EDITORIAL

"The switch" – a biologic miracle

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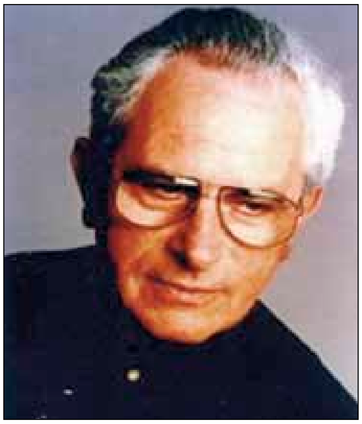

The access to air and food is accomplished at the laryngo-pharyngeal crossroad and beyond it they are morphologically separated: in the larynx opens the air tract, and in the pharynx opens the digestive tract (Figure 1). Let's call the crossroad zone simply: "the switch". Due to its neurocomplexity, "the switch" evolved into a bionic miracle of nature.

When did "the switch" appear in animal evolution? Based on his discovery of the fossil fish Tiktaalik (the "fish with hands") (Figure 2), the paleontologist Neil Shubin wrote in 2008 the book "*Your Inner Fish: A Journey into the 3,5-Billion-Year History of the Human Body"*. According to these findings , "the switch" present in humans appeared half a billion years ago (Figure 3) in the swallowing apparatus of the fish (Figure 4).

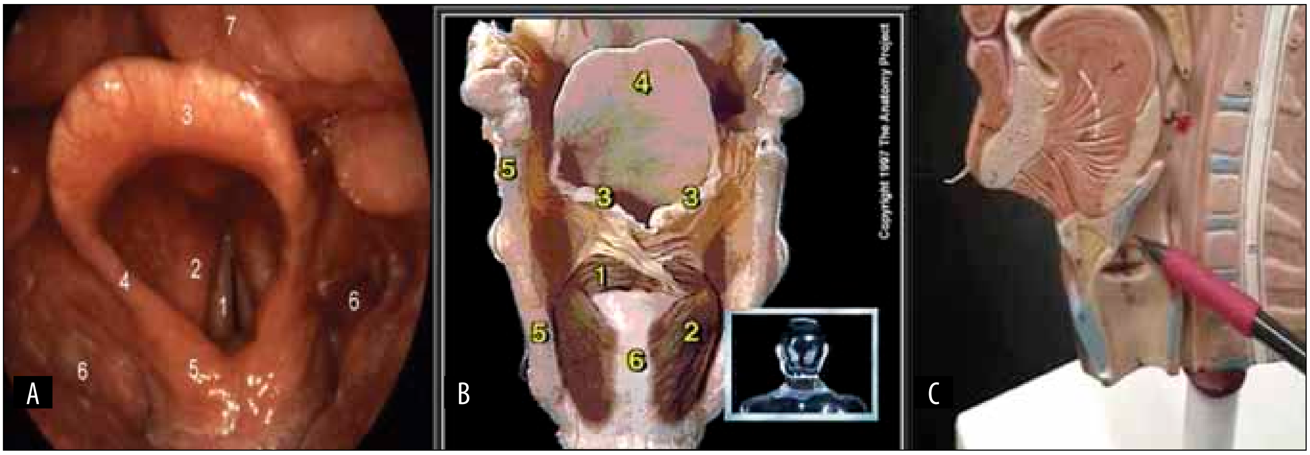

Figure 1 The larynx: **A.** from above: *1=vocal cords, 2=vestibular folds, 3=epiglottis, 4=aryepiglottic plica, 5=arytenoid cartilage, 6=pyriform sinus, 7=back of the tongue*; **B.** frontal section: *1. Oblique arytenoid and aryepiglottic muscles, 2. Posterior cricoarytenoid muscle, 3. Inlet of the larynx, 4. Epiglottis, 5. Cornu of thyroid cartilage, 6. Cricoid cartilage* **C.** lateral section

Figure 2 The fossil fish Tiktaalik (the "fish with hands")

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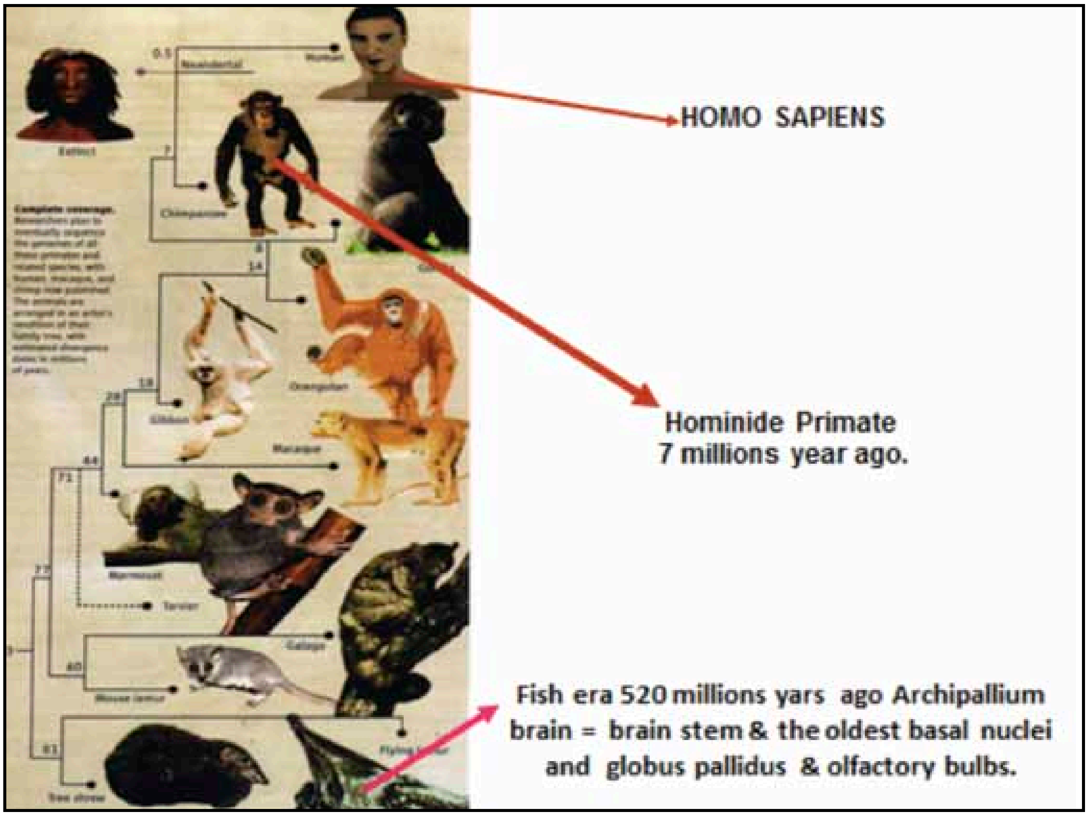

Figure 3 History of human switch

Figure 4 The fish swallowing

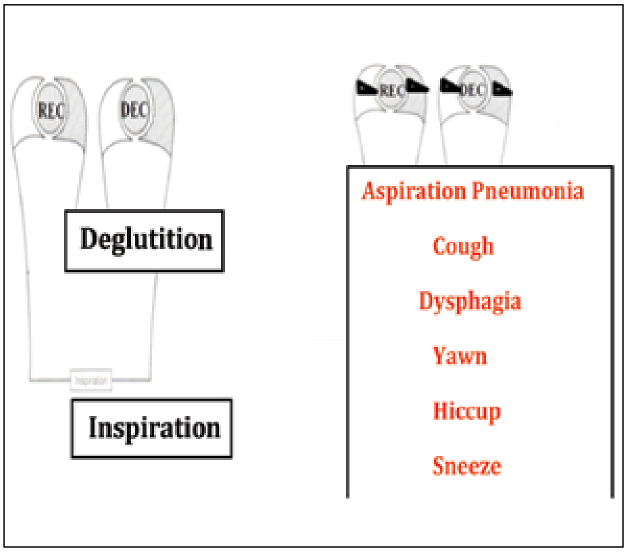

Figure 5 Normal switch function and switch dysrhythmia

In the digestive system, "the switch" serves as the "Digestive Epiglottic Complex" (DEC), whereas in the respiratory system it serves as the "Respiratory Epiglottic Complex" (REC).

For a normal dual function of breathing and eating, "the switch" has to fulfil two desiderata: a) shutting and opening, without allowing liquids to leak into the trachea, or air to enter the esophagus; b) correct alternation of the two processes. In order to realize this desiderata, DEC and REC interrelationship must be of reciprocal inhibition (Figure 5).

Activation of REC is a coordinated function that ensures inhalation and exhalation of air in the trachea: moves the epiglottis away, opens the glottis (allowing the free passage of air into the trachea) and activates the diaphragmatic muscle, the external intercostal muscles, the sternocleidomastoid muscle, the serratus anterior muscle, and the scalene muscles.

Table 1
Digestive Epiglottic Complex

1	Posterior tongue muscle contracture	9	Contraction of superior constrictor
2	Epiglottis back flexion	10	Contraction of palatopharyngeal muscle
3	Closing laryngeal aperture	11	Contraction of thyrohyoid
4	Raising the larynx	12	Contraction of thyroarytenoid
5	Closure of glottis	13	Contraction of cricothyroid
6	Contraction of mylohyoid	14	Contraction of inferior constrictor
7	Contraction of geniohyoid	15	Relaxation of esophageal sphincter
8	Contraction of middle constrictor	16	Activation esophageal peristaltic muscle

Likewise, coordinated of DEC (Table 1) moves the epiglottis back with a posterior movement of the tongue, shuts the laryngeal aperture, raises the larynx, brings together the vocal cords (closure of the glottis), contracts the hyoid and middle & superior constrictor muscles of the pharynx, relaxes the superior esophageal sphincter, and activates esophageal peristalsis (Figure 6). All these actions occur in 400 milliseconds, just like in a musical sequence.

The concomitant electromyographic recording of the muscles involved in deglutition reveals a sequential recruitment (Figure 7).

"The switch" function is coordinated by the nervous system from a supranuclear center located in the reticular substance of the brainstem: the "switch center" (supranuclear reticular center - SRC) (Figure 8).

Not far from the supranuclear center of "the switch", the breathing nuclei (DRG, VRG, PC), as

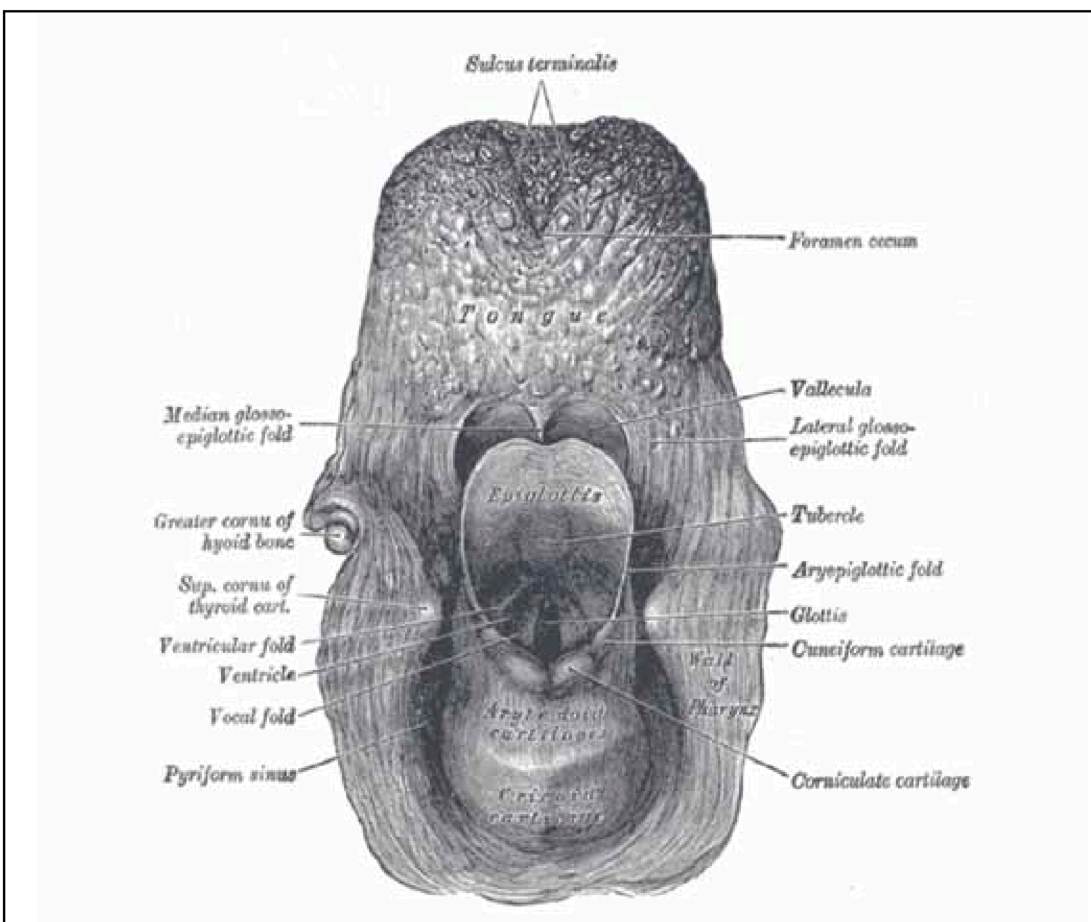

Figure 6 Anatomy of the Digestive Epiglottic Complex

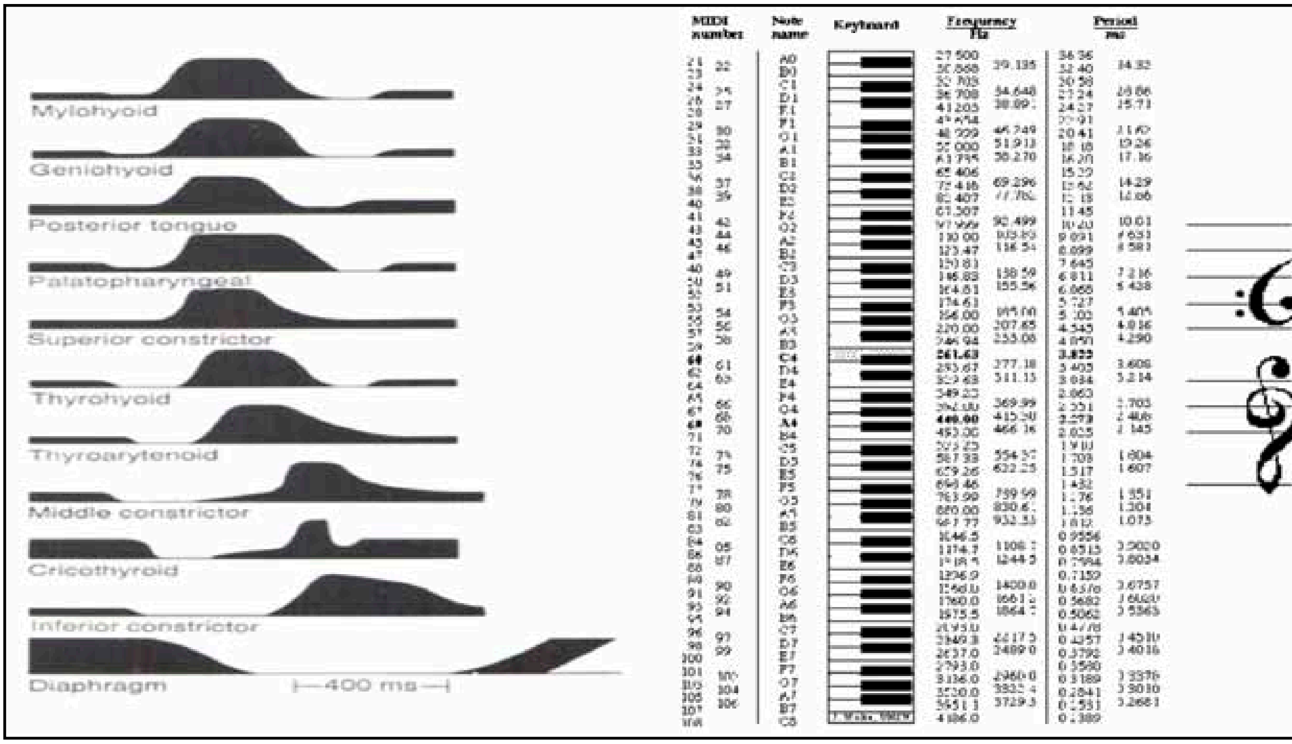

Figure 7 Electromyographic recording of the muscles involved in deglutition

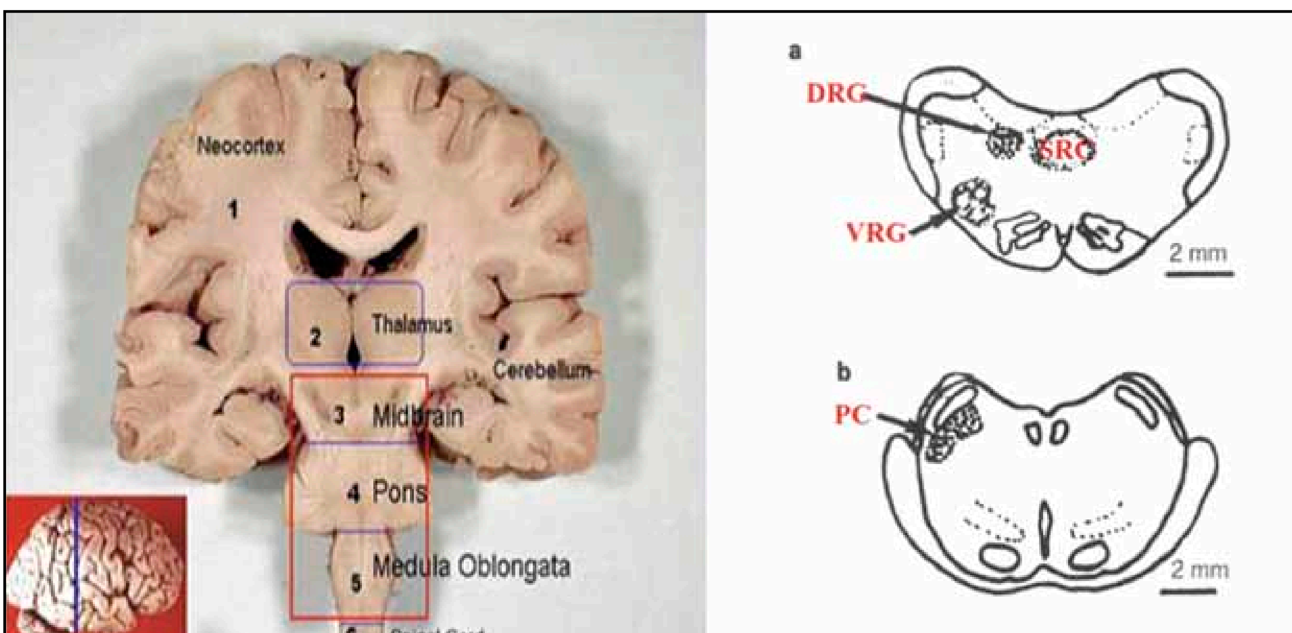

Figure 8 The "switch center" (supranuclear reticular center) - *DRG = dorsal respiratory group; VRG= ventral respiratory group; PC= pneumotaxic center; SRC= supranuclear reticular center*

well as of the cardiac regulation, are located. It has been suggested that 25 centers associated with behaviour are located in proximity. In the mid-20th century, Paul McLean elaborated the evolutionistic theory of the reptilian, paleo-mammalian and neo-mammalian brain, called "triune brain".

Nature placed the centers for breathing, eating and heartbeat in the brainstem, because even at rest, during sleep, or with the consciousness suspended, the essential life activities continue. Their cessation means brain death.

During the digestive act, the "switch center" sends impulses to the brainstem nuclei of cranial nerves V, VI, VII, IX, X, XI, XII and the nerve roots of C1-C5 and T6-T12, using an algorithm similar to the one detected by the EMG muscle contraction (Figure 9).

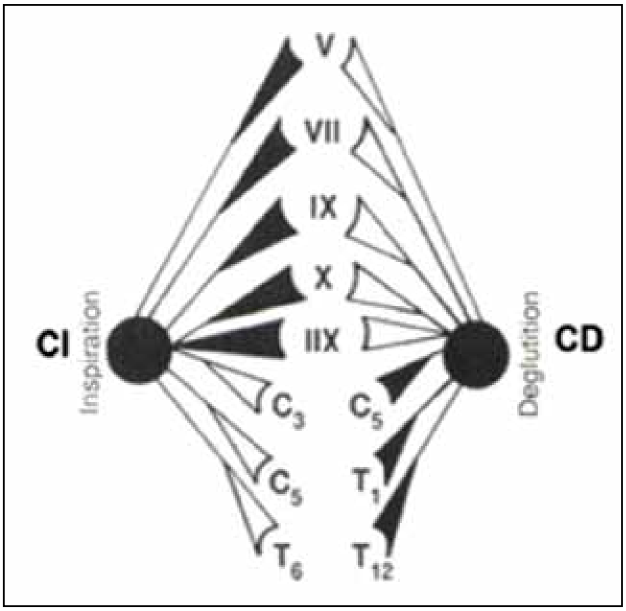

Figure 9 The "switch center" activity during the digestive act

With the evolution from fish to reptile and the appearance of the air breathing, the brainstem developed. In the palleomammalian phase of the evolution, the reticular system was enriched, with a new regulator, "the limbic system", and its compartments: the parasympathetic autonomic nervous system (PSNS), the sympathetic nervous system (SNS) and the hypothalamus.

Later on, the appearance of the neocortex in the neomammalian phase of evolution made possible the voluntary control of the switch, as proved by the Val-salva maneuver. The reciprocal inhibition of the switch enabled automatisms like hiccup, yawn and sneeze to appear only one at a time. In the reptilian era, the switch is missing. In the palleomammalian phase of the evolution, the rudimentary switch appeared.

Ramon Y Cajal, in 1889, impressed by the multitude of poorly defined neurons in the brainstem, elaborated the "*network*" concept.

Sherrington, in the monography "*The Integrative Action of the Nervous System*", published in 1906, summarized two decades of experimental observations. The central nervous system acts as the coordinator of various parts of the body and the reflexes are the simplest expressions of the interactive action of the nervous system. The brainstem enables the entire body to function toward one definite end at a time. He explains the incisive difference between his "Reticular Theory" versus Cajal's "Neuron Doctrine".

Morruzzi and Magoun (1949) and Magoon (1952) proposed the name of the *reticular ascending activating system* and *the reticular descending inhibitory system* when they have discovered the sleep/arousal effect of this area of the brainstem.

Three years before the Ad Hoc Committee of the Harvard Medical School elaborated the criteria of brain death, Oscar Sager, in his book dedicated to Gheorghe Marinescu and published in 1965, "Reticular Formation", writes: the reticular system is a "sine-qua non" of the nervous system (Figure 10, Figure 11).

The major nerve of "the switch" is the vagus – pneumogastric cranial nerve. This nerve is 85% sensory afferent and 15% motor efferent to the muscles of the switch (larynx + pharynx). It contains axons from the ambiguus, solitary and trigeminal nuclei. The vagus supplies motor parasympathetic fibers to all the organs except the suprarenal glands, lowers the heart rate, ensures peristalsis, sweating and muscle contraction.

The neurotransmitter of the vagus is the vagusstoff discovered by Otto Loewi, later found to be acetylcholine (Figure 12). The functions of the acetylcholine receptor are to lower the heart rate, to ensure peristalsis, sweating and to activate the switch.

It is an important neuromodulator of the peripheral and central nervous system. In the peripheral nervous system, acetylcholine activates muscles; in the cortex, it increases responsiveness to sensory stimuli (a form of attention), excites pyramidal cells and ensures the capacity of learning and plasticity. As the major

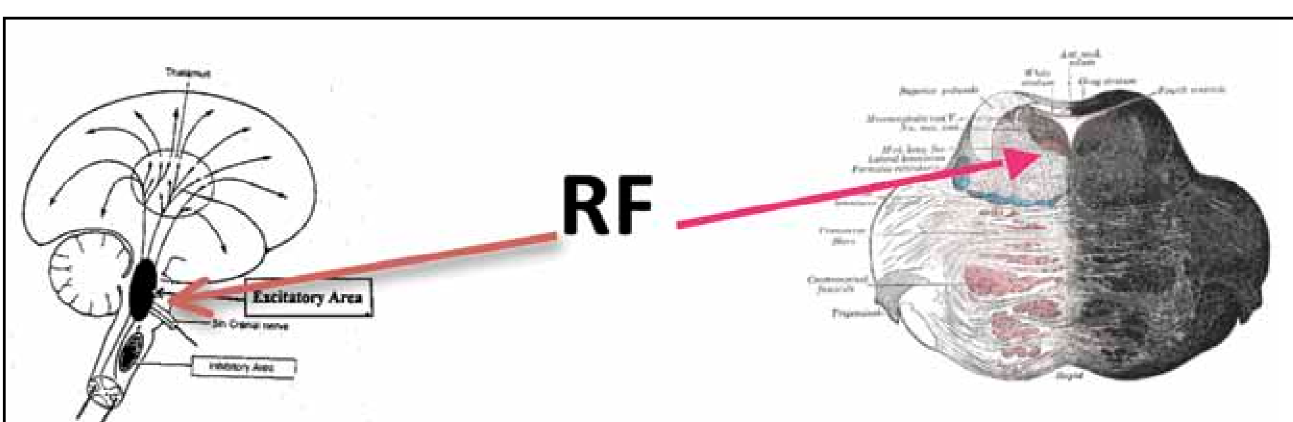

Figure 10 Reticular system activity

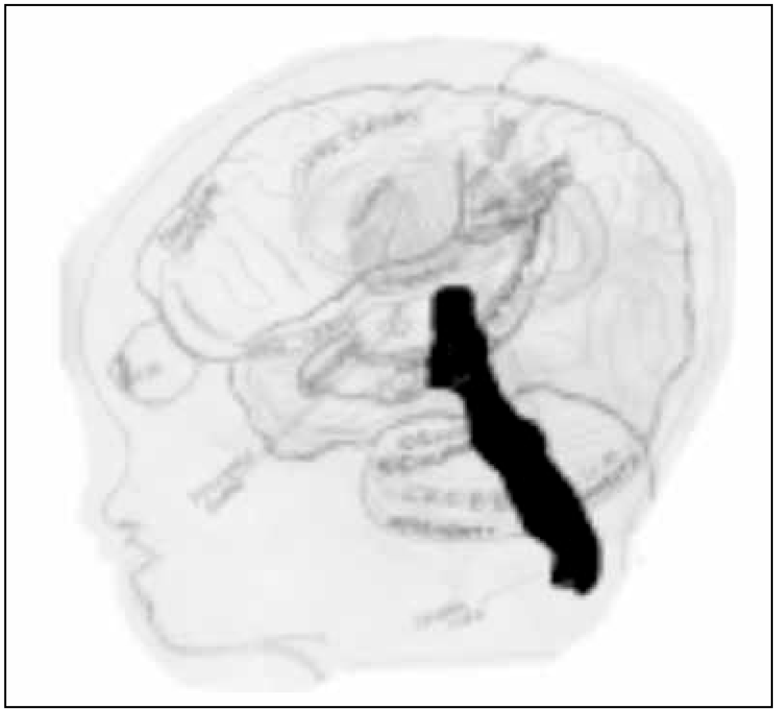

Figure 11 Reticular formation

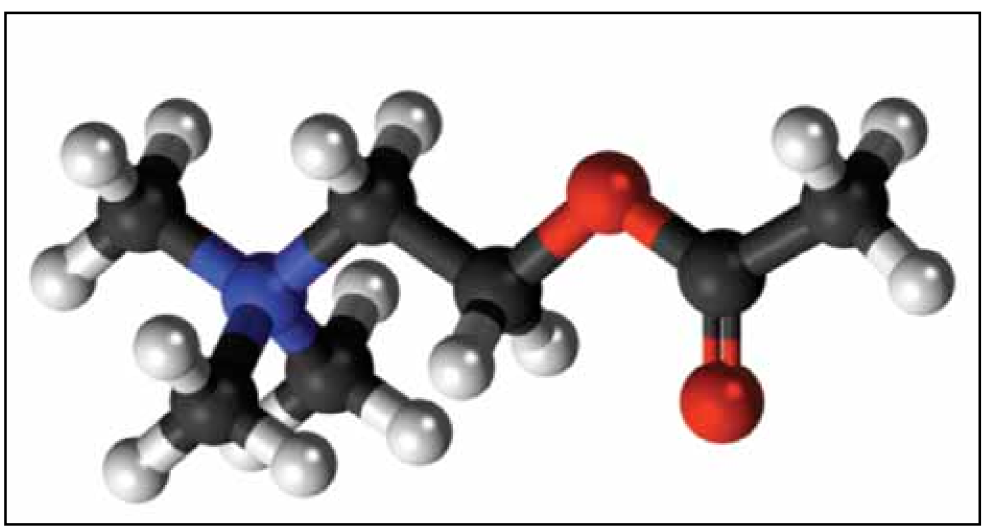

Figure 12 Acetylcholine (ACh)

neuro-transmitter in the autonomic nervous system, it activates all the viscera.

In 2011, Tracey and his colleagues Mauricio Rosas-Ballina and Peder Olofsson discovered a memory T cell subset that secretes acetylcholine in the T cells of mice spleens (Figure 13), when activated by signals arising in the vagus nerve.

Acetylcholine blocks inflammation, interfering with the immunologic activity of cytokines.

The last decades showed the involvement in the activity of the switch supercenter of norepinephrine, serotonin, GABA, endorphins, hormones and cytokines.

In the following nervous system disorders "the switch" activity is severely altered: ALS, Wallenberg's Syndrome, Cerebral Palsy, Multiple sclerosis, chronic progressive external ophthalmoplegia, Kearns-Sayre syndrome and myasthenia.

ALS destroys the motoneurons activating the switch, resulting in: respiratory failure and aspiration pneumonia of all degrees, followed by eating problems: losing the capacity of swallowing, malnutrition and dehydration. Switch disorders may be improved by using CPAP, tracheostomy and the feeding tube.

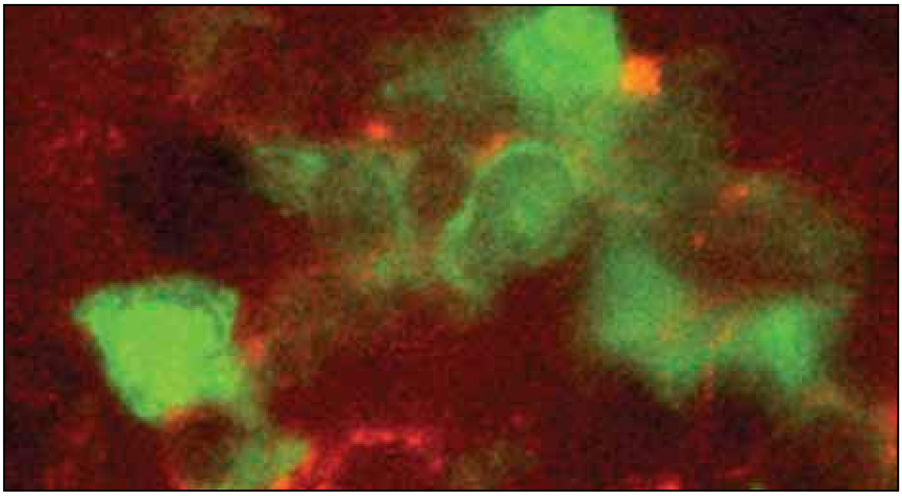

Figure 13 Green labeled lymphocyte cells are capable of producing acetylcholine

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