

# NEUROBIOLOGICAL BASIS OF ANGER

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## INTRODUCTION

Anger is a frequent destructive emotion that has an important role in society and the public health. But, do we know how anger structures in our brain? Do we know how we regulate such an important emotion?

## OBJECTIVE

The main objective is to show the knowledge that we have about **how anger work in the human brain** through a literature review of the current status of this area of cognitive neuroscience.

## CONTENT

### The RAGE SYSTEM

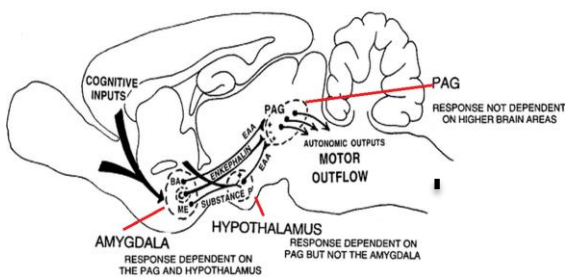


Fig. 1: Summary of the localization of RAGE circuit and the hierarchical control in the brain: BA, basal amygdala; ME, medial amygdala; EAA, excitatory amino acid; PAG, periaqueductal gray.

A very efficient and effective way to study the structures involved in anger is by observing the **rage system**. Based on studies of brain stimulation it has been considered that the structures involved in the circuit of rage are:

- Amygdala
- Hypothalamus
- Periaqueductal gray (PAG)

Rage circuit runs from the middle of the amygdala, through areas of the hypothalamus and down towards midbrain PAG.

The system is organized as a **hierarchical structure** such that aggression evoked by stimulation of the amygdala depend on the functional integrity of the medial hypothalamus and periaqueductal gray. However, the aggression evoked by stimulation of the medial hypothalamus does not depend on functional integrity of the amygdala but depend on the integrity of PAG.

### REGULATION and ACTIVATION

#### Seeking and Rage system

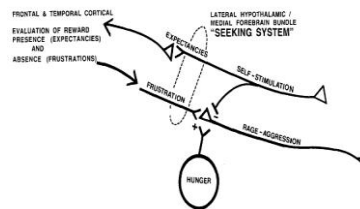


Fig2. Schematic suggestion of likely interactions between SEEKING and RAGE system; (+), excitation; (-), inhibition.

The most common causes that generate anger are caused by **irritation and frustration**, like:

- Restriction of freedom
- Restriction of access to resources

"Frustration-aggression hypothesis" suggests that the RAGE system must be anatomical and neurophysiological linked to the SEEKING system.

#### Neurochemistry of Anger

##### Serotonin (5-HT)

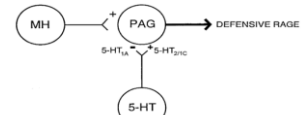


Fig3. Summary of the difference in modulating PAG between serotonin receptors: 5-HT<sub>1A</sub> and 5-HT<sub>2C</sub> / 1C of medial hypothalamus (MH) whose axons projecting in PAG.

Experiments show that the function is different depending on what 5-HT receptor is activated:

- 5-HT<sub>1A</sub> Suppress PAG **NO ANGER**
- 5-HT<sub>2/1C</sub> Activate PAG **ANGER!**

##### Substance P

Substance P works as a neurotransmitter and neuromodulator activating the hypothalamic receptor NK1 who promotes aggression and anger.

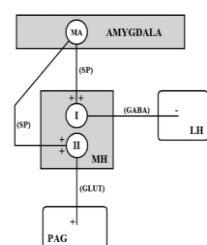


Fig4. Summary of the Rage system; role of substance P modulating the circuit. MA, medial amygdaloid nucleus; SP, substance P; MH, medial hypothalamus; I, II, neuronal groups within the MH; GABA, gamma aminobutyric acid; LH, lateral hypothalamus; GLUT, glutamate; PAG, periaqueductal grey; (+), excitation; (-), inhibition.

## CONCLUSIONS

- The way to know how anger works in the human brain and how we regulate that emotion is through the studies in the **RAGE system**.
- It is still necessary **to bet for a deeper understanding**, although recently there has been increased interest in this field.
- Finally, we could control and regulate anger and avoid **anti-social behaviour**.

## REFERENCES

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- **FIG.4- Katsouni E. et al** (2009). *The involvement of substance P in the induction of aggressive behavior*. *Peptides* 30; 1586–1591
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