

*Academic lectures for general medicine
Summer course 3rd year
Updated 2004- 2014*

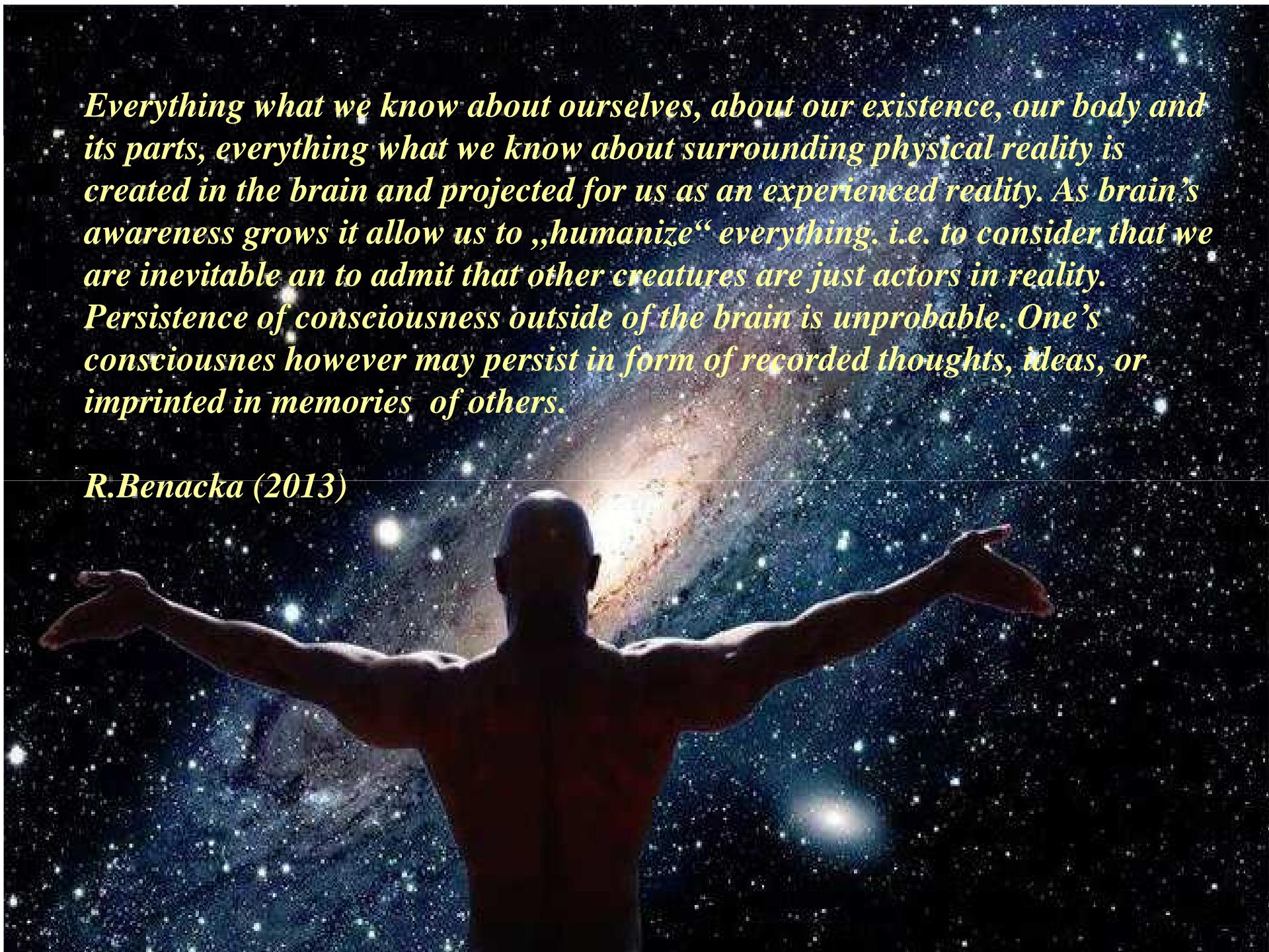
GENERAL PATHOPHYSIOLOGY

Pathophysiology of consciousness

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P.J. Safarik University, Košice, SR

Everything what we know about ourselves, about our existence, our body and its parts, everything what we know about surrounding physical reality is created in the brain and projected for us as an experienced reality. As brain's awareness grows it allow us to „humanize“ everything. i.e. to consider that we are inevitable an to admit that other creatures are just actors in reality. Persistence of consciousness outside of the brain is unprobable. One's consciousness however may persist in form of recorded thoughts, ideas, or imprinted in memories of others.

R.Benacka (2013)



Consciousness – general considerations

- **Consciousness** = various manifestation of neuronal assemblies of different size and complexity; no center in the brain; structural components of arousal, alertness, attentiveness, memory, emotion
- **Consciousness** = activation state achieved in the brain, maintained by the brain for the brain; outside of the brain consciousness has no real meaning
- **Consciousness** = continuum of behavioral states; changing throughout the night and day; also including somatic idiognosia
- **Consciousness** = morphed throughout the ontogeny; different in the kid, adulthood, man, woman; it is rather subjective than objective; similar to memory and emotions
- **Consciousness** = practical medicine through interviewing persons evaluates rather „awareness“ (Can you hear me ?, Where are you, Who are you ?)

Consciousness Tetrad (Singh & Singh, 2011)

- **Default consciousness:** basic manifestation of the life; differentiating living from dead; biological principle form non-living physical principle
- **Aware consciousness:** continuum of behavioural states (lucidity, somnolency, sleep) po patologické (somnolencia, stupor, koma)
- **Operational Consciousness:** ability to perform motor, sensoric, cognitive, creative, emotional, esthetical manifestations
- **Exalted Consciousness:** connection with the source; God meditation, creativity



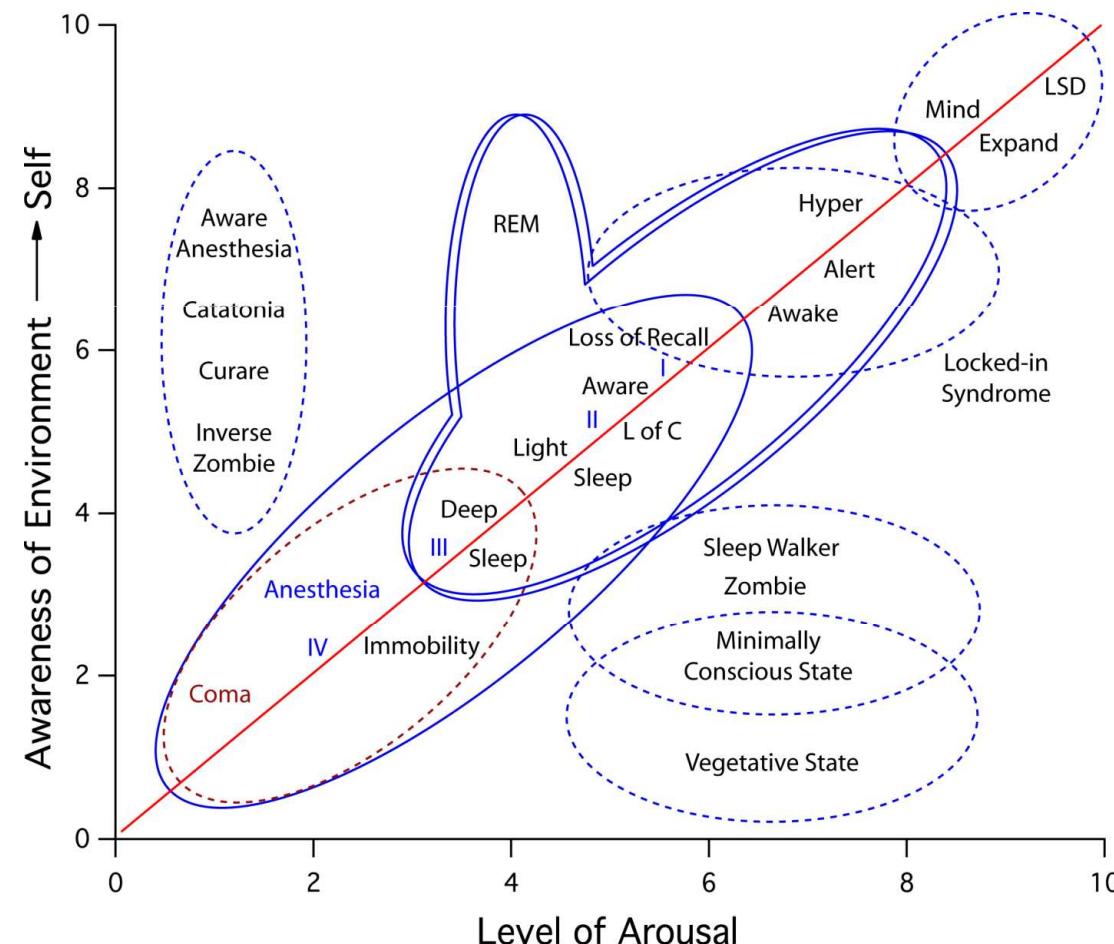
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Neuronal representation of consciousness

Various levels of consciousness – older view

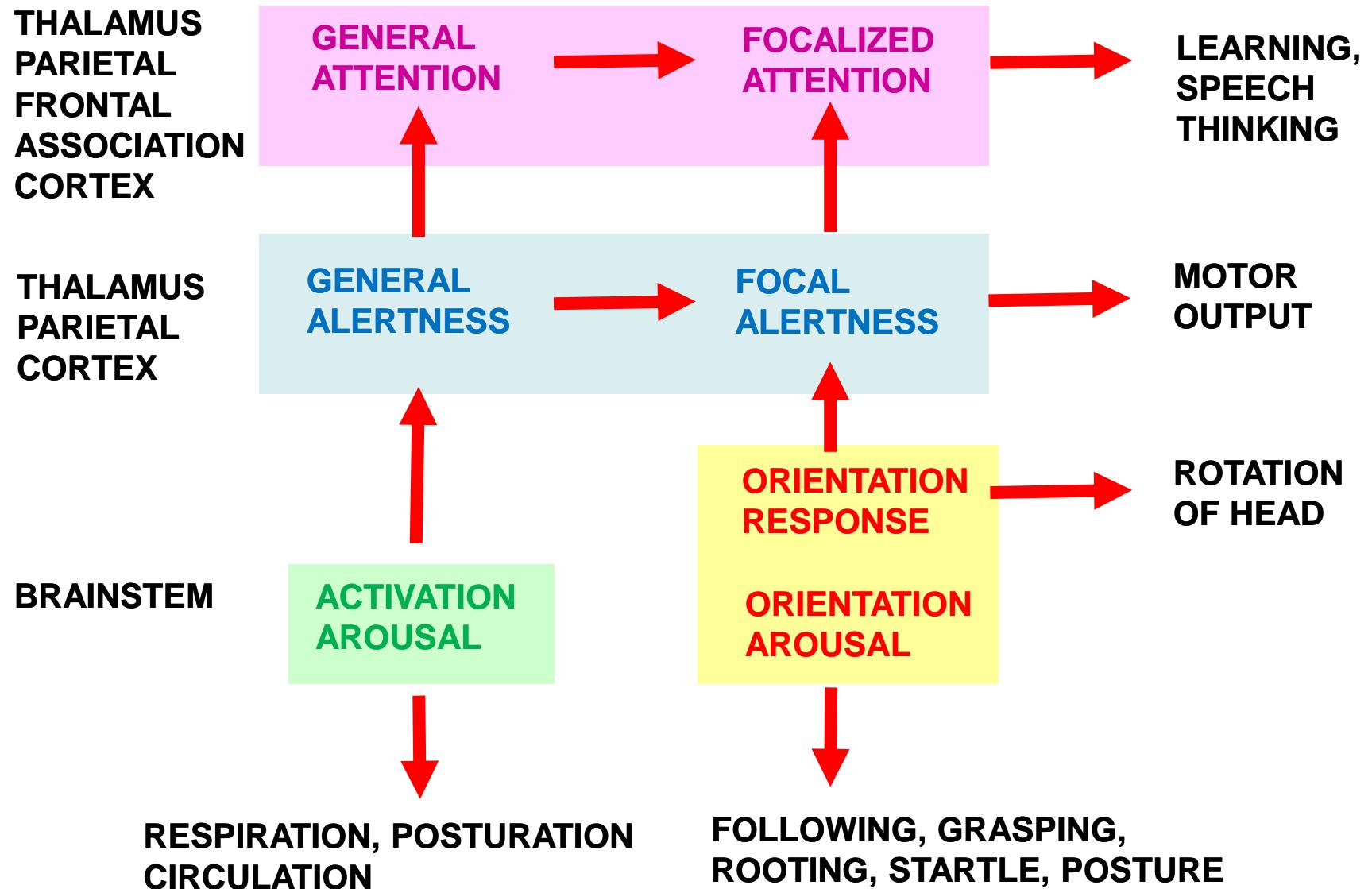
▪ Consciousness components

- **arousal** = activity level, charge, energy level
- **content** = awareness of self and awareness of environment

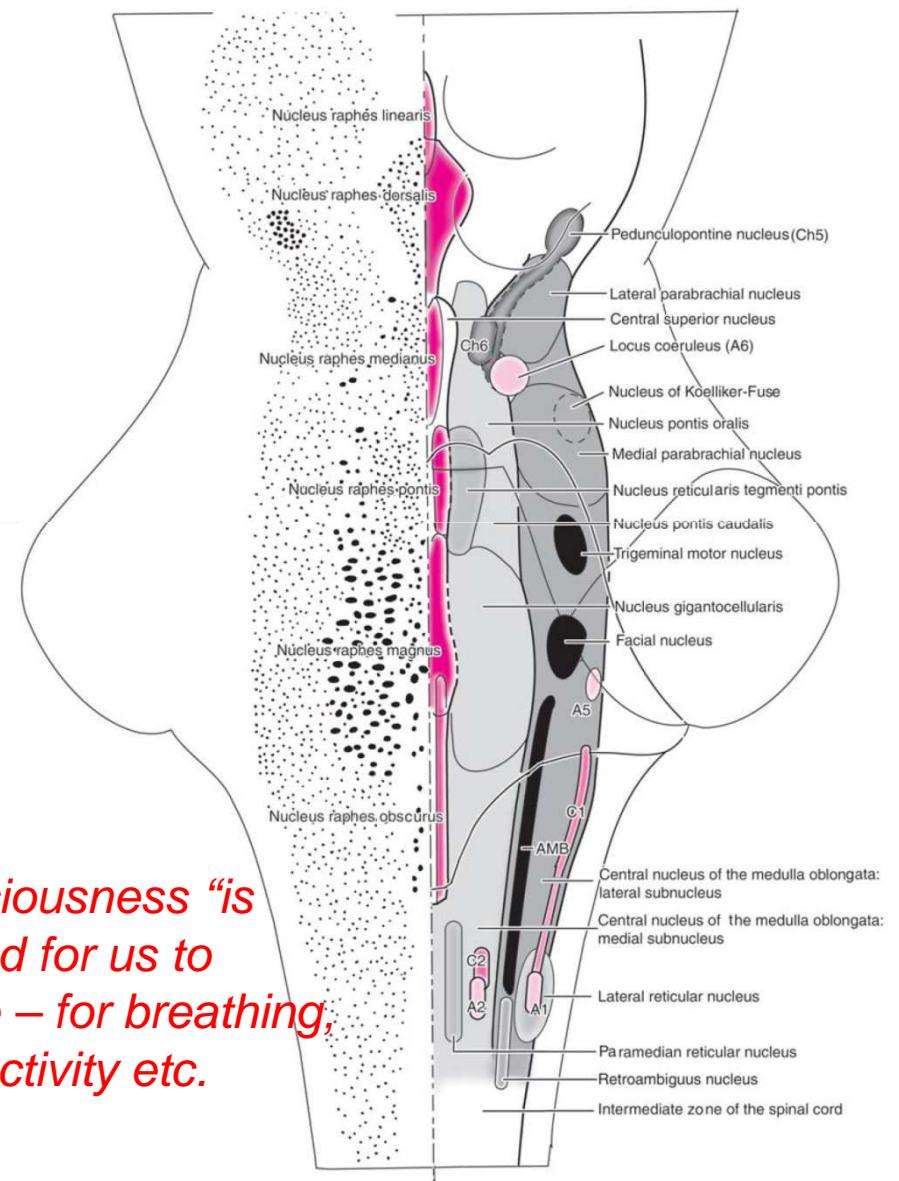
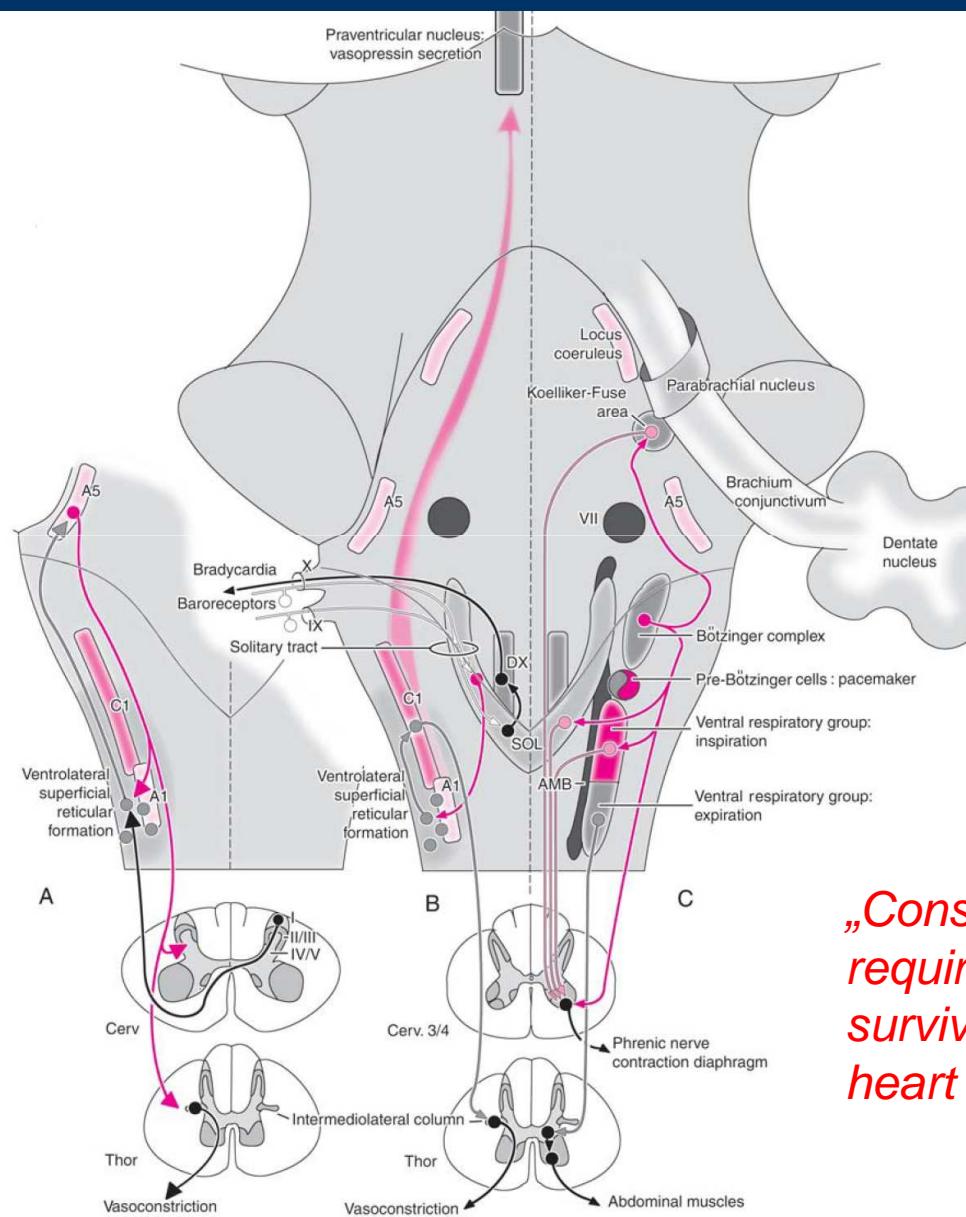


Laureys S: The neural correlate of (un)awareness: lessons from the vegetative state. *Trends Cogn Sci* 2005, 12:556-559.

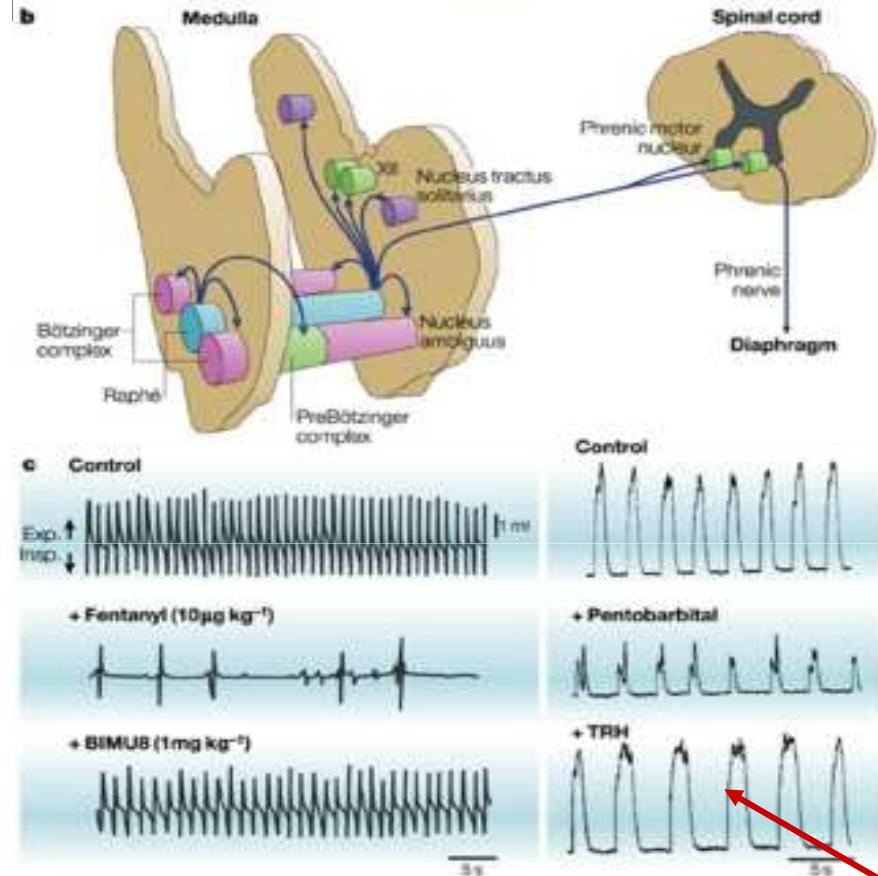
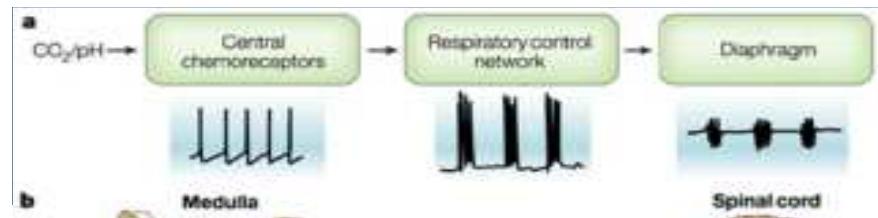
Continuum of behavioural states



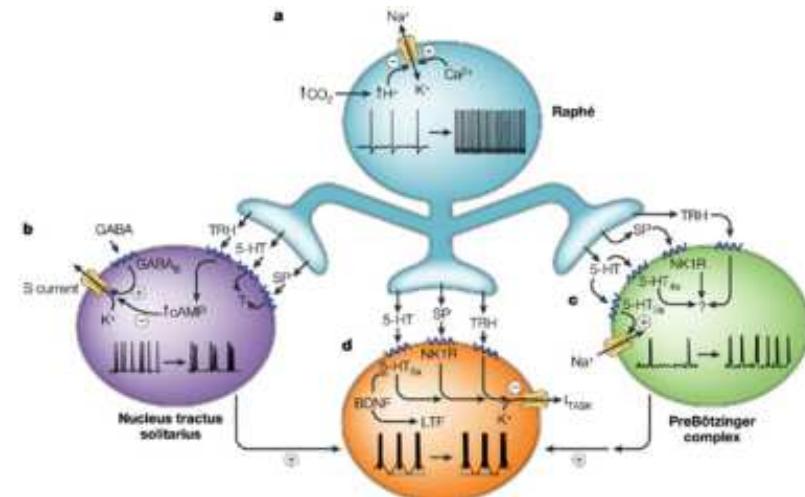
Brainstem – arousal system



“Consciousness “is required for us to survive – for breathing, heart activity etc.



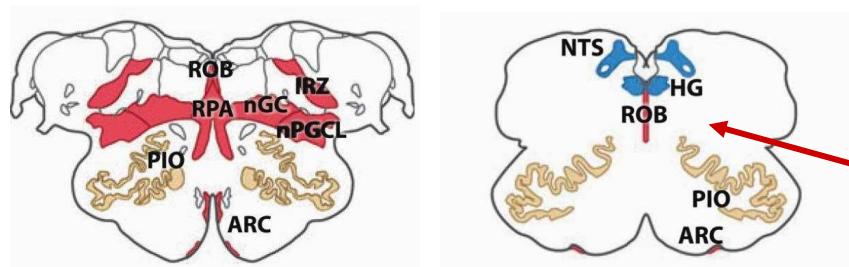
Chemoreception and wakefulness

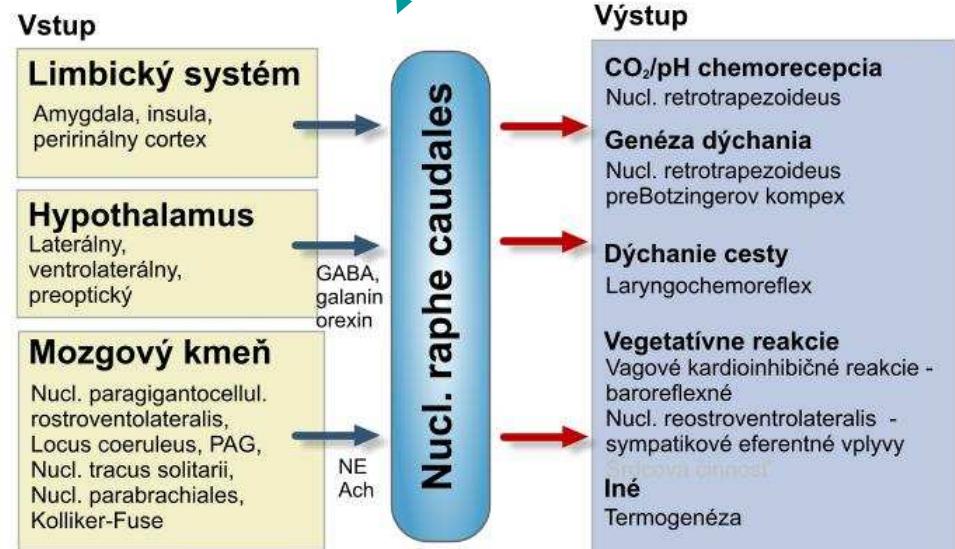
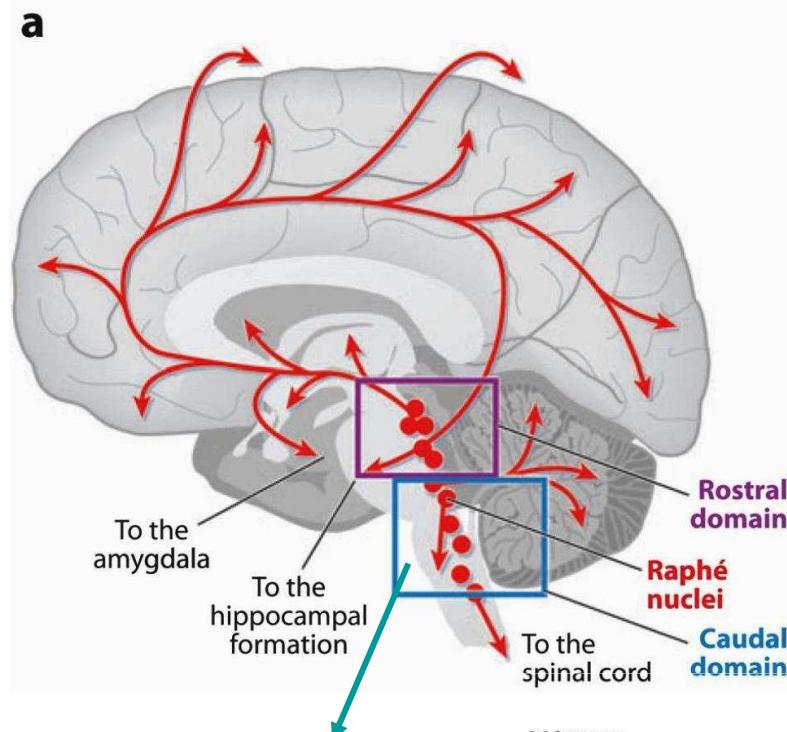
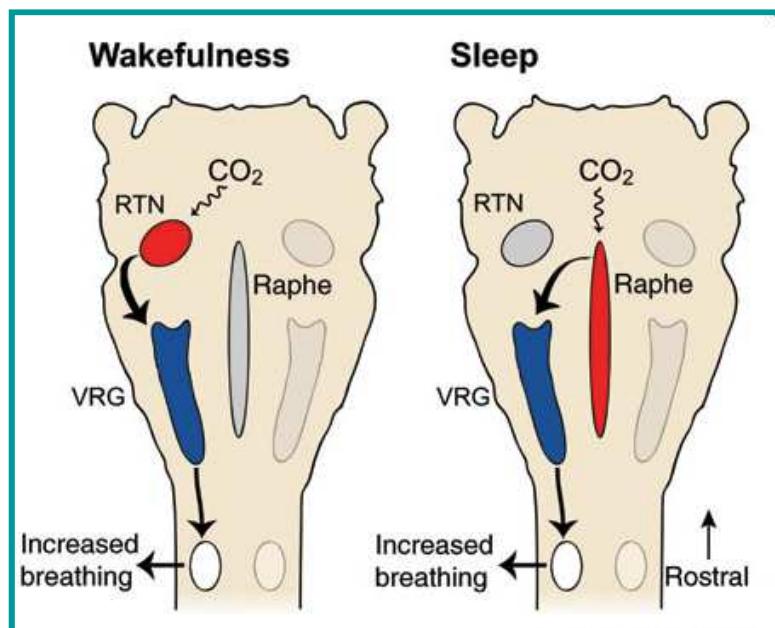
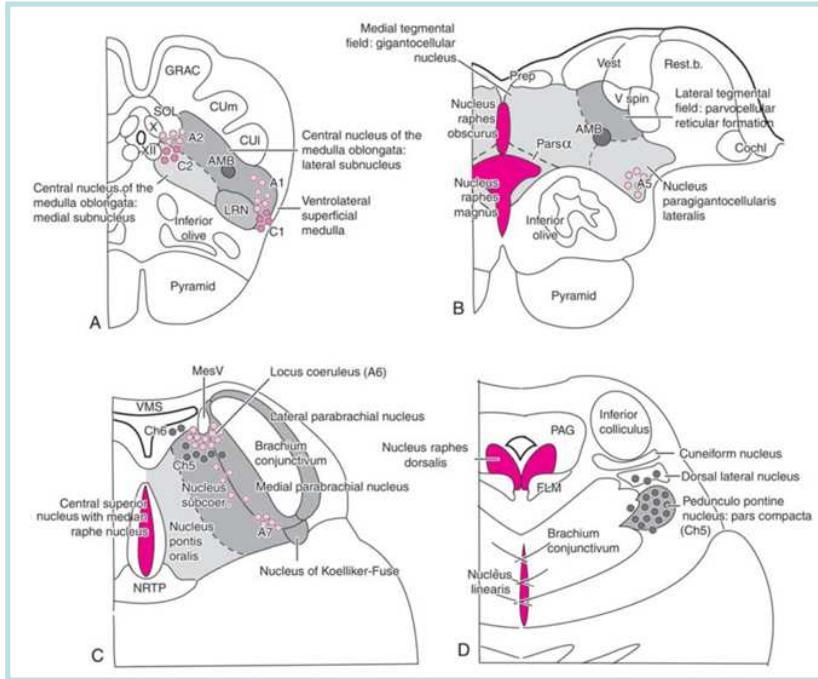


Nature Reviews | Neuroscience

CO₂ stimulates serotoninergic neurons. Respiratory motoneurons are stimulated via 5- HT, TRH a SP. Neurons in pre-BötC are stimulated through 5-HT4a, 5-HT2a as well as neurokinin1 (NK1)

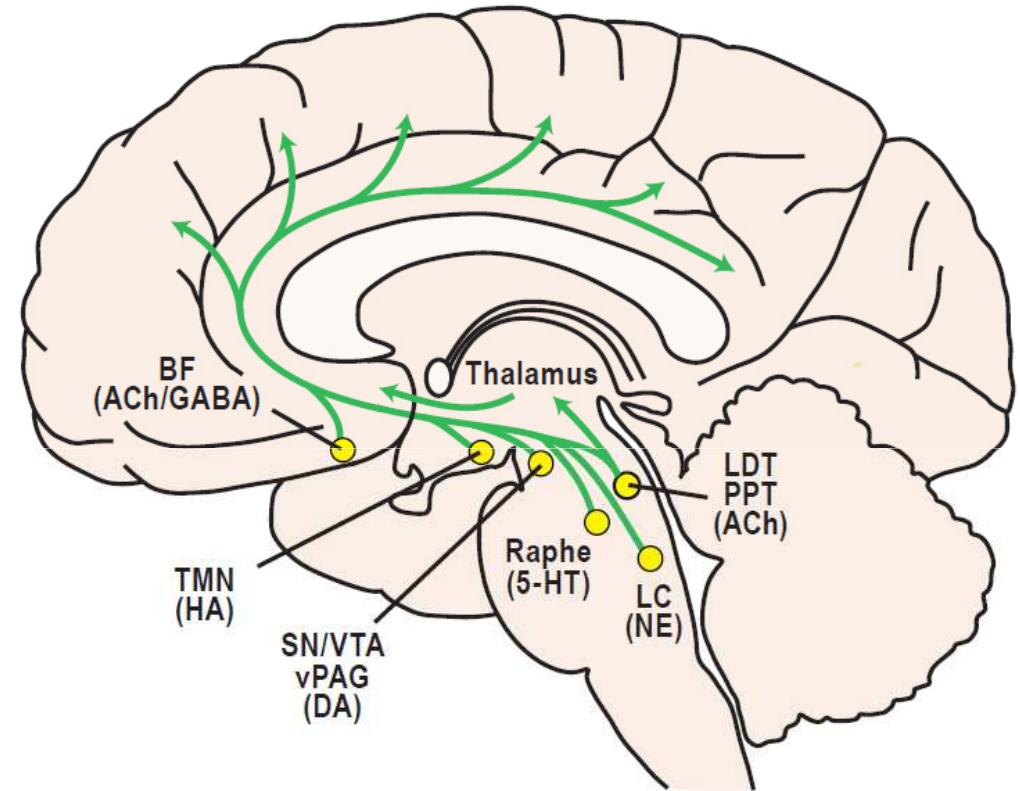
- Reversal of respiratory rhythm induced by anaesthetics (Fentanyl)
- projekcie do všetkých hlavných respiračných jadier (NTS, NA, preBöt, Böt complex, XII i frenikové motoneuróny).





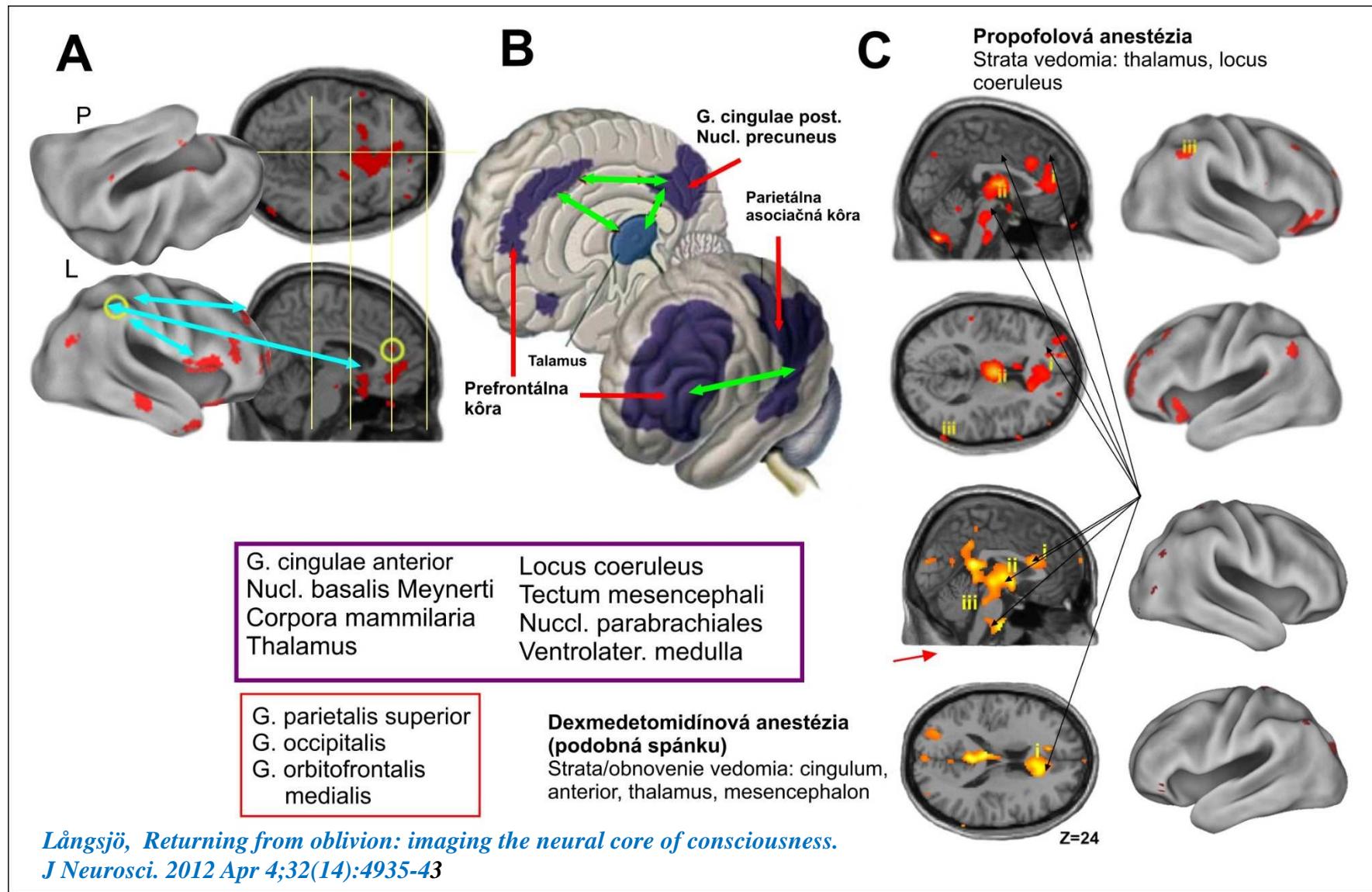
Arousing Diffuse Modulatory Systems (ADMS)

- **Norepinephrine (NE):** locus coeruleus (LC),
- **Serotonin (5-HT):** raphe nuclei,
- **Dopamine (DA):** substantia nigra (SN), ventral tegmental area (VTA), ventral periaqueductal grey (vPAG).
- **Acetylcholine (Ach) :** laterodorsal, peduncular - pontine tegmental nucleus (LDT/PPT), basal forebrain (BF)
- **Histamine (Hi):** tuberomamillary nuclei (TMN)

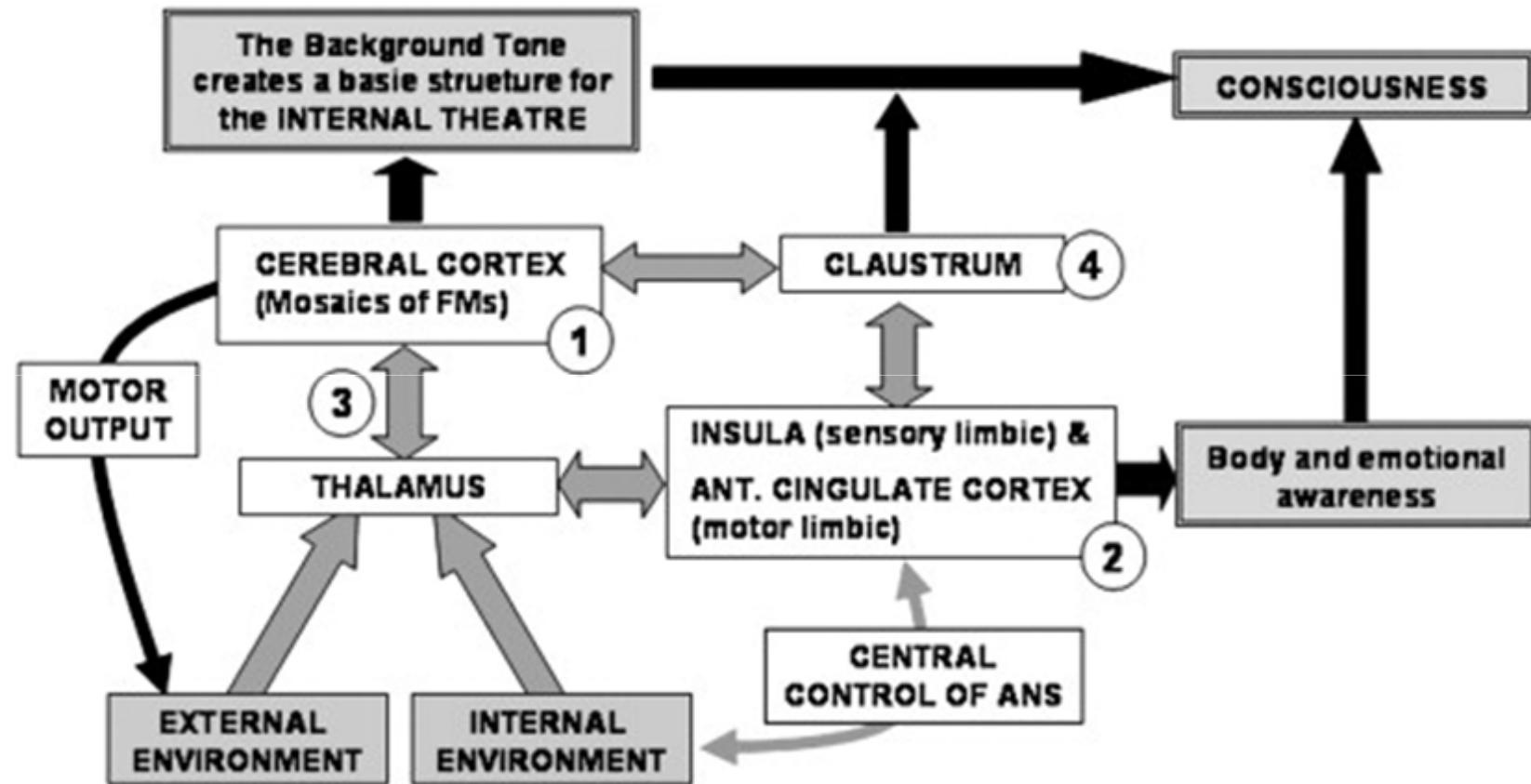


España, R. A., & Scamell, T. E. (2011). *Sleep Neurobiology from a Clinical Perspective*. *Sleep*, 34(7), 845-858.

Minimal neuronal substrate – experimental anesthesia

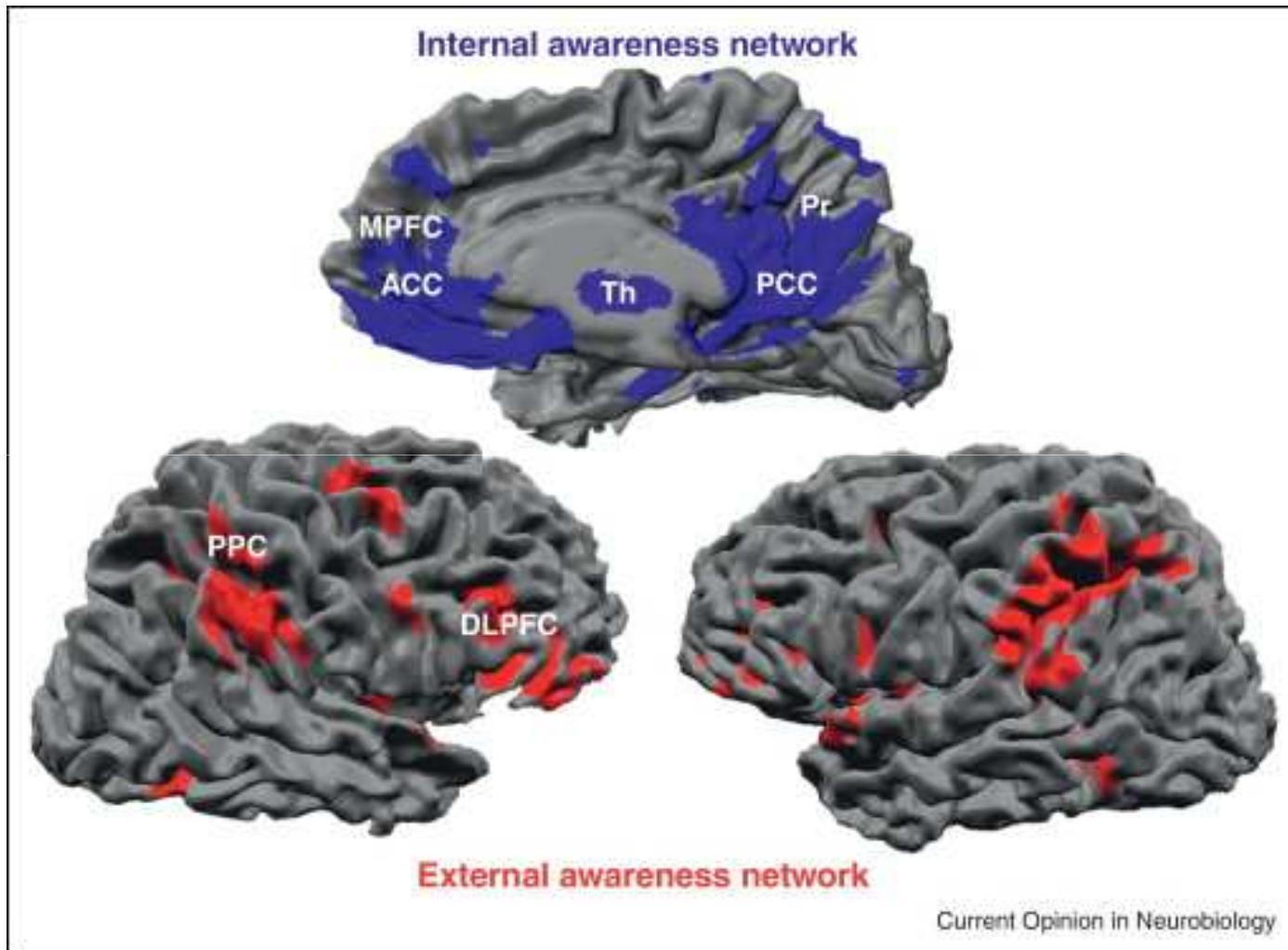


Principal parts of consciousness generator



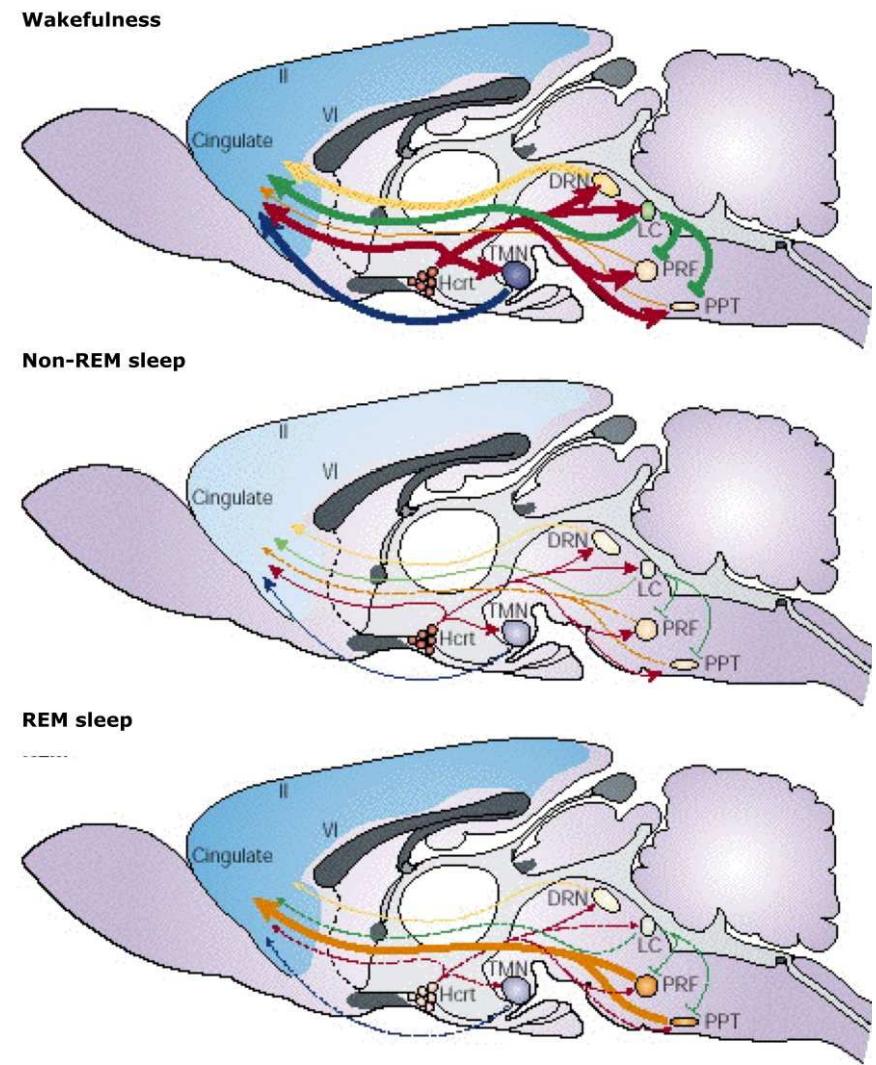
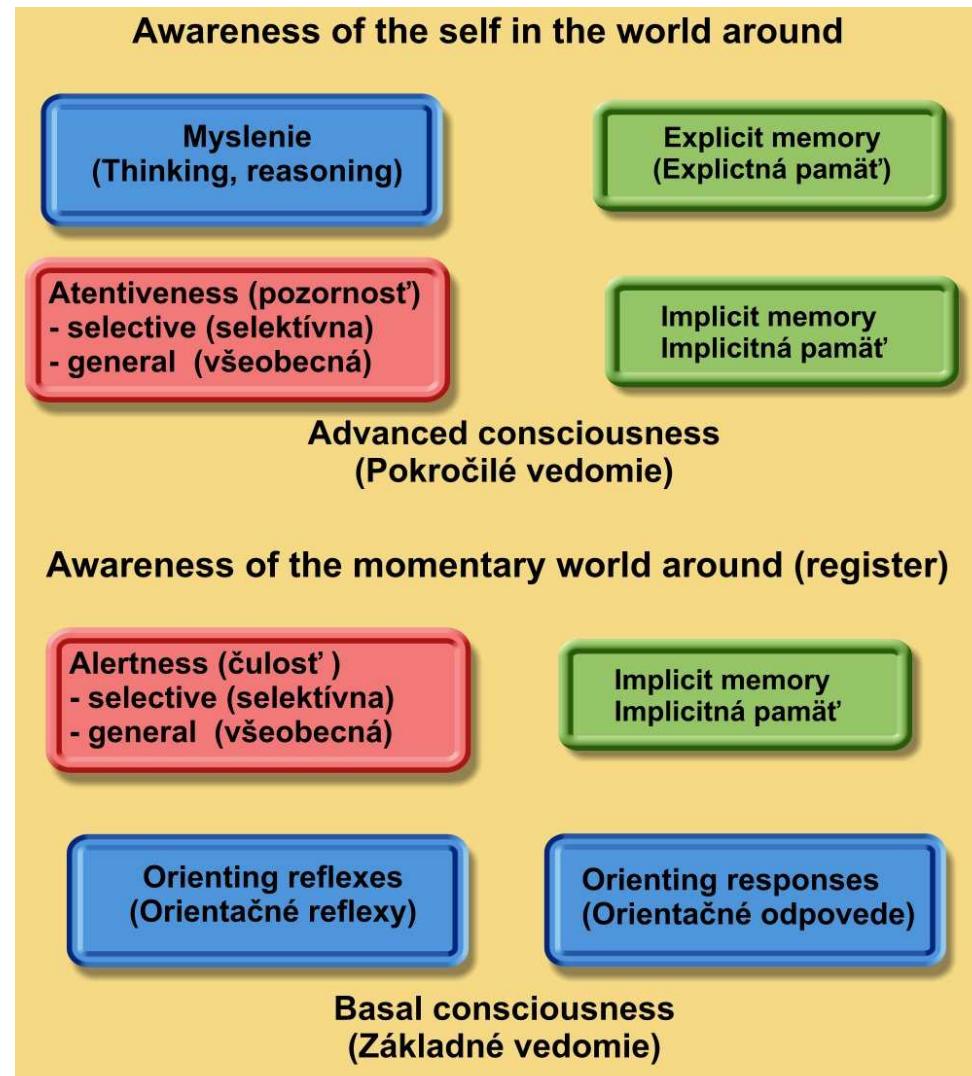
Schiff, N. D., Giacino, J. T., Fins, J. J.: Deep brain stimulation, neuroethics, and the minimally conscious state: moving beyond proof of principle. Arch. Neurol. 66, 697–702 (2009)

Principle of internal and external awareness network



Demertzi, A., Soddu, A., Laureys, S.: Consciousness supporting networks. Current Opinion in Neurobiology, 23 (2), 2013, p. 239–244

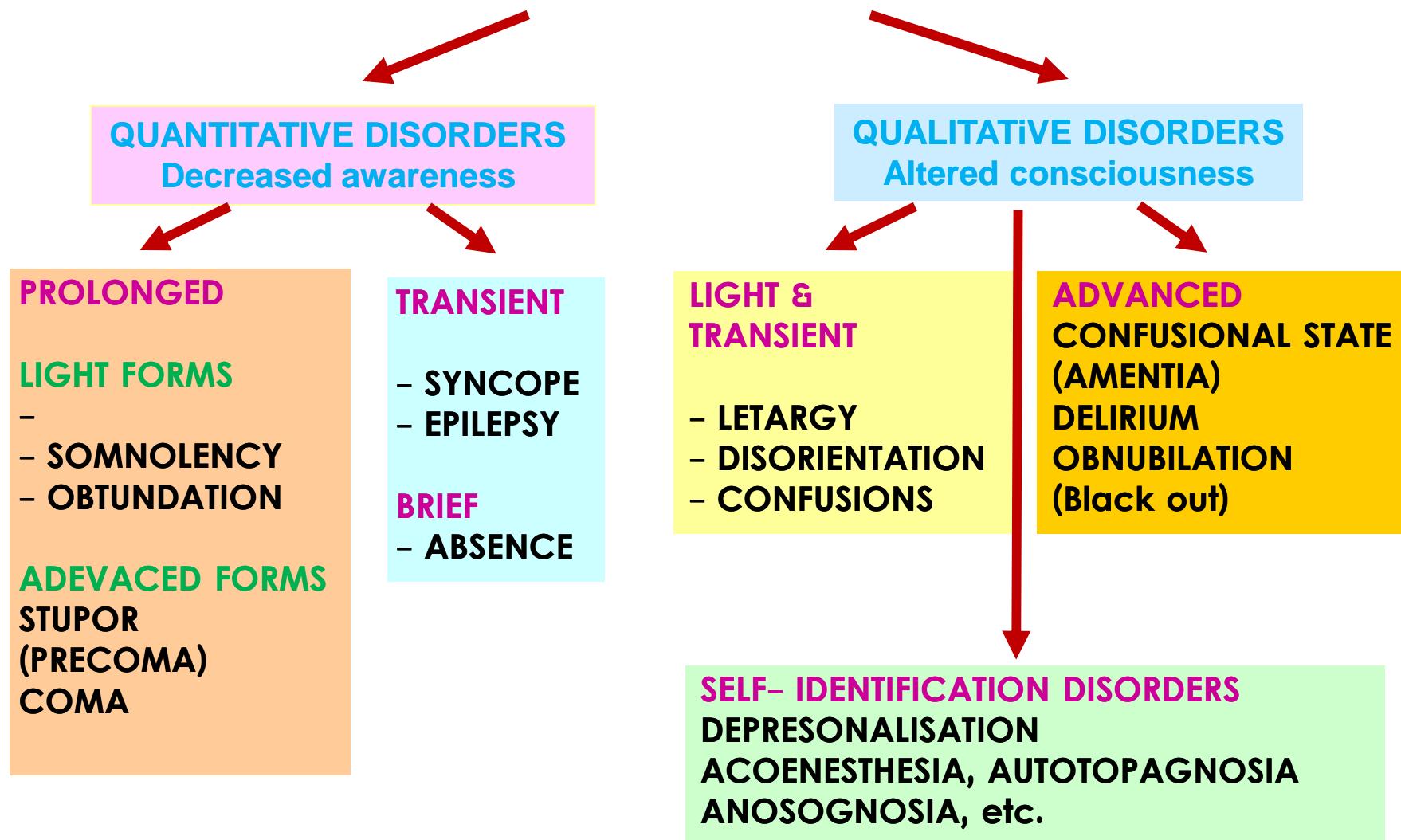
Continuum of behavioural states





2
**Disorders of
consciousness**

Disorders of consciousness



Quantitative disorders of consciousness

■ Transient (sec- min)

● **Syncope (faintness)** short disorder of consciousness

■ **systemic hypotension, resp. collaps**

(postural/ ortostatic synkopa), kardiálne (ischémia srdca, vazovagálna synkopa, ASM)

■ **disordered redistribution of blood –**
changes in intrathoracic pressure (cough syncope, laugh syncope, food jedlo (postprabdial defecation), psychogenic factors, (neurogenic syncope)

■ **changes in vessel lumen** (vertebro-basilar artery insufficiency, carotic stenotisation)

■ **disorders in electric stability** (brain commotio, brain contusion, electrical current shock, epilepsy, electroconvulsions)

■ Prolonged (hod- dni- týždne)

■ **Somnolency, lethargy** – pathological sleepiness, waking up upon light stimuli (opening eyes, orientation), response are correct, targeted, make sense, but are slowed

■ **Obtundation** – communication is difficult, person spontaneously fall asleep, can be waken up by stronger mechanicaô stimuli (rarely verbal), responses are not so precised, limited, not comprehensive, disorientation

■ **Stupor (precome)** – deep unconsciousness; person reacts to painful stimuli pain stimuli; reactions are delayed little localized, sporadic movements, verbalisation

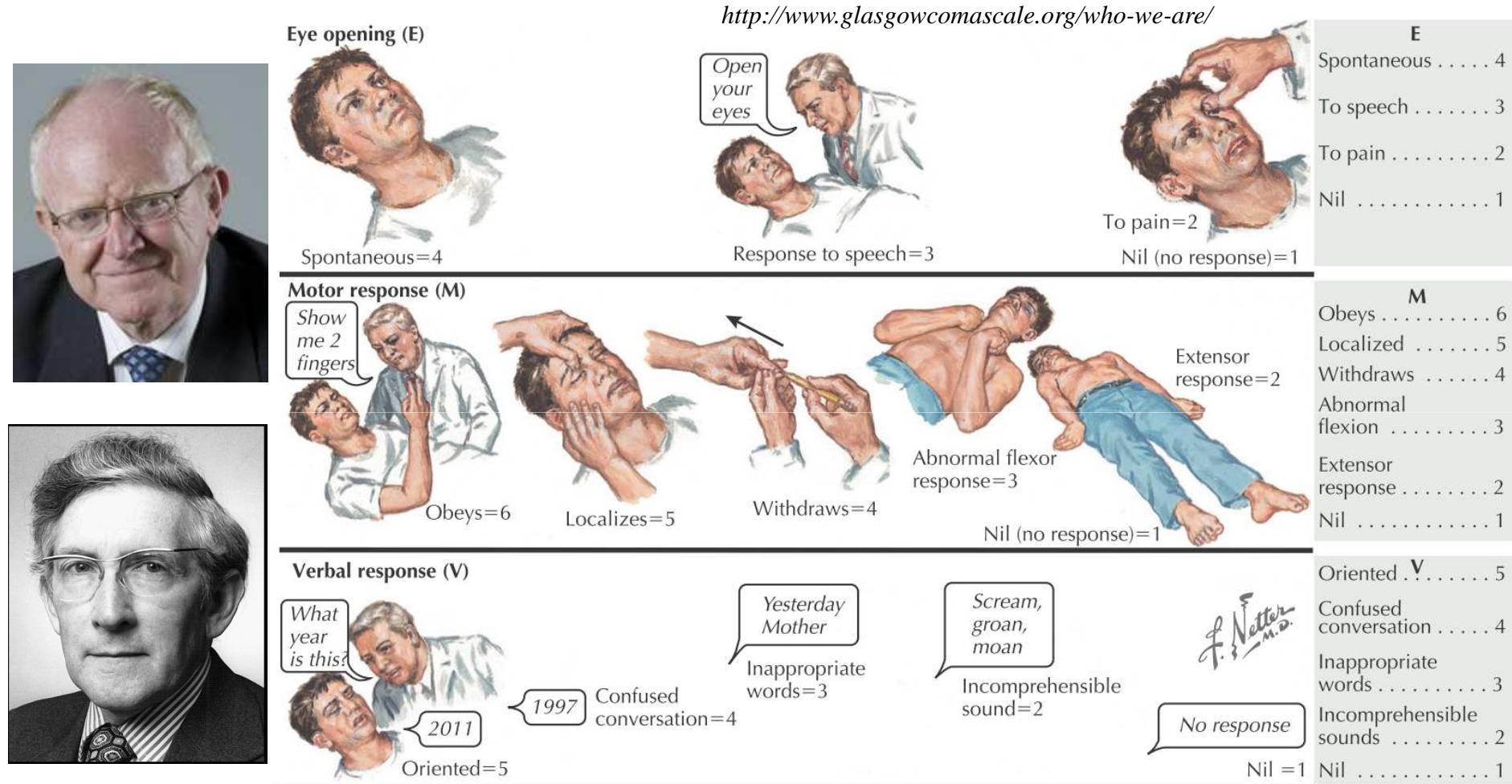
■ **Coma** - total unreactivity to outer stimuli, no spontaneous motor response, eyes are closed, breathing is shallow, vegetative responses present

Causes of disordered consciousness

Causes	Lesions	
Supratentorial Lesions	Epidural or Subdural Hematoma Large Ischemic Infarction	Intraparenchymal hemorrhage Trauma Abscess Tumor
Infratentorial Lesions	Basilar artery thrombosis Pontine or Cerebellar Hematoma	Ischemic Cerebellar Infarction Tumor Abscess
Diffuse Encephalopathies	Hypoglycemia Drug Intoxication Hepatic Encephalopathy Hyperosmolar States Hyponatremia Global Cerebral Ischemia	Hyperthermia Meningitis and Encephalitis Subarachnoid Hemorrhage Myxedema Renal Failure Hypercarbia Thiamine Deficiency Hydrocephalus
Psychogenic	Catatonic States Hysteria-malingering	Acute psychotic delirium

Gosseries O, Bruno MA, Chatelle C, Vanhaudenhuyse A, Schnakers C, Soddu A, Laureys S: Disorders of consciousness: what's in a name? NeuroRehabilitation 2011, 1:3-14.

Glasgow Coma scale



Sir Graham Teasdale & Bryan Jennett (1926-2008) – Glasgow
 neurosurgeons, introduced Glasgow Coma Scale (GCS); 1974 Lancet, entitled
 "Assessment of coma and impaired consciousness: a practical scale"

Coma score (E+M+V)=3 to 15

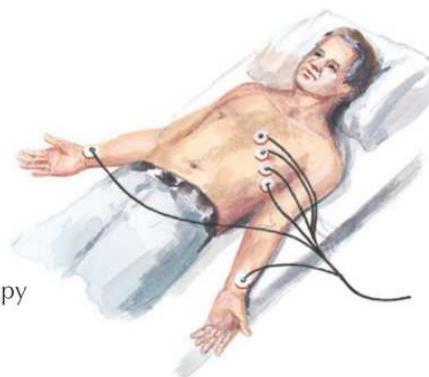
Maximum = 15 Healthy >12
 Minimum = 3 Critical <8

Syncope – four stage management

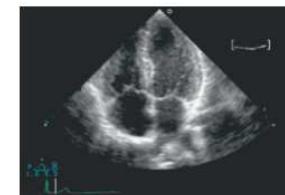
Step 1: Electrocardiogram



All patients with syncope should undergo electrocardiography. If ECG is abnormal, confirmatory testing and appropriate therapy should be instituted.

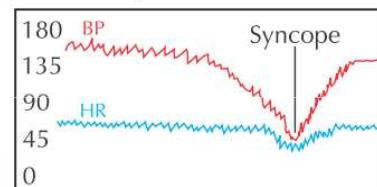


Step 2: Echocardiography



In most patients without a diagnosis, a structural evaluation with echocardiogram is required.

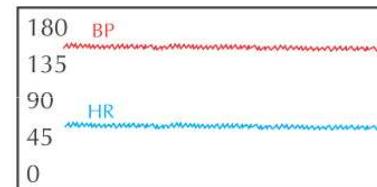
Step 3: Head-up tilt-table test



Positive neurocardiogenic tilt-table test shows drop in BP and heart rate.

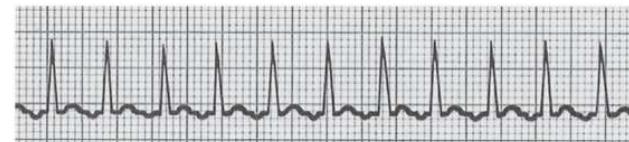
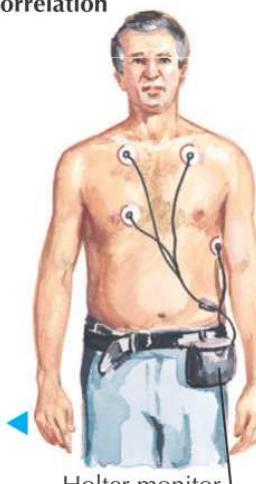
Should be considered if steps 1 and 2 are negative

JOHN A. CRAIG, MD
with
D. Mascaro



Normal tilt-table test shows maintenance of normal BP and heart rate.

Step 4: Monitoring for symptom-rhythm correlation



Ambulatory monitoring recommended for patients with negative evaluation; duration of monitoring dependent on frequency of episodes; for daily symptoms, 48-hour monitor adequate

Holter monitor

Pupils

Pattern	Description	Lesion
Dilated (bilateral)	∅ 7 mm , (-) reaction to light	<ul style="list-style-type: none">• Transtentorial herniation of both medial temporal lobes• Intoxication: anticholinergics, sympathicomimetic drugs
Narrowed (bilateral)	∅ 1-1,5 mm	<ul style="list-style-type: none">• Intoxication by opiates, organophosphates, cholinomimetics, miotic eye drops• Pontine haemorrhage, Neurosyphilis
Asymmetric (anisocoria)	∅ 1 mm difference	<ul style="list-style-type: none">• Normal ~ 20% of population; (+) photoreaction• (-) photoreaction - dilation: ipsilateral pressure in mesencephalon + nucl..III (tumors, bleeding)
Fixed pupils	∅ 5 mm , (-) fotoreaction	<ul style="list-style-type: none">• Mesencephalic lesions

Qualitative disorders of consciousness

- **Lighter forms** (often combined with quantitative disfunctions; patients are mostly aware of disorder)
 - **Apathy, letargy** – similar to tiredness (e.g. depression, toxic, infection, ictus, metabolic)
 - **Disorientation** – slowness, blunted attentiveness and preparedness, (e.g.. altitude sickness, hypoxia, cold , starvation, hypoglycemia)
 - **Confusion** – a person is not orientated to time, place and/or person; responses or behaviours to situations may be inappropriate. agitation, restlessness with sleepiness (somnolence) or even stupor (difficult to arouse or state)

■ Progressive forms (altered state of consciousness, cognition)

- **Acute confusion state** – disordered perception, disorientation, disorders of memory (intoxication – posttraumatic, post-narcotic, inflammation)
- **Delirium** – disorder of thinking, perception, hallucinations, disorders of memory, agitation, sleepiness, amnesia, organic damage (nádory, toxicky, abstinencia)
- **Obnubilation (blackout)** – disorder of perception of reality; amnesia
- **Depersonalisation**

Acute confusional state

(Alternatives: confusional state, organic brain syndrome, confusional insanity, transient psychotic reaction, organic psychosyndrome; Meynert-Korsakoff syndrome

Characteristics: amentia (behaviorálna demencia) patrí aj ku kognitívnym poruchám)

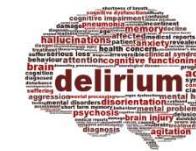
- forma delíria s prevahou deficitu percepcie, pozornosti a orientácie, dezorientovaný v čase a priestore, často je nadmieru aktívny – úniky; aktívna obrana
- schopnosť rozepamäťania (anterográdna, retrográdna amnézia), zasteté vedomie (neschopnosť presunu a fokalizácie pozornosti)
- Môže sa prejaviť úzkosť, strach, hnev, eufória, tras, potenie, búšenie srdca.

Causes:

- Intoxication (37% cannabis, marihuana), pooperative (probably post-narcotic or combination of effects) (in elderly surprisingly high incidence after hip fracture surgery), tramadol, infections,
- Diabetes – hypoglycaemia, cardiac decompensation, infarction,
- Confusional arousals (sleep terror),
- Alzheimer disease, kidney failure (uremia)
- Dehydratation, disorders of electrolytes



Delirium

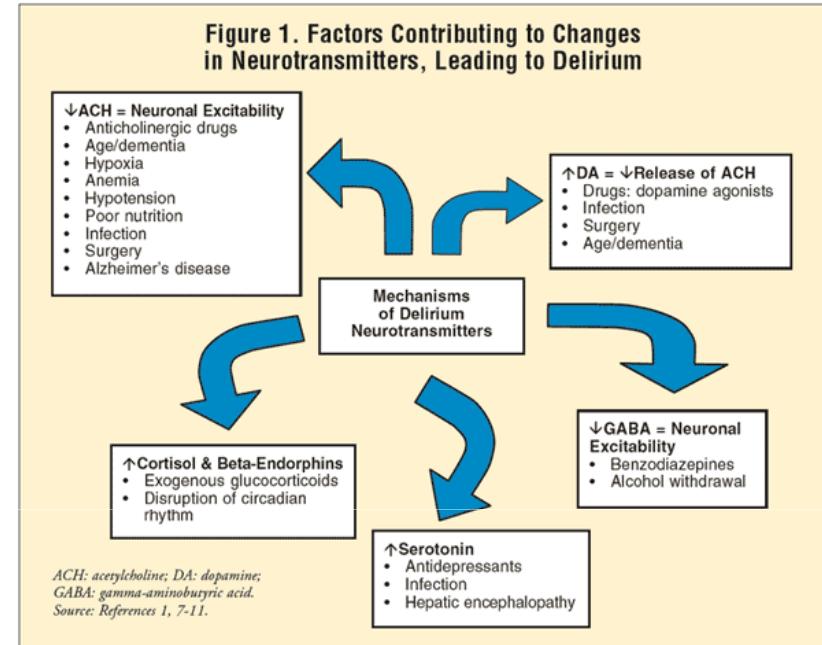


Delirium due to the substance withdrawal e.g., alcohol, benzodiazepines, or nicotine, etc.

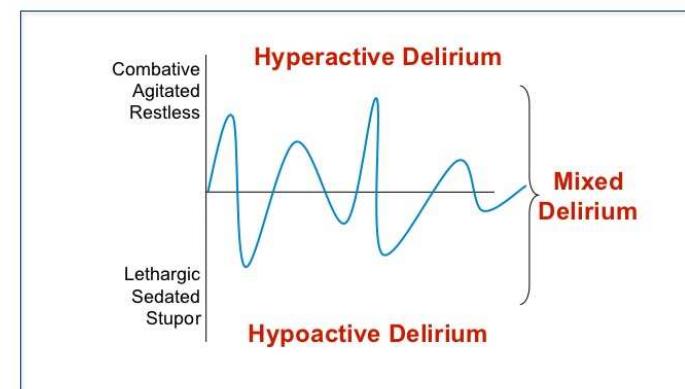
- **Mechanisms:** imbalance of inhibitory and excitatory neurotransmitter systems in brain; alcohol consumption leads to *inhibition of excitatory NMDA receptors and activation of the inhibitory GABA-A receptoric effect (cerebral inhibition)*; withdrawal leads to disinhibition of brain and reinforcement of alarm response > dopaminergic and noradrenergic effects -> marked sympathetic activation and a tendency toward epileptic seizures.
- benzodiazepine withdrawal causes delirium by way of decreased GABA-ergic transmission; epileptic seizures may occur.

Delirium not due to substance withdrawal

- **Mechanisms:** many different; final common pathway of delirious states seems to consist of a cholinergic deficit combined with dopaminergic hyperactivity.
- significance of other neurotransmitters – serotonin, noradrenaline less clear

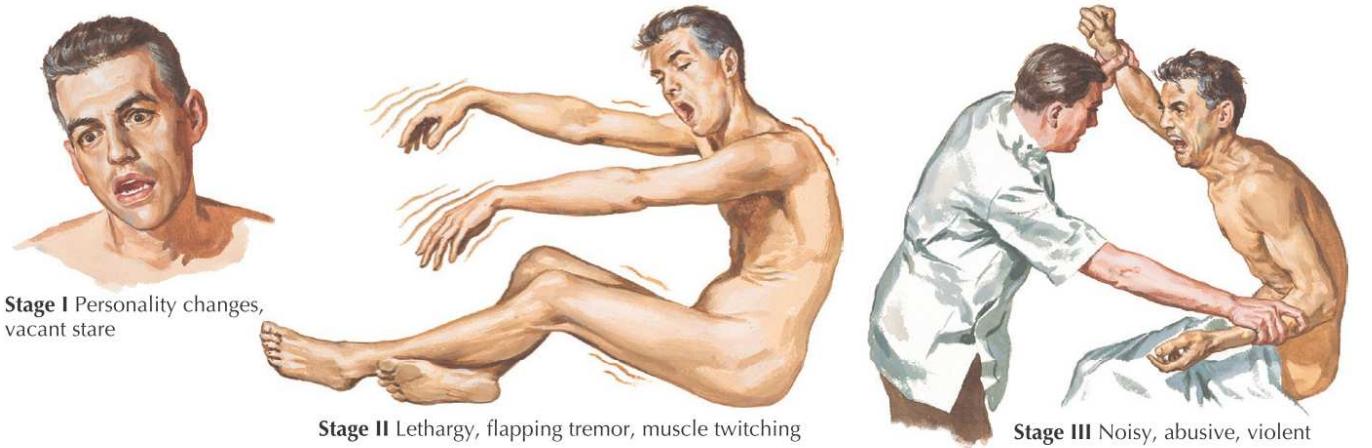
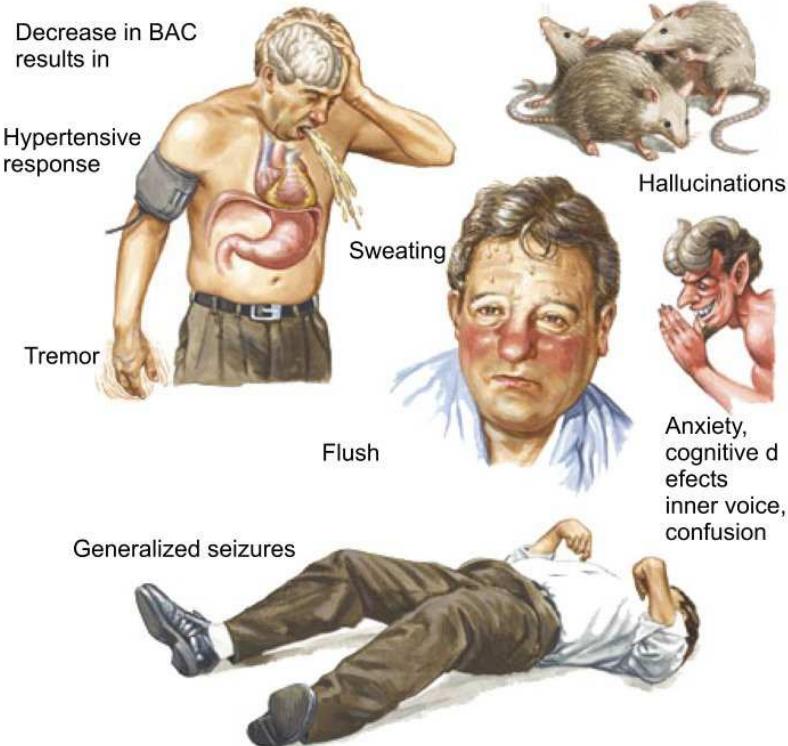


Delirium Subtypes

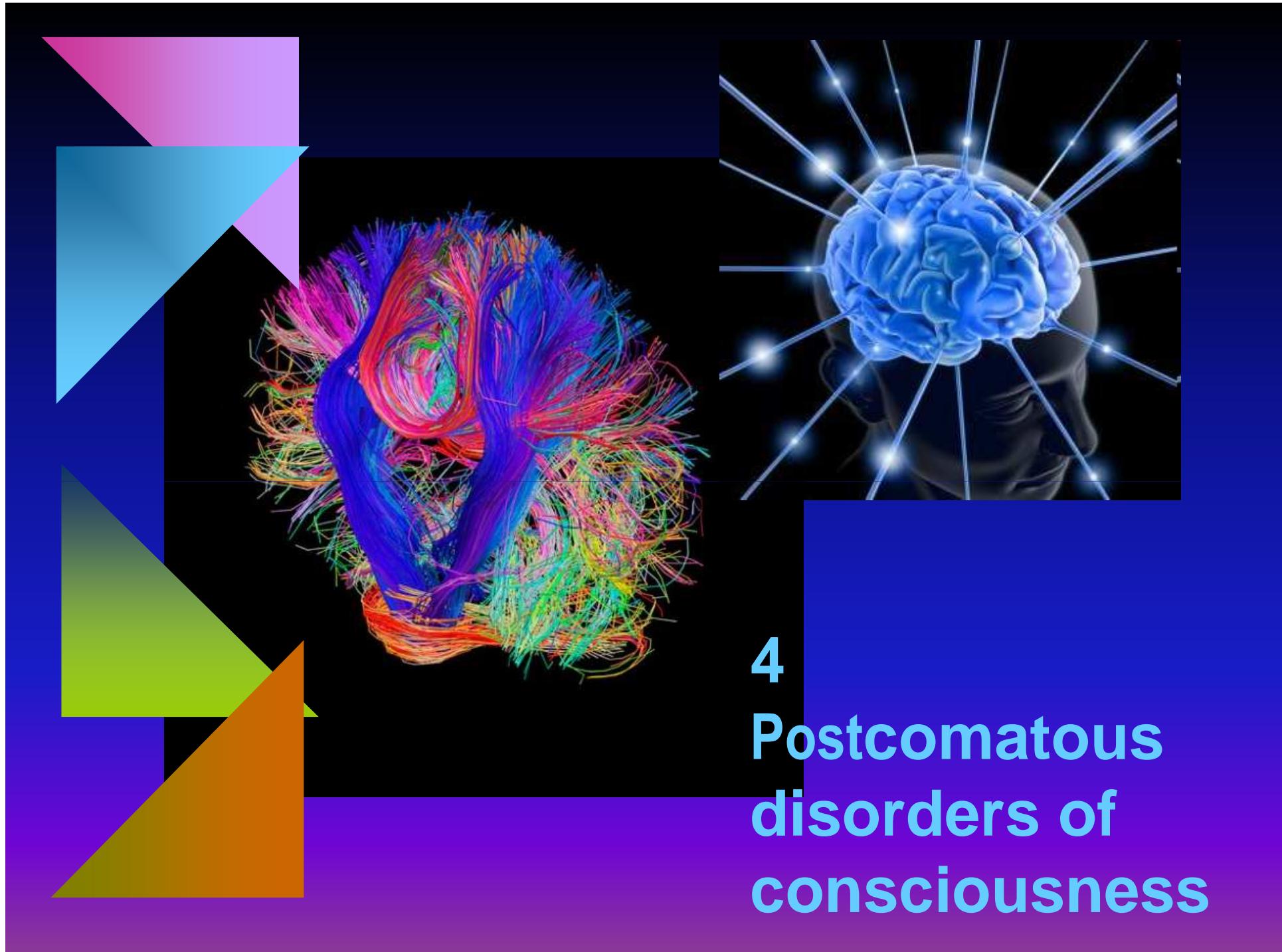


Delirium

Withdrawal symptoms in chronic alcohol abuse

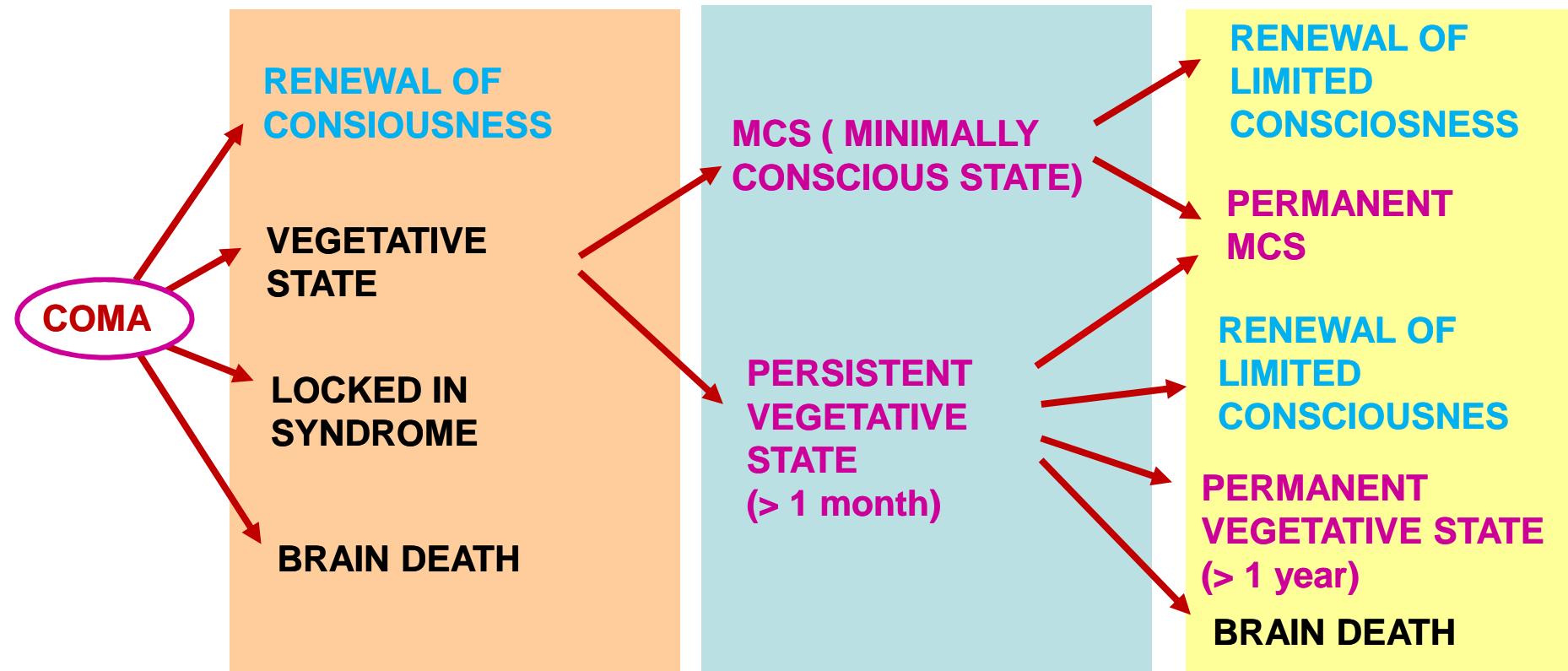


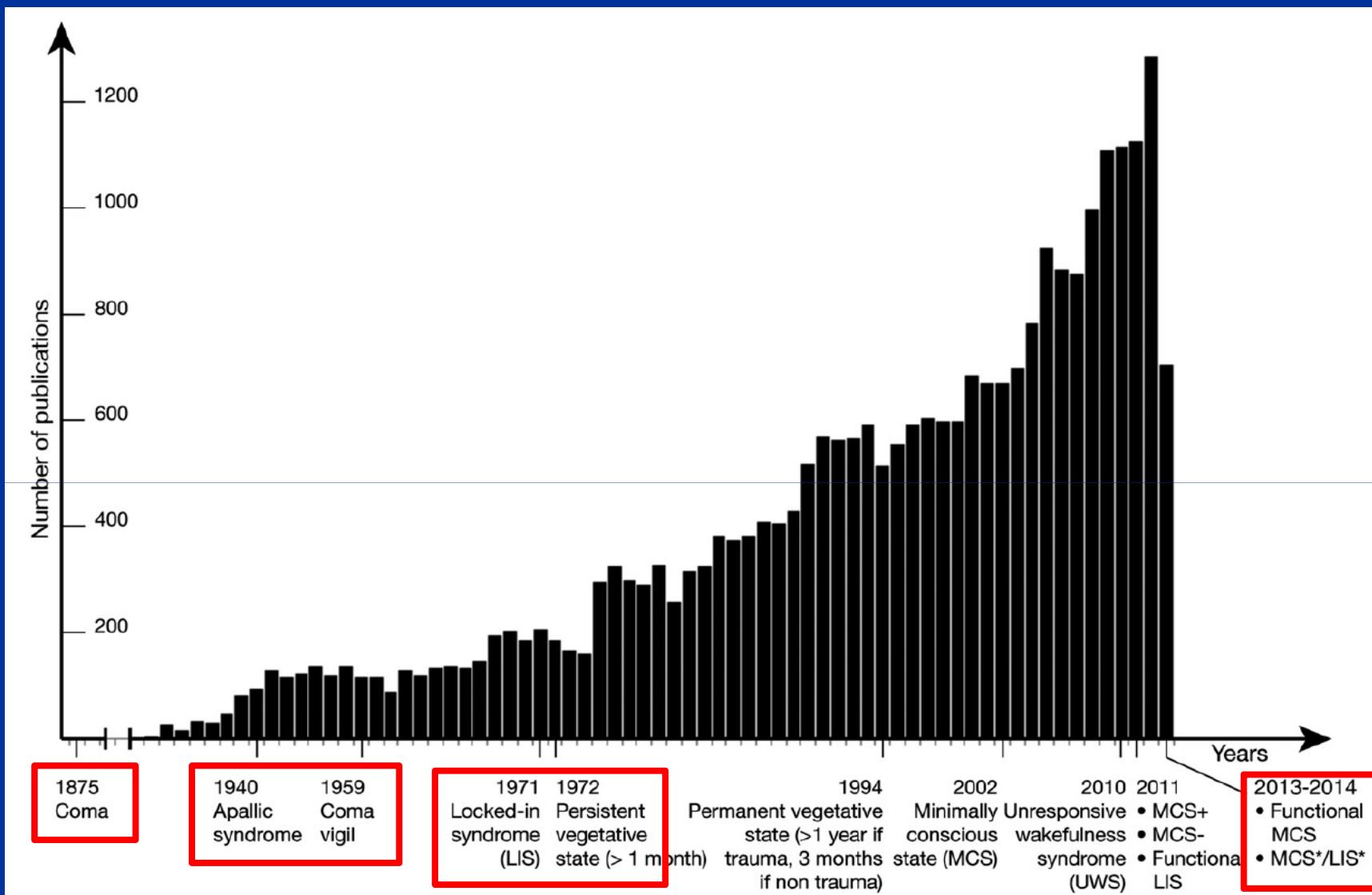
Stages in development of delirium due to the substance withdrawal



4 **Postcomatous disorders of consciousness**

Postcomatous disorders & coma like states





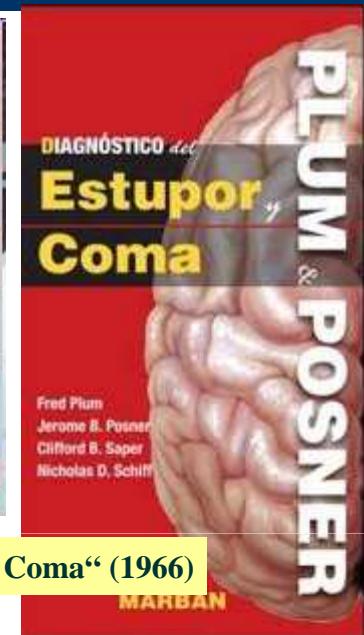
Number of published papers per year on patients with disorders of consciousness and evolution of the terminology. Medline search (7/2013) keywords used were 'coma', 'vegetative state', 'unresponsive wakefulness syndrome', 'minimally conscious state' and 'locked-in syndrome'

Honors

- **Fred Plum (1924 – 2010)** – american neurologist; he introduced the term "locked-in syndrome": together with Dr. Byron Jennett, they introduced the term "persistent vegetative state"

Jennett B, Plum F (1972) Persistent vegetative state after brain damage: a syndrome in search of a name. Lancet:734–737

- **Schiff, N.D. (1997)** tzv. deep brain stimulation
- **Laureys, S (2005):** usage of fNMR, PET in research



„Diagnosis of Stupor and Coma“ (1966)



Laureys S, Schiff ND: Coma and consciousness: paradigms (re)framed by neuroimaging. Neuroimage, 2012, 2:478-491.

Laureys S: Science and society: death, unconsciousness and the brain. Nat Rev Neurosci 2005, 11:899-909.

Jennett B, Plum F: Persistent vegetative state after brain damage. A syndrome in search of a name. Lancet 1972, 7753:734-737

Postcomatous disorders & coma like states

Vegetative state (Apallic syndrome 1940, Coma vigil 1952)

Unresponsive wakefulness syndrome (UWS) (2010)

Eti: traumatic/ atraumatic, drug dependencies/ independency

- severe global metabolic, toxic, ischaemic, traumatic cortical injury (cardiac arrest, brain surgery, etc.)
- bilateral damage of frontal lobe, lesion of upper brainstem,

Sy:

- return to wakefulness (eye opening), but without awareness of self and environment; with no communication, no visual contact with persons, nor surroundings, no verbal response
 - without paralysis, spontaneous movements exist, normal reflexes (breathing)
 - bulbar reflexes present, eye-ball movement, swallowing, yawning
 - occasionally decerebration or decortication rigidity, Babinski's sign
 - pupillary response to light often not present on both sides
 - vegetative response normal or hyperactive (CVS – tachycardia, hypertensive episodes, thermoregulation, neuroendocrine, bowel movement)
 - without sensory disturbances, reactions to pain are present but delayed
-
- **Persistent vegetative state** – lasting > 1 month
 - **Permanent vegetative state** – lasting > 1 year after traumatic brain damage or > 3 months after atraumatic brain damage

Post- comatose recovery outcomes

Persistent vegetative state

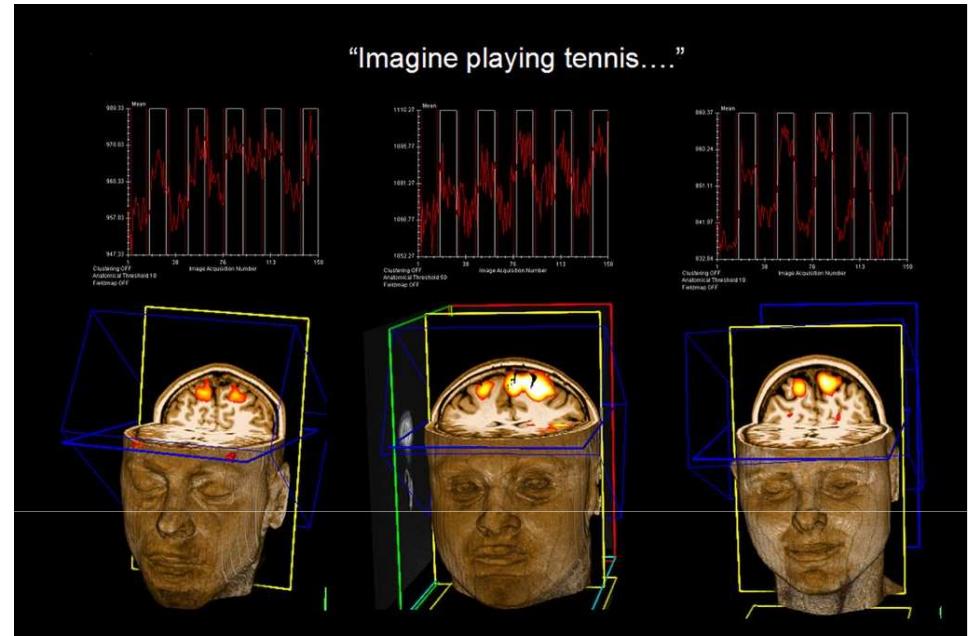
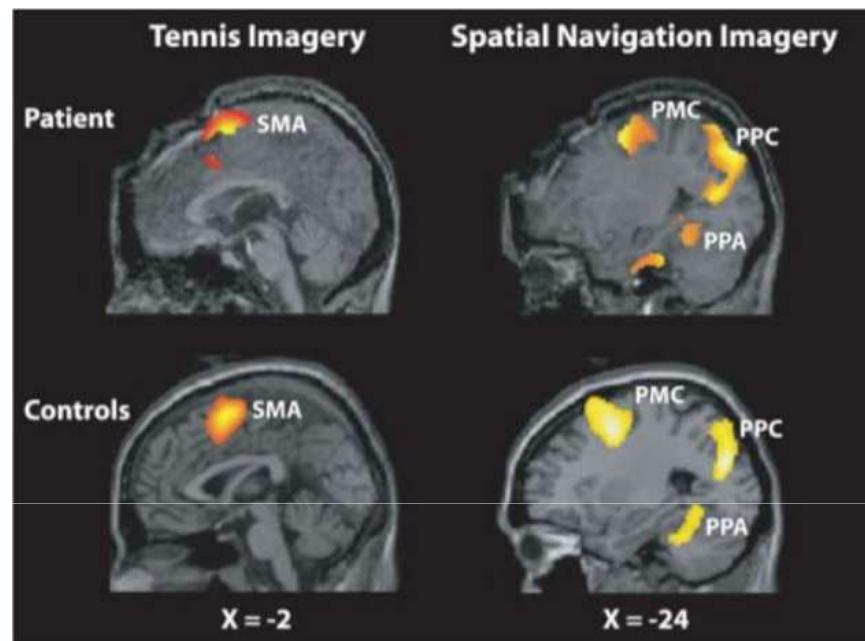


<http://www.usatoday.com>

Akinetic mutism



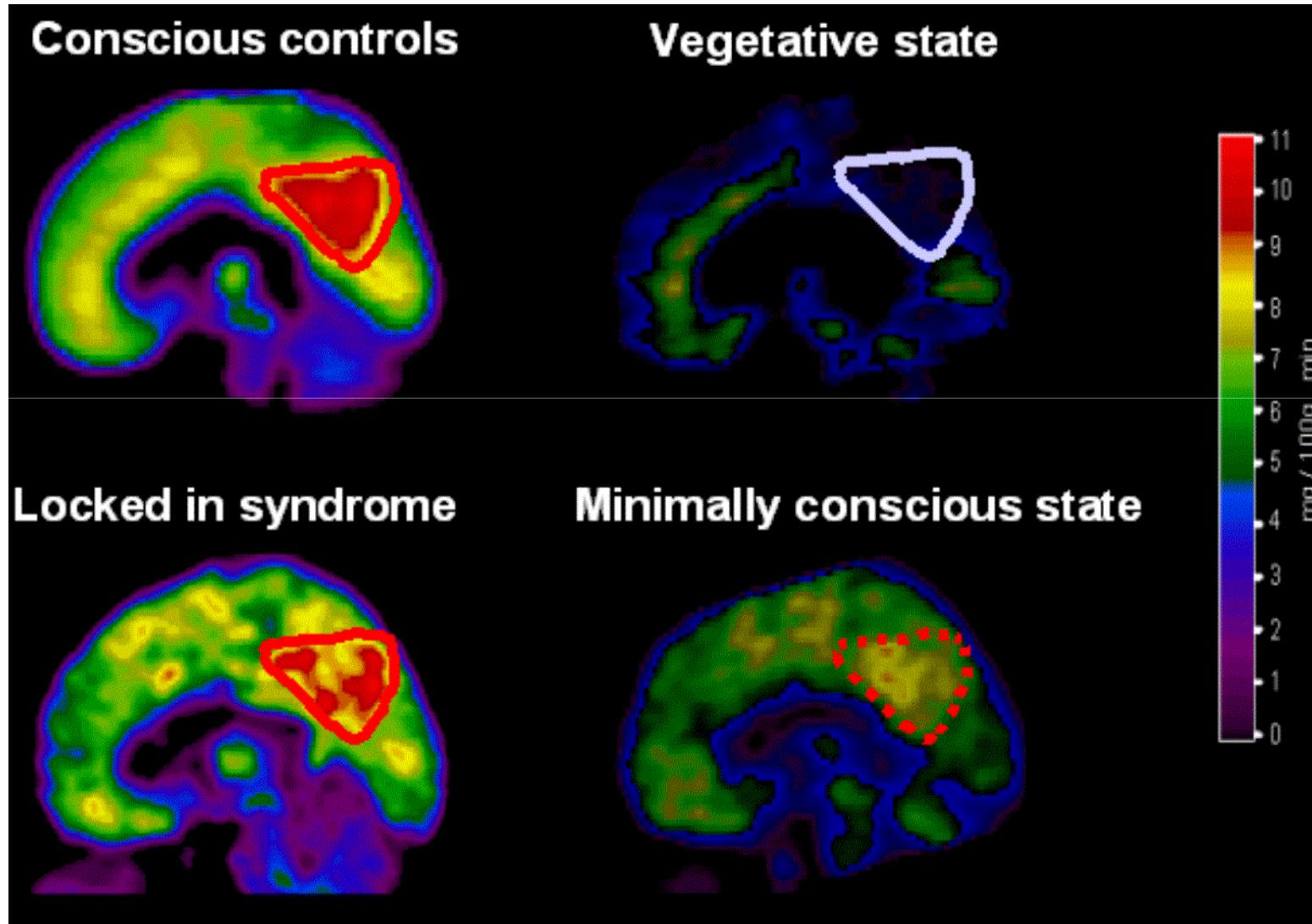
Vegetative state



Patients can imagine various activities; there is lack of outer manifestations of awareness

- **Gosseries O, Bruno MA, Chatelle C, Vanhaudenhuyse A, Schnakers C, Soddu A, Laureys S: Disorders of consciousness: what's in a name? NeuroRehabilitation 2011, 1:3-14.**
- **Schiff, N.D.: Recovery of consciousness after brain injury: a mesocircuit hypothesis. Trends Neurosci. 33, 1-9, 2010**
- **Demertzi, A., Soddu, A., Laureys, S.: Consciousness supporting networks. Current Opinion in Neurobiology, 23(2)? 239–244, 2013**
- **Laureys S, Schiff ND: Coma and consciousness: paradigms (re)framed by neuroimaging. Neuroimage 2012, 2:478-491.**

Using NMR and PET scans in diagnostics

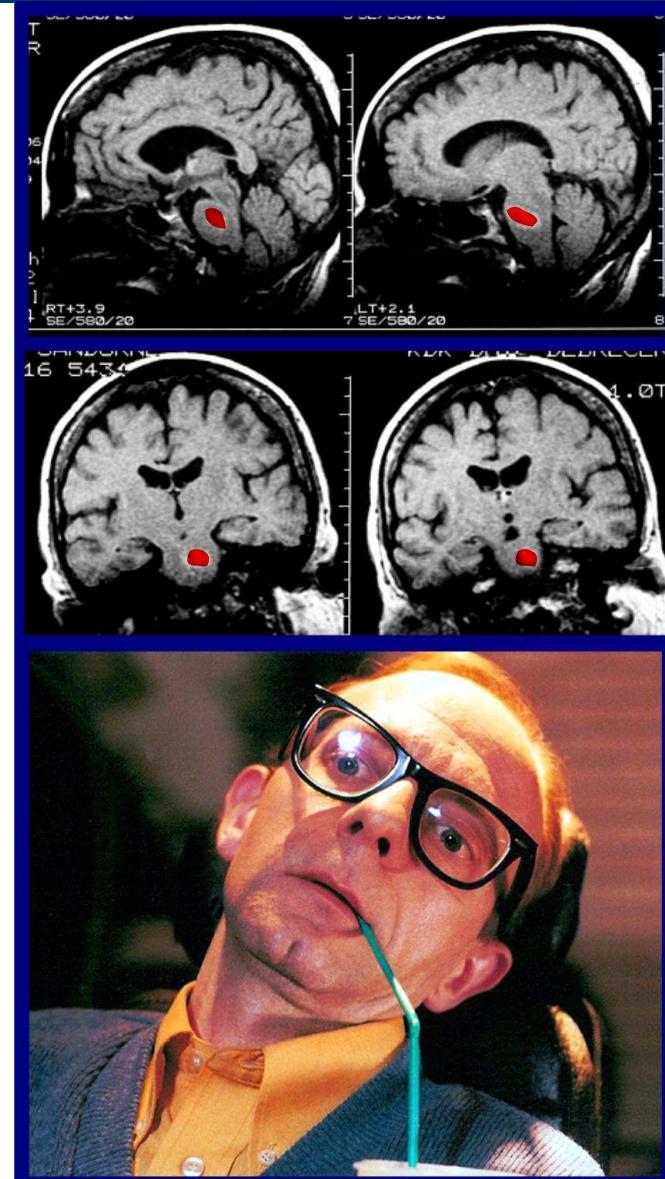


Postcomatous disorders & coma like states

Locked in syndrome (LIS)

- Alt.: pseudocoma, deafferentation sy.)
- Eti: rare clinical entity results typically from a ventral pontine infarction (rarely pontine tumours, haemorrhage, central pontine myelinolysis, head injury or brain stem encephalitis.) that damages cortico-spinal tracts below the level of the III.n. nuclei., leading to complete paralysis of voluntary muscles except for eye movements
- Sy:
 - total paralysis (tetraplegia loss of voluntary movement);
 - Bulbar paralysis (dysarthria, amimia, dysphagia) – arteficial feeding
 - patients can open their eyes and elevate and depress eyes to command. ; horizontal eye movements are usually lost
 - Patients are on arteficial ventilation
 - No sensoty defect; reactivity to pain present ↗
 - Recovery is exceptional

Damasio A, Meyer K: Consciousness: an overview of the phenomenon and of its possible neural basis. In The Neurology of Consciousness: Cognitive Neuroscience and Neuropathology. Laureys S, Tononi G. (Ed) Oxford:UK: Academic Press; 2009: 3-14



Other disorders of consciousness

Akinetic mutism

- **Eti:** first described in patients that suffered from diencephalic damage; lesions that interfere with reticular cortical/integration (but spare the corticospinal pathways); hydrocephalus, tumors close to 3rd ventricle; gross bilateral lesion of gyrus cinguli, frontal lobe, periaqueductal mesencephalon
- **Sy:** immobility, eye closure, little or no vocalisation; little movement to painful stimuli
 - the relative paucity of signs indicating damage to descending motor pathways, despite the immobile state (as in LIS); spasticity and rigidity are not usually evident (as in vegetative state)
 - Sleep/wake cycles can be seen, as indicated by eye opening.
 - !! debate about whether or not the syndrome should be clearly differentiated from the vegetative state; indistinguishable from early stages of the vegetative state

Abulia = lighter form of akinetic mutism: hypokinesis (bradykinesia instead of akinesis (delayed verbal and other motor reactions)

Psychogenic coma (Hysterical pseudocoma)

- eyelids are kept firmly shut and are resistant to opening
- oculocephalic responses are unpredictable (nystagmus is evident on caloric testing)
- motor tone is normal or inconsistent and limb reflexes retained.
- EEG shows awake rhythms

Catatonia

1874-Karl Ludwig Kahlbaum (Die Katatonie oder das Spannungsirresein)

Eti: associated with psychiatric illness (affective) schizophrenia; metabolic/ drug induced disorders; no organic lesions

Sy:

- no spontaneous movement, patients seem unresponsive to their surroundings, but appear conscious.
Neurological examination is normal. passive limb positioning in postures “waxy flexibility”.
- eyes open and unblinking, pupils dilated but reactive, oculocephalic responses absent or impaired, and caloric responses intact. EEG: low voltage, fast record rather than the “slowing” of true coma.
- difficult to distinguish from organic disease, particularly in lethargic unresponsiveness



Comparison of coma-like disorders of consciousness

	Minimally conscious state	Vegetative state	Coma	„Locked in“ syndrome
Vigilance - communication	Reduced, partial	Absent	Lost	Full
Sleep - Wake cycle	Present	Present	Absent	Present
Motor functions	Localized response to pain; touches and hold things;	Minimal spontaneous movements; withdrawal response to pain	Reflex and postural responses	Quadriplegia
Auditory functions	Localises source of sound; turn the head	Startle (orientation) after recovery some remember	None; after recovery some remember what they heard	Present
Visual functions	Visual fixation (prezerá; akoby do práz dna)	Startle (orientation), no focusing	No	Present
Communication	No words, sounds		No	Present; limited to vertical eye movement
Cognition understanding	Present but limited	Limited, little or missing	No	Present; cannot react
Emotions	Smiling, crying, clenching, mimics	Reflex smiling, crying	No	Present ; cannot react

Bruno MA, Vanhaudenhuyse A, Thibaut A, Moonen G, Laureys S: From unresponsive wakefulness to minimally conscious PLUS and functional locked-in syndromes: recent advances in our understanding of disorders of consciousness. J Neurol 7:1373-1384. 2011,

Assessment

Standardized validated scales

- bedside assessment neurologist, internist
- Glasgow coma scale (GCS)
- Coma Recovery Scale-Revised (CRS-R)
- Full Outline of Unresponsiveness scale (FOUR)

Specific assessment tools:

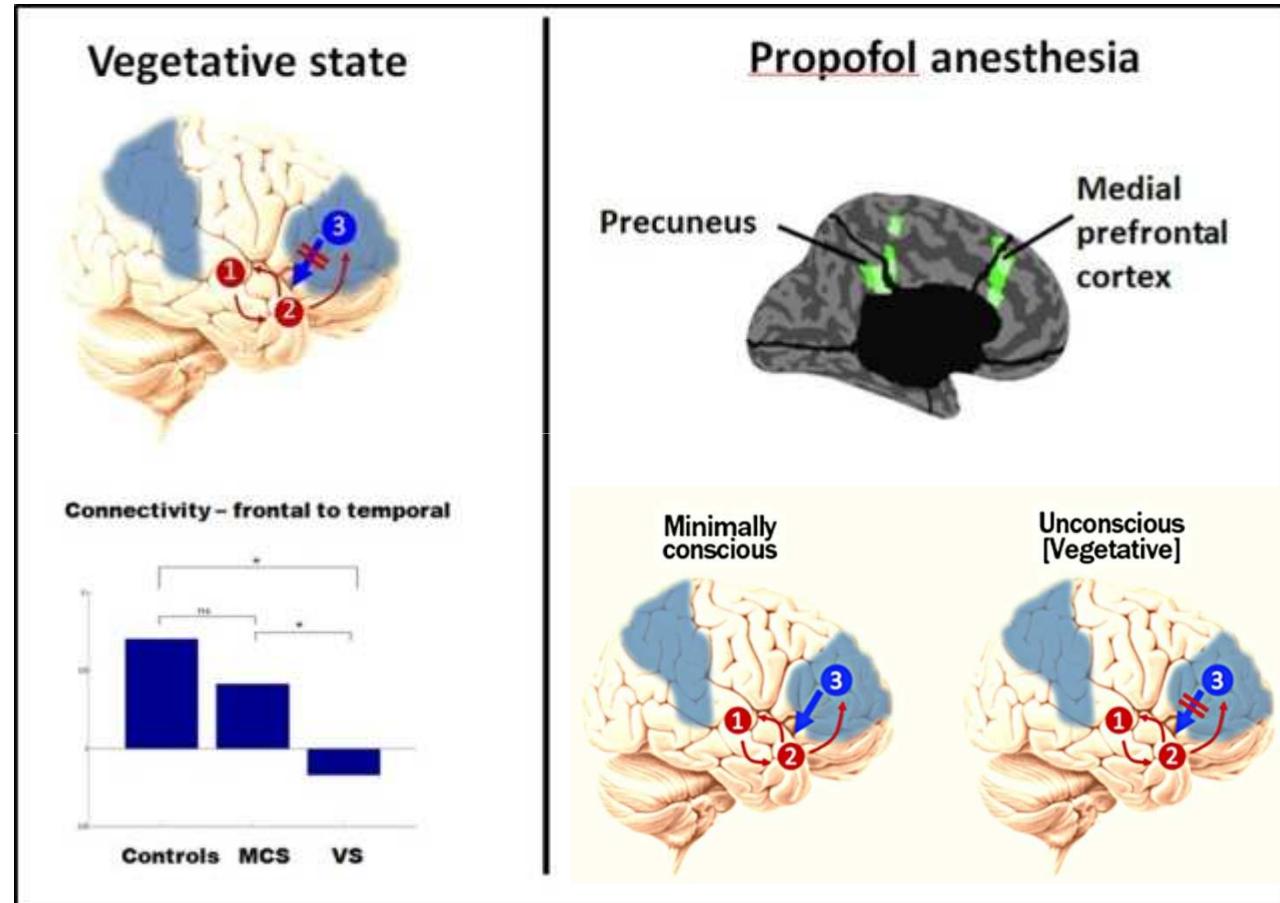
- mirror (to evaluate visual pursuit), patient's own name (to assess auditory localization),
- self-referential stimulus (their own face)
- written commands (absence of response to oral commands)

What are not the signs of consciousness

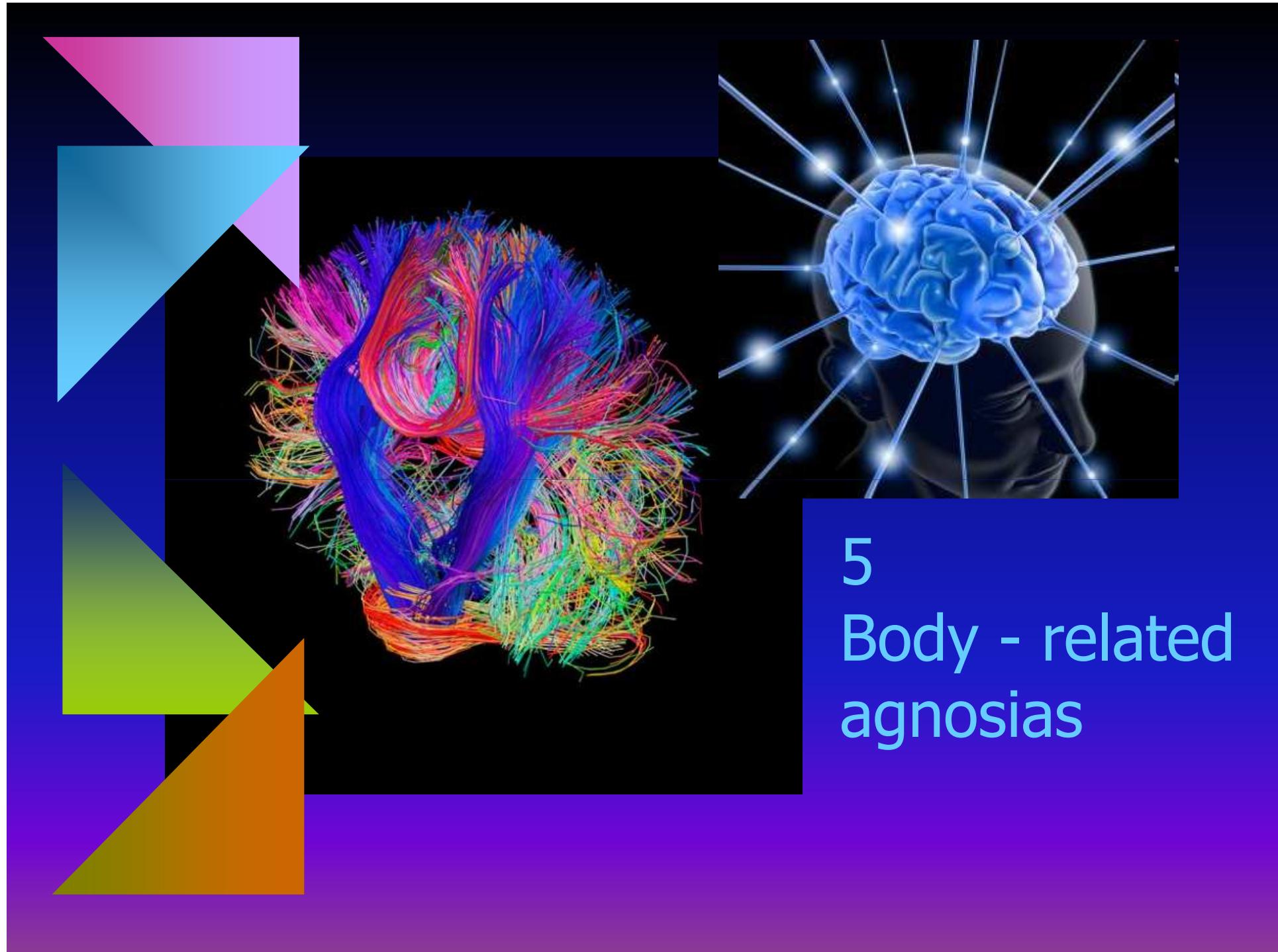
- blinking in response to a threat (blink reflex may be elicited due to corneal stimulation by air flow)
- visual fixation (at least in patients with anoxia)
- resistance to eye opening is related to consciousness

Frontal- parietal disconnection

- PET studies hypometabolism in frontal-parietal regions
- Strata spojení medzi frontálnou a parietálnou kôrou pri VS a propofolovou anestéziou



Boly, M., Garrido, M.I., Gosseries, O., et al.: Preserved feedforward but impaired top-down processes in the vegetative state. Science 2011, 6031: 858-862



5 Body - related agnosias

Disorders of self-recognition and its parts

Autopagnózia	neschopnosť rozoznať dráždené miesto na povrchu tela
Dermoalexia	neschopnosť rekonštrukcie priestorovej mapy povrchu tela. Prejavuje sa tým že postihnutý nie je schopný rozoznať rôzne tvary, písmená ktoré sa mu kreslia na kožu
Alloestézia	je porucha stálosti lokalizácie podnetu. Pri opakovanom dráždení toho istého miesta cíti chorý dráždenie stále v iných oblastiach
Dyzestézia	je porucha, pri ktorej sa podnet jednej modality interpretuje ako vnem inej modality, napr. dotyk ako pálenie, chlad ako teplo a pod
Stereoagnózia	strata schopnosti rozoznať predmety hmatom pri zatvorených očiach. Táto porucha sa prejavuje dvomi, relatívne samostatnými formami
Amorfognózia	neschopnosť rozoznať tvary predmetov (napr. kocku, guľu, knihu). Porušená je centrálna integrácia podnetov z povrchových i hĺbkových mechanoreceptorov i proprioreceptorov

Qualitative disorders

Ahygnozia	neschopnosť rozoznávať látkovú podstatu ohmatávaných predmetov (napr. sáčok s vodou, pieskom a pod.). Porušená je centrálna reprezentácia podnetov z termoreceptorov chladu, tepla a povrchových mechanoreceptorov
Akinestézia	neschopnosť rozoznávať pohyb tela a jeho jednotlivých segmentov, napr. chôdzu, pohyby ruky nohy a pod.
Statanestézia	neschopnosť rozoznávať statické postavenie tela alebo jeho jednotlivých častí, napr. stoj
Hypopallestézia	neschopnosť vnímať hĺbkovú tzv. vibračnú citlosť. Vzniká poruchou rýchlo sa adaptujúcich vibračných mechanoreceptorov v tlaniye okolo svalov a kĺbov
Hypobarestézia	neschopnosť vnímať tupý, do hĺbky pôsobiaci tlak. Vzniká poruchou pomaly sa adaptujúcich nízkoprahových hĺbkových mechanoreceptorov
Acoenesthesia	neschopnosť vnímať vlastné telo a jeho jednotlivé časti. Vzniká integratívnom poruchou barorecepcie, termorecepcie, povrchovej a hlavnej hĺbkovej mechanorecepcie, propriocepcie
Amorphognosia	

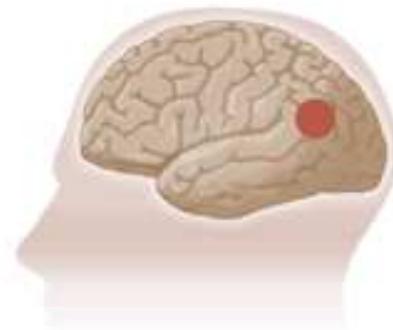
Self-location, self-consciousness

Gyrus angularis – speech processing (aphasia), acalculia, space cognition, attentiveness, memory (Brodmann 39)

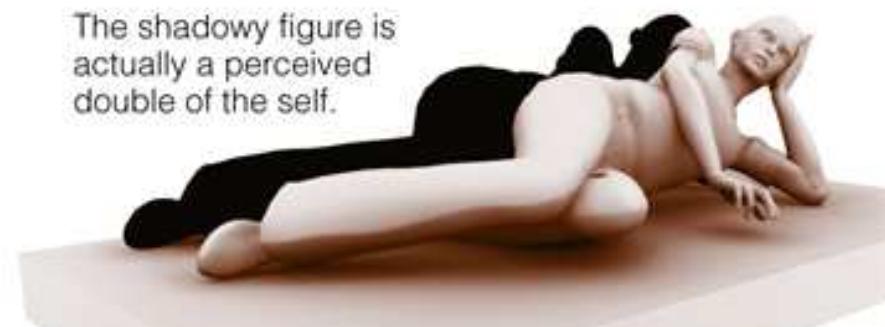


A PRESENCE BEHIND

Stimulation of the **left angular gyrus** gave the patient a sensation of a shadowy person lurking behind.

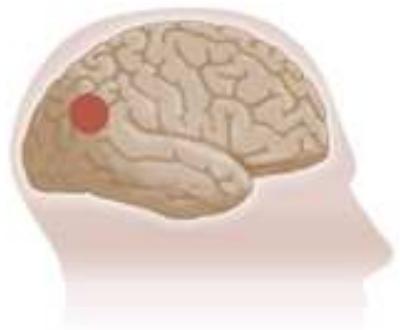


The shadowy figure is actually a perceived double of the self.



OUT-OF-BODY

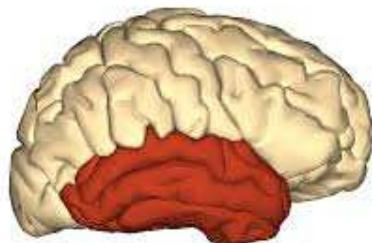
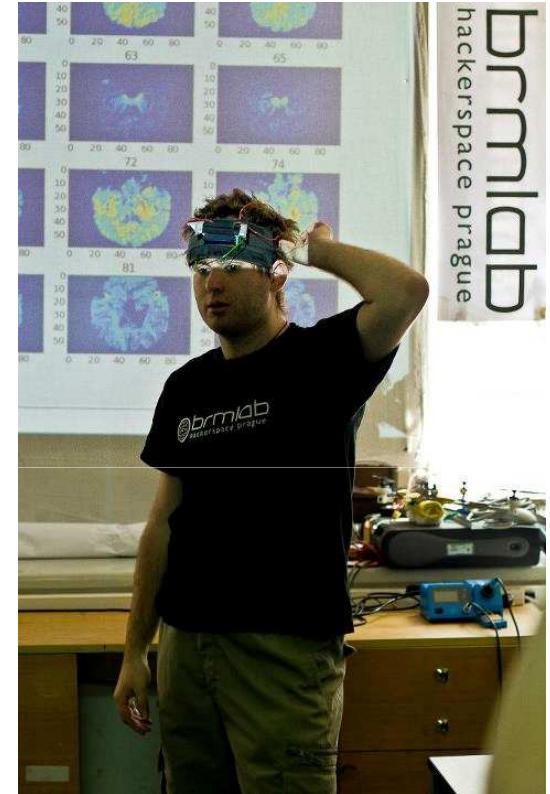
Stimulation of the **right angular gyrus** resulted in an out-of-body experience, as if the patient were floating from the ceiling, looking down at herself.



Blanke O (2012) Multisensory brain mechanisms of bodily self-consciousness. *Nature Reviews Neuroscience*: 13: 556-571.

Ionta S, Heydrich L, Lenggenhager B, Mouthon M, Gassert R, Blanke O (2011): Temporo-parietal cortex encodes self-location and first-person perspective. *Neuron* 70:363-374.

Temporal cortex – mystical experiences



- Persinger, M: Stimulation of temporal lobe by weak magnetic stimuli may evoke special feeling and mystical experiences of encountering with God (well – beeing, absolute safety, endless love, http://en.wikipedia.org/wiki/God_helmet)