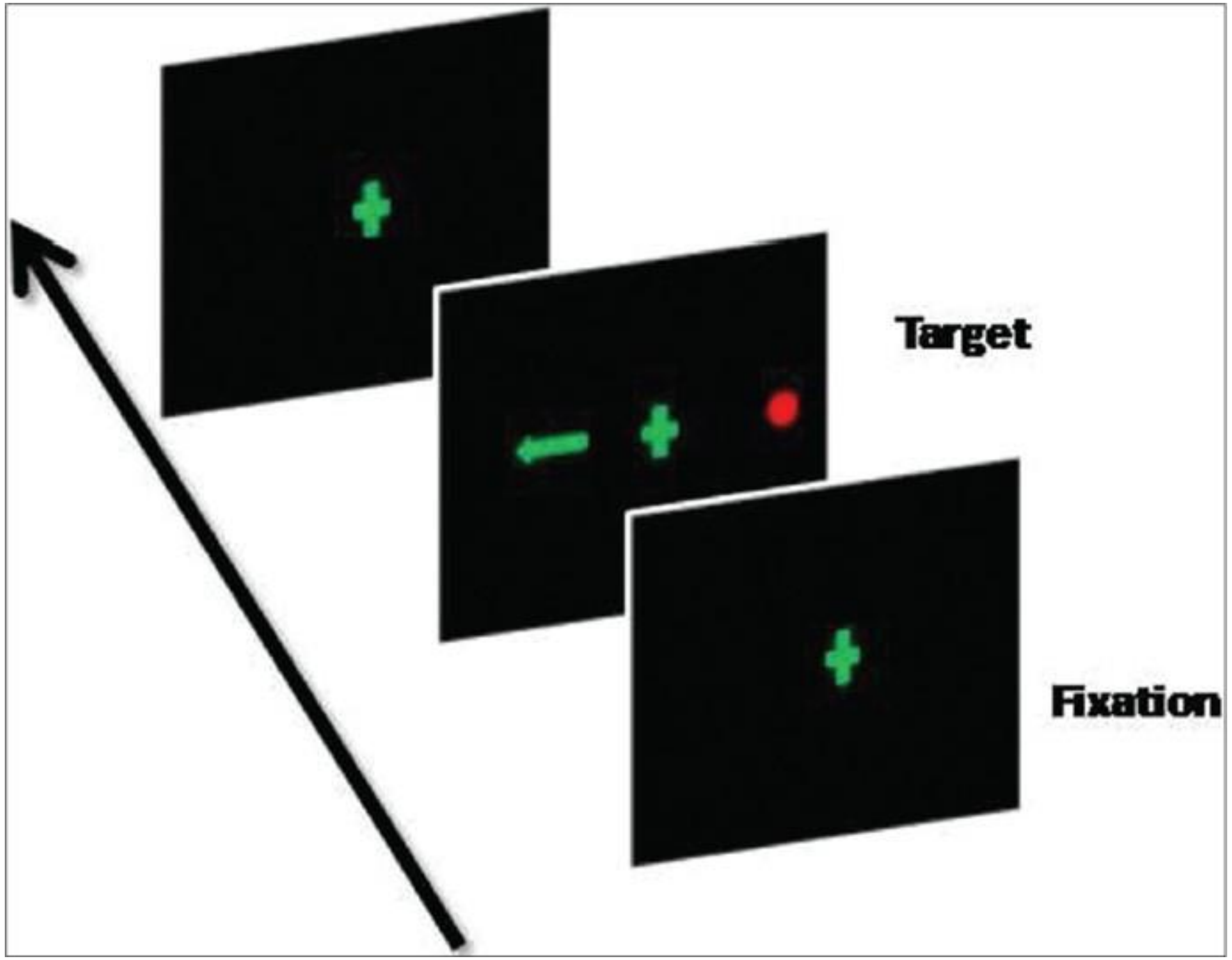
Antisaccades: an overview

Sofia Krasovskaya

8th VML Research Seminar

Nov 9th, 2018

What is an antisaccade?



- A voluntary eye movement made in the direction opposite to the side where a stimulus is presented.
- The subject is asked to fixate a small dot (cross) for some time. A stimulus is presented to one side and the subject is asked to inhibit a reflex eye movement towards it but to make a saccade in the opposite direction.
- Analysis of the errors and latencies indicate dysfunction in the frontal lobe, which controls saccades.

- Millodot: Dictionary of Optometry and Visual Science, 7th edition. © 2009 Butterworth-Heinemann
- Srivastava A, Sharma R, Sood SK, Shukla G, Goyal V, Behari M. Saccadic eye movements in Parkinson's disease. Indian J Ophthalmol [serial online] 2014 [cited 2018 Nov 9];62:538-44. Available from: http://www.ijo.in/text.asp?2014/62/5/538/133482

Why do we need antisaccades?

PRIMARY AND SECONDARY SACCADES TO GOALS DEFINED BY INSTRUCTIONS

P. E. HALLETT

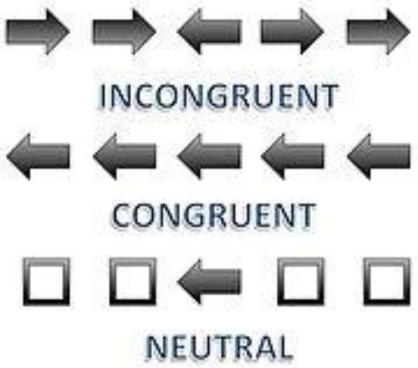
Department of Physiology, University of Toronto, Toronto, Ontario, Canada, M5S 1A8

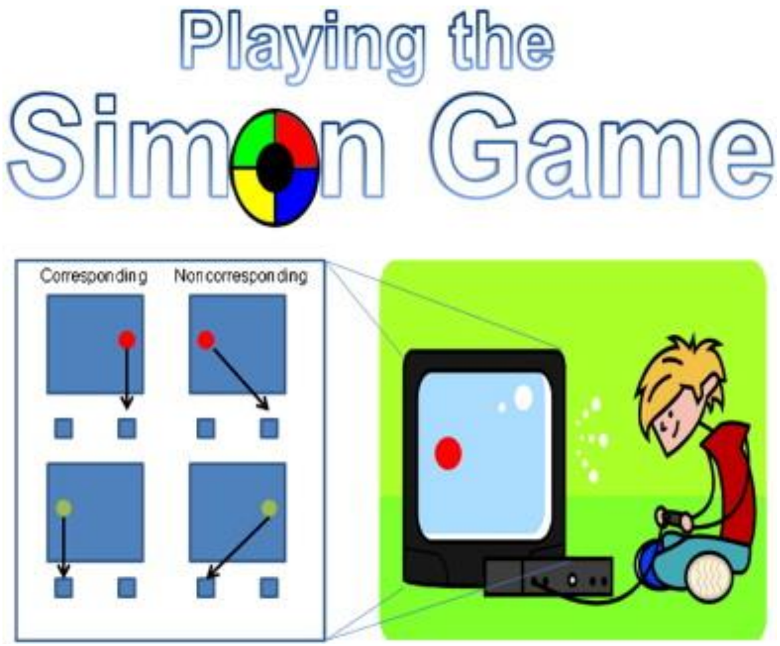
(*Received 6 July 1977; in revised form 7 December 1977*)

Abstract—A luminous point steps horizontally in the dark, and the subject tracks it (normal task), or is instructed to respond by some other horizontal eye movement (e.g. an equal and opposite movement—the "anti-saccade" task). Eye movements in the "anti-task" are characterized by long latency, inaccurate primary saccades which sometimes show minor anomalies in velocity profile. The secondary saccades are large, corrective, of shorter than primary latency, and are not based on retinal feedback. Thus, the human saccadic system is optimized for, but not restricted to, foveation. The highly idiosyncratic "anti" latency data can be normalized by reference to the Wheeless 2-step paradigm. A mechanism is proposed.

- The anti-saccade test was initially described by **Peter Hallet (1978).**
- an important task for investigating the flexible control that we have over behaviour.
- This ability to control behaviour flexibly, responding automatically to stimuli in one situation and suppressing this automatic response in favour of an alternative response in a different situation, is the hallmark of **executive control.**
- The Saccadic eye movement system provides an excellent model for investigating this ability of the brain because eye movements are easy to measure in the laboratory and because we have considerable knowledge of the neural networks that participate in controlling gaze.

Studying flexibility

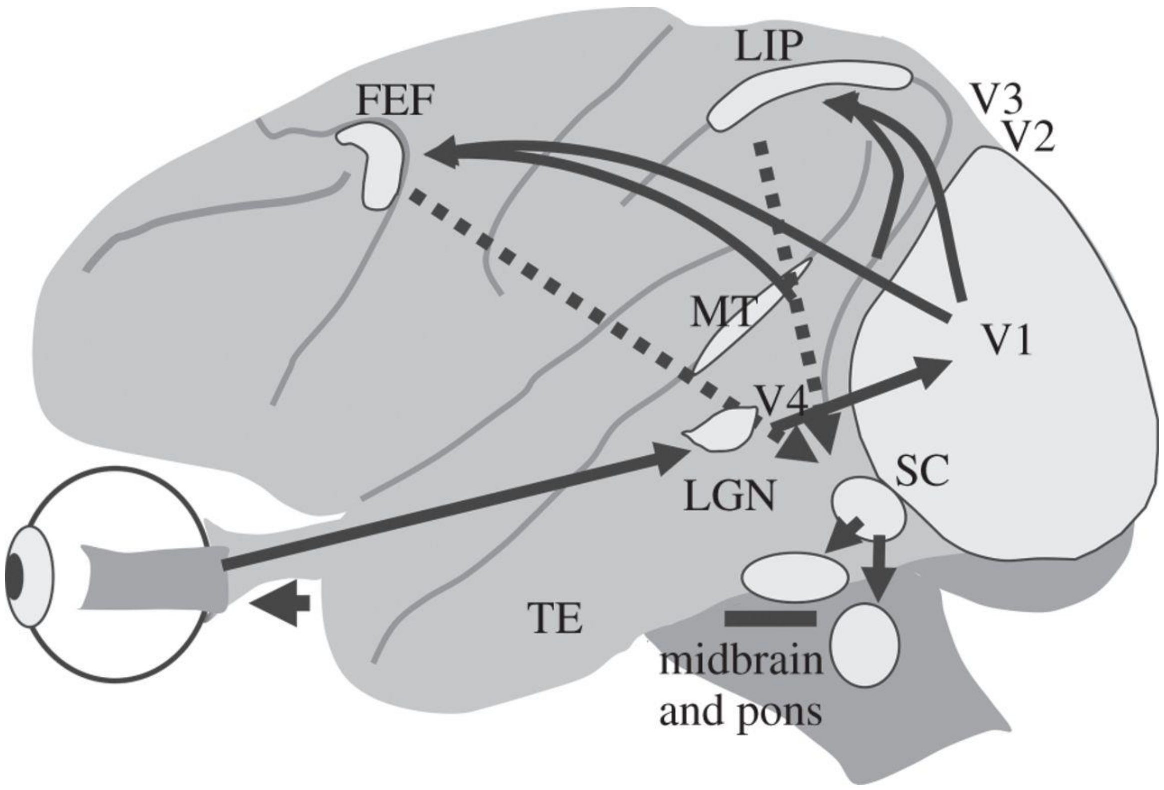


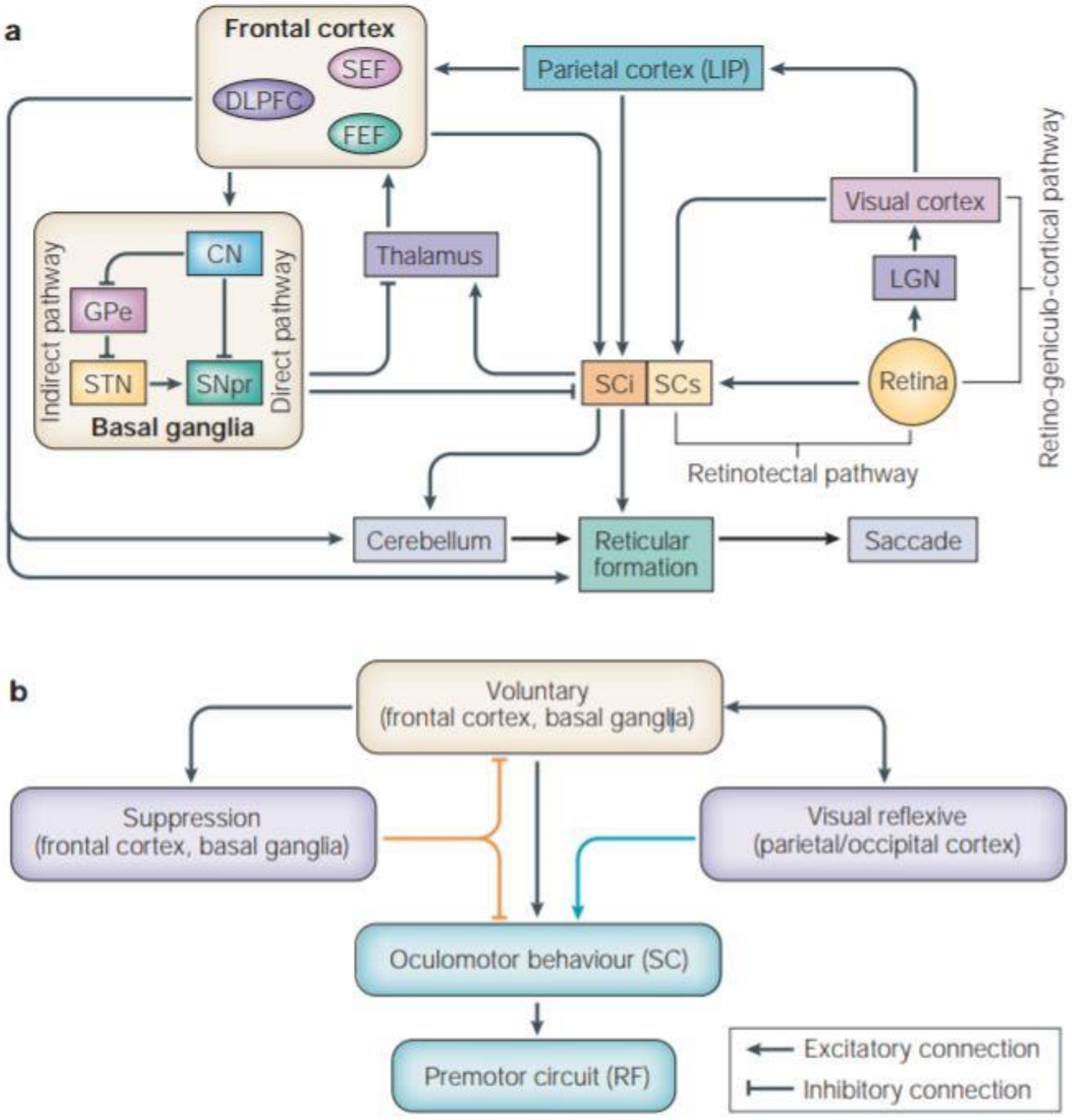


- Different behavioural paradigms have been developed to study the ability of the brain to respond flexibly to our environment (antisacc, Stroop, Eriksen's Flanker, Simon task).
- The anti-saccade task contains a manipulation of stimulus–response compatibility that decouples stimulus encoding and response preparation.
- 2 steps for correct performance:
    1) Suppression of the automatic response to look at the target (pro-saccade);
    2) Vector inversion: transformation of the location of the stimulus into a voluntary motor command to look away from the target (anti-saccade).

Neurophysiological circuits

- **Munoz, D. P., & Everling**, S. (2004). Look away: the anti-saccade task and the voluntary control of eye movement. Nature Reviews Neuroscience, 5(3), 218–228. doi:10.1038/nrn1345
- Many cortical and subcortical structures are involved in the suppression and/or generation of saccadic eye movements
- Single-neuron activity has been recorded in a number of these brain areas in monkeys performing the anti-saccade task, including the dorsolateral prefrontal cortex (**DLPFC**), the lateral intraparietal area (**LIP**), the supplementary eye fields (**SEF**), the Frontal eye fields (**FEF)** and the Superior Colliculus (**SC).**
- The SC forms a vital node in the saccade network because it **receives convergent input** from almost all of the cortical and subcortical structures that are involved in controlling saccades. The FEF & SC project directly to the paramedian pontine reticular formation to provide the necessary input to the saccadic premotor circuit for **saccade initiation**.
- Understanding how neurons in the SC and FEF participate in the suppression of automatic responses and the generation of goal-directed saccades is crucial for explaining behaviour in the anti-saccade task.





Direct Pathway:

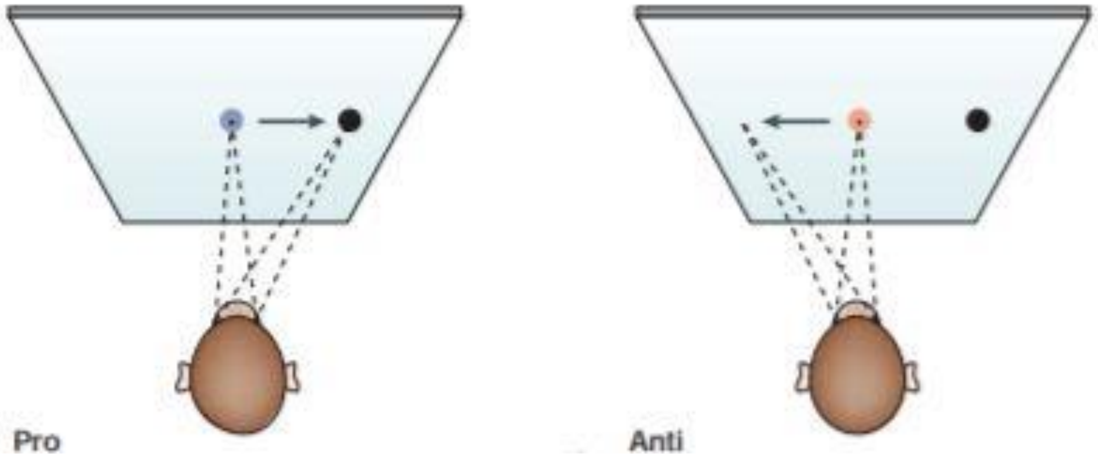
1) The retino-geniculo-cortical pathway to the primary visual cortex and the retinotectal pathway to superficial layers of the SC. Visual information is processed through several extrastriate visual areas (V3, V4, MT) before it is passed on to motor structures to affect action.
2) The lateral intraparietal area (LIP) is at the interface between sensory and motor processing. The LIP projects to the intermediate layers of the SC and the frontal cortical oculomotor areas: FEF, SEF and DLPFC.
3) FEF – execution of voluntary saccades. SEF - internally guided decision-making and sequencing of saccades. DLPFC - executive function, spatial working memory and suppressing automatic, reflexive responses. All these frontal regions project to the SC - a vital node in the premotor circuit where cortical and subcortical signals are integrated.
4) The FEF, SEF and SC project directly to the paramedian pontine reticular formation to provide necessary input to the saccadic premotor circuit so that a saccade is initiated or suppressed.
5) Frontal cortical oculomotor areas also project to the CN. GABA neurons in the CN project through the direct pathway to the SNpr. Neurons in the SNpr form the main output of the basal ganglia circuit: they contain GABA and project to the intermediate layers of the SC and to nuclei in the thalamus that project to the frontal cortex.
6) Cortical inputs to the direct pathway lead to disinhibition of the SC and thalamus because these signals pass through two inhibitory synapses.

Indirect Pathway:

1) Through the basal ganglia, in which a separate set of GABA neurons in the CN project to the external segment of the globus pallidus (GPe).
2) GABA neurons in GPe then project to the subthalamic nucleus (STN). Neurons in the STN send excitatory projections to neurons in the SNpr, which in turn project to the SC and thalamus.
3) Cortical inputs to the indirect pathway lead to inhibition of the SC and thalamus because these signals pass through three inhibitory synapses.

Suppression of the automatic pro-saccade

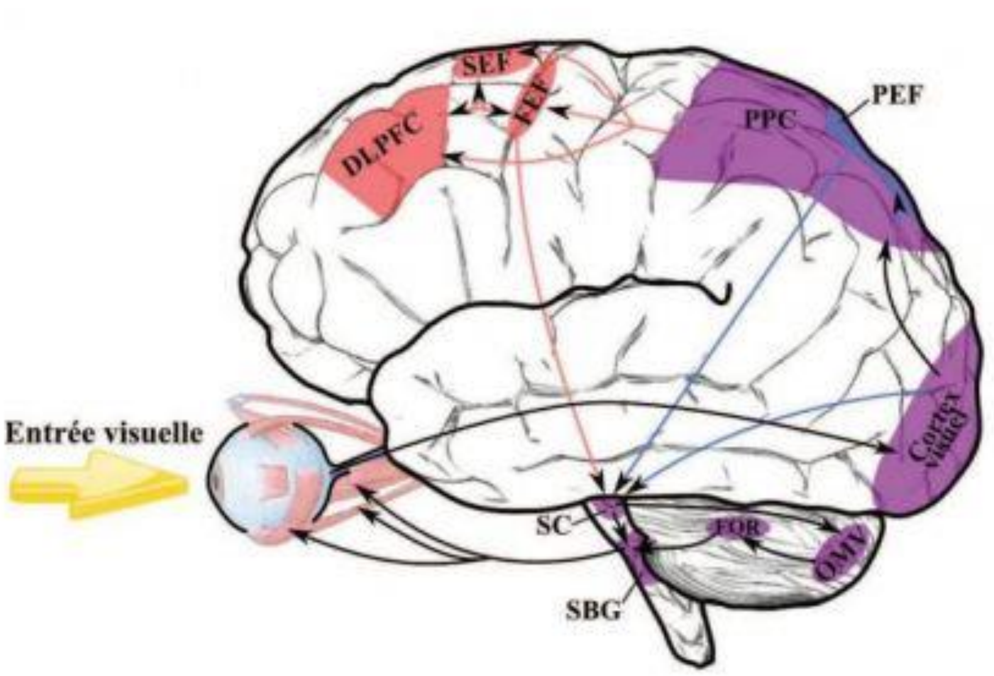
- SC and the FEF contain distinct populations of fixation and saccade neurons, whose discharges are modulated in a reciprocal manner in the anti-saccade task.
- Fixation neurons are tonically active during visual fixation and they cease to discharge during the execution of saccades.
- Saccade neurons have a reciprocal pattern of activity; they are silent during fixation and discharge a high-frequency burst of action potentials for saccades to a certain region of the contralateral visual field that defines their response field.
- It has been hypothesized that a network of inhibitory interneurons participates in shaping the reciprocal discharges of fixation and saccade neurons.



Sources of FEF & SC saccade neuron inhibition

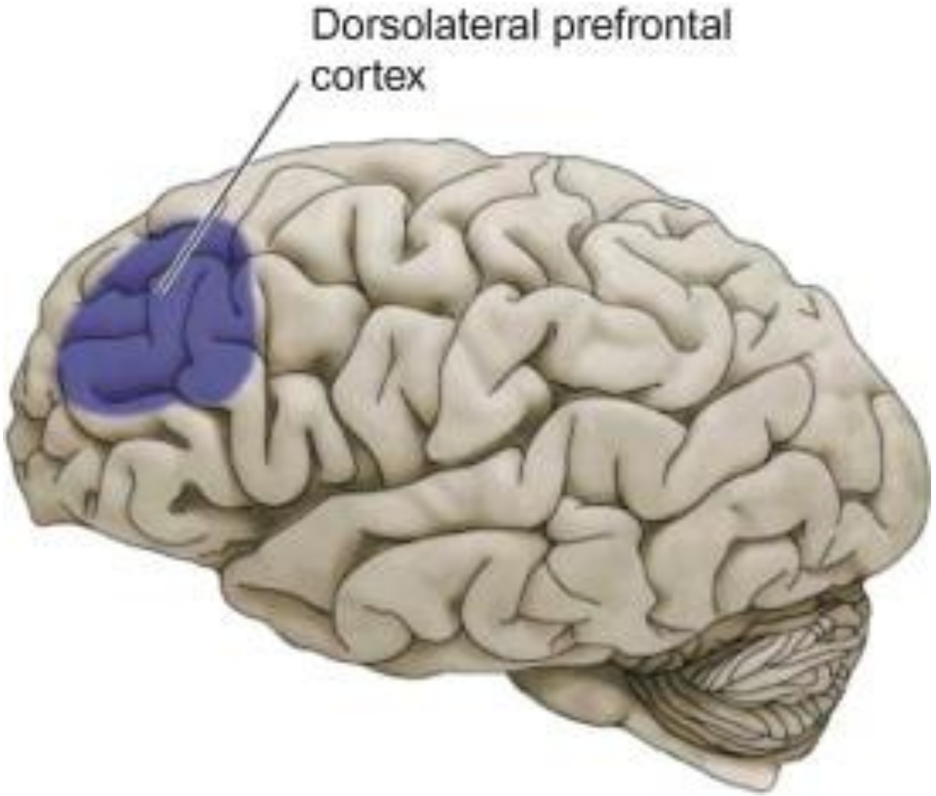
1) SEF

- The visual and saccade-related responses of many neurons in the SEF are greater for anti-saccades than for pro-saccades.
- Many SEF neurons, especially fixation neurons, show increased activation on anti-saccade trials during the instruction period that precedes target presentation, and the activity of these neurons is lower on trials in which the monkey generates a direction error.
- The SEF projects directly to the FEF and SC, so SEF efferents could excite local inhibitory interneurons to exert inhibition of saccade neurons in these structures



https://theworldnews.net/fr-news/vous-aimez-parier-gros-on-sait-desormais-quelle-zone-du-cerveau-est-activee

Sources of FEF & SC saccade neuron inhibition



2) **DLPFC**

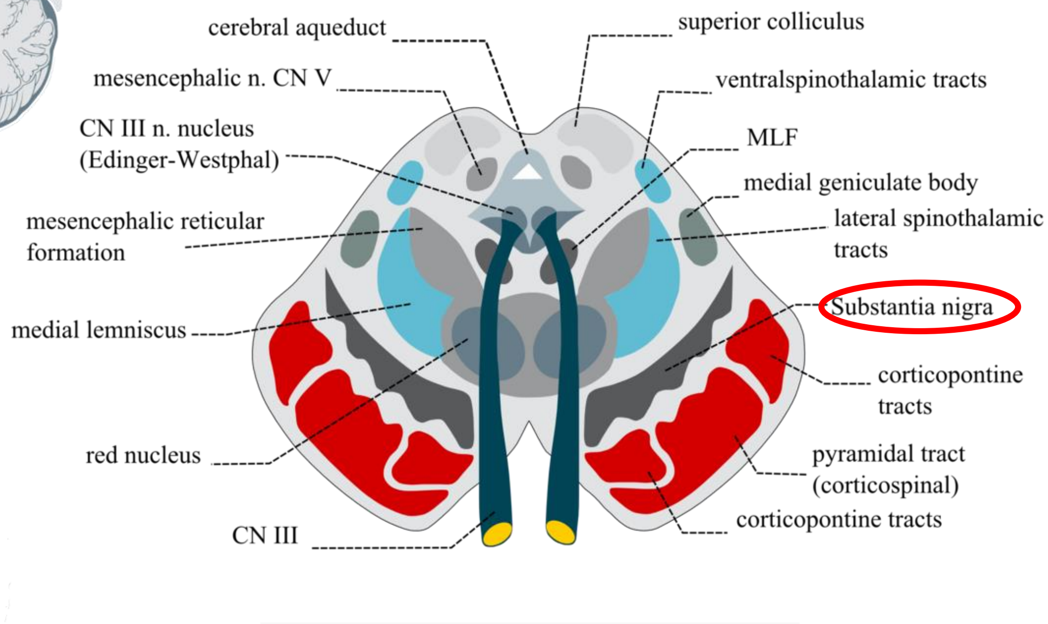
- Neurons in the DLPFC project directly to the SC and the FEF, but the function of these projections remains unknown.
- Funahashi and colleagues (1993) recorded DLPFC neurons when monkeys performed a delay version of the pro- and anti-saccade tasks. They found that some neurons coded the stimulus location whereas other neurons coded the required response direction during the delay period.
- A large proportion of DLPFC neurons showed differences in their baseline activity between a spatial, object and association task while monkeys were looking at a central fixation marker before a stimulus was presented.
- These differences in activation probably reflect differences in preparatory set and could be involved in pre-setting the excitability of neurons in the SC and FEF. Alternatively, other populations of neurons in the DLPFC that have yet to be recorded in the anti-saccade task could provide inhibition to the saccade neurons in the FEF and SC.

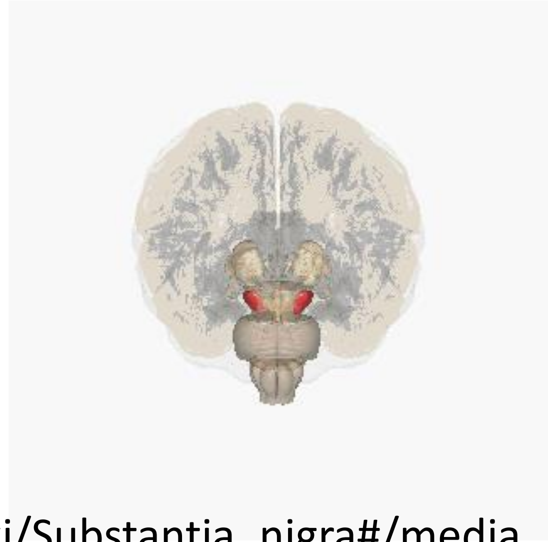
https://www.sciencedirect.com/topics/neuroscience/dorsolateral-prefrontal-cortex

Sources of FEF & SC saccade neuron inhibition

3) Substantia nigra pars reticulata (SNpr)

- A subset of neurons in the SNpr discharges tonically during fixation and pauses for saccades.
- Some of these neurons project directly to the SC and the thalamus, which in turn projects to the FEF.
- So, tonic neurons in the SNpr, which contain GABA, could exert tonic inhibition over saccade neurons in both the SC and FEF, and this inhibition could be enhanced on anti-saccade trials

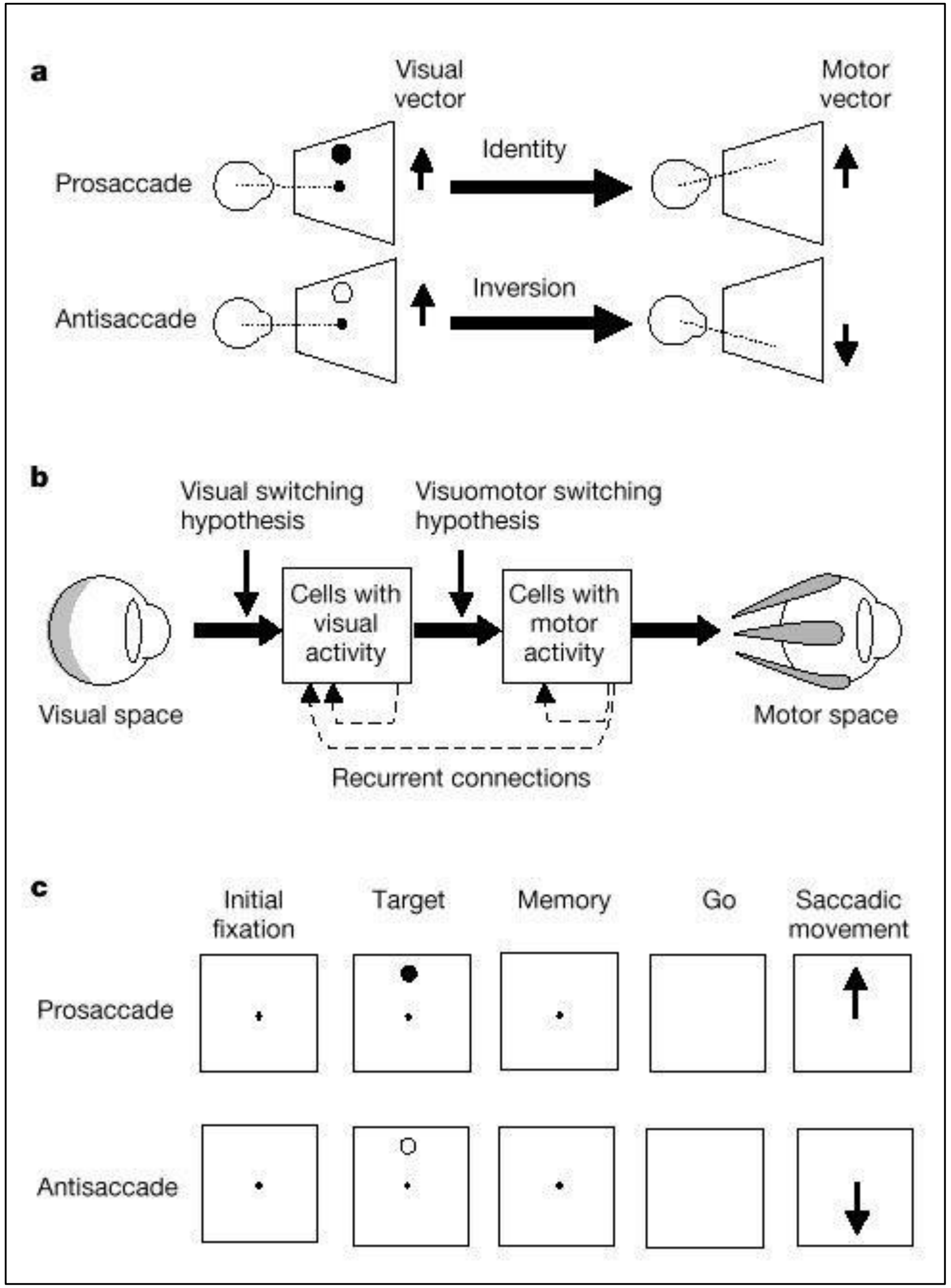




https://en.wikipedia.org/wiki/Substantia_nigra#/media

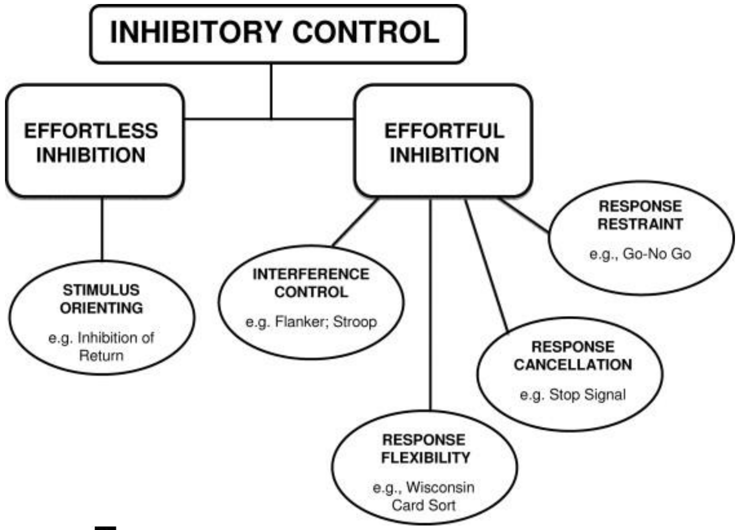
Vector inversion

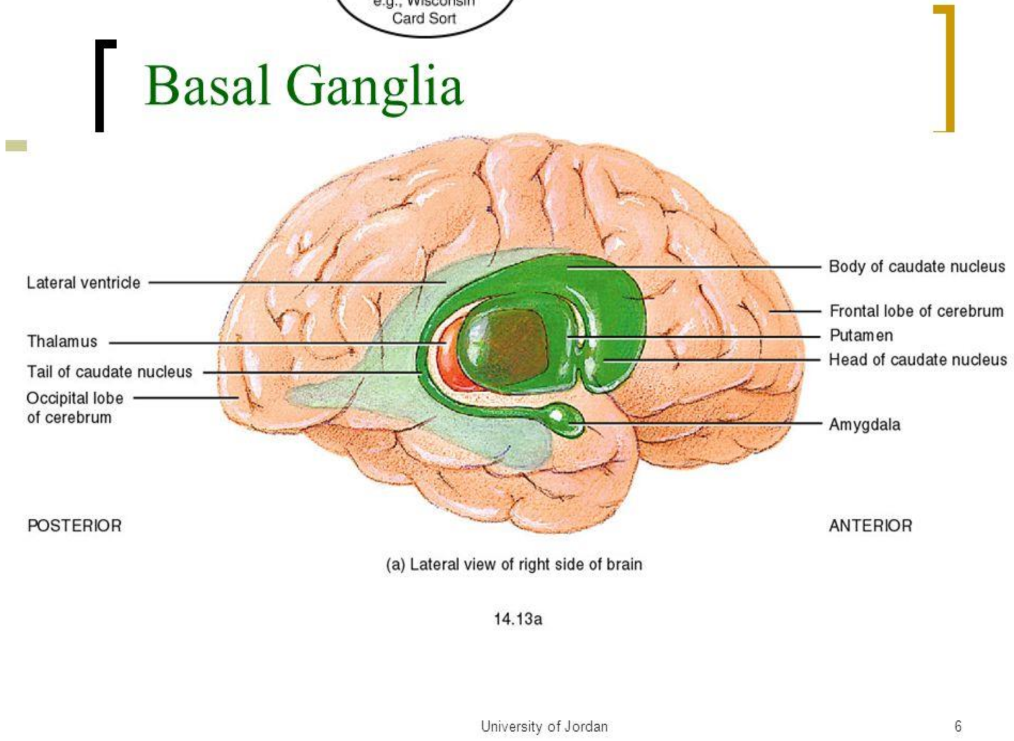
- How is the location of the visual stimulus transformed into the appropriate motor command for the execution of saccades?
- This problem is straightforward for pro-saccades because the visual response is mapped directly onto the saccade neurons in the FEF and SC.
- Not trivial in the anti-saccade task because the visual response is initially mapped to the wrong population of saccade neurons in the SC and FEF.
- This activity must be suppressed and instead a saccade response must be generated by saccade neurons on the opposite side of the brain.
- Somewhere between the initial registration of target appearance and the generation of the saccadic burst in the FEF and SC, the target vector must be transformed (inverted) into the movement vector.
- evidence has accumulated to indicate that neurons in both the LIP and the FEF participate in vector inversion.



Zhang & Barash, Neuronal switching of sensorimotor transformations for antisaccades, 2000 https://doi.org/10.1038/35050097

Clinical studies





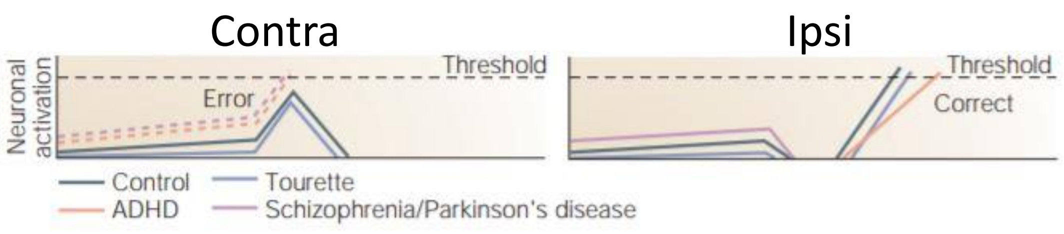
- Because of the dependency on frontal and basal ganglia structures, the anti-saccade task has emerged as an important clinical tool for investigating development and dysfunction in various neurological and psychiatric disorders
- Young children (<8 years of age) have difficulty in suppressing the automatic pro-saccade in the anti-saccade task. Many of the direction errors that are triggered by children are corrected quickly, revealing that these young subjects have no difficulty in understanding the task. Rather, their difficulty is in suppressing the automatic pro-saccade to the target. This suppression ability develops gradually and is achieved only at about 18 years of age.
- Because young children have reduced inhibitory control, they will have difficulty in pre-setting the excitability of saccade neurons in the FEF and SC before the target appears.
- On the other hand, normal adults can selectively inhibit pretarget activity in saccade neurons so that it is easier to suppress automatic pro-saccades in the anti-saccade task.

Schizophrenia

- **increased error rates and prolonged RT's** for correct anti-saccades. Similar to patients with DLPFC lesions, have a reduced ability to suppress the activity of saccade neurons in the FEF and SC on anti-saccade trials and a reduction in the rate of accumulation of activity for the correct anti-saccade

Parkinson's disease (PD)

- difficulty in generating voluntary responses. **Increased RT's** for correct anti-saccades, indicating that the activity required to trigger them accumulates more slowly in these patients. Faster than controls at generating the automatic responses in the pro-saccade task, making more **express saccades**. Leads to more **direction errors** on antisaccade trials. As a result of this reduced inhibitory control in PD, inappropriate top-down saccadic suppression might be present at stimulus onset, resulting in **excessive activity in saccade neurons**.



ADHD:

- **deficit in response inhibition**. Difficulties in suppressing the automatic pro-saccade on anti-saccade trials. Despite the increase in direction errors, there is no change in the mean reaction time of correct anti-saccades, implying no deficit in the ability to initiate a voluntary response. **Compromised top-down control of saccade neurons in the FEF and SC.** This results in **excessive pretarget activity** in the FEF and SC so that direction errors are easily triggered after appearance of the visual stimulus.

Tourette's syndrome:

- **increased RT's** in both pro- and anti-saccade tasks and they generate **few direction errors**. Perhaps as a consequence of adapting to the symptoms of the disorder, the patients have **increased top-down inhibition** acting on the saccade-generating system, thereby making it harder for activity to accumulate to trigger saccades in either pro- or anti-saccade conditions

ELSEVIER

Vision Research

Volume 84, 24 May 2013, Pages 1-5

An internationally standardised antisaccade protocol

Chrystalina Antoniades [a, b], Ulrich Ettinger [c], Bertrand Gaymard [d], Iain Gilchrist [e], Arni Kristjánsson [f], Christopher Kennard [b], R. John Leigh [g], Imran Noorani [a], Pierre Pouget [d], Nikolaos Smyrnis [h], Adam Tarnowski [i], David S. Zee [j], R.H.S. Carpenter [a]

⊞ Show more

https://doi.org/10.1016/j.visres.2013.02.007