Österreichische
Wachkoma
Gesellschaft

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in Kooperation mit der Österreichischen Gesellschaft für Neurorehabilitation und dem Wiener Krankenanstaltenverbund

Univ.Prof. Dr. Roland Beisteiner

„Hirnaktivitäten bei Menschen im Wachkoma
–
was können wir mit der funktionellen MRT erfassen“

NATURE REVIEWS | NEUROLOGY VOLUME 10 | JULY 2014

DISORDERS OF CONSCIOUSNESS

Diagnostic accuracy of brain imaging in the vegetative state

Adrian M. Owen

Vegetative state / Unresponsive wakefulness / Wakefulness without awareness:

- It is now well accepted that when these patients are examined by specialized clinical teams, up to 43% will show inconsistent but reproducible behavioural signs of awareness, and will be reclassified as being in a minimally conscious state. Nevertheless, some covertly aware patients will escape detection altogether, even by experienced teams.

Brain–Computer Interfaces for Communication with Nonresponsive Patients

Lorina Naci, PhD,[1] Martin M. Monti, PhD,[2] Damian Cruse, PhD,[1] Andrea Kübler, PhD,[3] Bettina Sorger, PhD,[4] Rainer Goebel, PhD,[4] Boris Kotchoubey, PhD,[5] and Adrian M. Owen, PhD[1]

A substantial number of patients who survive severe brain injury progress to a nonresponsive state of wakeful unawareness, referred to as a vegetative state (VS). They appear to be awake, but show no signs of awareness of themselves, or of their environment in repeated clinical examinations. However, recent neuroimaging research demonstrates that some VS patients can respond to commands by willfully modulating their brain activity according to instruction. Brain–computer interfaces (BCIs) may allow such patients to circumvent the barriers imposed by their behavioral limitations and communicate with the outside world. However, although such devices would undoubtedly improve the quality of life for some patients and their families, developing BCI systems for behaviorally nonresponsive patients presents substantial technical and clinical challenges. Here we review the state of the art of BCI research across noninvasive neuroimaging technologies, and propose how such systems should be developed further to provide fully fledged communication systems for behaviorally nonresponsive populations.

ANN NEUROL 2012;72:312–323

Coma:
There are no signs of wakefulness—no spontaneous eye opening, even to intense stimulation—and no signs of awareness. Usually it is transient: a few days or weeks. In rare cases, it is chronic.

Vegetative state / Unresponsive wakefulness / Wakefulness without awareness:
There are signs of wakefulness, including eye opening and stimulus-induced arousal, but no signs of awareness of oneself or of the environment. The state is considered permanent 1 year after a traumatic brain injury, or 3 months after brain damage from lack of oxygen.

Minimally conscious state:
There are signs of wakefulness and inconsistent, but reproducible signs of awareness, including sustained visual pursuit, command following, and intelligible verbalization. It may be chronic or permanent, although no time intervals have been defined.

Locked-in state:
Patients are usually aware, but unable to move or speak, and unless completely locked in, they may communicate via small eye movements. In the acute phase, awareness may be impaired.

Functional Neuroimaging Methods	Advantages	Limitations
fMRI	Noninvasive; global brain coverage; high spatial resolution (millimeter range); sophisticated analysis methods; first to demonstrate plausibility of communication with patients deemed to be in a VS.	High cost; lack of portability; physical impositions (eg, patient must stay still and in supine position for an extended period of time); no paramagnetic equipment can be present; noisy; susceptible to movement artifacts; lower temporal resolution than EEG (second range).
fNIRS	Noninvasive; portable; relatively low cost; nearly noiseless; less sensitive to movement artifacts than fMRI; easier to operate than fMRI; no restriction on paramagnetic medical equipment.	A relatively new methodology; limited experience with BCI applications; limited spatial resolution (~3cm); especially poor resolution of deep brain structures; some susceptibility to movement artifacts; analysis methods under development.
EEG	Noninvasive; portable; relatively low cost; high temporal resolution (millisecond range); silent; no physical impositions (eg, can be applied in the seated and supine positions or when the patient is asleep); vast BCI experience with different patient populations.	Limited spatial resolution (~3cm); especially poor resolution of deep brain structures; susceptible to artifacts from cranial muscles and eye movements; the majority of existing paradigms have limited use for DOC patients (but see Cruse et al[30]).

fNIRS - Functional Near Infrared Spectroscopy

- Naito and colleagues mapped 2 mental imagery tasks, calculation and singing, to yes/no responses, and were able to detect responses with fNIRS in 40% of 17 CLIS patients. The brain response for these patients could be decoded with 74% accuracy.

Naito M, Michioka Y, Ozawa K, et al.
Communication means for totally locked-in ALS patients based on changes in cerebral blood volume measured with near-infrared light. IEICE Trans Inf Syst 2007;90:1028–1037.

- The spatial resolution of fNIRS is in the range of a few cubic centimeters… thus BCI paradigms that employ fNIRS must be based upon neural responses that are relatively broad. Future improvements in the development of multichannel fNIRS systems promise to address this issue.

EEG - Electroencephalography

- the P300 can be elicited by passive paradigms (eg, just listening), especially for stimuli of particular significance, like a participant's own name, and increases substantially when participants actively attend.

- the modulation of the P300 by manipulations of conscious perception, such as stimulus masking, attention manipulations, and anesthesia, highlights its usefulness as a marker of awareness.

- About 20 to 25% of patients with Disorders Of Consciousness show a P300 effect.

- amplitude increase in active paradigms, as compared to passive paradigms, is likely to be a more reliable indicator of awareness than the mere presence of this component, as the P300 can be elicited even when participants are not conscious of the stimuli.

EEG - Electroencephalography

Schnakers and colleagues tested 14 DOC (MCS and VS) patients … MCS patients exhibited a P300 to their own names, in both active (counting) and passive (listening) conditions. Like controls, this P300 was larger in the active condition than in the passive condition, suggesting voluntary compliance with task instructions.

Voluntary brain processing in disorders of consciousness

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ABSTRACT

Background: Disentangling the vegetative state from the minimally conscious state is often difficult when relying only on behavioral observation. In this study, we explored a new active evoked-related potentials paradigm as an alternative method for the detection of voluntary brain activity.

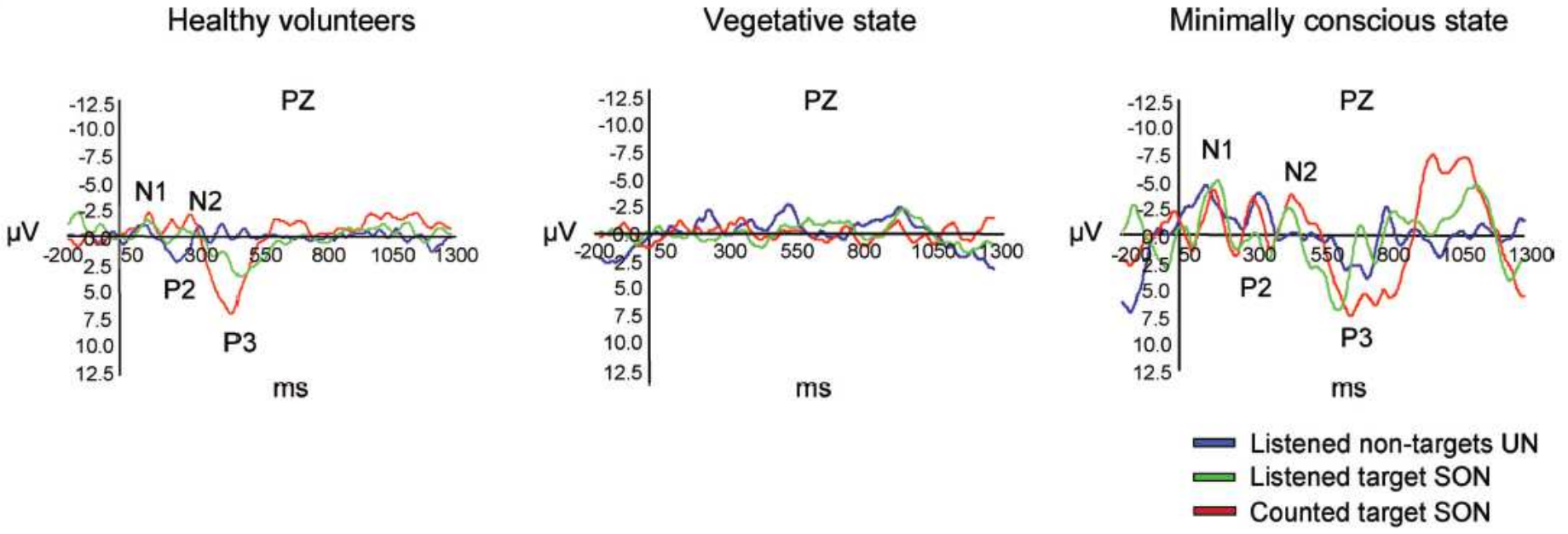
Methods: The participants were 22 right-handed patients (10 traumatic) diagnosed as being in a vegetative state (VS) (n = 8) or in a minimally conscious state (MCS) (n = 14). They were presented sequences of names containing the patient's own name or other names, in both passive and active conditions. In the active condition, the patients were instructed to count her or his own name or to count another target name.

Results: Like controls, MCS patients presented a larger P3 to the patient's own name, in the passive and in the active conditions. Moreover, the P3 to target stimuli was higher in the active than in the passive condition, suggesting voluntary compliance to task instructions like controls. These responses were even observed in patients with low behavioral responses (e.g., visual fixation and pursuit). In contrast, no P3 differences between passive and active conditions were observed for VS patients.

Conclusions: The present results suggest that active evoked-related potentials paradigms may permit detection of voluntary brain function in patients with severe brain damage who present with a disorder of consciousness, even when the patient may present with very limited to questionably any signs of awareness. *Neurology*® 2008;71:1614–1620

By contrast, the Vegetative State patients did not show any P300 differences between the active and passive conditions, suggesting that they were unable to comply with task instructions in the active condition.

Figure Grand-averaged evoked-related potentials in healthy volunteers (n = 12), vegetative patients (n = 8), and minimally conscious patients (n = 14) at Pz



PET – Positronen Emissions Tomographie

Diagnostic precision of PET imaging and functional MRI in disorders of consciousness: a clinical validation study

Johan Stender*, Olivia Gosseries*, Marie-Aurélie Bruno, Vanessa Charland-Verville, Audrey Vanhaudenhuyse, Athena Demertzi, Camille Chatelle, Marie Thonnard, Aurore Thibaut, Lizette Heine, Andrea Soddu, Mélanie Boly, Caroline Schnakers, Albert Gjedde, Steven Laureys

Lancet 2014; 384: 514–22

41 patients with unresponsive wakefulness syndrome, four with locked-in syndrome, and 81 in a minimally conscious state.

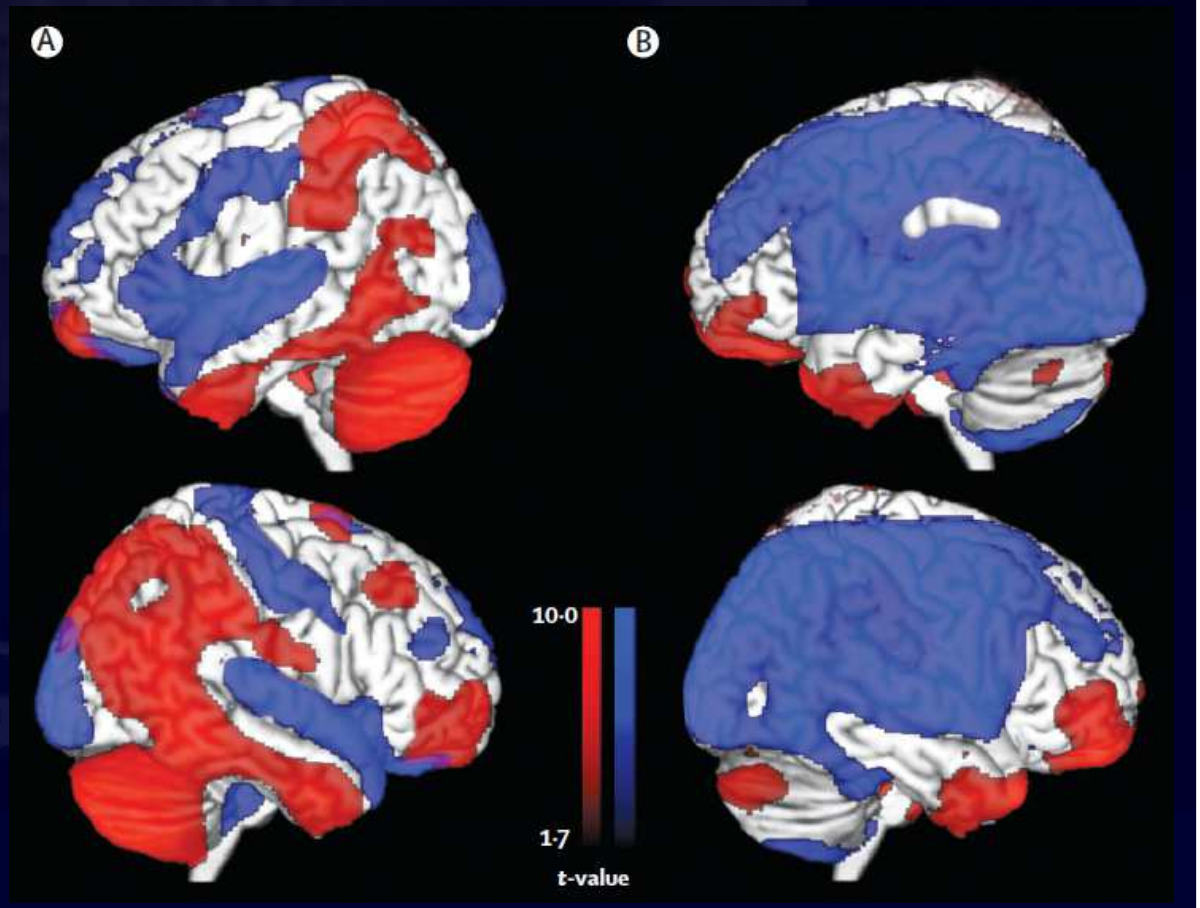
Repeated standardised clinical assessments with the Coma Recovery Scale–Revised (CRS–R), cerebral 18F-fluorodeoxyglucose (FDG) PET, and fMRI during mental activation tasks. We calculated the diagnostic accuracy of both imaging methods with CRS–R diagnosis as reference. We assessed outcome after 12 months with the Glasgow Outcome Scale–Extended.

PET – Positronen Emissions Tomographie

-18F-FDG PET had high sensitivity for identification of patients in a minimally conscious state (93%) and high congruence (85%) with behavioural Coma Recovery Scale–Revised (CRS–R) scores.
- 18F-FDG PET correctly predicted outcome in 75 of 102 patients (74%).
- 13 of 41 (32%) of the behaviourally unresponsive patients (ie, diagnosed as unresponsive with CRS–R) showed brain activity compatible with (minimal) consciousness on at least one neuroimaging test; 69% of these (9 of 13) patients subsequently recovered consciousness.

(A) Minimally conscious state.
(B) Unresponsive wakefulness syndrome compared with 39 healthy.

Blue=areas with significantly lowered metabolism.
Red=areas with preserved metabolism.



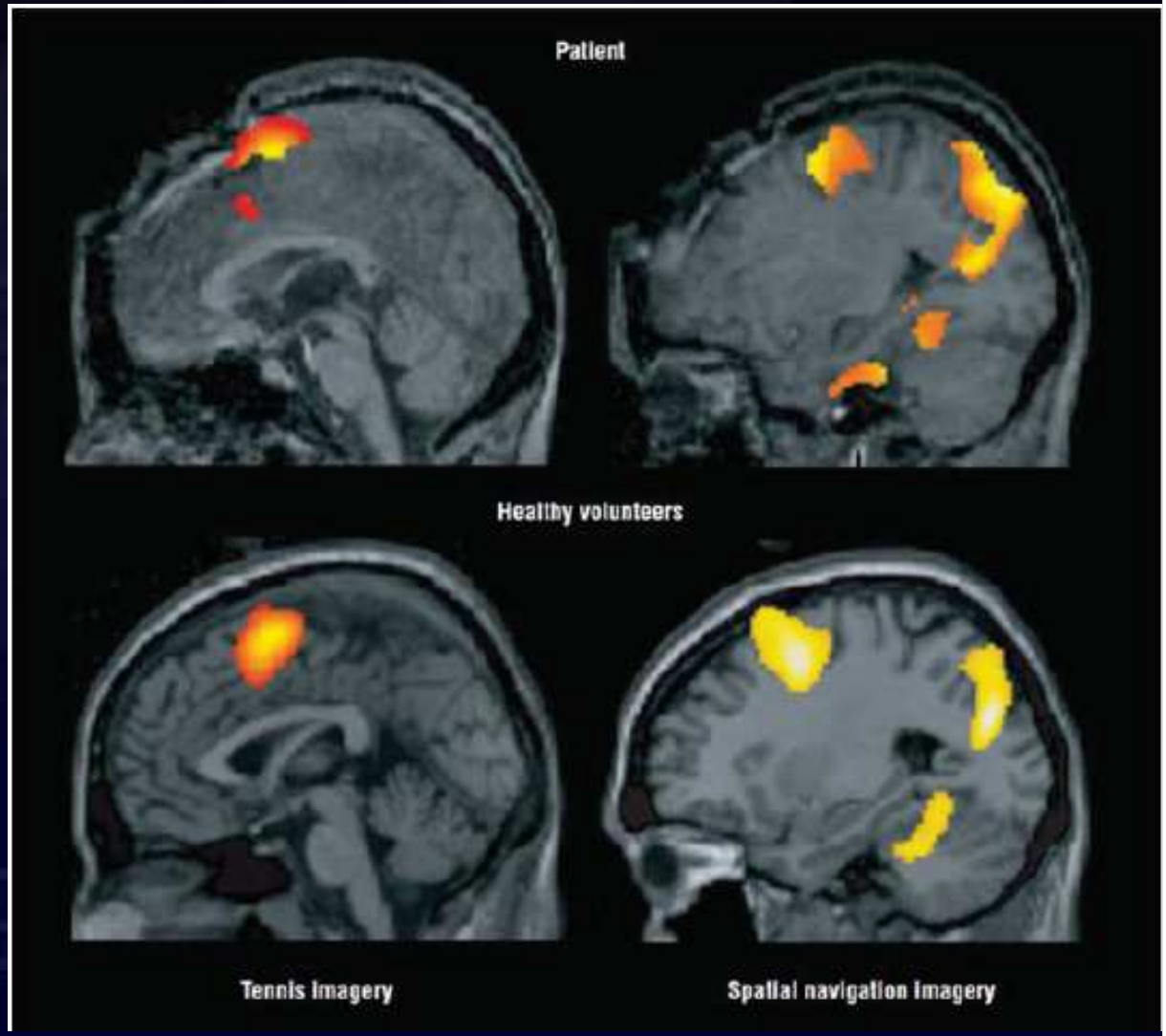
fMRI – functional Magnetic Resonance Imaging

Monitoring of Brain Activation

Conscious responses to stimuli in a patient who fulfilled all the clinical criteria defining the vegetative state.

Responses were indistinguishable from that of a group of healthy volunteers (n = *12)*

Owen AM, Coleman MR, Boly M, et al. Detecting awareness in the vegetative state. Science 2006;313:1402.



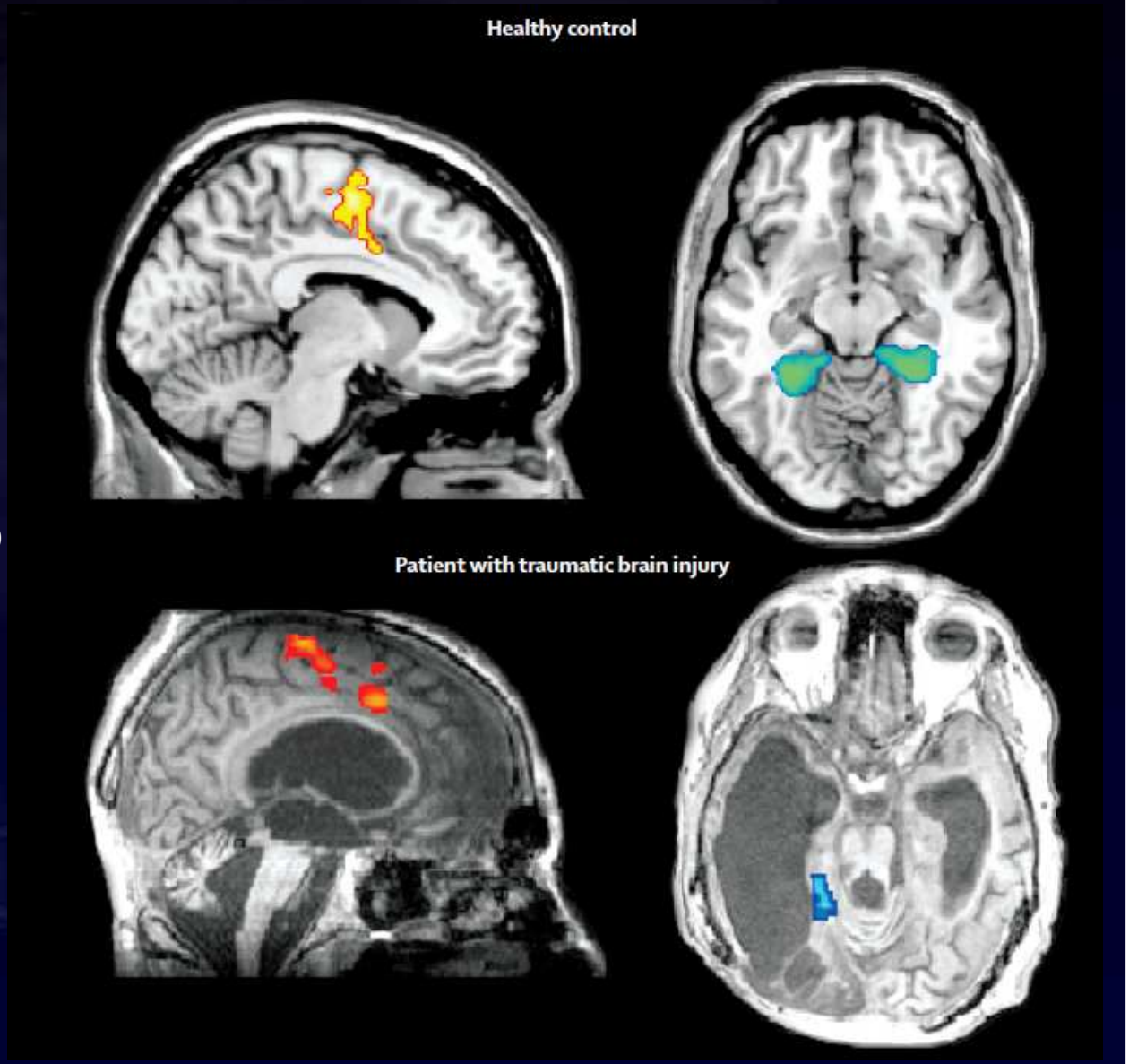
fMRI – functional Magnetic Resonance Imaging

Monitoring of Brain Activation

Monti et al extended this approach to demonstrate that fMRI could also be used to communicate with a patient in VS.

Tennis was mapped to a yes response, spatial navigation to a no response.

Monti MM, Vanhaudenhuyse A, Coleman MR, et al. Willful modulation of brain activity in disorders of consciousness. N Engl J Med 2010;362:579–589.

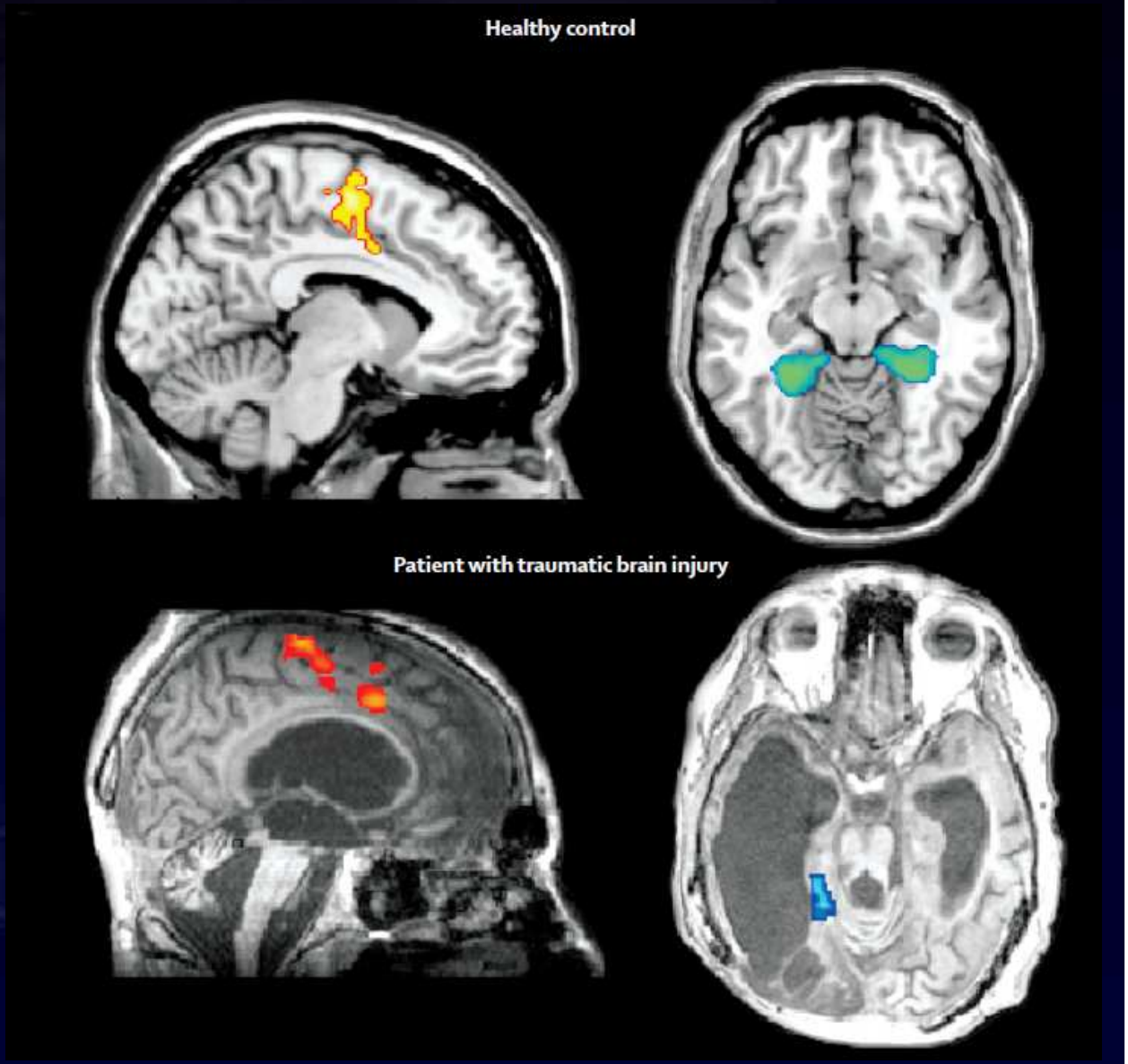


fMRI – functional Magnetic Resonance Imaging

Monitoring of Brain Activation

Following 6 autobiographical questions (eg, "Is your father's name Thomas?"), the answers that were decoded from the brain activity matched the factually correct answers (in 5 of the 6 questions), which were unknown to the experimenters at the time.

This study demonstrated that the presence of voluntary, reliable, and sustained brain activity in response to command could be used as a proxy for physical behavior, such as movement or speech.



fMRI – functional Magnetic Resonance Imaging

Monitoring of Functional Connectivity
(Funktionelle Konnektivität = Hohe Korrelation der Signalverläufe von 2 Hirnregionen)

NeuroImage: Clinical 4 (2014) 240–248

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journal homepage: www.elsevier.com/locate/ynicl

Altered network properties of the fronto-parietal network and the thalamus in impaired consciousness

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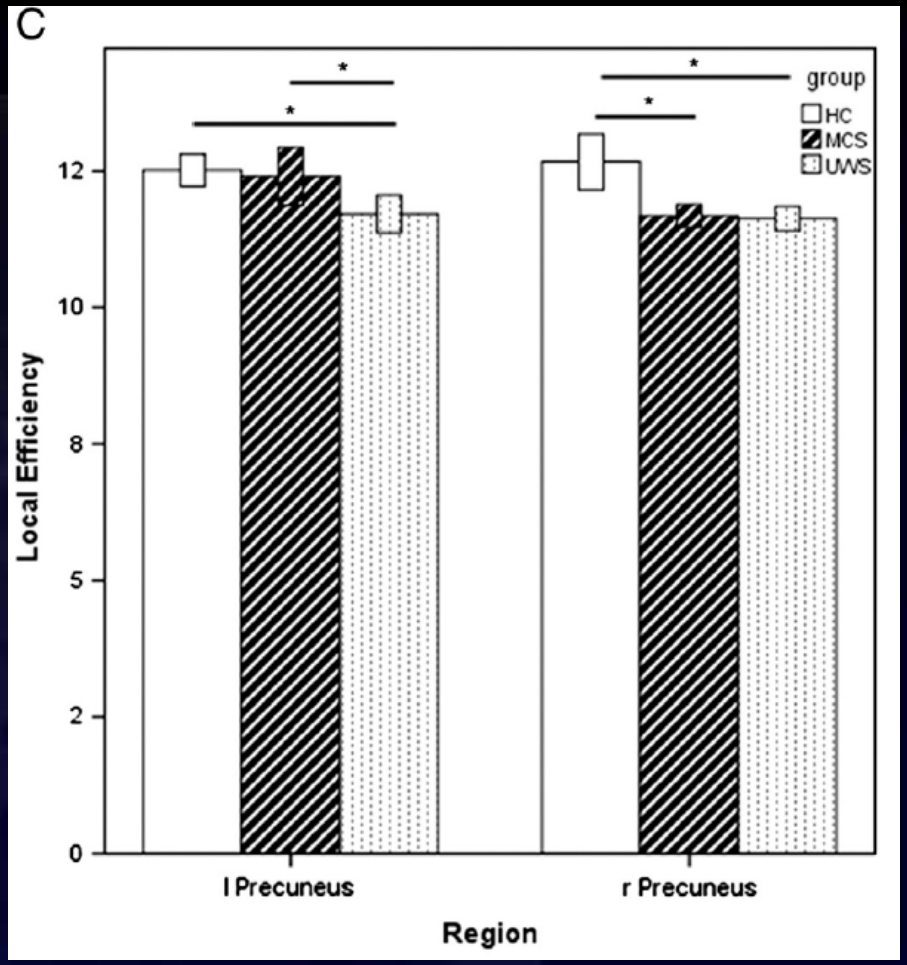
fMRI – functional Magnetic Resonance Imaging

Monitoring of Functional Connectivity
(Funktionelle Konnektivität = Hohe Korrelation der Signalverläufe von 2 Hirnregionen)

Laureys and Schiff (2012) proposed a model of recovery of consciousness focusing on the connectivity between and within frontal and parietal regions influenced by specific circuit modulations of the thalamus.

Resting state fMRI data of 34 patients with unresponsive wakefulness syndrome and 25 in minimally conscious state were compared to 28 healthy controls.

Network properties were altered in several regions which are associated with conscious processing (medial parietal, and frontal regions, thalamus). Between minimally conscious and unconscious patients medial parietal regions differed.
Alterations in the thalamus were particularly evident in non-conscious patients.
Most of the regions affected in patients with impaired consciousness belong to highly interconnected central nodes. Their disturbance has severe impact on information integration probably leading to a total breakdown of consciousness.



Precuneus:
Local efficiency reflects the efficiency of parallel information transfer, robustness, and fault tolerance of a local network.

Current Biology 22, 1333–1338, July 24, 2012 ©2012 Elsevier Ltd All rights reserved DOI 10.1016/j.cub.2012.05.022

Report

A Real-Time fMRI-Based Spelling Device Immediately Enabling Robust Motor-Independent Communication

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For now, our study constitutes only a proof of concept working with 6 healthy volunteers.

Besonderheit dieser neuen fMRT Technik:

1.) Interaktive Kommunikation mit dem Patienten während er im Scanner liegt (real time fMRI).

Klassisches fMRT: erst Stunden nach der Untersuchung steht fest, ob der Pat. auf die Aufgaben reagiert hat.

2.) Völlig freie Kommunikation (kein ja/nein) über Auswahl der 26 Buchstaben des Alphabets

3.) Geringe Anstrengung, kaum Vorbereitung/Vortraining erforderlich

4.) Aktueller Stand: freie Beantwortung von 2 beliebigen Fragen in ca. 1h Messzeit

To intentionally generate 27 distinguishable hemodynamic activation patterns, participants voluntarily influenced three fMRI signal aspects:

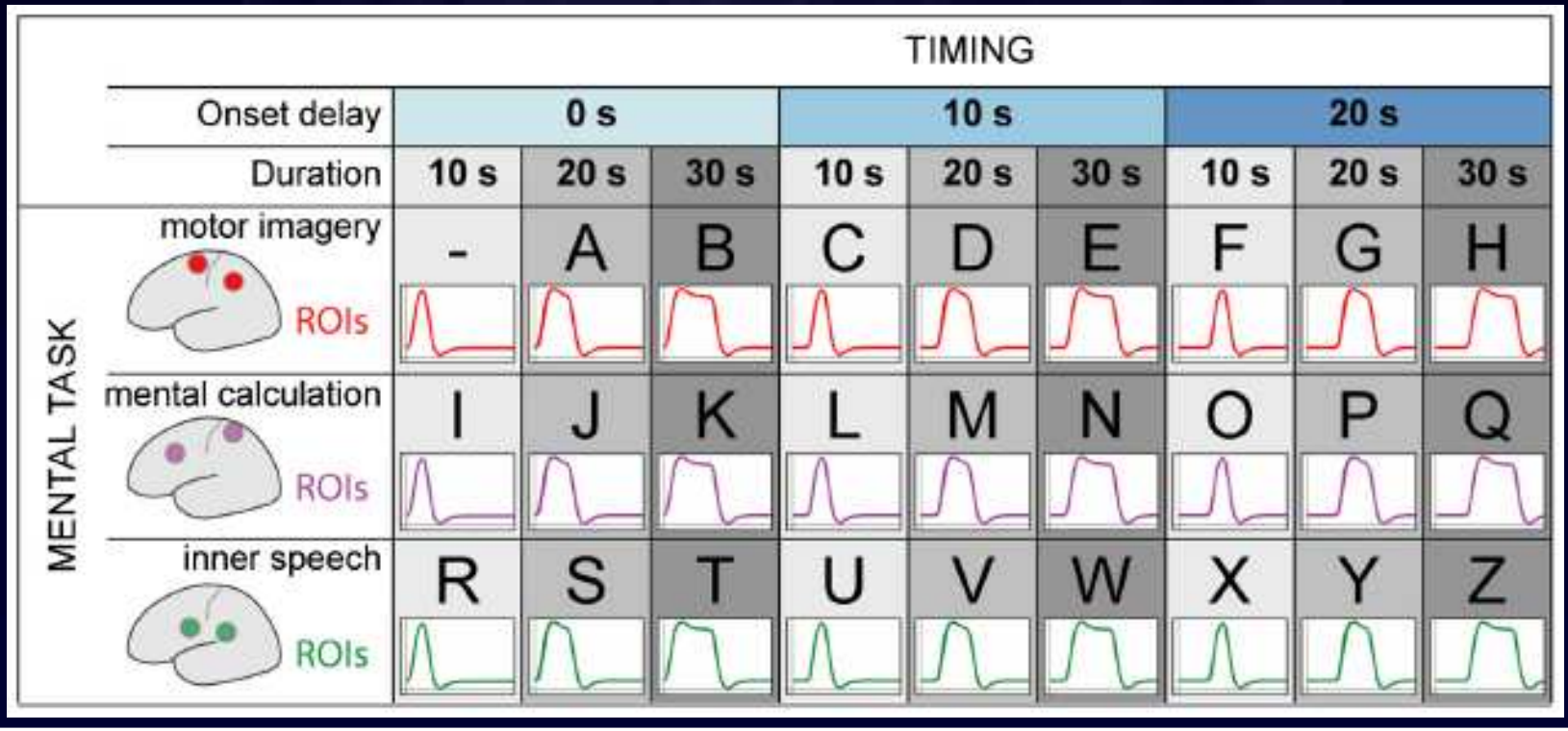
(1) location of the signal source by performing three different mental tasks

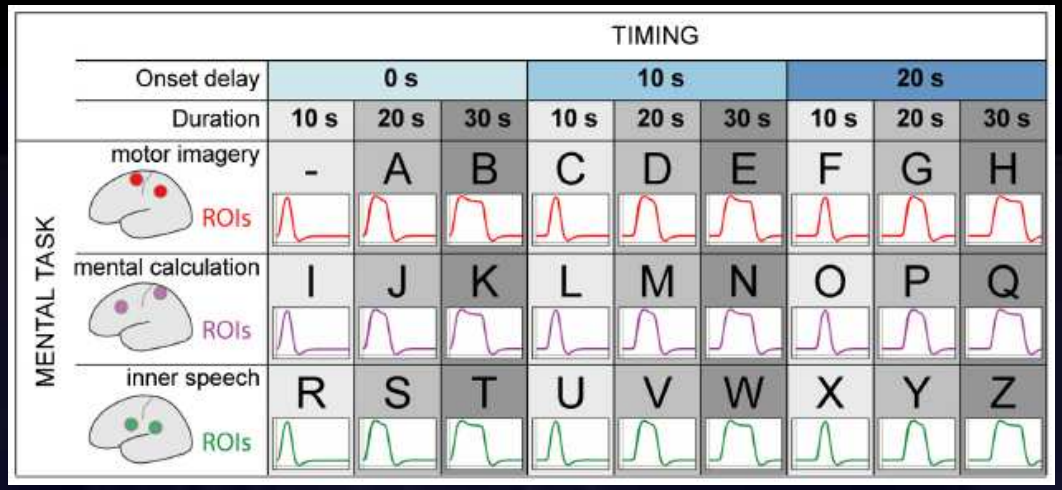
To intentionally generate 27 distinguishable hemodynamic activation patterns, participants voluntarily influenced three fMRI signal aspects:

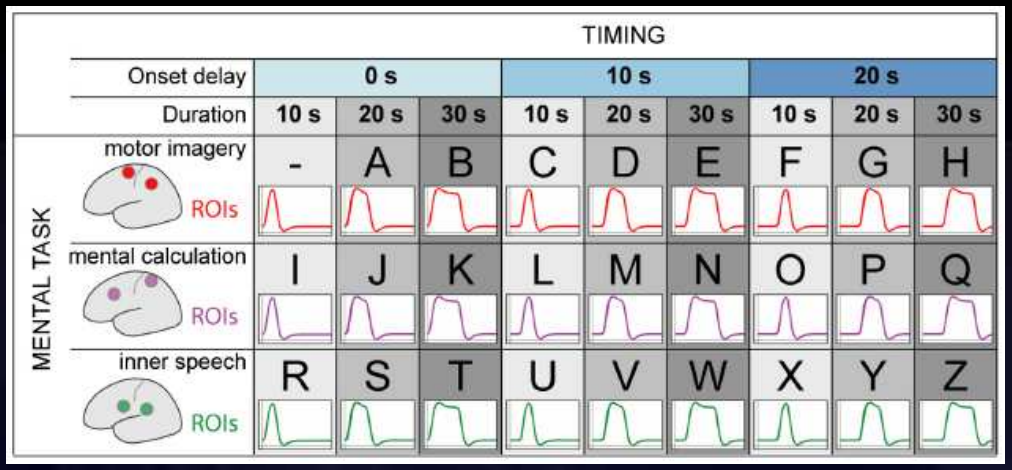
(1) location of the signal source by performing three different mental tasks (see Movie S1 available online)

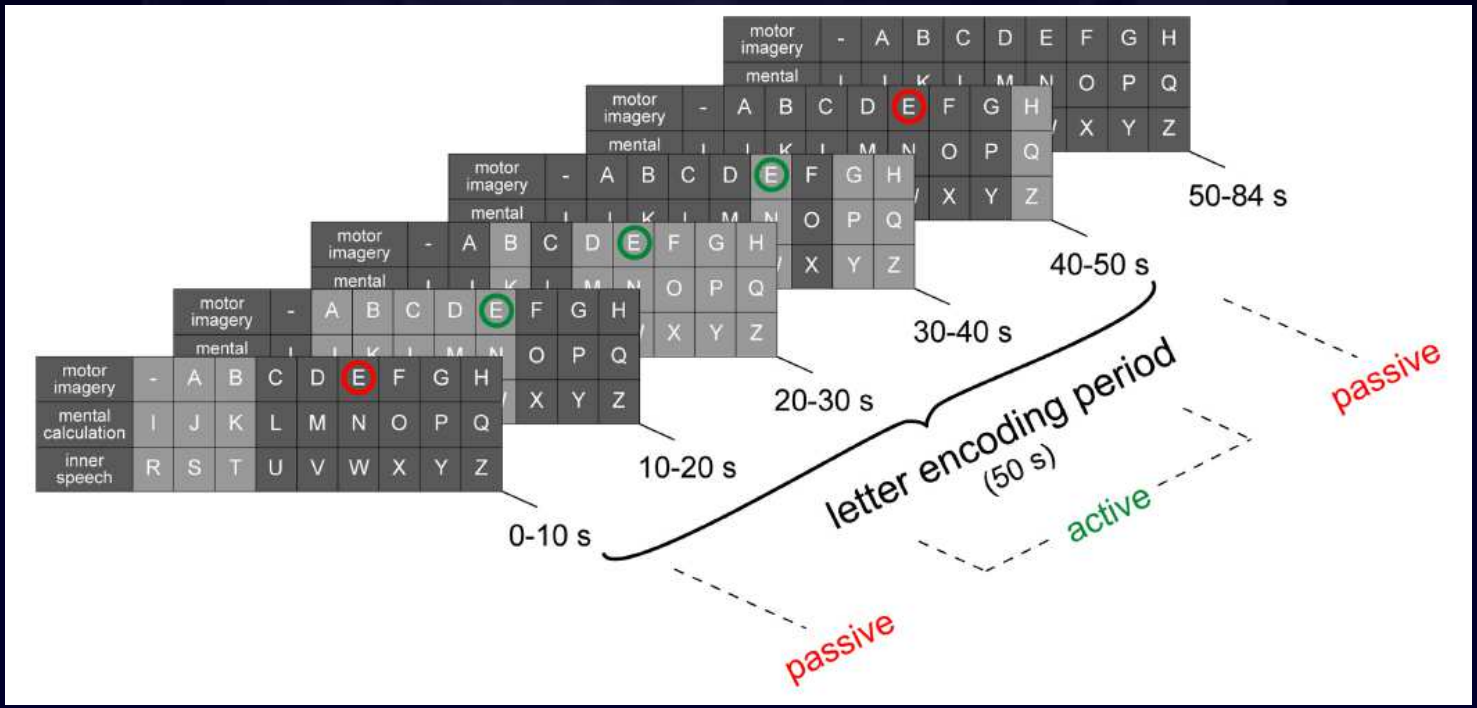
(2) signal onset delay by delaying the start of the mental task for 0 s, 10 s, or 20 s, and

(3) signal duration by varying the mental task duration between 10 s, 20 s, and 30 s.

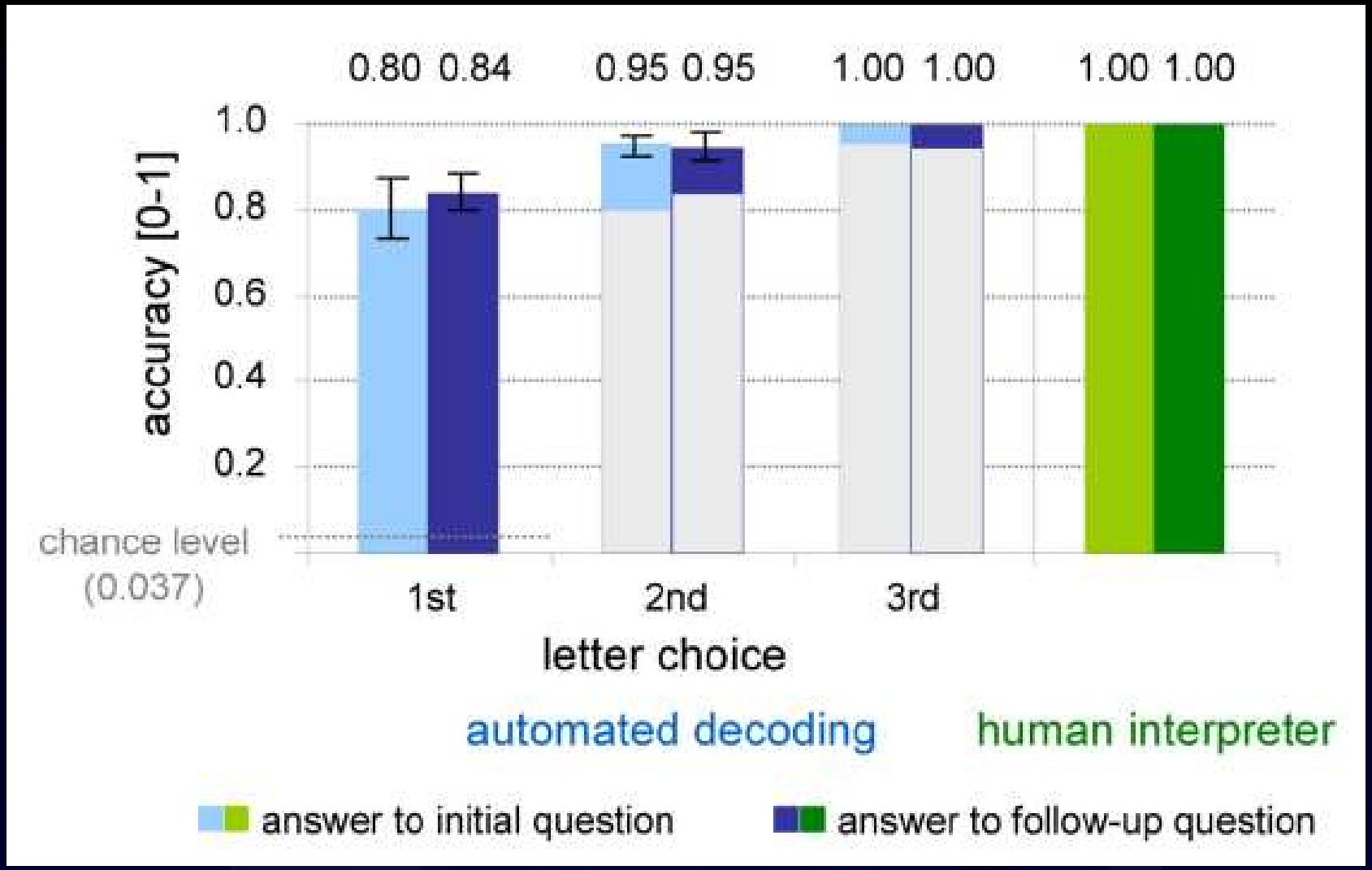



TIMING
Onset delay
0 s
10 s
20 s
Duration
10 s
20 s
30 s
10 s
20 s
30 s
10 s
20 s
30 s
MENTAL TASK
motor imagery
ROIs
-
A
B
C
D
E
F
G
H
mental calculation
ROIs
I
J
K
L
M
N
O
P
Q
inner speech
ROIs
R
S
T
U
V
W
X
Y
Z


TIMING
Onset delay
0 s
10 s
20 s
Duration
10 s
20 s
30 s
MENTAL TASK
motor imagery
ROIs
mental calculation
ROIs
inner speech
ROIs
- A B C D E F G H
I J K L M N O P Q
R S T U V W X Y Z


motor imagery
mental calculation
inner speech
0-10 s
10-20 s
20-30 s
30-40 s
40-50 s
50-84 s
letter encoding period
(50 s)
passive
active
passive

participant	initial question		follow-up question	
	stated question	decoder output/ human interpreter's decision	stated question	decoder output/ human interpreter's decision
1	"What is your hobby?"	P H O T O G R A P H Y - - Q G M X X E I C N G W R R N E P S V H S - Y Z X I I P H O T O G R A P H Y - -	"What did you PHOTOGRAPH last?"	- O Y - H O M E - R M W R Z M O G R A T Z S G V T W A - M Y - H O M E -
2	"Where did you spend your most recent vacation?"	- I N D C N E R C A - A F Q F M M G S I - A I R O B O O F J D C B - I N D O N E S I A -	"What did you like most in INDONESIA?"	- T E K P L E S - I R G M X U O J I A S D L Q M G R A - T E M P L E S -
3	"Where did you spend your most recent vacation?"	- I N D I A - S - E B - C A U A M E A B B - I N D I A -	"What do you consider most typical for INDIA?"	- C L O S H I N G - A A J X T G R M E A R O U P R E A V O R - C L O T H I N G -
4	"What is your hobby?"	- D R S C U S R R N G - R C I T U S U S I P E R A B - R S T R U F M F I - D I S C U S S I N G -	"What is your favorite DISCUSSION topic?"	- A W Y T H I N G - A - N Z S G R P E I B K P W V Z J W H A - A N Y T H I N G -
5	"What are you interested in?"	- X O V I D R A V M U R E S I M X W - N J - M O V I E S	"Which MOVIE did you watch last?"	T O P F U N - V X N N L M I U Y O G J P A T O P G U N -
6	"Where did you spend your most recent vacation?"	- - U D - O E S T - I A V C A P C U U I A B C F B Y D R V A - B U D A P E S T -	"What did you like most in BUDAPEST?"	- S W N - E O F U E - A U X L A G X E V D A J T Y M O F M G S C R - S Y N A G O G U E -



The top-ranked letter choice was correct in 82%, when considering the first two and three letter choices, in 95% and 100% of the cases.
The experimenters correctly deciphered all answers of the participants online, enabling back-and-forth communication within the ongoing MRI session.

Probleme / Limitationen:

1) Visuelle Aufgaben für Unresponsive Wakefulness Patienten nicht möglich (Transfer in akustische Modalität!)

2) Mögliche Ursachen niedriger Erfolgsraten in vielen Studien:
- Die Diagnose ist korrekt (kein Bewusstsein)
- Sensitivität/Technische Reife der Methoden für Bewusstseinssignale zu gering
- Aufgaben zu schwierig da Defizite bei:
    - Sprachverständnis
    - Arbeitsgedächtnis
    - Entscheidungsfindung
    - Exekutiven Funktionen
    - Aufmerksamkeitsspanne

3) Klassifikationsfragen: Klinisch Unresponsive Wakefulness Patienten welche Hirnaktivität modulieren können = neue Patientenkategorie?

Wissenschaftliches Programm

- Methodische Entwicklungen
- Kognitive Organisation & Plastizität
- Reorganisation & Plastizität im erkrankten Gehirn
- Funktionserhalt im Alter

Jeweils mit Impulsvortrag und freien Beiträgen zu den Themen

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Dr. J. Rath (Wien)
Dr. Kunz (Salzburg)

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Informationen u.a. auch zum vorgeschalteten Curriculum am 12.12.2014 finden Sie auf der Homepage der ÖGFMRT unter www.oegfmrt.org

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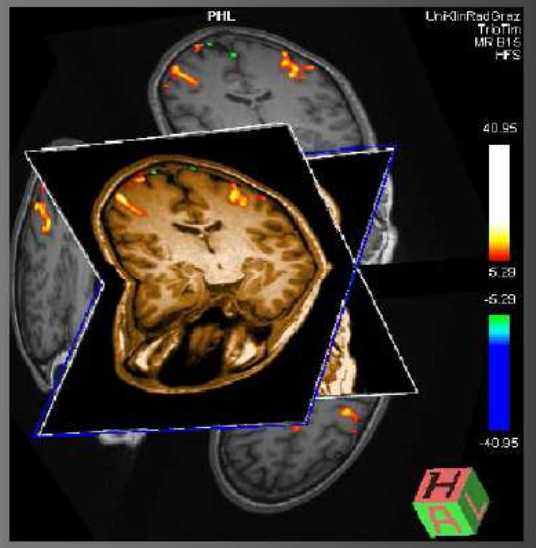
Interdisziplinarität schafft Innovation



14. Österreichisches fMRT Symposium

Graz 13. Dezember 2014

Österreichische Gesellschaft für fMRT (ÖGFMRT)

Institut für Psychologie, Universität Graz
Neurologie & Radiologie, Medizinische Universität Graz
Inst. Semant. Datenanalyse, Technische Universität Graz