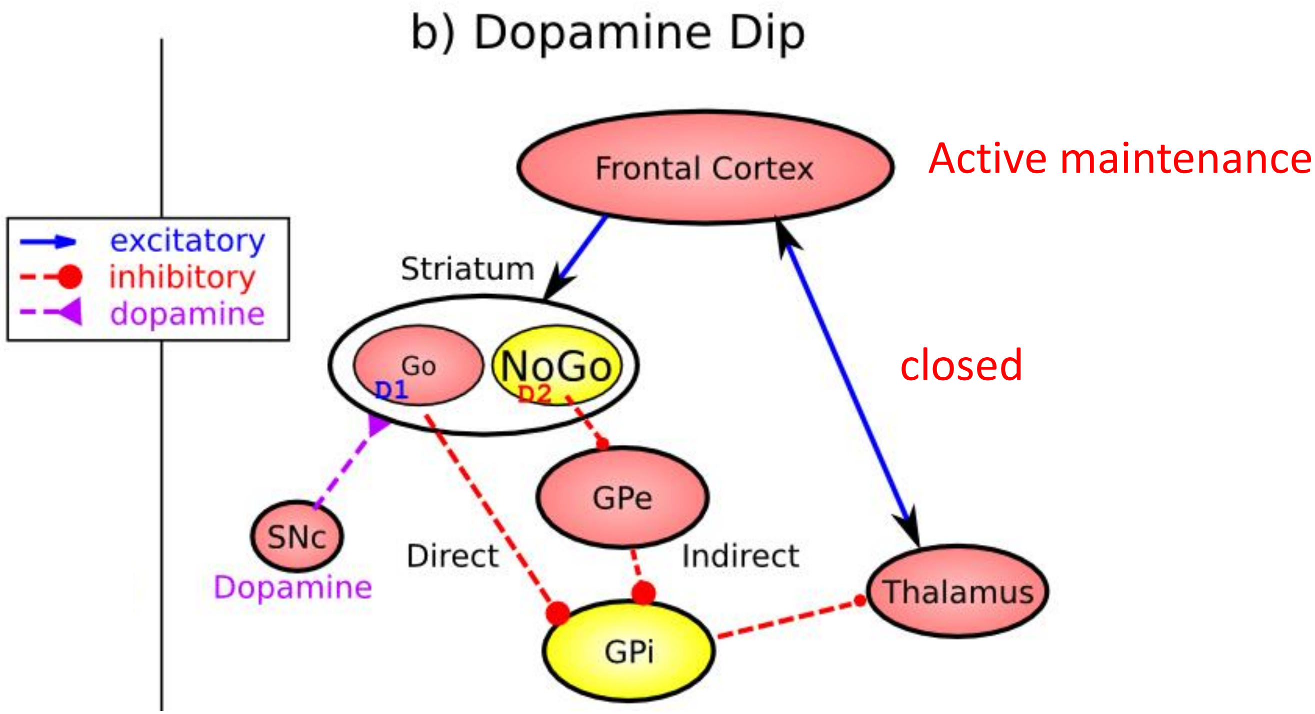
Prefrontal cortex and dopamine

- A critical biological mechanism for executive function, is the firing of **Dopamine neurons in the midbrain** (ventral tegmental area (VTA) and substantia nigra pars compacta (SNc)).

- The level of release of dopamine oscillates based on the presence or absence of a reward.

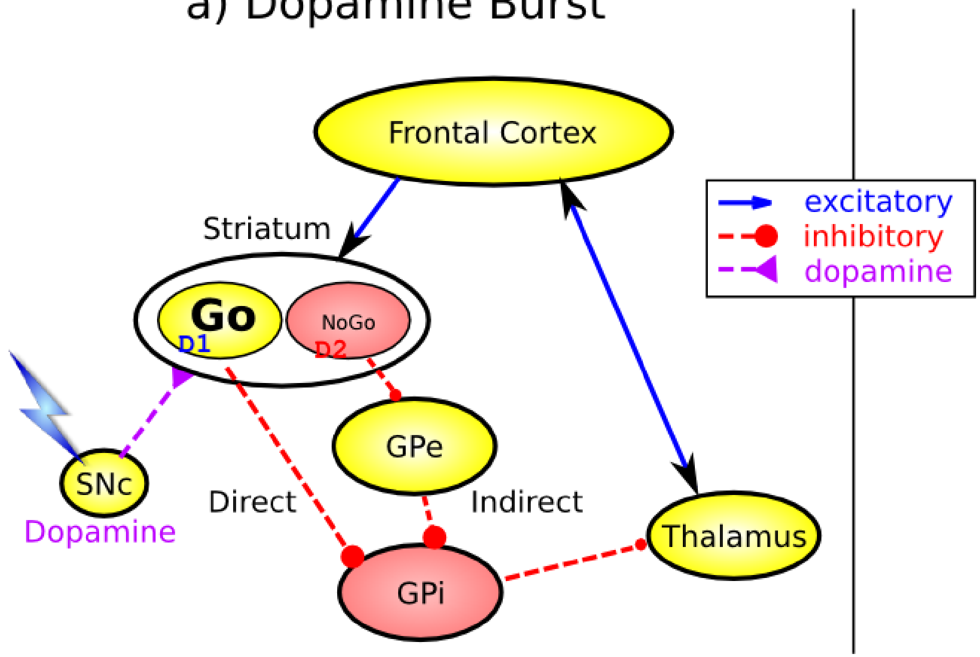
- Reward is evaluated by the PFC and the PFC itself modulates the dopamine release in the midbrain.





- DA dip (decrease in DA neuron firing in SNc) leads to preferential activity of indirect "**NoGo**" pathway neurons in the striatum, which inhibit the external segment globus pallidus neurons (GPe), that inhibit the GPi.
- Increased **NoGo** activity thus results in disinhibition of GPi, making it more active and thus inhibiting the thalamus, preventing initiation of a new reverberant activity in the thalamo-cortical loop, i.e. TC loop is silent.
- Since the thalamus acts as a gate, no new information is allowed to the PFC, which maintains an old activity pattern.

a) Dopamine Burst

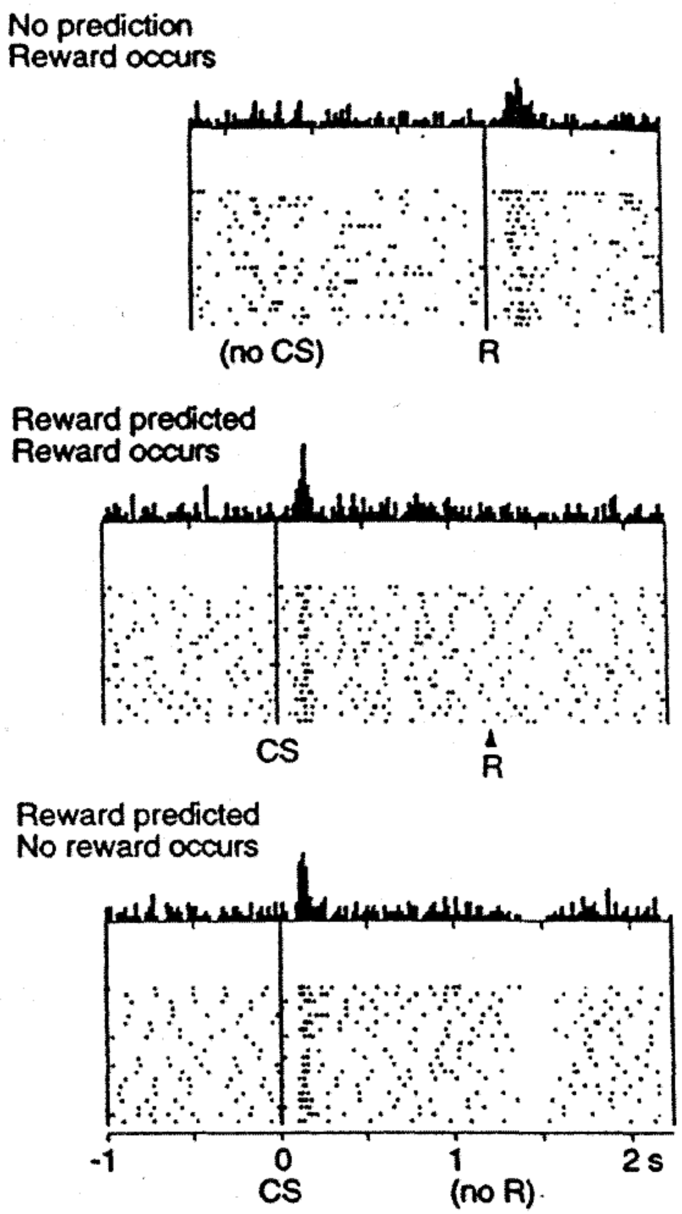


- DA burst activity drives the direct "**Go**" pathway neurons in the striatum, which then inhibit the activation in the globus pallidus internal segment (GPi), which releases specific nuclei in the thalamus from inhibition, allowing them to complete a bidirectional excitatory circuit with the frontal cortex, resulting in the initiation of an updating to a new pattern of neural firing.
- The increased **Go** activity during DA bursts results in potentiation of cortico-striatal synapses, and hence learning to select actions that tend to result in positive outcomes.

Phasic DA and temporal credit assignment

- Dopamine neurons in the midbrain initially respond to primary rewards (e.g., apple juice), but then learn to fire at the onset of conditioned stimulus (CS) that reliably predicts the primary reward.

- *This is caused by the shift of the DA release to the time of the onset of CS due to reinforcement learning that something nice will follow CS –* ***temporal credit assignment (expectation).***



Relation of robust maintenance to working memory (WM)

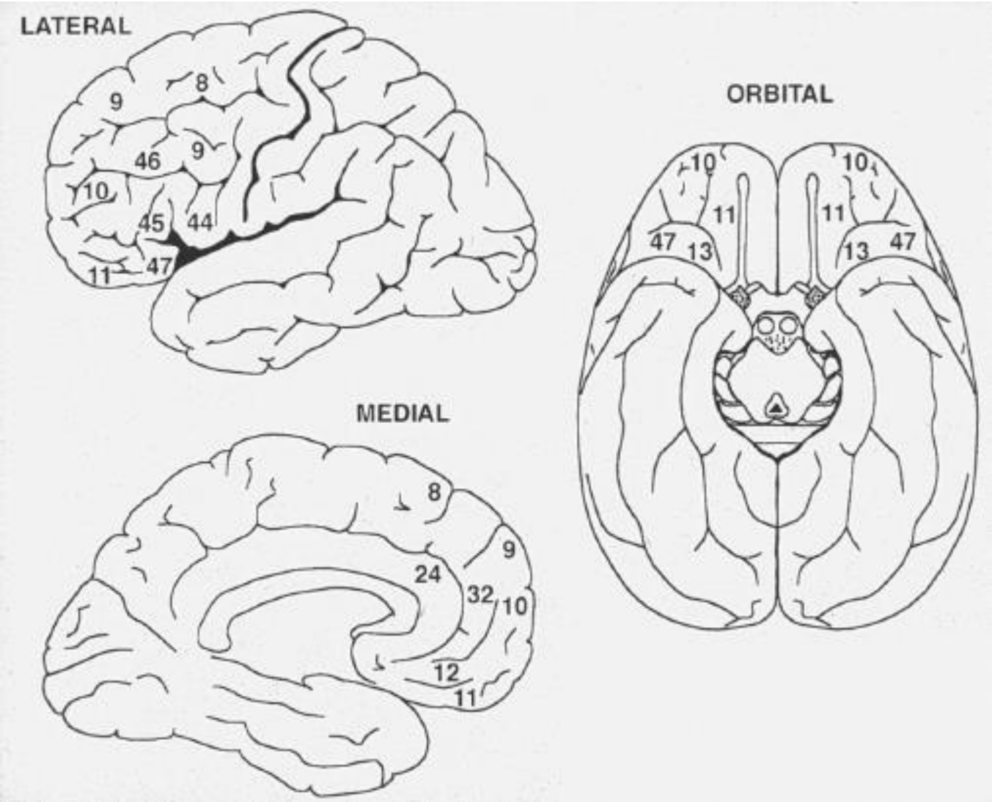
- Working memory (WM), a core executive function, is a memory buffer that is responsible for the transient holding of information. It is the ability to remember information over a brief period (in the order of seconds).
  - Other suggested names have been short-term memory, operant memory, and provisional memory.

- **Working memory** is generally considered to have a **limited capacity**. The earliest quantification of the capacity limit was the "magical number seven" suggested by Miller in 1956, i.e., the capacity of young adults is around seven simultaneous elements, which he called "chunks“.

- Later research revealed this number depends on the category of chunks used (e.g., span may be around seven for digits, six for letters, and five for words). It seems this limited capacity is related to how many relationships between the variables we can actively maintain.

Functional specialization of PFC

- The mechanisms for robust active maintenance exist across the PFC, but different PFC areas have been associated with different contributions to overall executive function.
- Lateral, orbital, medial areas of the prefrontal cortex display differences in connectivity with other parts of the brain.



The lateral and medial PFC

- **The lateral PFC** areas are interconnected with **sensory and motor** areas and play a role in controlling the processing in these areas.

- **The medial PFC** areas are more strongly interconnected with subcortical brain areas associated with **affective and motivational** functions.

- Functionally we can characterize the lateral areas as being important for "cold" cognitive control, while the medial areas are important for "hot" emotional and motivational processing.

- However, this distinction is not as clear cut as it sounds, as even the lateral areas are subject to modulation by motivational variables and BG/dopamine gating signals based on the maintained cognitive information being predictive of a task success (reward).

Dorsal and ventral areas in the **lateral PFC**

- The dorsal lateral PFC areas interconnect more with the dorsal pathway in the posterior cortex, while ventral PFC interconnects with the ventral posterior cortical pathway.

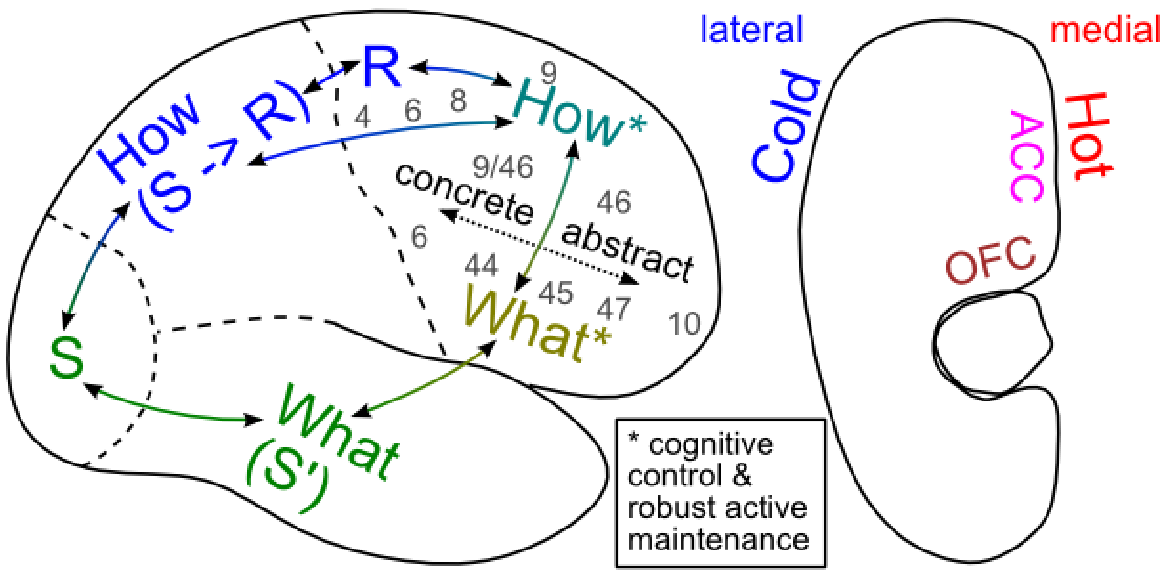
- The **dorsal** pathway in the posterior cortex is specialized for perception-for-action (**How** processing): extracting perceptual signals to drive motor control, while the **ventral** pathway is specialized for perception-for-identification (**What** processing).

- The **dorsal lateral PFC** (DLPFC) areas are particularly important for executive control over motor planning and top-down for the parietal cortex.

- while **ventral lateral PFC** (VLPFC) areas are particularly important for control over the temporal lobe pathways that identify entities in the world, and also form rich semantic associations about these entities.

Dorsal and ventral areas in the lateral PFC

- *Left figure*: the What versus How distinction for lateral posterior cortex can be carried forward into the PFC, to understand the distinctive roles of the **ventral (What)** and **dorsal (How)** areas of PFC (O'Reilly 2020).



- *Right figure*: distinction between the functions of lateral (cold) versus medial and orbitofronal PFC (hot).

Dorsal and ventral areas in the **medial** PFC

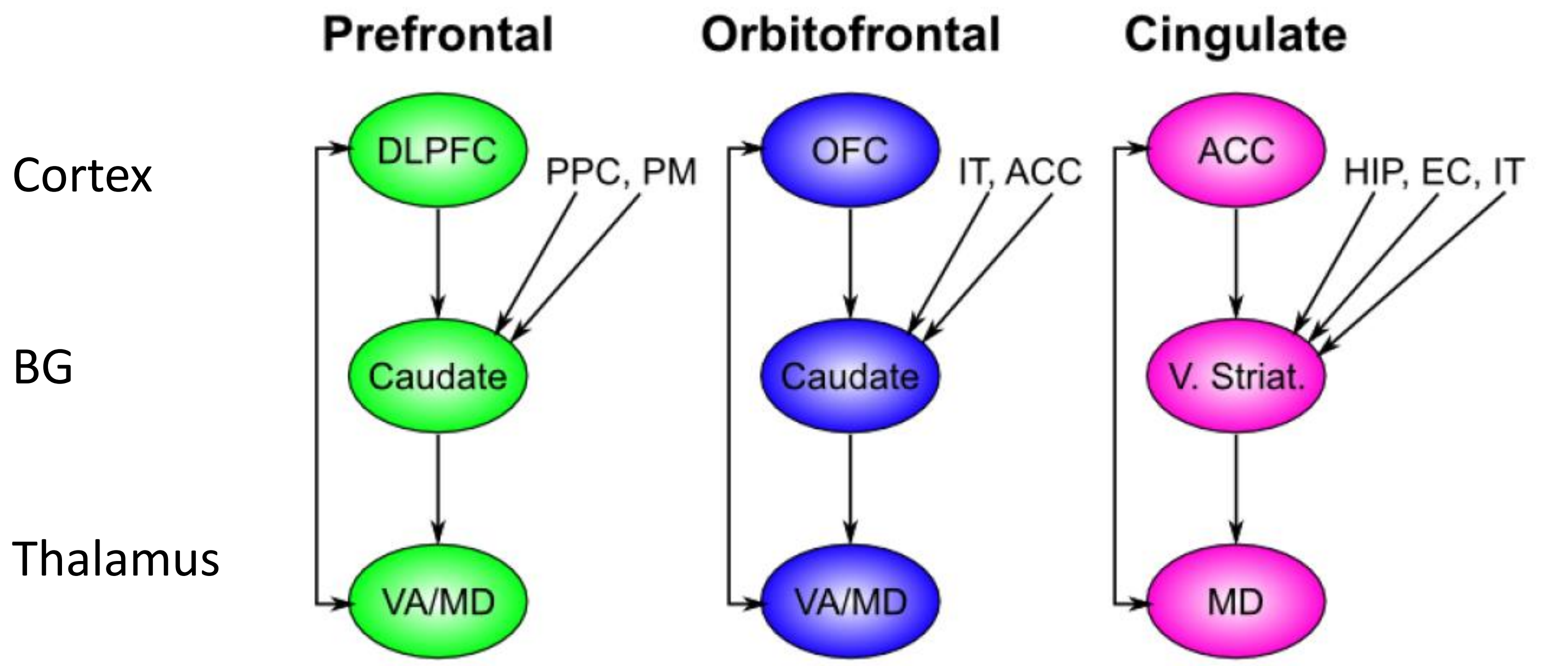
- The **dorsal medial** PFC is also known as the *anterior cingulate cortex* (ACC), which has been shown to encode the **affective aspects of motor** control variables (e.g., how much effort will an action take, how much conflict and uncertainty is there in selecting a response), which is consistent with a **"hot how"** functional specialization.
  - Dorsomedial PFC areas also project to the subthalamic nucleus and serve to delay motor responding to prevent impulsive choice under difficult response selection demands.

- The **ventromedial** areas of PFC (VMPFC) including the **orbital frontal cortex** (OFC) have been shown to encode the **affective value of different sensory** stimuli, consistent with the idea that they are the **"hot what"** areas.

Other executive functions of PFC

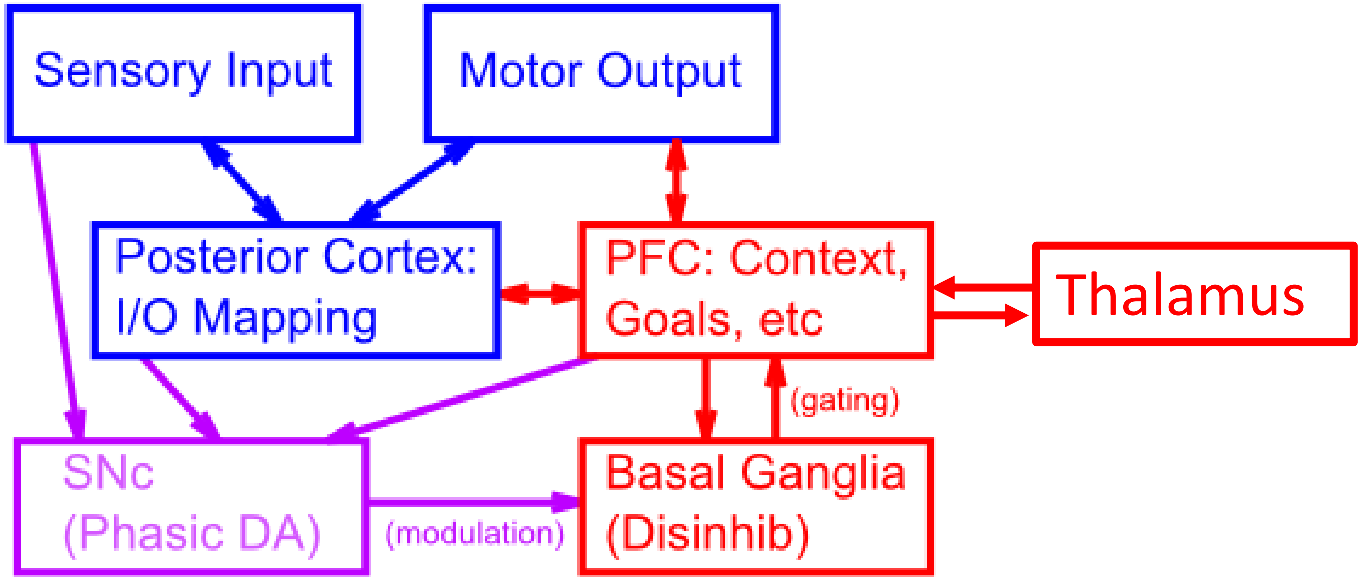
- Highly structured cognitive activities, often involving formal **symbol systems**:
  - learning and/or using mathematics, formal logic, computer programming,
  - creative writing, and structured, rational decision-making.
- All of these require temporally-extended maintenance of task-relevant information, especially of a highly abstract, symbolic nature. The role of **language** in these and many other executive functions is a very important aspect.
- Control over **encoding and retrieval of episodic information** in the hippocampus – it is highly likely that the hippocampus and PFC/BG systems interact significantly in many forms of executive function, with the rapid learning abilities of the hippocampus complementing the transient, flexible active maintenance properties of the PFC.

Cortex, Basal Ganglia and action selection



- **Parallel circuits** through the basal ganglia for different regions of the frontal cortex – each region of frontal cortex has a corresponding basal ganglia circuit.
- **Prefrontal loop**: DLPFC also controlled by posterior parietal cortex (PPC), and premotor cortex (PM). **Orbitofrontal loop**: OFC = orbitofrontal cortex, also receives from inferotemporal cortex (IT), and anterior cingulate cortex (ACC). **Cingulate loop**: ACC also modulated by hippocampus (HIP), entorhinal cortex (EC), and IT.

PFC and BG WM (PBWM) model



- **PFC** provides top-down context and control over posterior cortical processing pathways to ensure that interpretation of data is task and context appropriate.
- The **BG** exert a disinhibitory gating over PFC, switching between robust maintenance and rapid updating.
- The **SNc** (substantia nigra pars compacta) exhibits phasic dopamine (DA) release that modulates the BG circuits, thereby training the BG gating signals in response to the external reward signals.

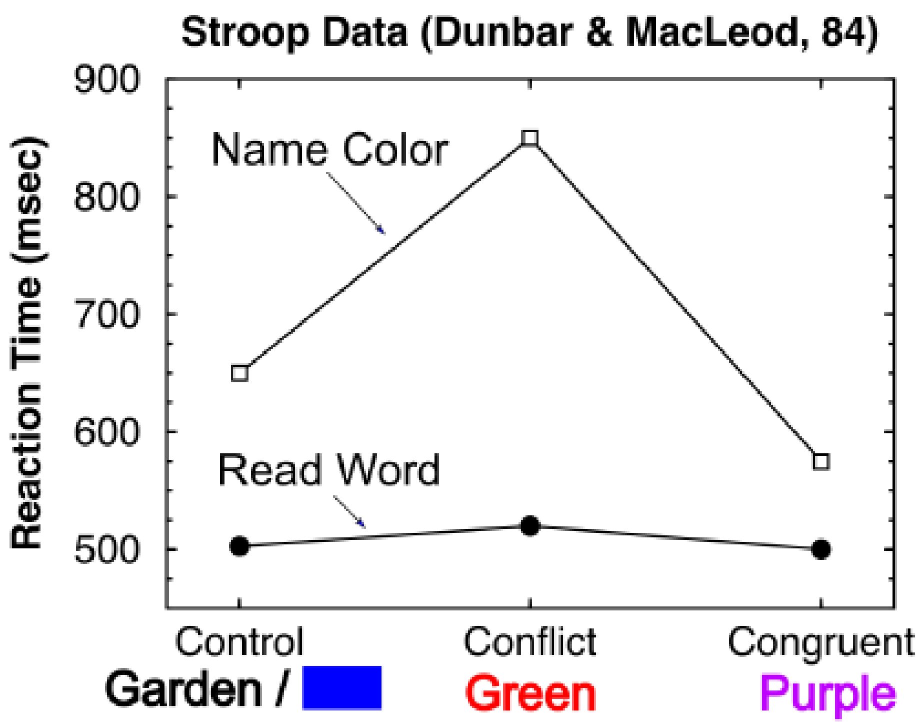
Top-down Cognitive Control: the Stroop effect

- Subjects are presented with colour words (e.g., "red", "green") one at a time and are required to either read the word (e.g., "red"), or name the colour of the ink that the word is written in.
- When asked to name the colour of the word it takes longer and is more prone to errors when the colour of the ink does not match the name of the colour (John Ridley Stroop 1935).

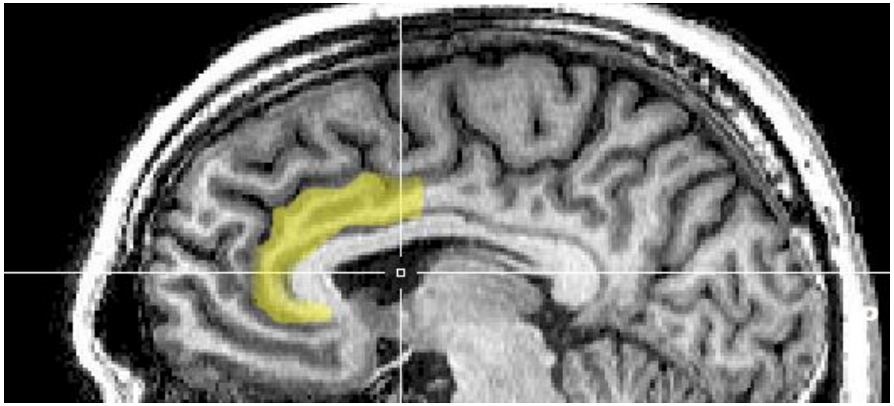
congruent	incongruent
RED	RED
GREEN	GREEN
BLUE	BLUE
PURPLE	PURPLE
RED	RED
BLUE	BLUE

Typical data from neurologically intact participants

- The "Stroop effect" is that error rates and response times are larger for the incongruent condition, i.e., in the case of colour naming.
- The effect has been attributed to the relatively "automatic", well-practiced nature of reading words, so that the natural tendency to read the word interferes with attending to, and naming, the colour.
- https://www.psytoolkit.org/lessons/experiment_stroop.html



Stroop task: neuroimaging



- Two main areas are the anterior cingulate cortex (conflict and uncertainty in selecting a response), and the dorsolateral prefrontal cortex (extracting perceptual signals to drive motor control).
- ACC is responsible for what decision is made (i.e. whether someone will say the written word or the ink colour).
- DLPFC provides for activating the areas of the brain involved in colour perception, but not those involved in word encoding.
- DLPFC does it by an excitatory top-down support to the weaker pathway (colour naming), which then enables this pathway to better compete with the more dominant word reading pathway.

Stroop effect: uses

- Among the most important uses is the creation of validated psychological tests based on the Stroop effect permit to measure a person's selective attention capacity and skills, as well as their processing speed ability.

- It is also used in conjunction with other neuropsychological assessments to examine a person's executive processing abilities, and can help in the diagnosis and characterization of different psychiatric and neurological disorders.

- Researchers also use the Stroop effect during brain imaging studies to investigate regions of the brain that are involved in planning, decision-making, and managing real-world interference (e.g., texting and driving).

PFC strength and the A-not-B task

- Devised by the developmental psychologist Jean Piaget (1896-1980).
- The task involves hiding a desirable object at location A for several trials and then hiding it at a new location B.
- The error is that infants < 12 months perseverate in searching at A from where they have successfully retrieved the object several times, sometimes even when the object is visible at the new location B.

- The task requires infants both to hold a retrieval plan in mind and to suppress a previously reinforced response.
- A short-term (working) memory constraints have to be overcome in order to perform the task correctly.

Summary of key points

- The PFC encodes information in an active state through **sustained neural firing**, which is more flexible and **rapidly updatable** than using synaptic weight changes.
- The basal **BG drives updating** of PFC active memory states through dynamic gating via the thalamus (Go and No-Go pathways).
- Dopamine neurons in the midbrain initially respond to primary rewards but can learn to fire at the onset of conditioned stimulus (CS) that reliably predicts the primary reward.
- The **PFC influences cognitive processing** elsewhere in the brain via top-down excitatory biasing (e.g., the Stroop effect).
- Medial and ventral areas of PFC (orbital prefrontal cortex (OFC) and anterior cingulate cortex (ACC)) convey affective and emotional information about stimuli and actions, respectively, and are important for properly evaluating potential actions to be taken.