



Karl Landsteiner Institute
of Neurorehabilitation and
Space Neurology

Diagnosis and Prognosis of Patients in Apallic Syndrome and Defect State of Apallic Syndrome

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Istanbul,

Consciousness

F.Plum and J.B.Posner

The limits of consciousness are hard to define satisfactorily and quantitatively and we can only interfere the self-awareness of others by their appearance and by their acts.

Consciousness

- Awareness
- Alertness
- Wakefulness
- Attention
- Arousal
- Intact Default Mode Network

Awareness

- Self awareness
- Subjective awareness
- Visual awareness
- Auditive awareness
- Emotional awareness
- Interoceptive awareness

Cognitive Abilities I

- Perception
- Comprehensiveness
- Recognition
- Assessment
- Processing
- Reliability

Cognitive Abilities II (Self recognition)

- Self reliability
- Responsiveness
- Conceptuality
- Assessment
- Subjectivity
(Cogito ergo sum)

Basis of Brain Functions

- Cortical network for the different brain functions
- Activation system of the cortical network (ascending reticular system)
- Functioning working system to accept and evaluate incoming stimuli as well as control of outgoing messages
- Access to the archive of memories and ability to add new experiences

Main Operating System in Consciousness

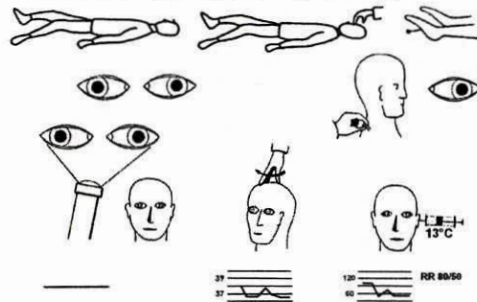
- Ascending reticular system
 - Functioning
 - undisturbed
 - Activation with different methods
 - Stimulation with all incoming sensory stimuli
 - Optic and acoustic stimulation, etc.
 - Stimulation of proprioceptive system
 - Medication
- Functional, biochemical, physical activation
 - Function like a “joy stick”
- “Switcher” unknown

Hierarchy in fMRI Paradigms (Kotchoubey, Schwarzbauer)

- Silent Paradigma (no stimulation)
- Vibro Stimulation
- Emotional Paradigma (cry/laughing, face)
- Language Paradigma (semantic discrimination)
- Memory Paradigma (Warrington Test)
- Mental Imagary

Reversible Coma

Acute Midbrain Syndrome, central, phase V

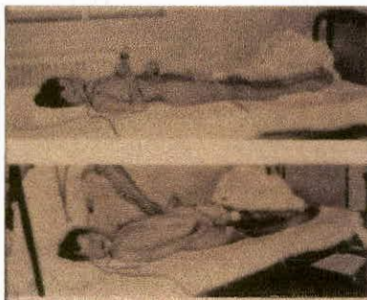


Vollbild des akuten traumatischen Bulbärhirnsyndroms. Schematische Darstellung. Nähere Erläuterung und Text s. Abb. 2.

Phase V, Stretch position, disinhibition of autonomic system

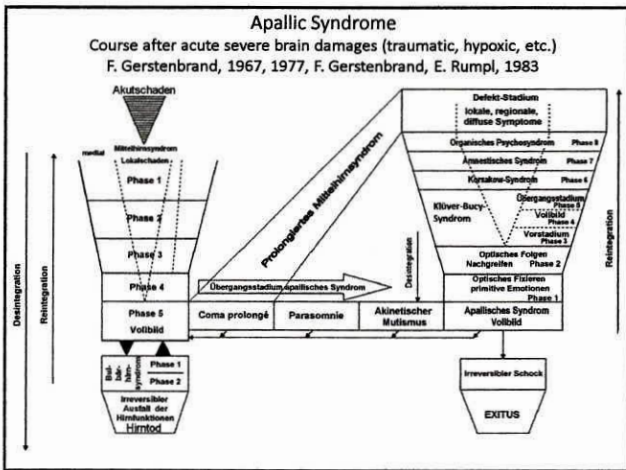
Acute Secondary Midbrain Syndrome

Traumatic brain injury, brain edema



Phase IV, V

STADIEN DER HIRNSTAMMSCHÜDEN NACH SUPRATENTORIELLER RAUMFORDERUNG	ZENTIL. HESITATION	MHS				BHS		
		I	II A	II B	III	IV	I	II
VIGILANT		SCHNELLER	SOPOR	COMA	COMA	COMA	COMA	COMA
REAKTION	AUSLÖSISCHE REIZE	GERINGE VERZÖGERT MIT ZUWENDUNG	VERZÖGERT OHNE ZUWENDUNG	FEHLEND	FEHLEND	FEHLEND	FEHLEND	FEHLEND
	SCHMERZREIZE	PROMPT GERICHTETE ABWEHR	VERZÖGERT UNGERICHTETE ABWEHR	RESTE UNGERICHTETER ABWEHR	BEUGESTRECKSTELLUNG	STRECKSYNERGISMEN	RESTSTRECKSYNERGISMEN	FEHLEND
OPFOMOTORIK	STELLUNG	NORMAL	NORMAL	BEGINNENDE DIVERGENZ	DIVERGENZ	DIVERGENZ	DIVERGENZ	DIVERGENZ
	BULBUS-BEWEGUNG	PENDELND	SCHWIMMEND	DYSKUNULGIERT	FEHLEND	FEHLEND	FEHLEND	FEHLEND
	PUPILLENWEITE	ISOKOR	ISOKOR	ISOKOR	ISOKOR	ISOKOR	ISOKOR	ISOKOR
KÖRPERMOTORIK	LICHTREAKTION	ISOKOR	ISOKOR	ISOKOR	ISOKOR	ISOKOR	ISOKOR	ISOKOR
	KÖRPERHALTUNG	ISOKOR	ISOKOR	ISOKOR	ISOKOR	ISOKOR	ISOKOR	ISOKOR
	SPONTANMOTORIK	MASSEN- UND HALSBEWEGUNGEN	MASSENBEWEG. ARME STRECKBEWEG. BEINE	MASSENBEWEG. ARME STRECKBEWEG. BEINE	BEUGESTRECKHALTUNG	STRECKHALTUNG	REST- NACHSTRECKHALTUNG	SCHLAFTE HALTUNG
	TONUS	NORMAL	BEINE GERING ERHÖHT	BEINE ERHÖHT	ERHÖHT	STARK ERHÖHT	GERING ERHÖHT	SCHLAF
OBLIGAT	BARANSKI PHÄNOMEN	↓↓	↑↓	↑↑	↑↑	↑↑	↑↑	↑↑
	ATMUNG	REGELMÄSSIG	REGELMÄSSIG	REGELMÄSSIG	REGELMÄSSIG	REGELMÄSSIG	REGELMÄSSIG	REGELMÄSSIG
VEGETATIV	PULS	LEICHT ERHÖHT	NORMAL	BESCHLEUNIGT	BESCHLEUNIGT	STARK BESCHLEUNIGT	BESCHLEUNIGT	VERLANGSAMT
	RR	NORMAL	NORMAL	NORMAL	LEICHT ERHÖHT	ERHÖHT	NORMAL	ERNIEDRIGT
NICHT OBLIGAT	KÖRPERTEMPERATUR	NORMAL	NORMAL	LEICHT ERHÖHT	ERHÖHT	STARK ERHÖHT	ERHÖHT	NORMAL ERNIEDRIGT



- ### Symptoms of Apallic Syndrome
- Coma Vigile
 - No recognition of the surrounding
 - No contact to the surrounding
 - No reaction to external stimuli
 - Sleep-wake-rhythm fatigue regulated
 - Optomotoric disturbances
 - Flexed-stretched position of the extremities and trunk
 - Rigido-spasticity
 - Primitive motor patterns (oral, grasping, etc.)
 - Dysregulation of the vegetative system

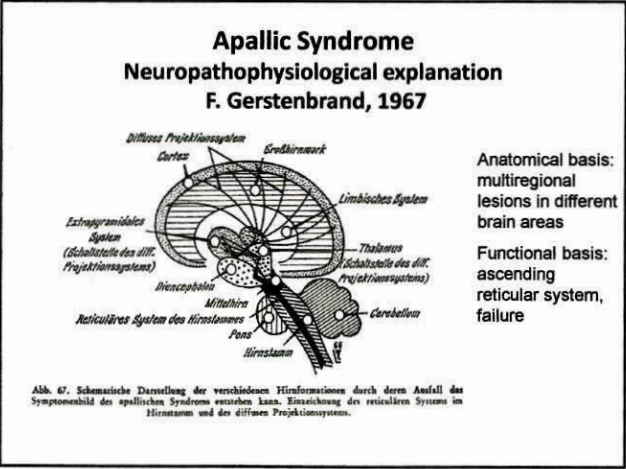
Apallic syndrome, pat. E.S., 19^a traumatic brain injury, 1992

Treatment program in special center for apallic syndrome
No tertiary lesions, minimal secondary lesions
Remission after 5 months to minimal defect state

Apallic Syndrome Full stage, traumatic

Abb. 20: Vollstadium des traumatischen apallicsches Syndroms (Fall 2), tonisches Greifen.
Abb. 21: Vollstadium des traumatischen apallicsches Syndroms (Fall 10/40), phasisches Greifen.

- Grasping reflex
 - Abb. 20: tonic
 - Abb. 21: phasic

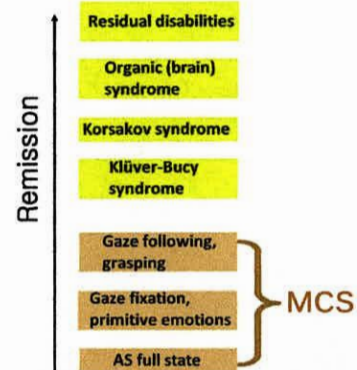


- ### Apallic Syndrome - Remission Stages Innsbruck Remission-Scale - 1
- Phase I: Optic fixation – reduction of Coma vigile, sopor
 - Phase II: Optic tracking – sleep-wake-rhythm normalizing, stupor
 - Phase III: Pre-Klüver-Bucy-Phase – combination in the primitive motor reflexes, hypersomnia – wakeful
 - Phase IV: Klüver-Bucy-Phase – typical Klüver-Bucy reflexes, obnubilation

Apallic Syndrome - Remission Stages Innsbruck Remission-Scale - 2

- Phase V: Post-Klüver-Bucy-Phase – hypersomnia, communication possible
- Phase VI: Korsakov syndrome – voluntary behavior, disorientation, confusional state
- Phase VII: Amnestic phase – emotional irritaion, flat emotions
- Phase VIII: Psycho-organic syndrome – normal consciousness, aware

Remission States of posttraumatic Apallic Syndrome (Innsbruck scale, Gerstenbrand 1977)

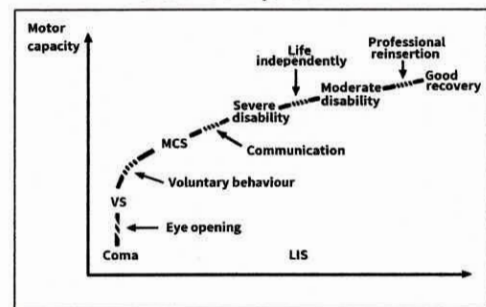


Minimally Conscious States

(Giacino et al, 1997)

- Crude consciousness: alertness
- Phenomenal consciousness: registration of external and internal phenomena
- Access consciousness: directed attention, cognitive awareness, decision making
- Critics:
 - No detailed neurological symptomatology
 - Phenomenological description
 - Etiology generally open
 - Comparable with different remission phases of AS/VS

Restauration of a Coma State after Laureys et al



Acute coma, vegetative state, minimally consciousness state, good recovery

Locked-- In Plus Syndrome LIS-additional Symptoms

- Acinetic mutism (Cairns et al, Skultety)
 - Lesion region 3rd ventricle, periaqueductal
- Sopor
- Stupor (Plum, Posner)
 - Lesion intralaminar nucleus thalami
- Hypersomnia (Jefferson)
 - Lesions mesodiencephal
- Parasomnia (Facon et al)
 - Lesion periaqueductal

Examination for Disorders of Consciousness

- Neurological bed side examination
- Coma recovery scale revised (CRS-R)
 - EEG (event related potentials)
 - semantic oddball paradigm - SOP
 - own name paradigm - ONP
- fMRI (event related potentials)
 - semantic oddball paradigm - SOP
 - own name paradigm - ONP

Functional Magnetic Resonance Imaging (fMRI)

- Method to register incoming stimulations in the different brain regions
- Using the BOLD effect (Blood Oxygenation Level Depend)

Stimulation of Brain Functions

- Silent stimulation (no stimulation)
- Sensory Stimulation
 - Vibro stimulation
 - Acoustic stimulation
 - Visual stimulation
 - Pain stimulation
- Cognitive Stimulation
 - Language stimulation
 - Imagery stimulation
 - Memory stimulation

Functional Neuroimaging

Functional neuroimaging studies suggest that specific brain activity in response to speech and hearing the own first name can remain in patients in the vegetative state or in early remission

(e.g. Coleman, Brain, 2007; Davis, PNAS, 2007; Di, Neurology, 2007; Schiff, Neurology 2005; Kampe, The Journal of Neuroscience, 2003; Owen, Neurocase, 2002).

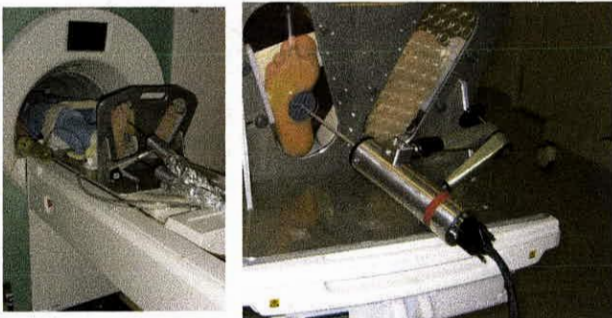
Paradigms in fMRI

Stimulus related paradigms

- Sensoric paradigms
 - Reaction on sensible stimulation (vibro stimulation)
 - Reaction of pains (electric medianus stimulation)
 - Visual stimulation, acoustic stimulation
- Cognitive paradigms
 - Language paradigm (semantic discrimination)
 - Own name paradigm (self awareness)
 - Emotional paradigm (reaction on cry/ laughing, face)
 - Memory paradigm (Warrington Test)
 - Motor-Imagery (tennis play, mental navigation)

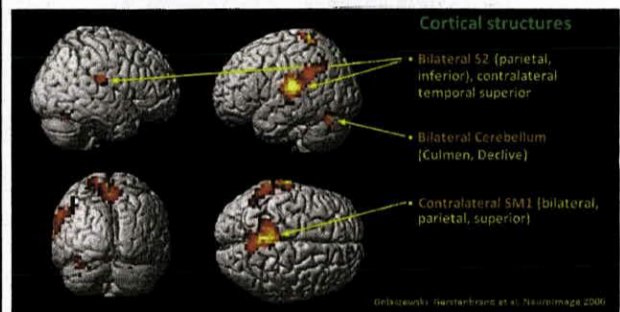
Stimulation unindepent paradigma (silent paradigma)
Default Mode Network

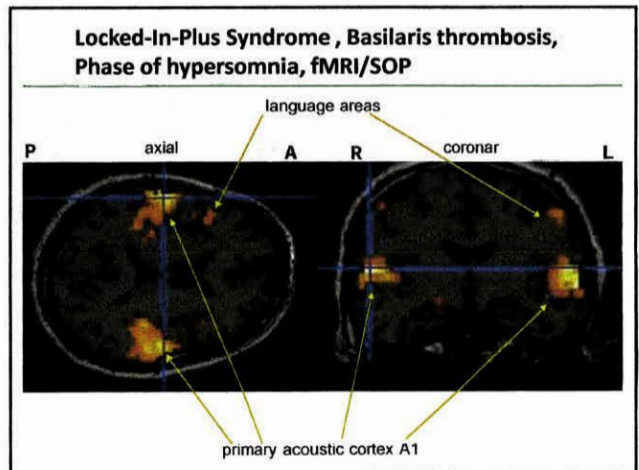
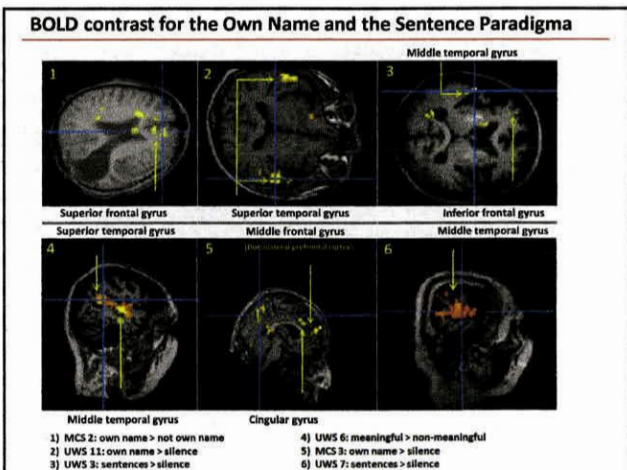
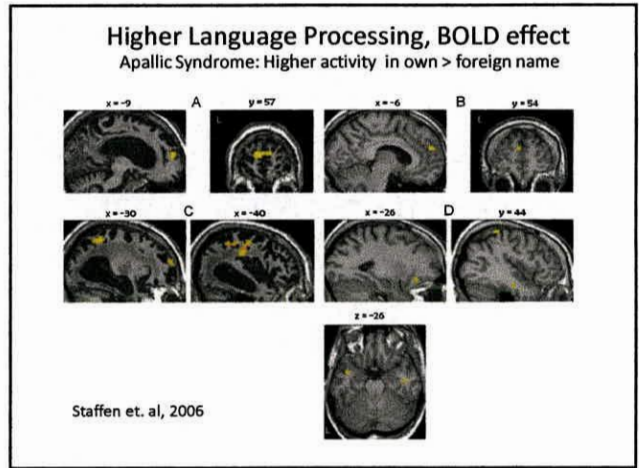
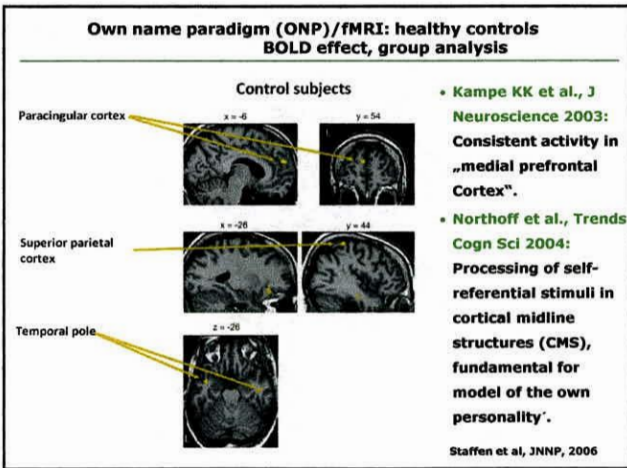
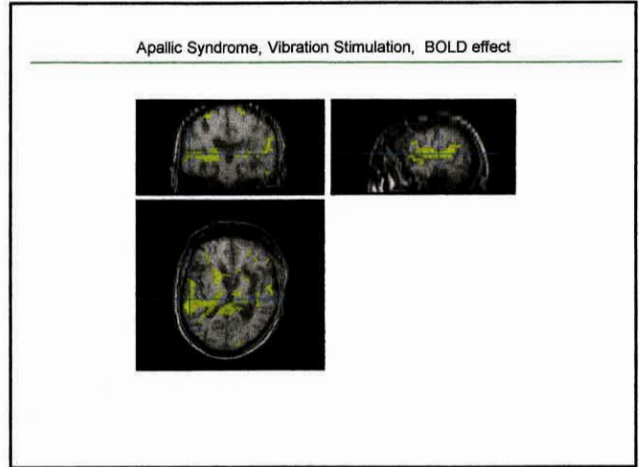
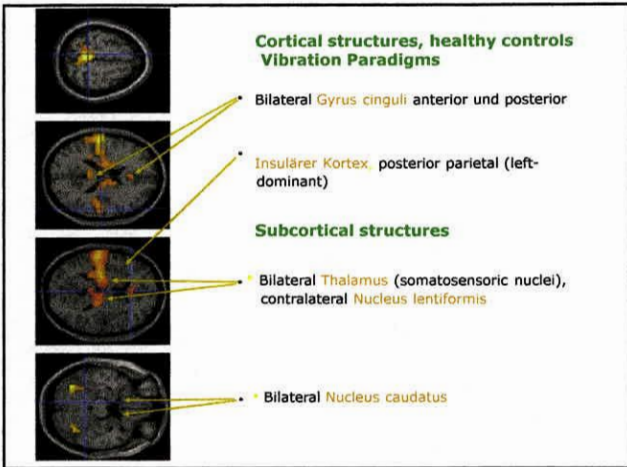
Vibration to the foot sole: amplitude 1 mm, frequency 50 Hz



Foot sole vibration BOLD effect, healthy controls

Stimulus: 50 Hz, A=1mm / Group analysis





Specific fMRI response in VS patients

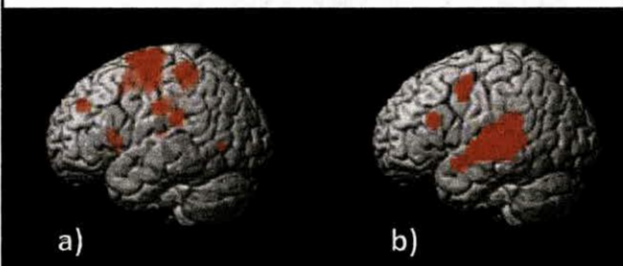
patient number	vibrotactile stimulation	silence vs name	own name vs foreign name	silence vs sentence	semantic oddball
VS#1	no	no	no	no	no
VS#2	no	no	yes	yes	no
VS#3	no	no	no	yes	no
VS#4	yes	yes	yes	yes	yes
VS#5	no	yes	no	yes	no
VS#6	yes	yes	yes	yes	yes
VS#7	no	yes	no	no	no
VS#8	no	yes	yes	yes	yes
VS#9	yes	no	no	no	no
VS#10	yes	no	no	no	no
VS#11	no	yes	no	yes	no
VS#12	yes	no	no	no	no
VS#13	yes	no	no	yes	no
VS#14	no	yes	yes	yes	no
VS#15	no	no	no	no	no

⇒ 8 patients with higher order speech processing and cortical response to a self-referential stimulus, 3 patients AS in remission

Specific fMRI response in MCS patients

patient number	vibrotactile stimulation	silence vs name	own name vs foreign name	silence vs sentence	semantic oddball
MCS#1	no	yes	yes	yes	no
MCS#2	no	yes	yes	yes	yes
MCS#3	no	yes	no	yes	no
MCS#4	on	yes	no	yes	yes
MCS#5	no	yes	yes	yes	no

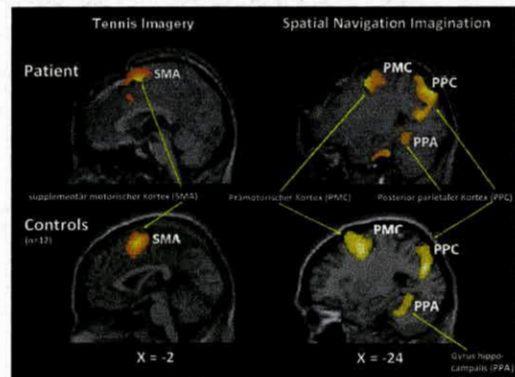
Mental Imagery in fMRT: healthy volunteer, 25a, f



a) Mental Imagery: Tennis play = „Yes“

b) Mental Imagery: walking through own flat in fixed sequence = „No“

Mental Imagery of a patient with Apallic Syndrome in fMRI



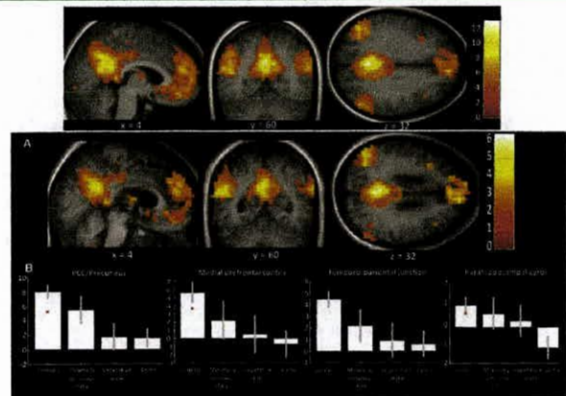
(Owen et al, Science 2006)

Default Mode Network

Raichle 2001

- **Function:**
Attention-demanding cognitive task
Cognitive processes (day dreaming, mind wandering, stimulus, independent source, self related source)
- **Anatomical basis:**
Precuneus bilateral
Temporo-parietal junctions
Medial prefrontal cortex
- **Level of consciousness, paraclinical brain marker**

Default Mode Net Work



(Vanhaudenhuyse et al, Brain, 2010)

Misdiagnosis in disorders of consciousness

Patients with severe chronic disorders of consciousness of different origin (TBI, hypoxia, stroke), in an Apallic Syndrome, full state or early remission state and patients in minimally conscious state are misdiagnosed up to 43%.

(Andrews et al,1996; Schnakers et al, 2009)

Conclusion

- In unresponsive patients diagnosed as Apallic Syndrome/Vegetative State the fMRI shows brain activity in language regions and regions of self-awareness, the diagnosis has to be revised. Patients are able for processing of language, memory differentiation and self-referential stimuli at a higher cortical level.
- Knowledge about the perception of language and self-referential stimuli in patients with severe disorders of consciousness is very important for planning of an individual neurorehabilitation program, also for relatives, for therapists and for caregivers to improve the outcome.
- Up to now, there are no data for a prognostic value of the detected specific brain activity in fMRI.



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ISTANBUL, TURKEY, 31 MAY – 3 JUNE 2014

FINAL PROGRAMME



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