Wos lejnger a blinder lebt, alz mer set er.

The longer a blind lives the more he sees.

Je länger ein Blinder lebt, umso mehr sieht er.

Yiddish Saying

Jiddisches Sprichwort

Tübingen:

Ernesto Soares (Engeneering)

Tamara Matuz (Psychol.)

Ute Strehl (Psychol.)

Boris Kotchoubey (Physiol.)

Ranganatha Sitaram (Engeneering)

Jürgen Mellinger (Physics)

Ander Ramos (Engeneering)

Sebastian Halder (Bioinform.)

Femke Nijboer (Psychol.)

Surjo Soekadar (Psychiatry)

Andrea Kübler (Psychol.)

Marcos Tagagiba (Neurosurg)

Alireza Gharabaghi (Neurosurg.)

Ralf Veit (Psychol.)

Andrea Caria (Engeneer.)

Sangyun Lee (Mathematics)

NIH,Bethesda,USA:

Leonardo Cohen (Neurol.)

Cornelia Weber (Psychol.)

Ethan Buch (Beh.Sciences)

Max-Planck-Inst., Tübingen

Bernhard Schölkopf (Mathem.)

Kamil Uludag (Neuroradiol)

Jeremy Hill (Bioinformatics)

Tel-Aviv, Israel:

Einer Onav (Rehab.)

Ulm, Germany

Albert Ludolph (Neurology)

Dorothe Lule (Biol.)

Tokyo, Japan (Riken)

H.Hoshi (Psychiatry)

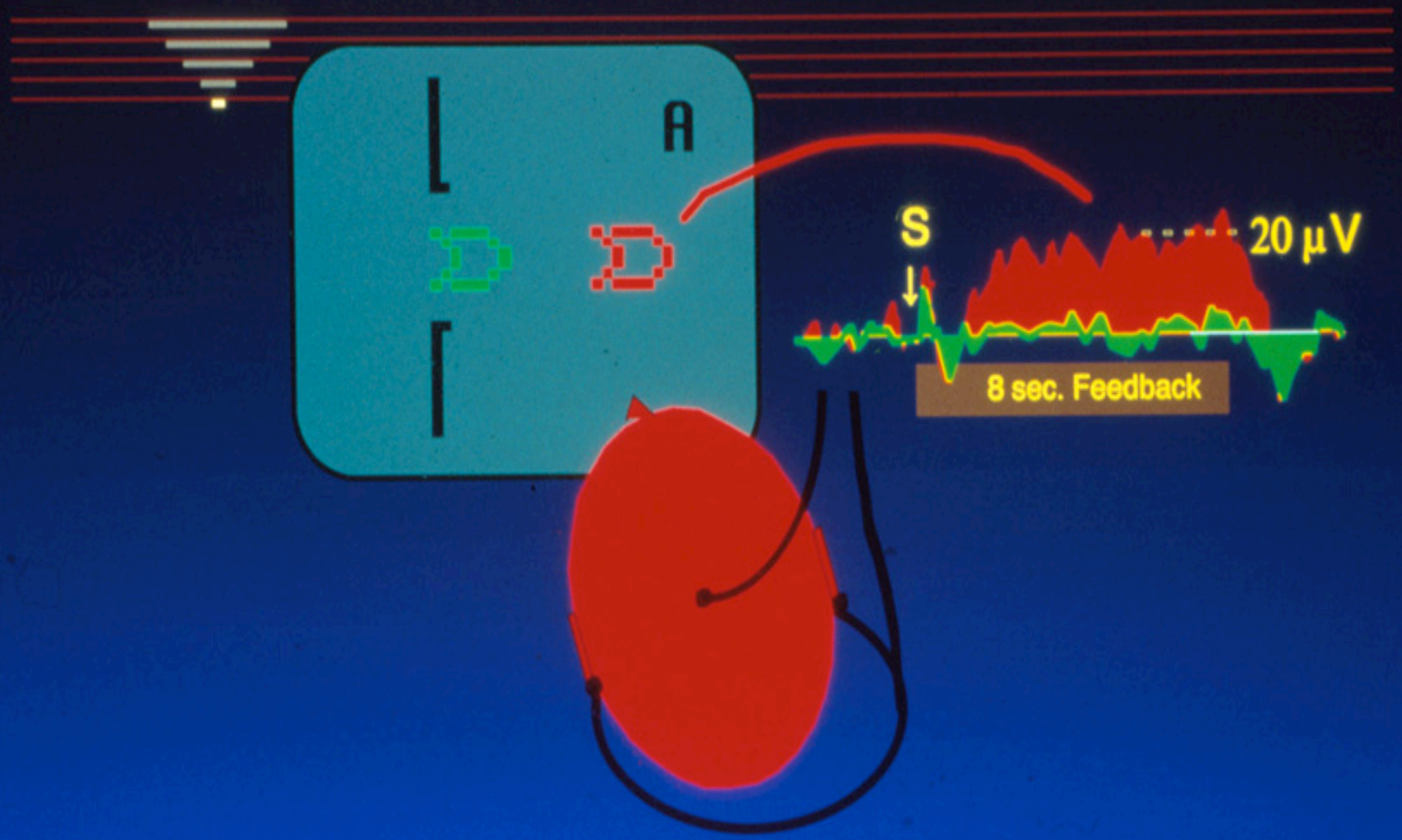
Freiburg, Germany

Ad Aertsen (Neuroscience)

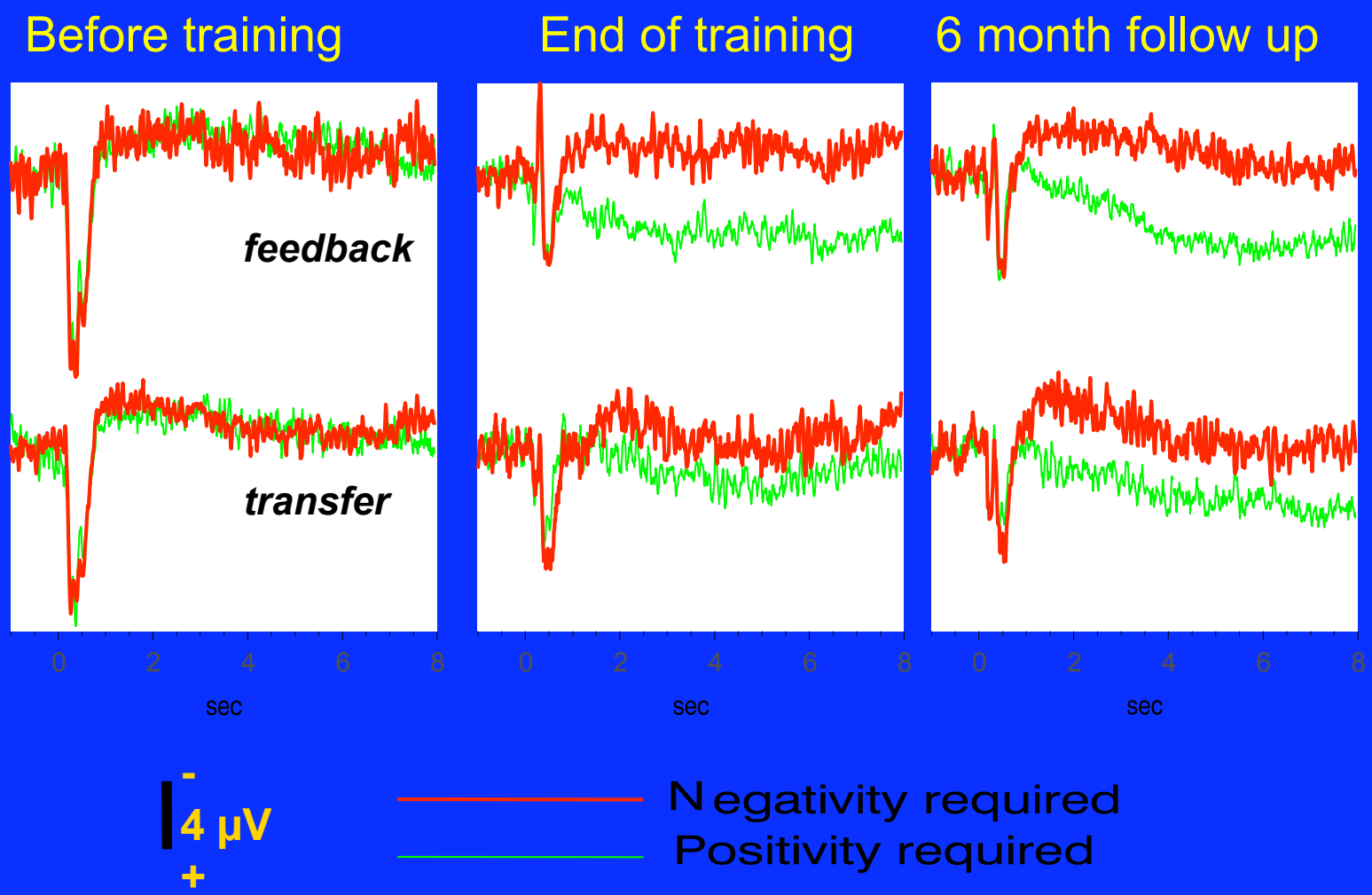
Stefan Waldert (Physics)

Carsten Mehring (Bioinformatics)

Biofeedback of Slow Potentials



slow cortical potentials



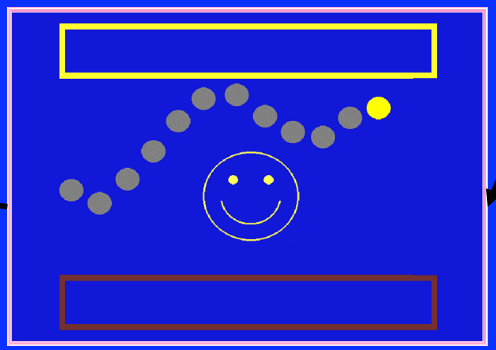
Koutchoubey et al, Epilepsia, 2001

A Brain-Computer-Interface for ADHD

patient

amplifier

trainer‘s screen



patient‘s screen

training

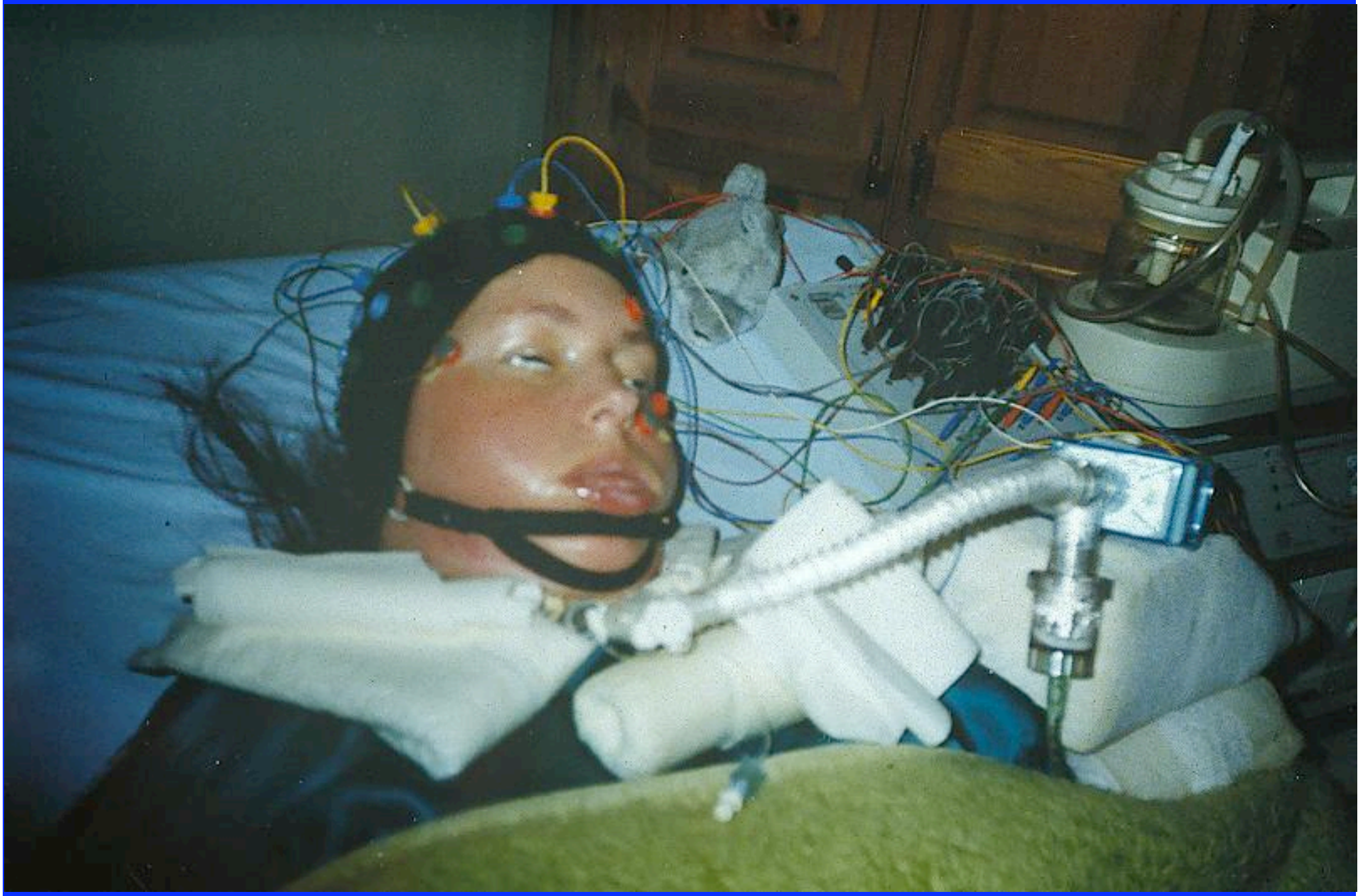
Strehl et al. Pediatrics (2006)

Near Infrared Spectroscopy-BCI in Attention Deficit Disorder

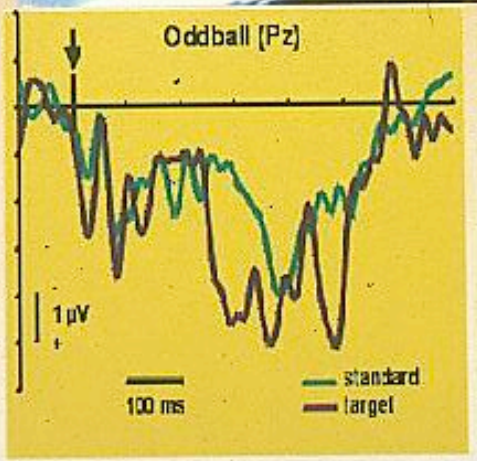
Figure 4 *Measurement being performed using the port - able, telemetric NIRS system.*

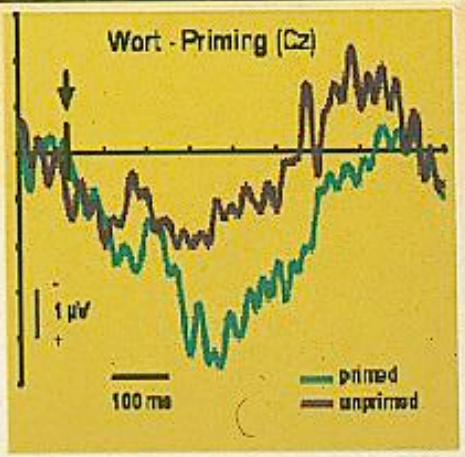
From Ranganatha Sitaram et al Neuroimage, 2007

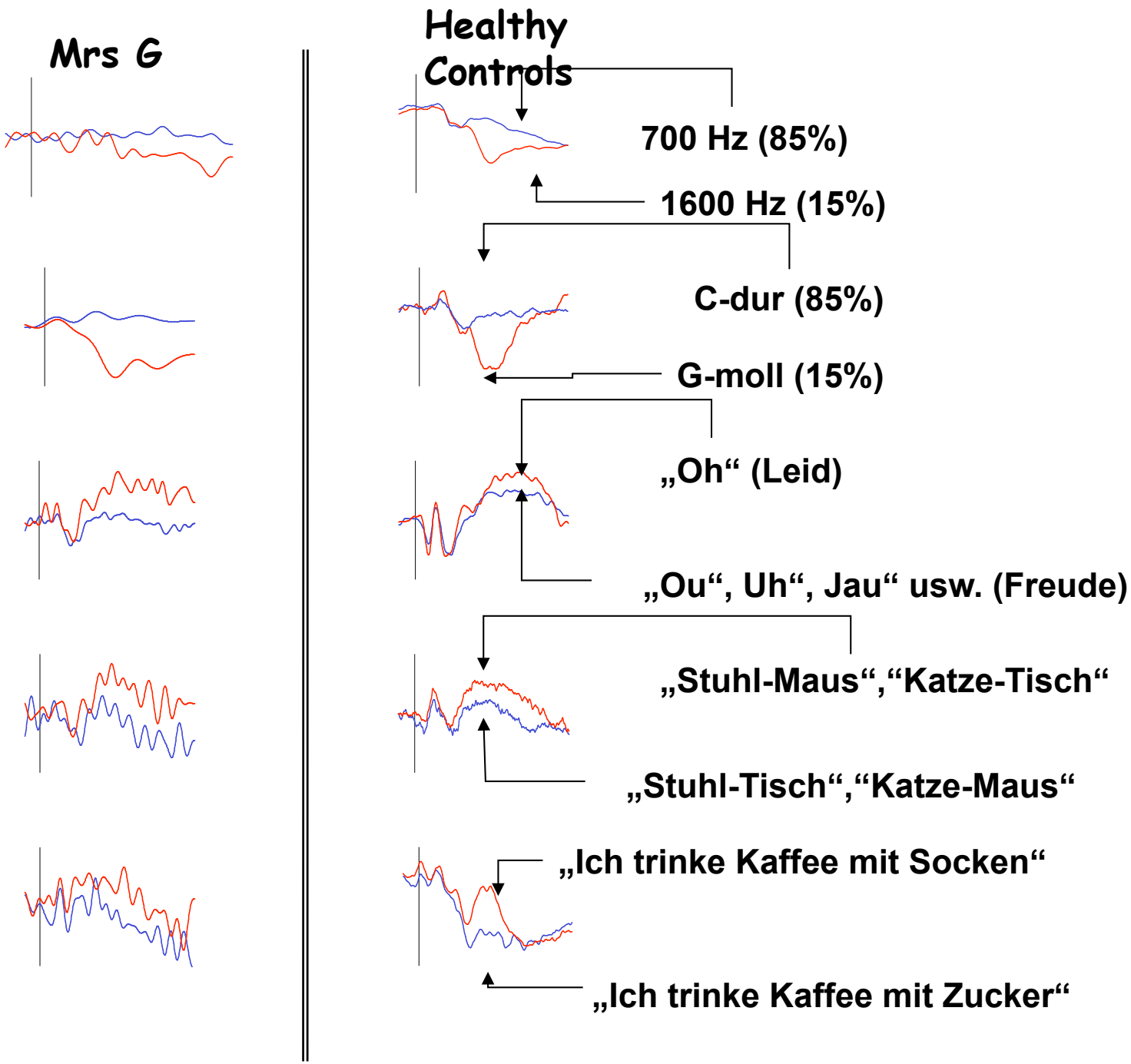
Science, 2002



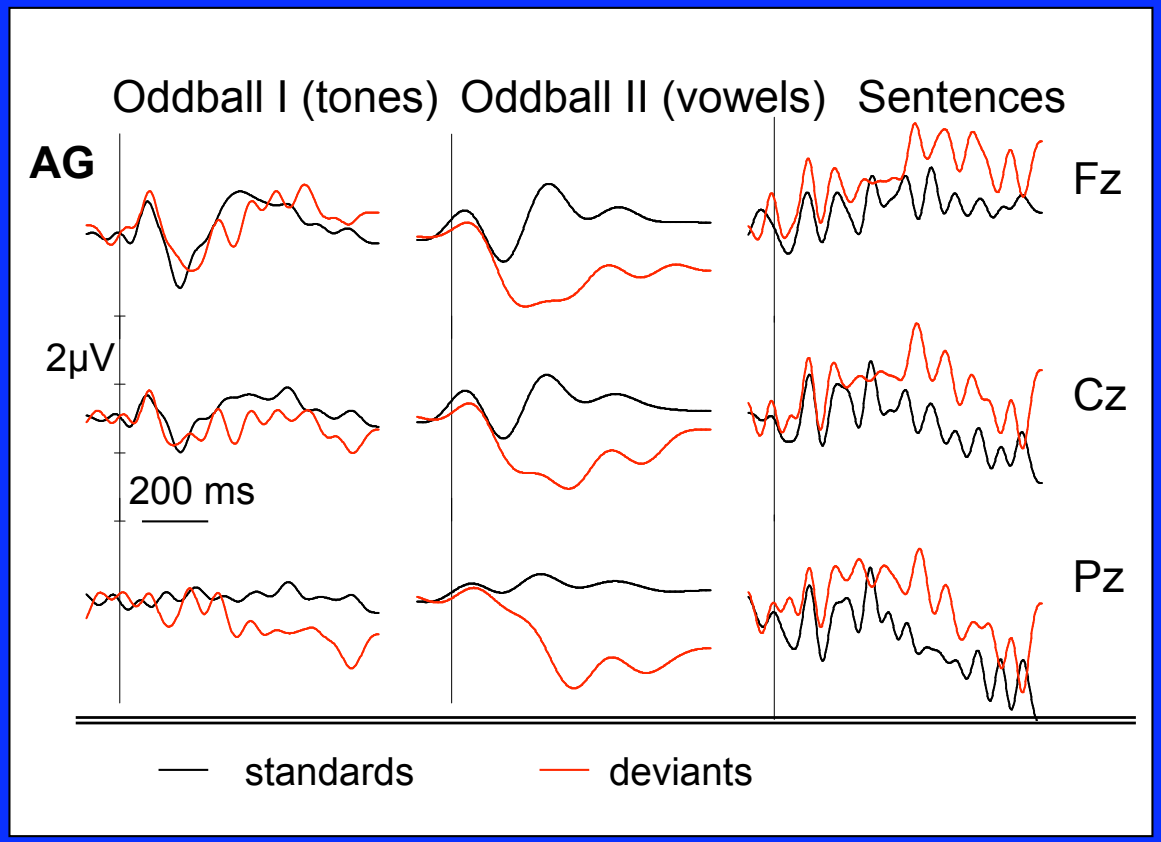
Pat TY. F, 23. Persistent vegetative state since 1995 after traumatic injury






Mrs G
Healthy Controls
700 Hz (85%)
1600 Hz (15%)
C-dur (85%)
G-moll (15%)
„Oh“ (Leid)
„Ou“, Uh“, Jau“ usw. (Freude)
„Stuhl-Maus“,“Katze-Tisch“
„Stuhl-Tisch“,“Katze-Maus“
„Ich trinke Kaffee mit Socken“
„Ich trinke Kaffee mit Zucker“

Detection of Cognition



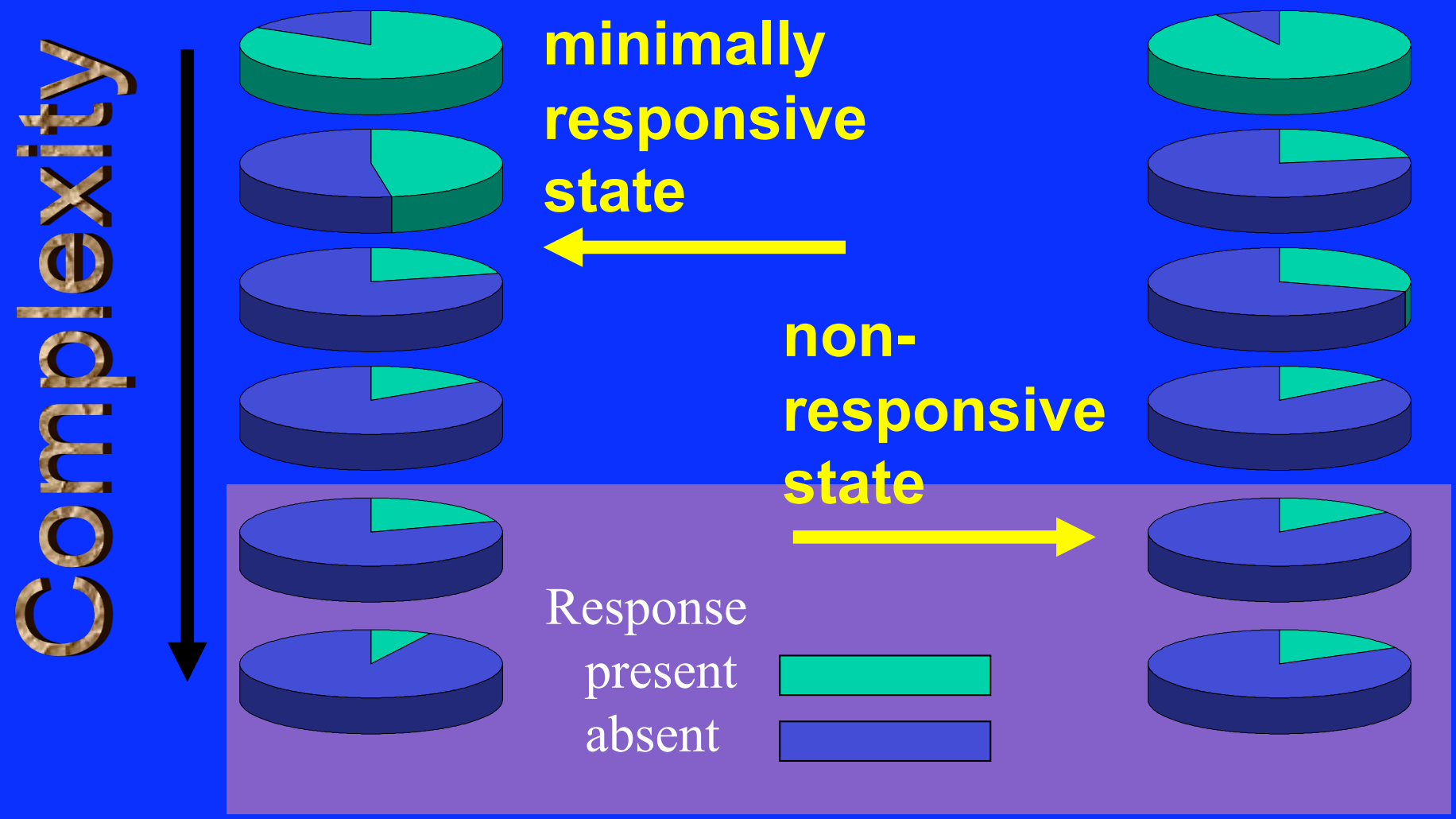
Kotchoubey et.al., News in Physiol.Sciences,2003

Patient NB, age 40, ALS

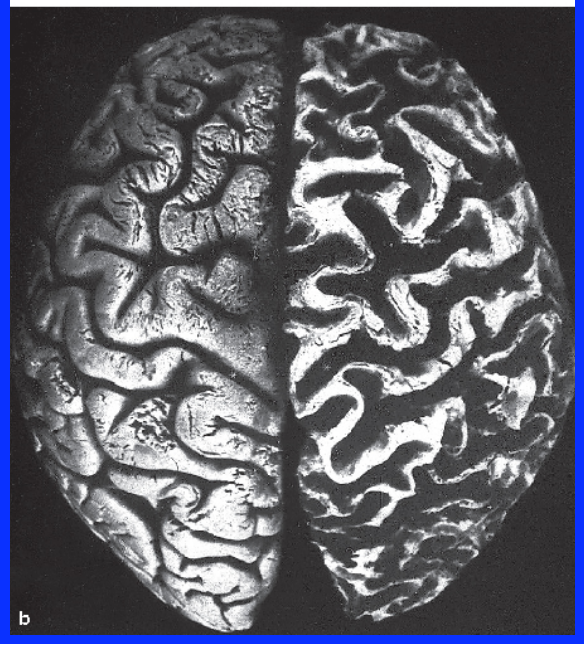
Patient AG, age 38, Guillain-Barré-Syndrome

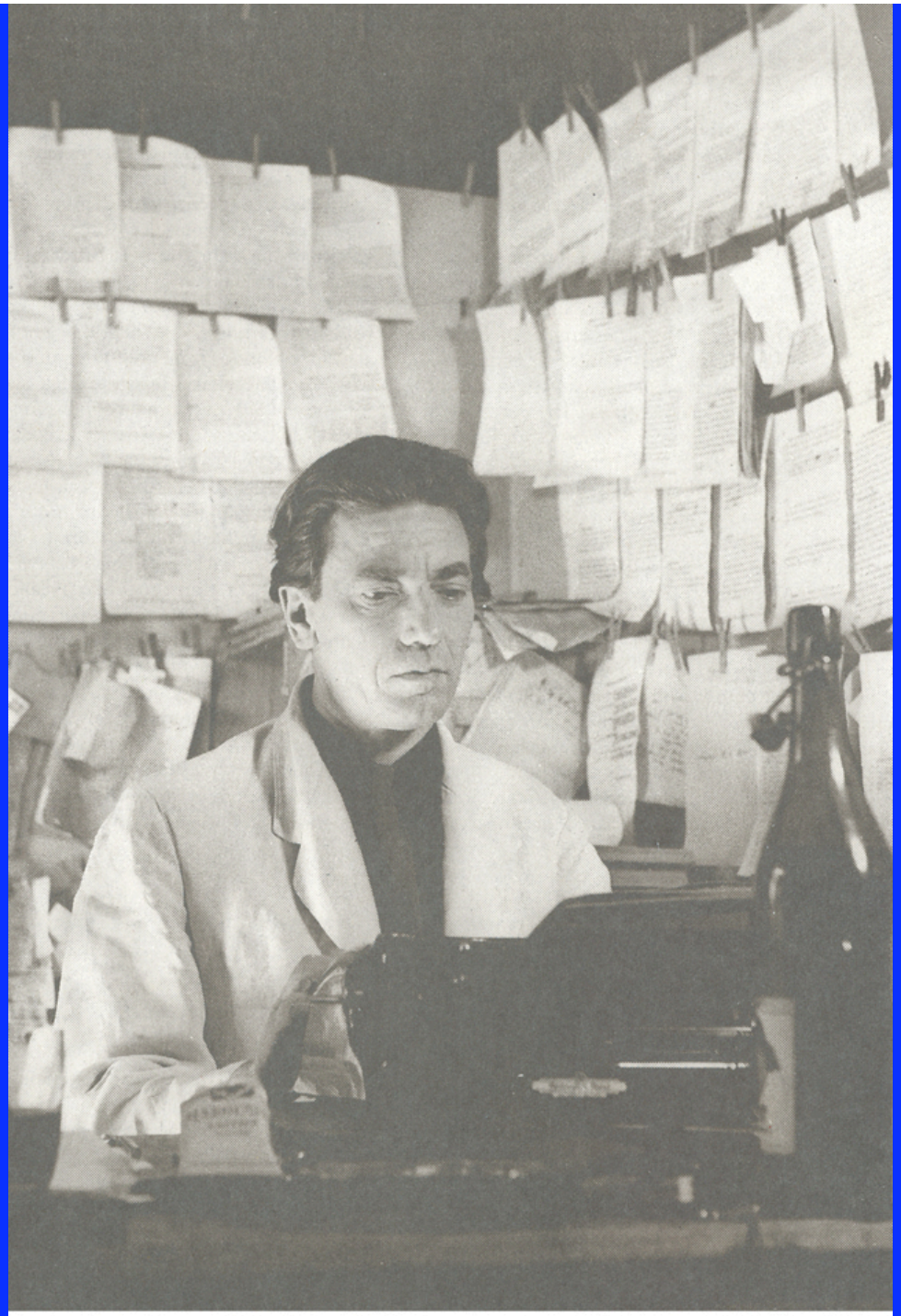
Koutchoubey et.al., News in Physiol.Sciences (2003)

Probabilities of cortical responses as a function of the complexity of stimulation




a


b

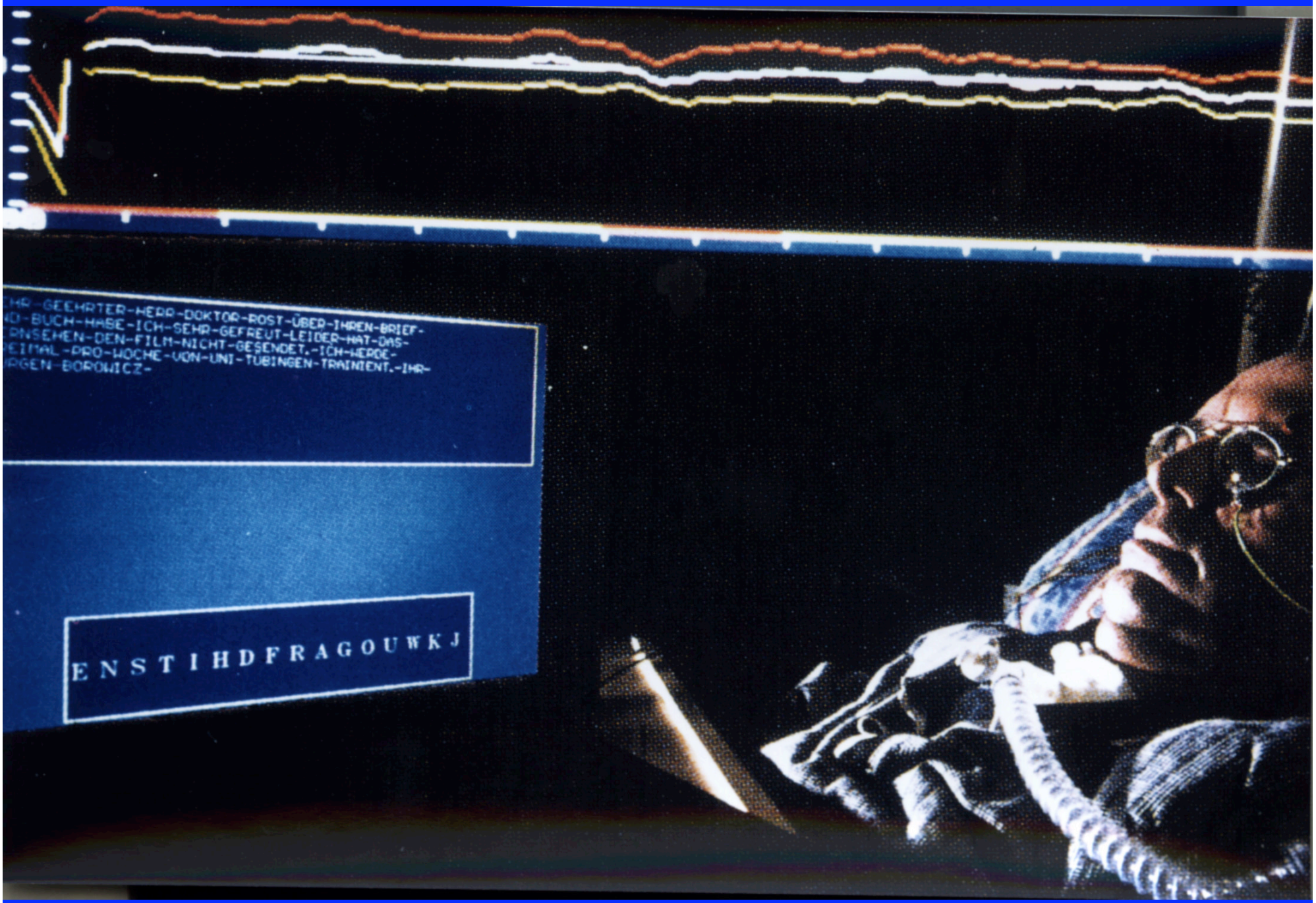


Ludwig Hohl (9. 4. 1904–3. 11. 1980) in seinem legendären Genfer Keller

Der Mensch lebt in dem Maße, wie er kommunikationsfähig ist: ist die Kommunikationsfähigkeit vorbei, so ist auch das Leben vorbei.

The human being lives according to its communication capacity: loosing the capacity for communication means loosing live.

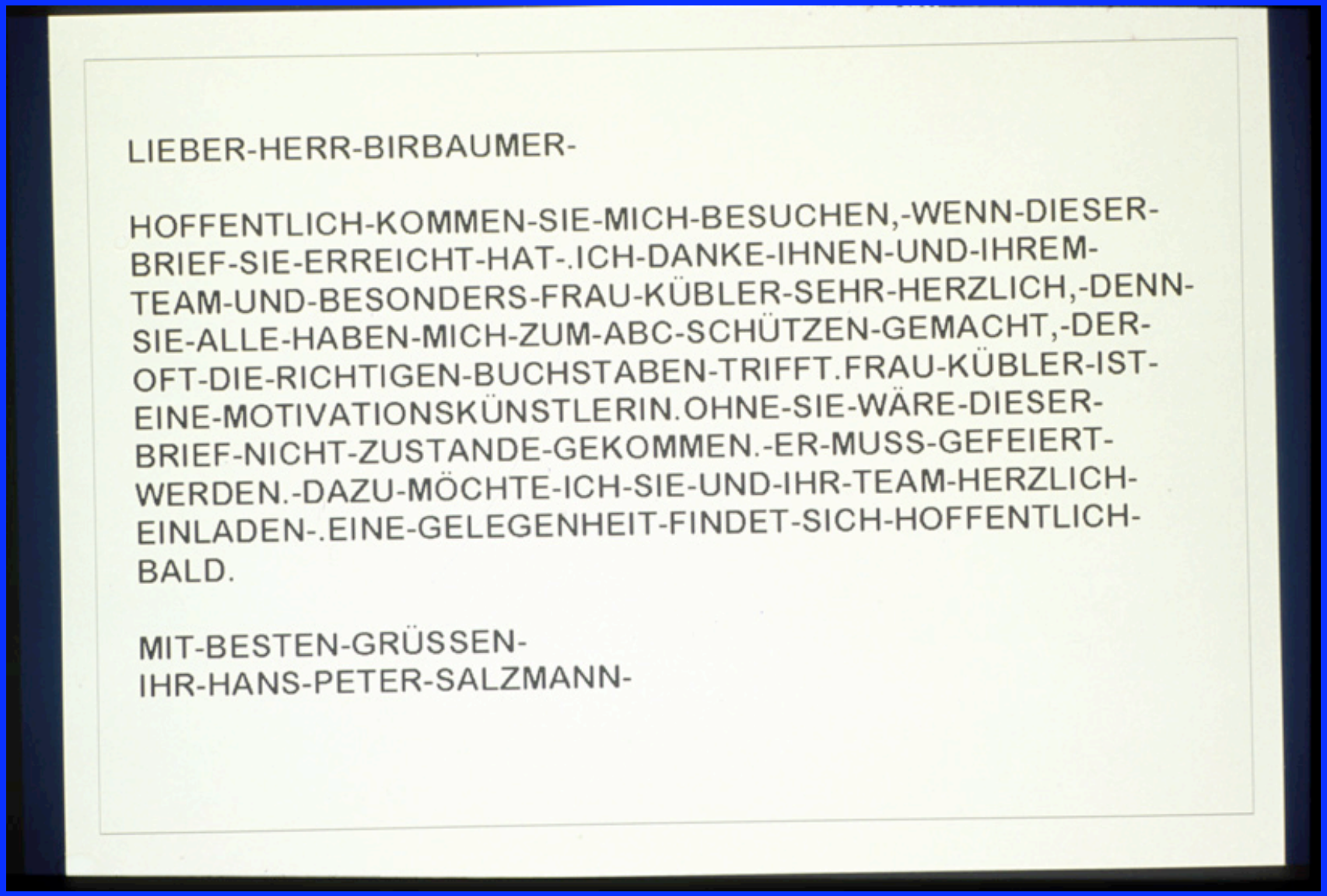
Ludwig Hohl



Source:Report in Newsweek of Birbaumer et al. Nature (1999)

LIEBER-HERR-BIRBAUMER-
HOFFENTLICH-KOMMEN-SIE-MICH-BESUCHEN,-WENN-DIESER-BRIEF-SIE-ERREICHT-HAT-.ICH-DANKE-IHNEN-UND-IHREM-TEAM-UND-BESONDERS-FRAU-KÜBLER-SEHR-HERZLICH,-DENN-SIE-ALLE-HABEN-MICH-ZUM-ABC-SCHÜTZEN-GEMACHT,-DER-OFT-DIE-RICHTIGEN-BUCHSTABEN-TRIFFT.FRAU-KÜBLER-IST-EINE-MOTIVATIONSKÜNSTLERIN.OHNE-SIE-WÄRE-DIESER-BRIEF-NICHT-ZUSTANDE-GEKOMMEN.-ER-MUSS-GEFEIERT-WERDEN.-DAZU-MÖCHTE-ICH-SIE-UND-IHR-TEAM-HERZLICH-EINLADEN-.EINE-GELEGENHEIT-FINDET-SICH-HOFFENTLICH-BALD.

MIT-BESTEN-GRÜSSEN-IHR-
(vollständiger Name des Patienten)



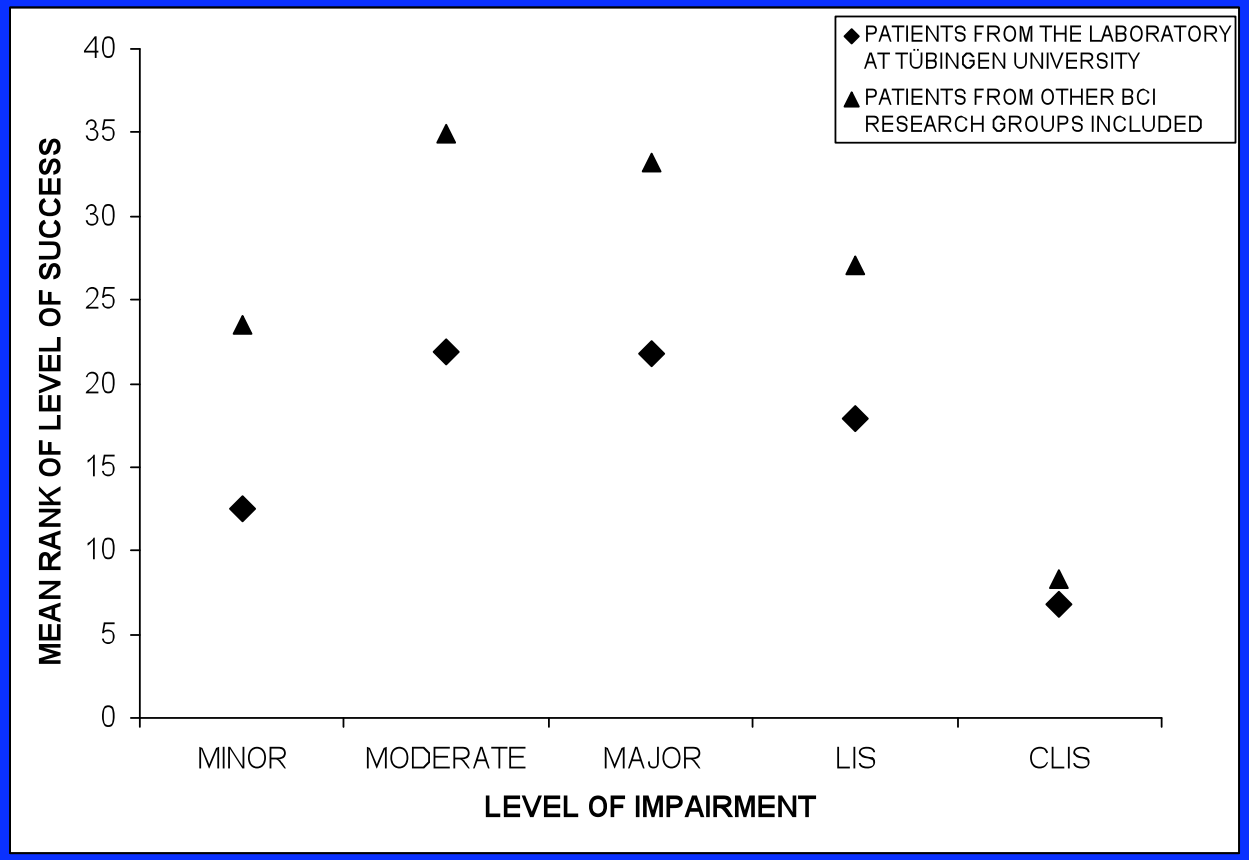
LIEBER-HERR-BIRBAUMER-

HOFFENTLICH-KOMMEN-SIE-MICH-BESUCHEN,-WENN-DIESER-
BRIEF-SIE-ERREICHT-HAT-.ICH-DANKE-IHNEN-UND-IHREM-
TEAM-UND-BESONDERS-FRAU-KÜBLER-SEHR-HERZLICH,-DENN-
SIE-ALLE-HABEN-MICH-ZUM-ABC-SCHÜTZEN-GEMACHT,-DER-
OFT-DIE-RICHTIGEN-BUCHSTABEN-TRIFFT.FRAU-KÜBLER-IST-
EINE-MOTIVATIONSKÜNSTLERIN.OHNE-SIE-WÄRE-DIESER-
BRIEF-NICHT-ZUSTANDE-GEKOMMEN.-ER-MUSS-GEFEIERT-
WERDEN.-DAZU-MÖCHTE-ICH-SIE-UND-IHR-TEAM-HERZLICH-
EINLADEN-.EINE-GELEGENHEIT-FINDET-SICH-HOFFENTLICH-
BALD.

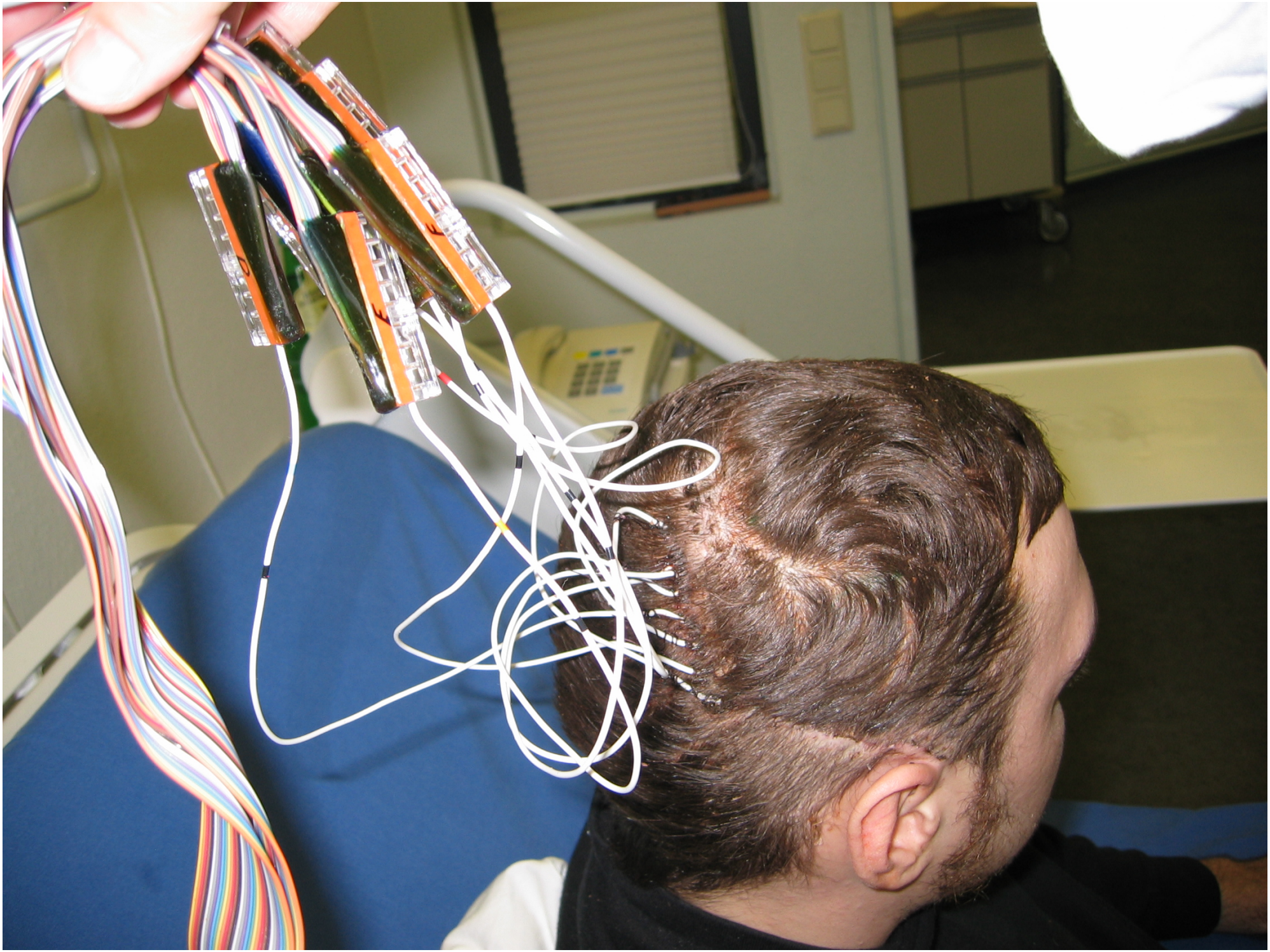
MIT-BESTEN-GRÜSSEN-
IHR-HANS-PETER-SALZMANN-

Birbaumer et al., Nature (1999)

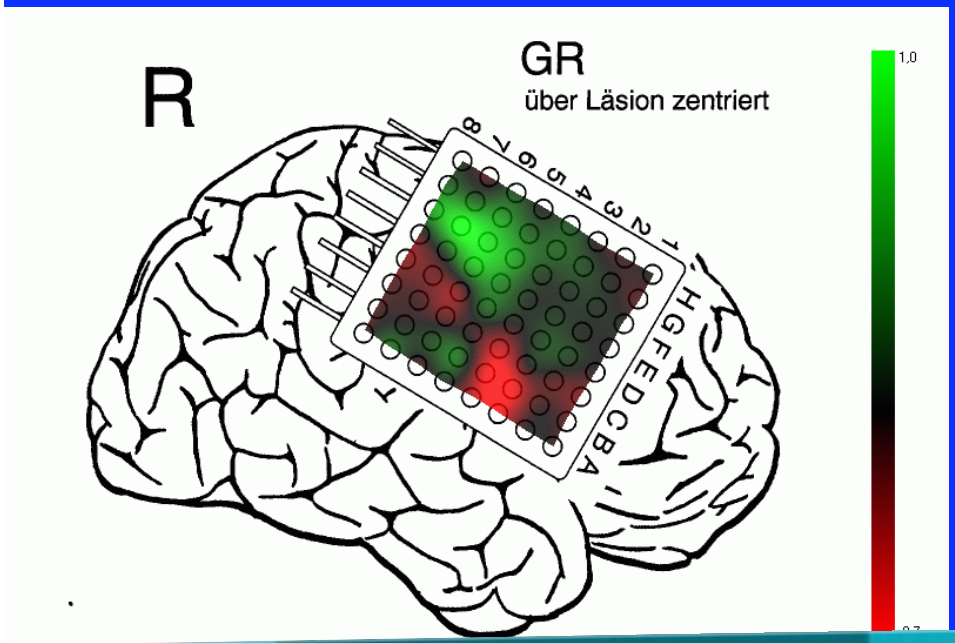
Levels of impairment and BCI-control

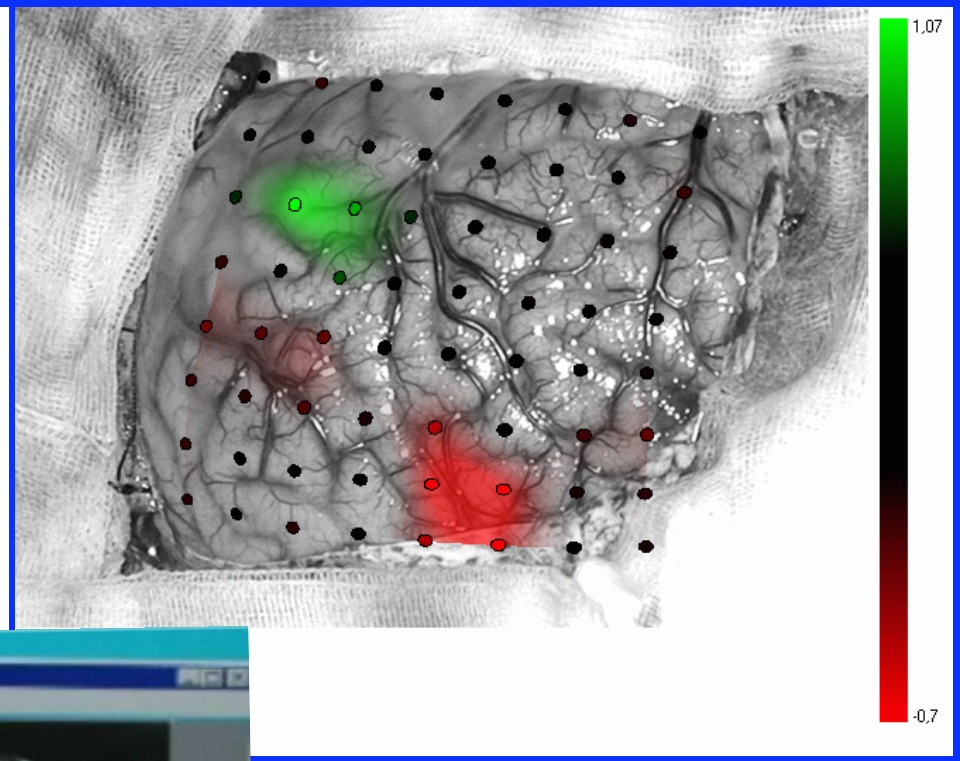


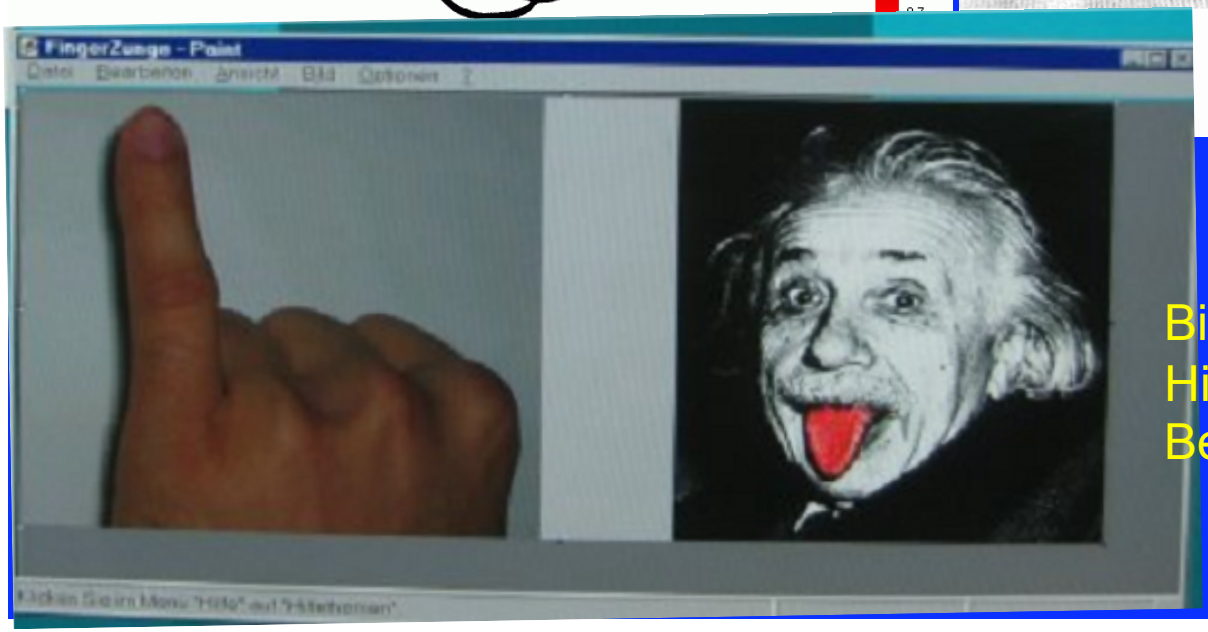
Kübler & Birbaumer, (2008)



Classification of brain activity during imagery





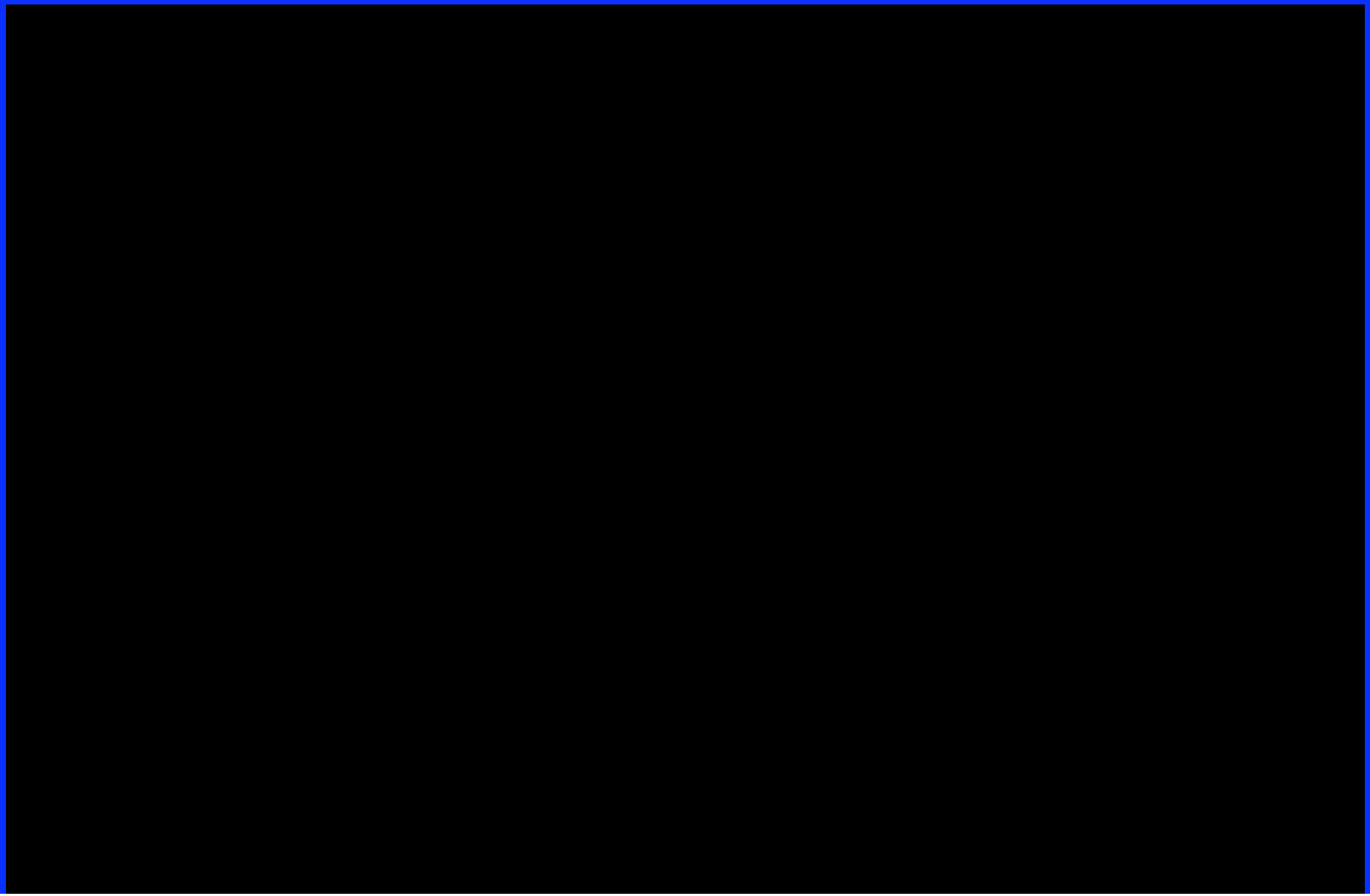


Birbaumer, Psychophysiology (2006)
Hinterberger et al.Epilepsy and Behavior (2008)

Completely locked-in patient IR with permission of family and judge

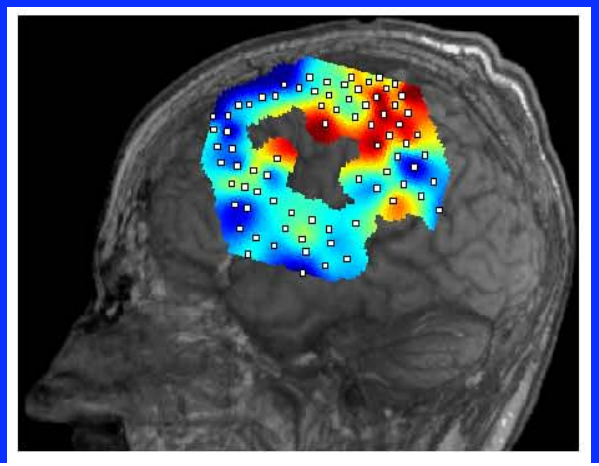
George

(with patient‘s permission)

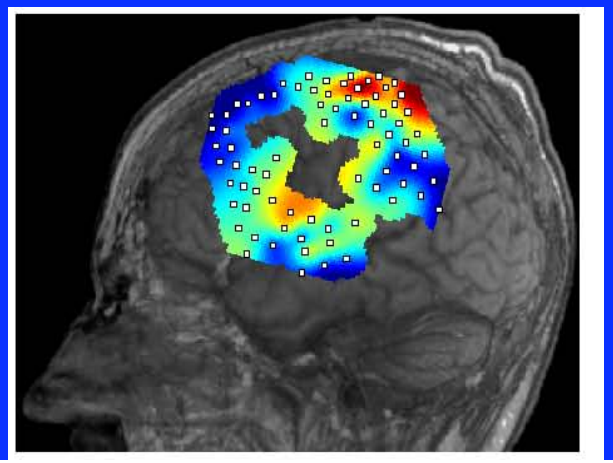


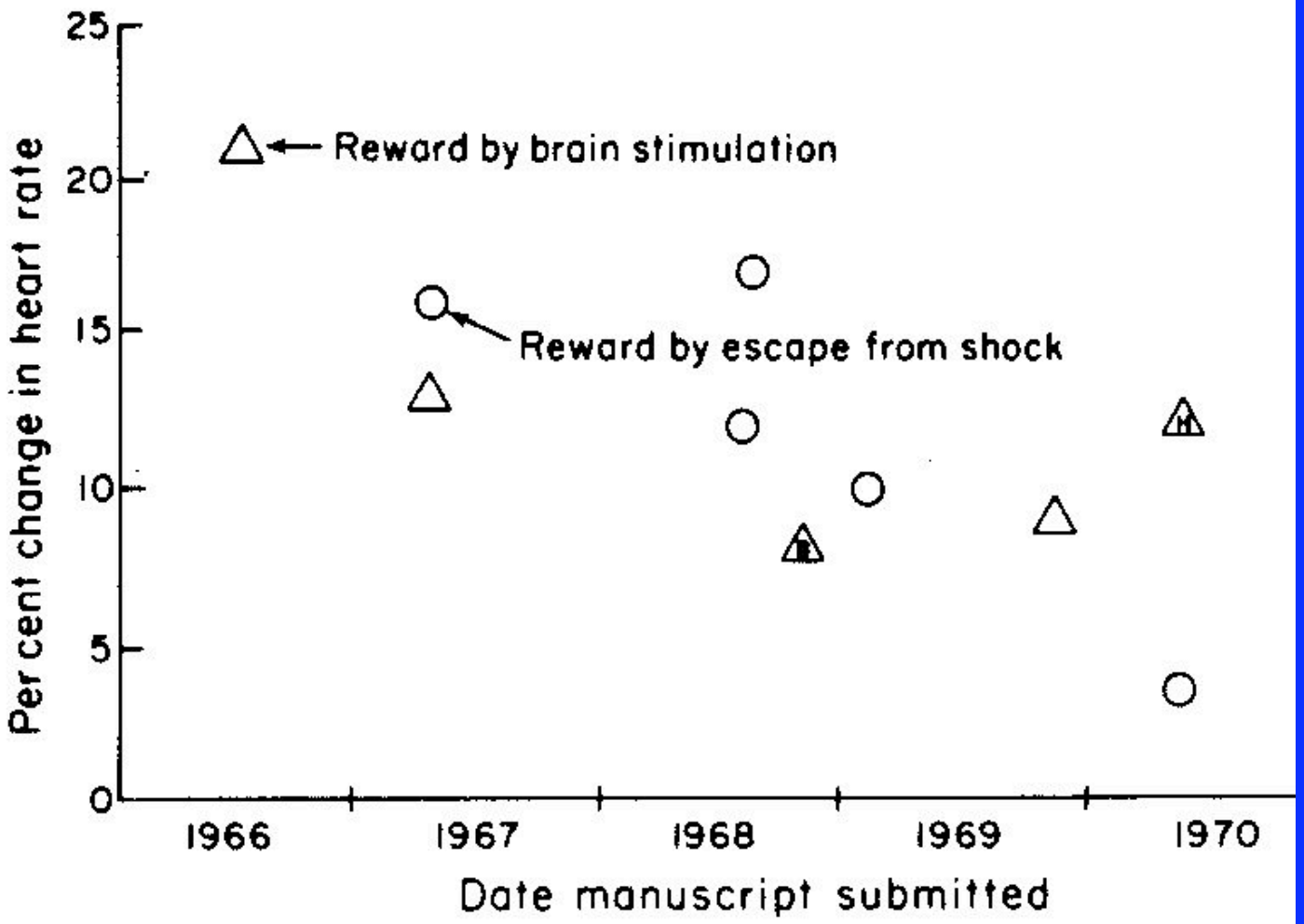
Completely locked-in patient GR with 120 electrode grid implanted êpidurally left fronto-central cortex

Imagery of hand movement „yes“



Imagery of foot movement „no“





Dworkin&Miller ,Behav.Neurosc(1986)

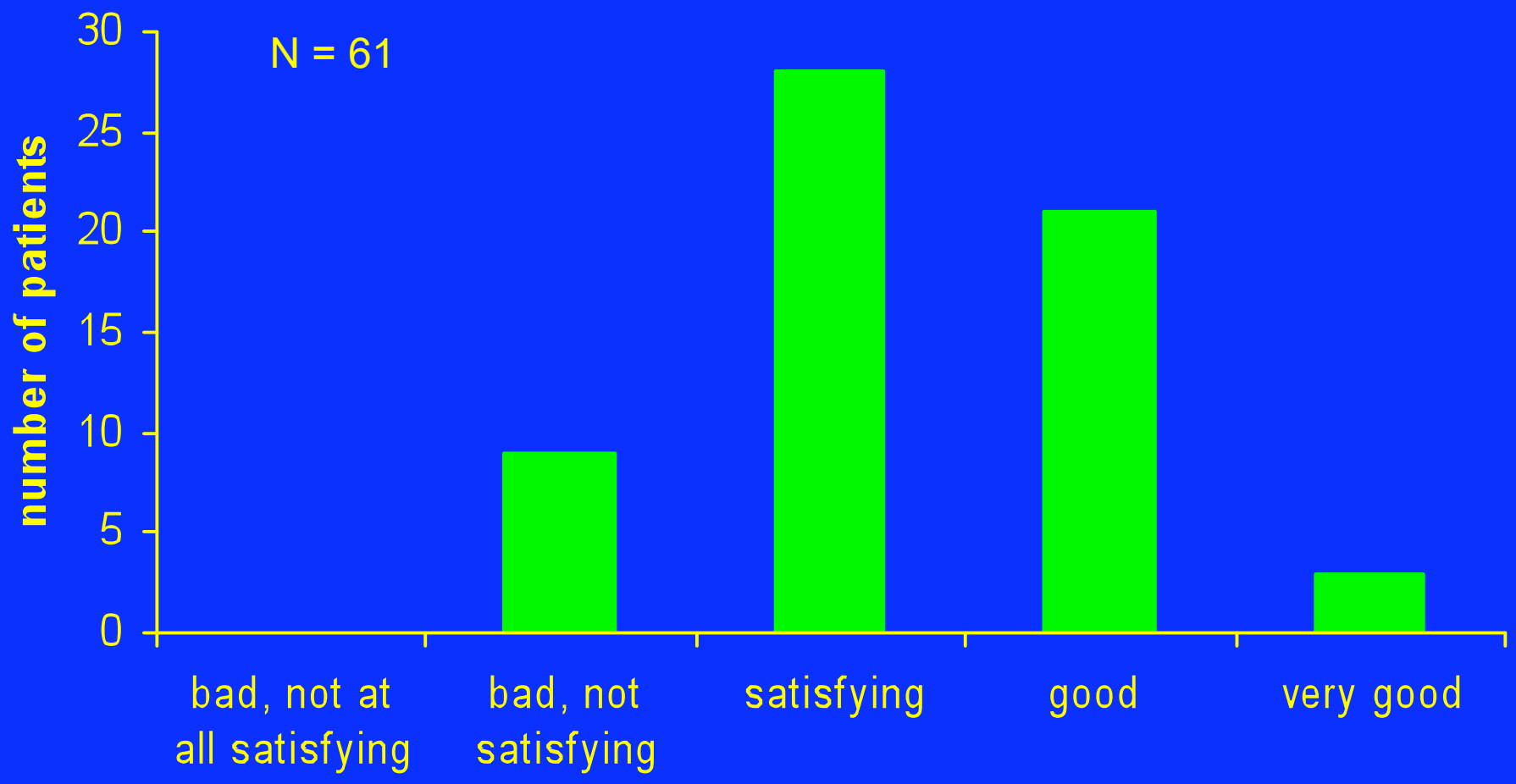
Si nos dejan solos, todo esta de mas.

Wenn wir allein gelassen werden, ist alles zu viel.

If we are left alone, everything becomes too much.

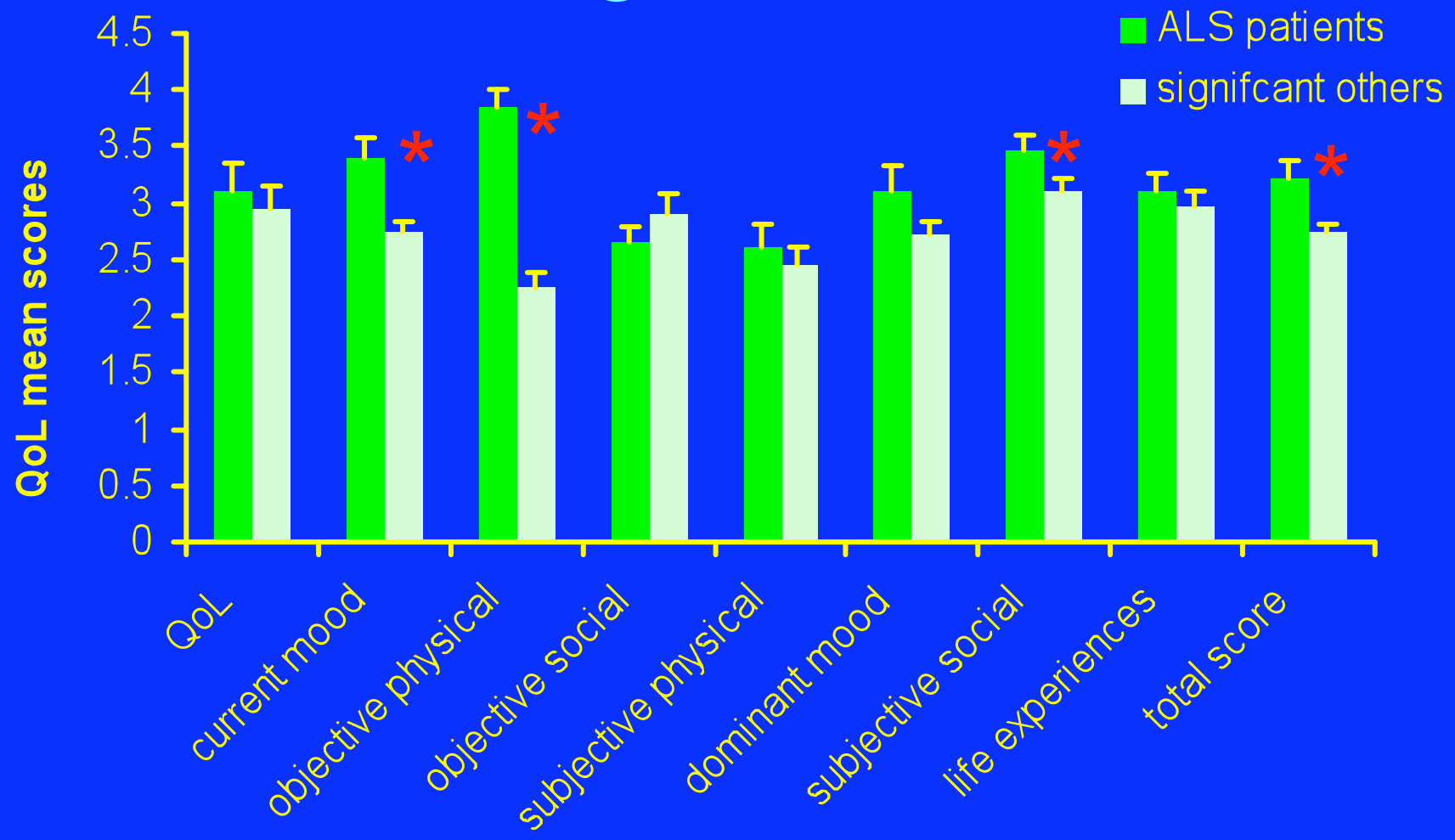
Antonio Porchia

Quality of life in ALS-patients



Kübler et al. , 2005

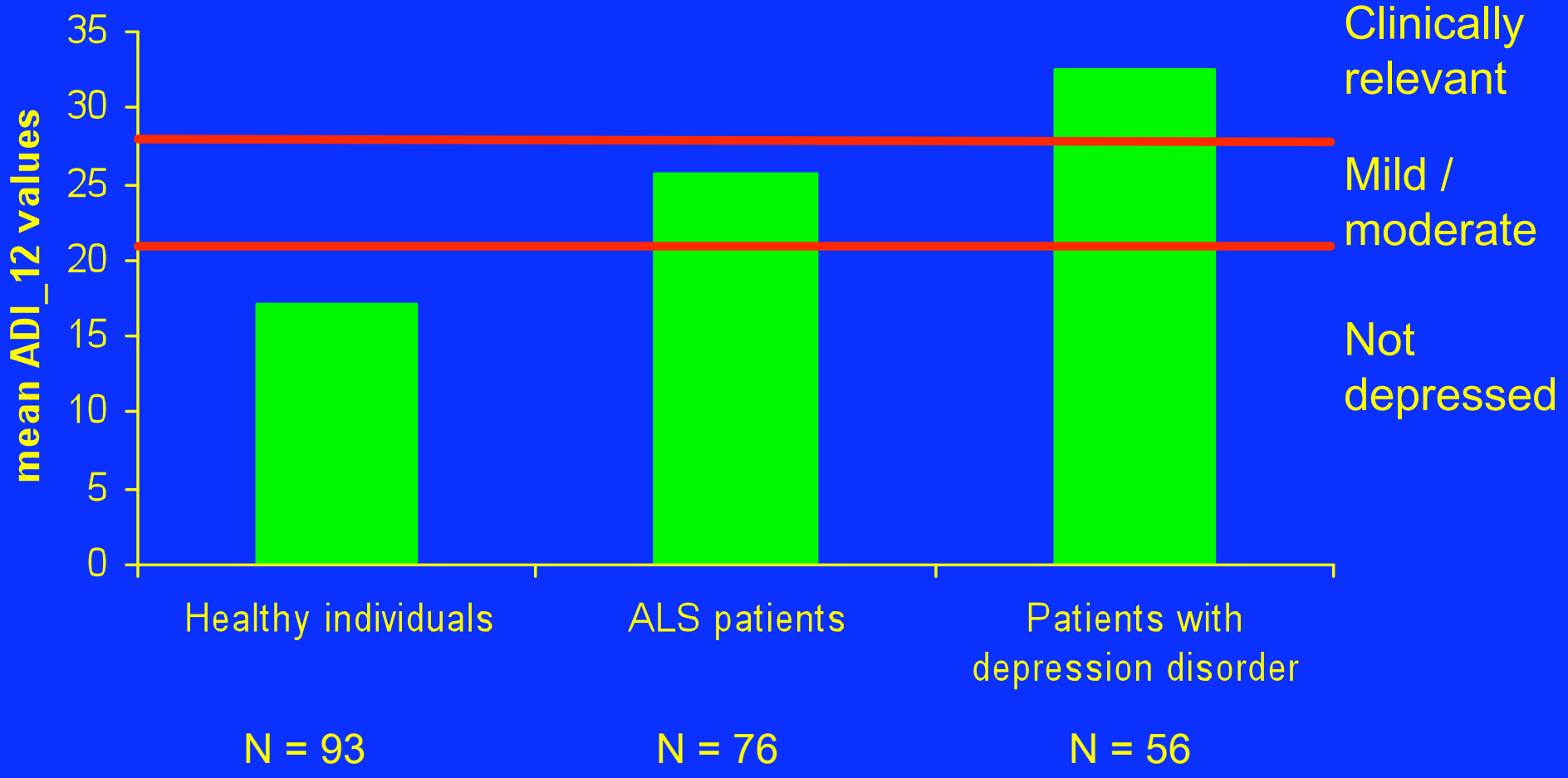
Quality of life– patients and the bias of significant others



N = 19; $t_{18} = 2.75$, $p < .05$

Kübler et al.Neuroreh.&Repair 2005

Mean scores of depression

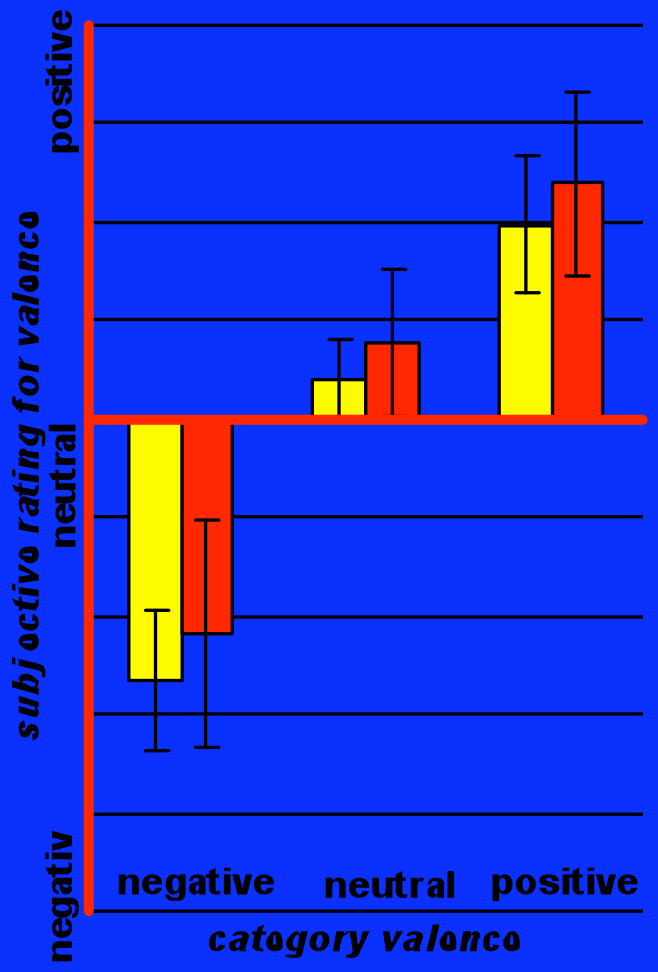


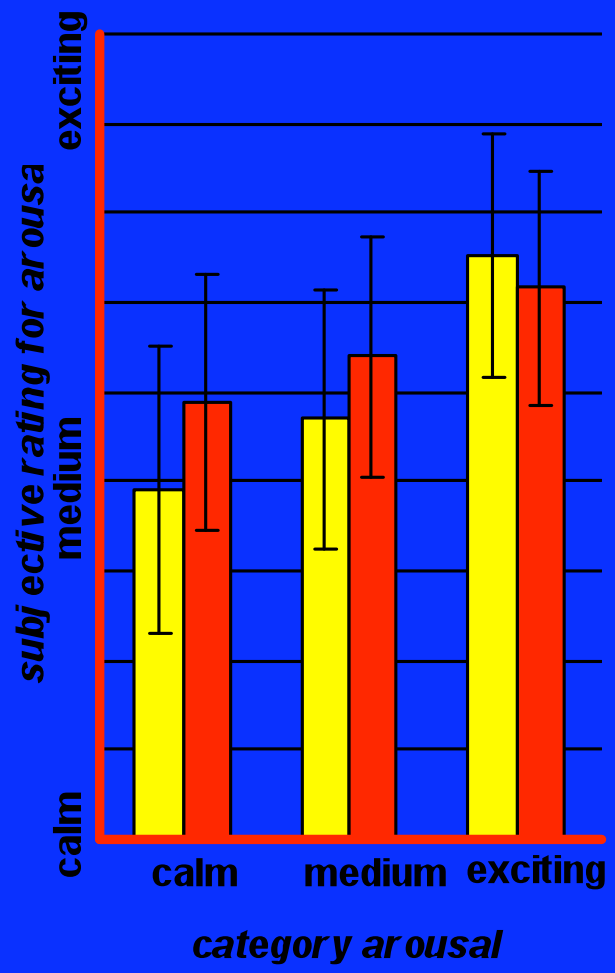
Kübler et al., in press

Subjective responses to emotional slides

ALS-patients rate more positive

Arousal is diminished in ALS-patients





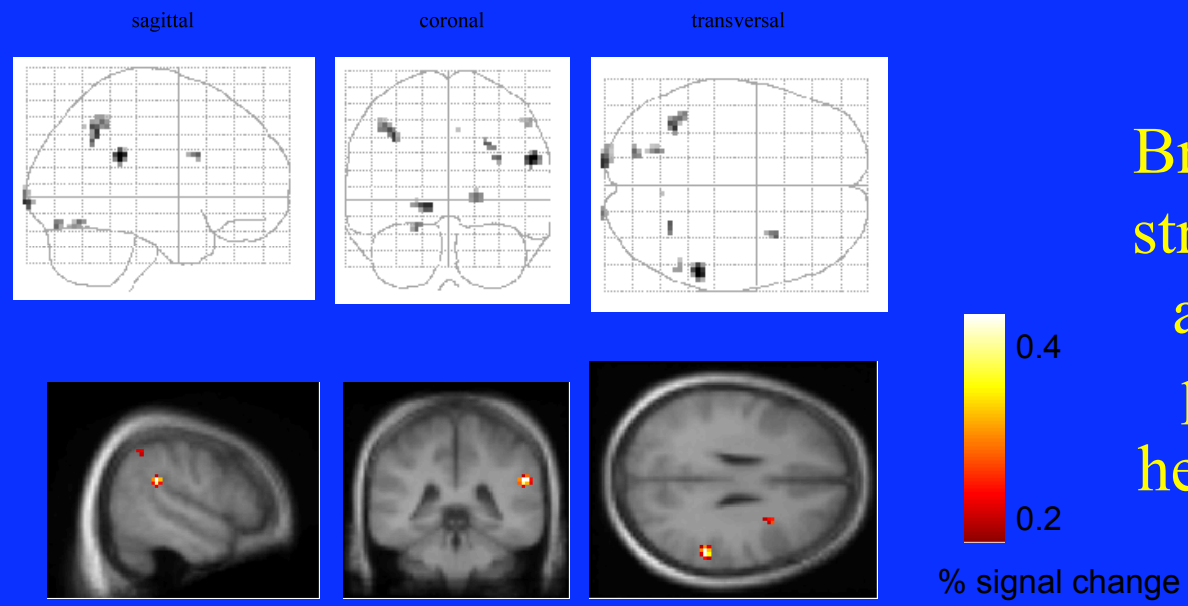
ALS patients

Healthy controls

Lule et al. Neurology 2004

ALS-patients minus healthy participants (IASP. Lang, Bradley & Cuthbert)

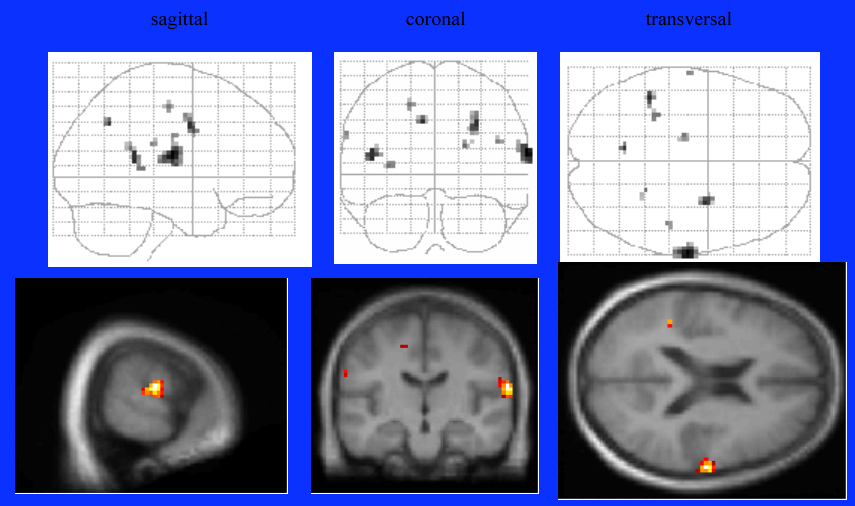
a.)



Brain areas with stronger BOLD-activations in patients than healthy controls

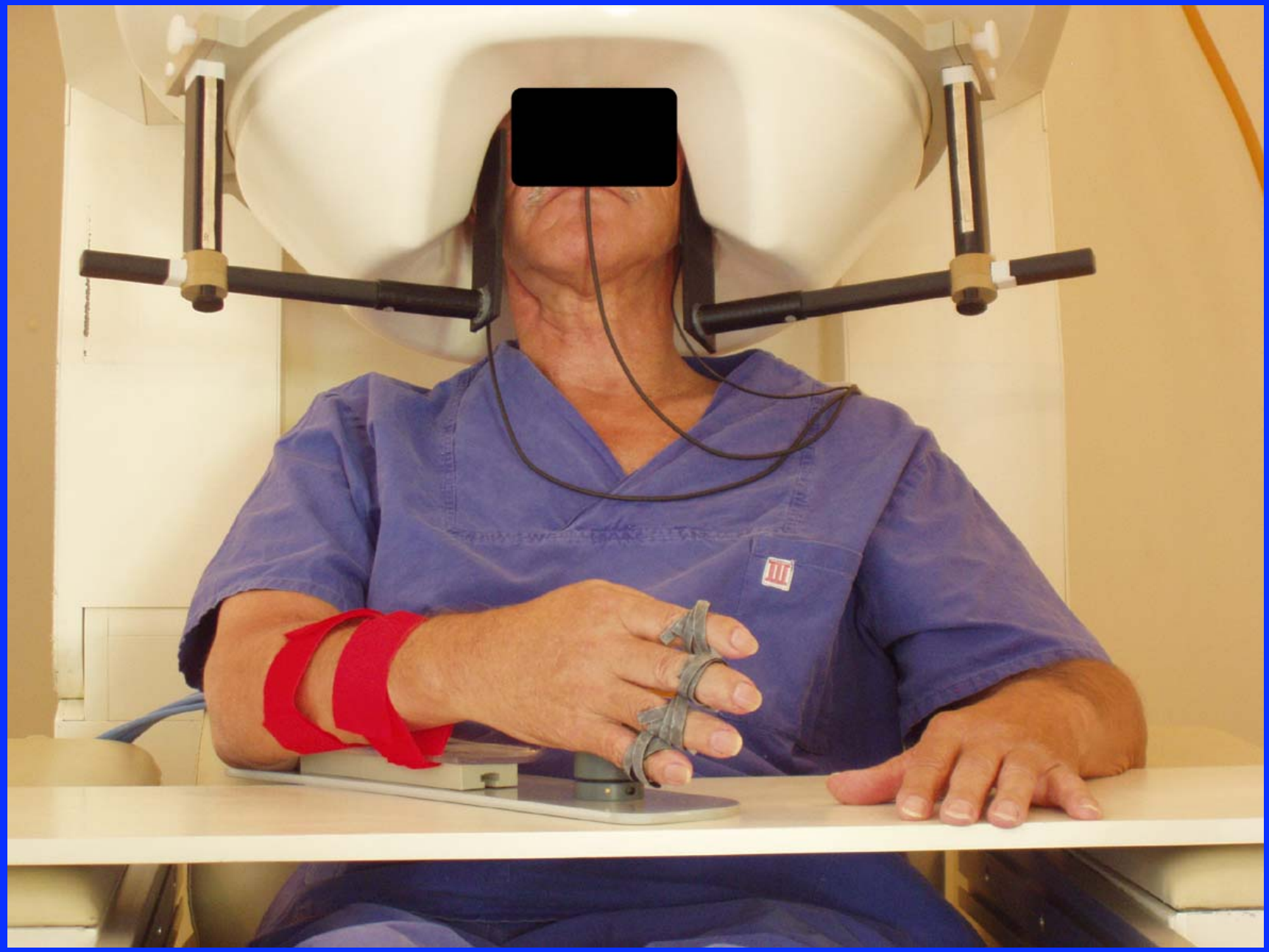
b.)

after 6 months



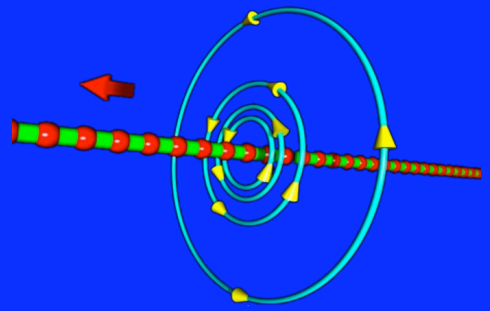
Larger activation in right supramarginal gyrus (BA 40) involved in social processing increases in the course of the disease

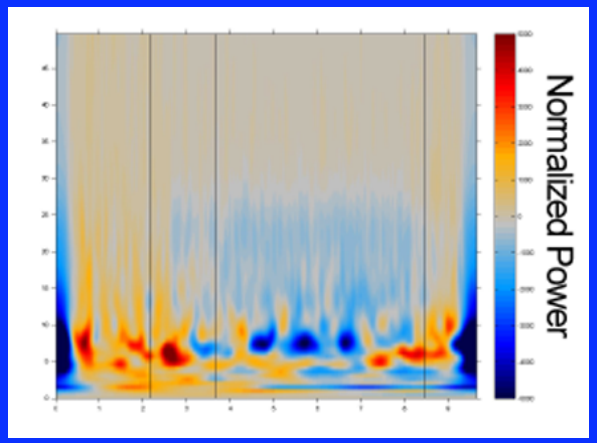
Lule et al,Neurology (2007)



Birbaumer & Cohen, J.Physiol. (2007)

The Training Paradigm





Whole-head MEG

Target Presentation

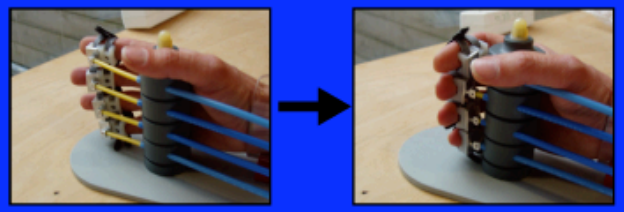
Realtime Spectral Analysis of MEG Control Channel Signals

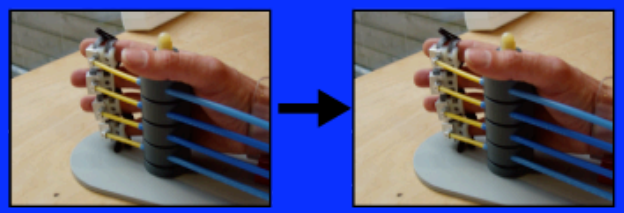
Screen Cursor Feedback

Successful Result Presentation

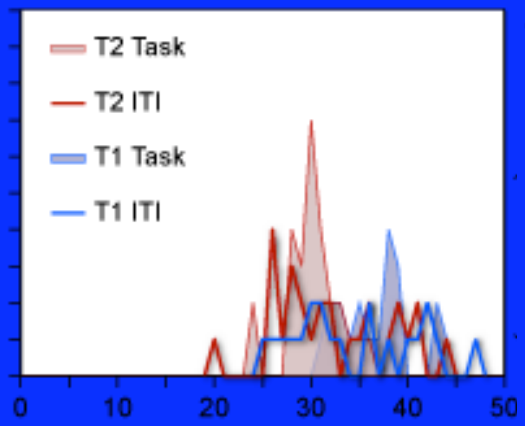
Unsuccessful Result Presentation

Orthosis closes hand





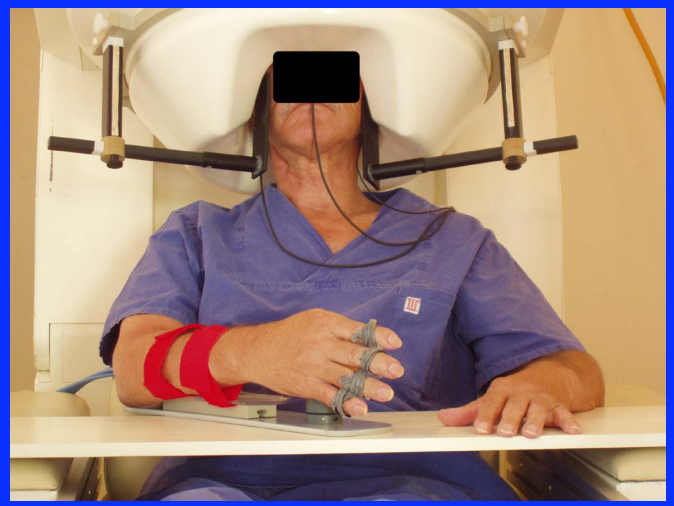
Hand position unchanged



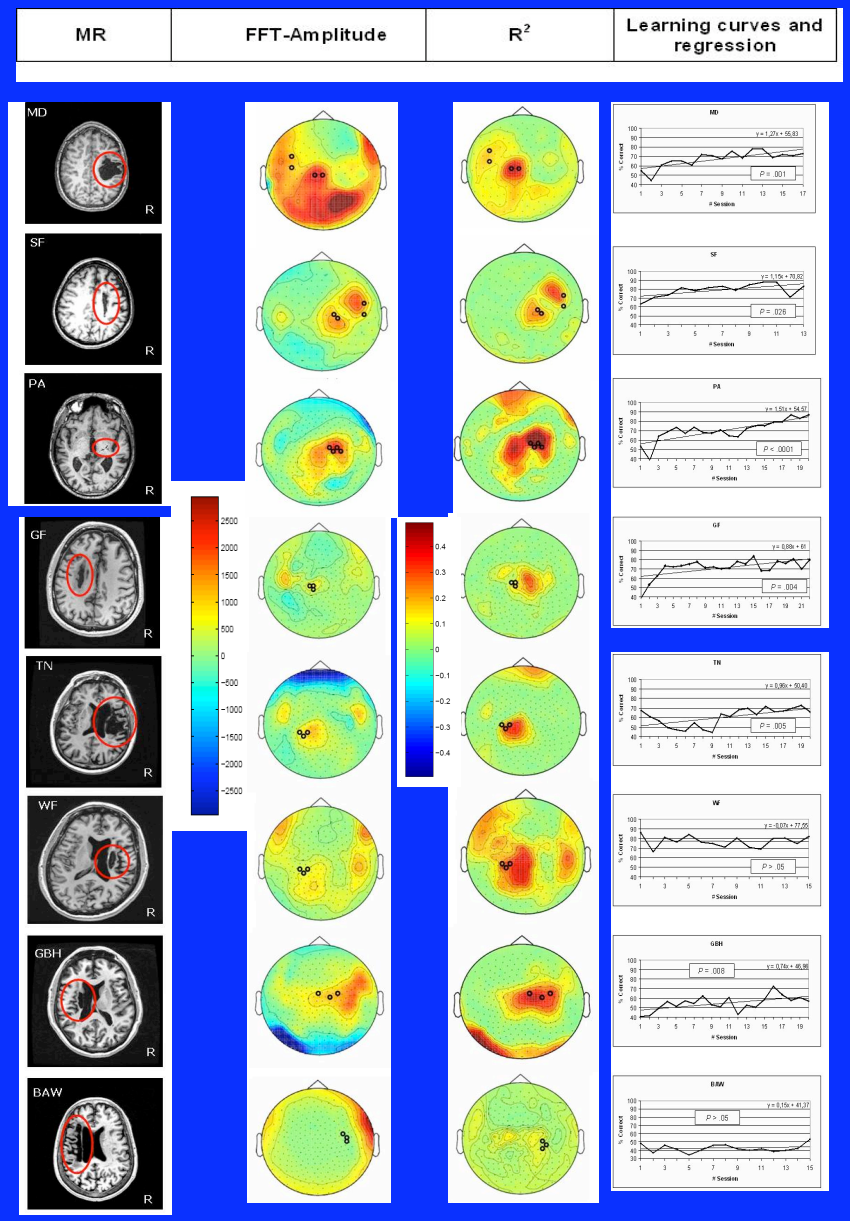
Bandwidth Power
(3 Hz BW; 12 Hz central frequenc

Buch et al, Stroke (2008)

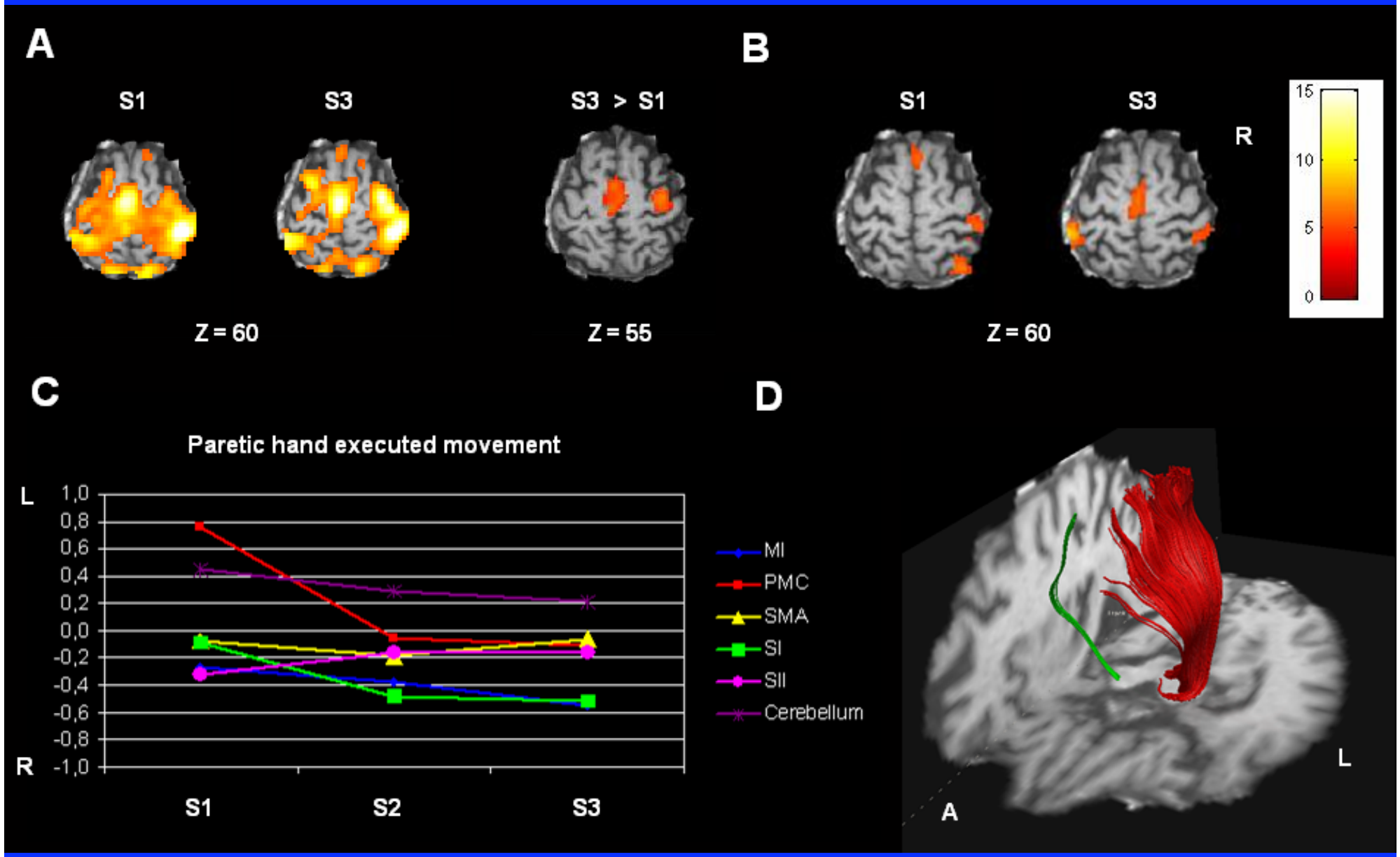
MEG-BCI training in chronic stroke



MEG-BCI: hand orthosis controlled by ipsilesional central mu-rhythm



Buch et al. Stroke (2008)


A
S1
S3
S3 > S1
Z = 60
Z = 55
B
S1
S3
R
15
10
5
0
Z = 60
C
Paretic hand executed movement
L
R
1,0
0,8
0,6
0,4
0,2
0,0
-0,2
-0,4
-0,6
-0,8
-1,0
S1
S2
S3
MI
PMC
SMA
SI
SII
Cerebellum
D
A
L

Die einzige Wahrheit auf der Erde ist unser Gefühl.

The only truth on earth is our emotion.

Gustav Mahler

fMRI-BCI system

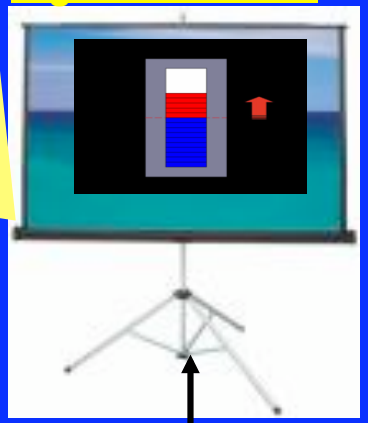
Signal Acquisition

Custom-built scanner program

raw images

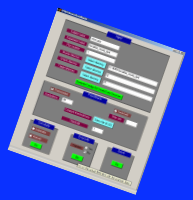
Signal Analysis

Signal Feedback



Participant

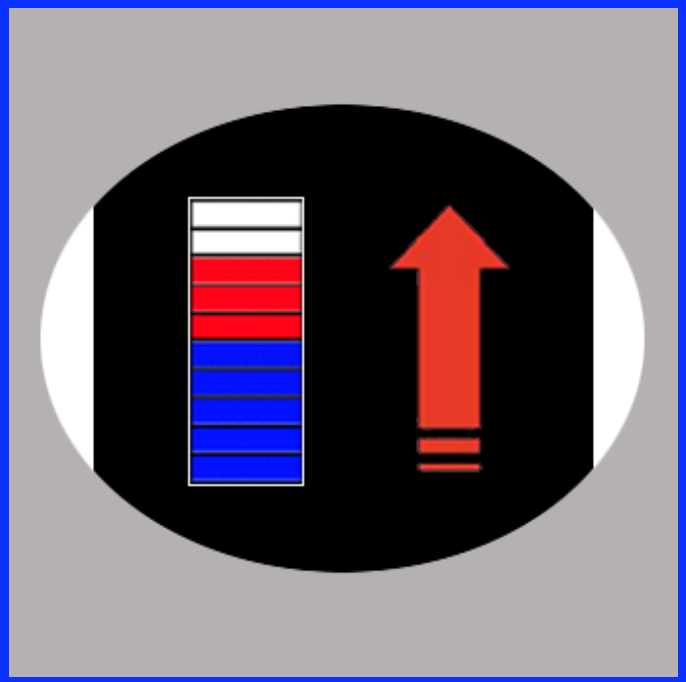
BCI Program

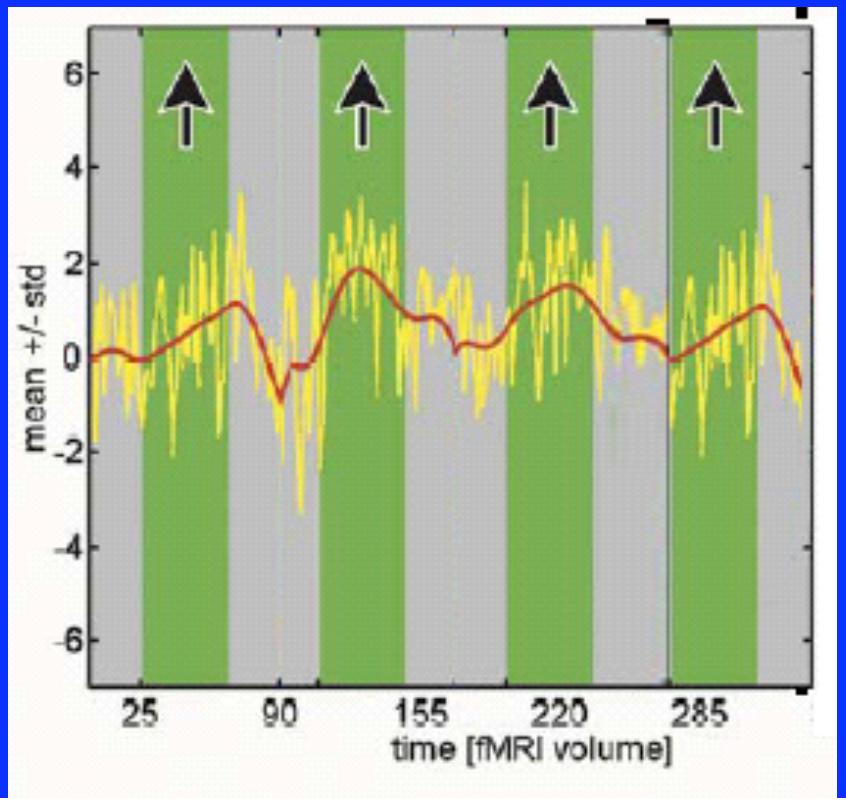


preprocessed
brain activity

pattern classification (Support Vector Machine)
•performance measures

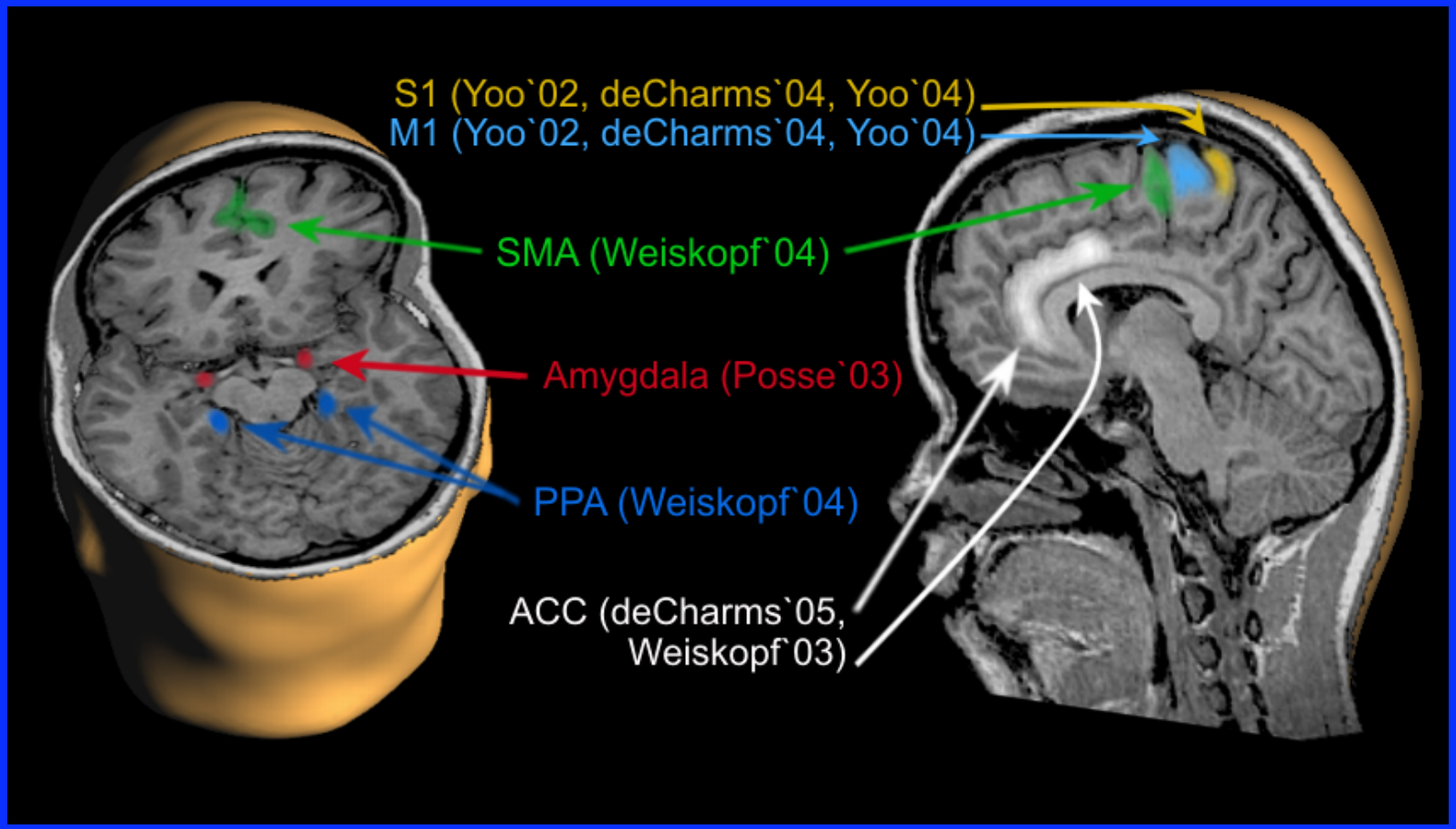
Rückmeldung der Hirnaktivität [Training]





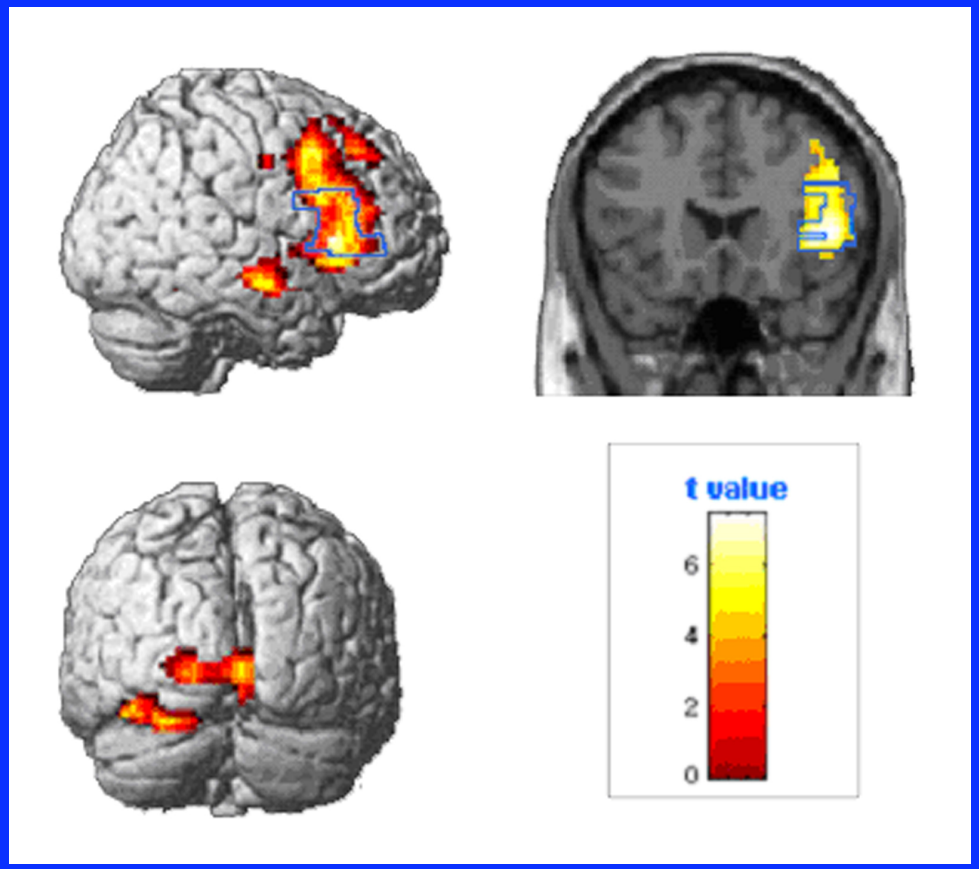
Weiskopf et al. J.Physiol (Paris) 2005

Operant Conditioning of BOLD



Weiskopf et al. Magn.Res. Imaging (2007)

Learning of right inferior frontal gyrus activation

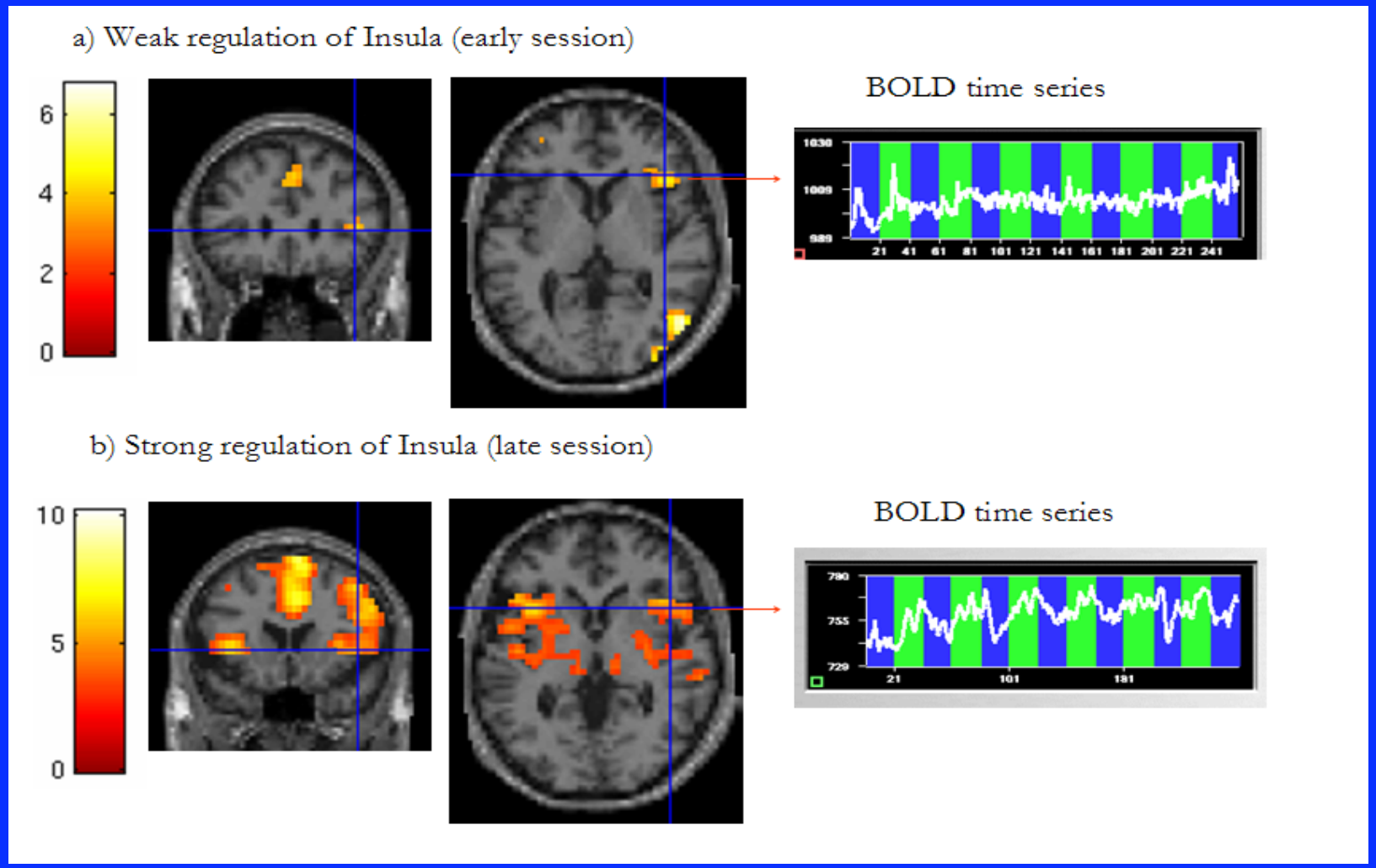


NE, SK = 12 sessions
SP, KL = 8 sessions

Rota et al., Human Brain Mapping, (2008)

Rota et al. Human Brain Mapping(2008)

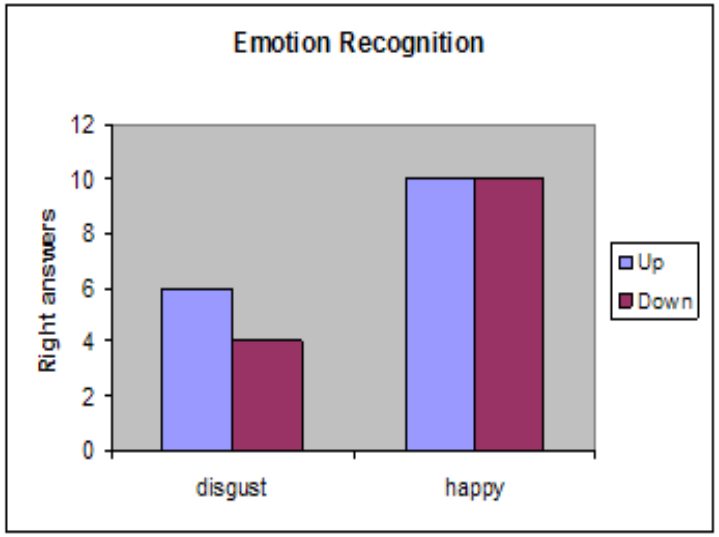
- Both schizophrenic subjects were able to regulate BOLD magnitude in the right anterior insula within the sessions. Percent BOLD signal increased from an early-weak regulation session, to a late-strong regulation session ($p<0.05$) (Fig. 2)



SPM analysis of subject FM, showing the contrast up-regulation vs baseline during an early and a late session. The time-series of BOLD signal for each session is also shown.

Emotional Face Recognition after 42 sessions of insula up-training in schizophrenia

- Patient FM, schizophrenia negative symptoms, better accuracy in the recognition of disgust faces after Up regulation compared to Baseline. Both emotions (happy and disgust) were rated as more intense after Up regulation



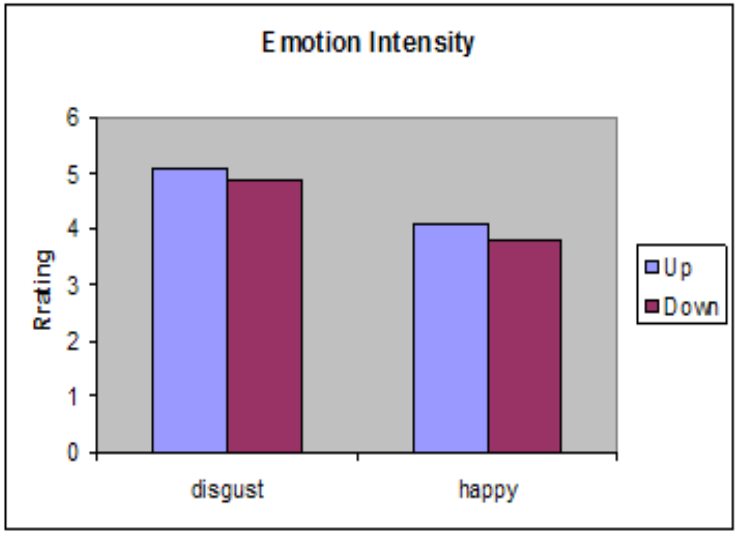
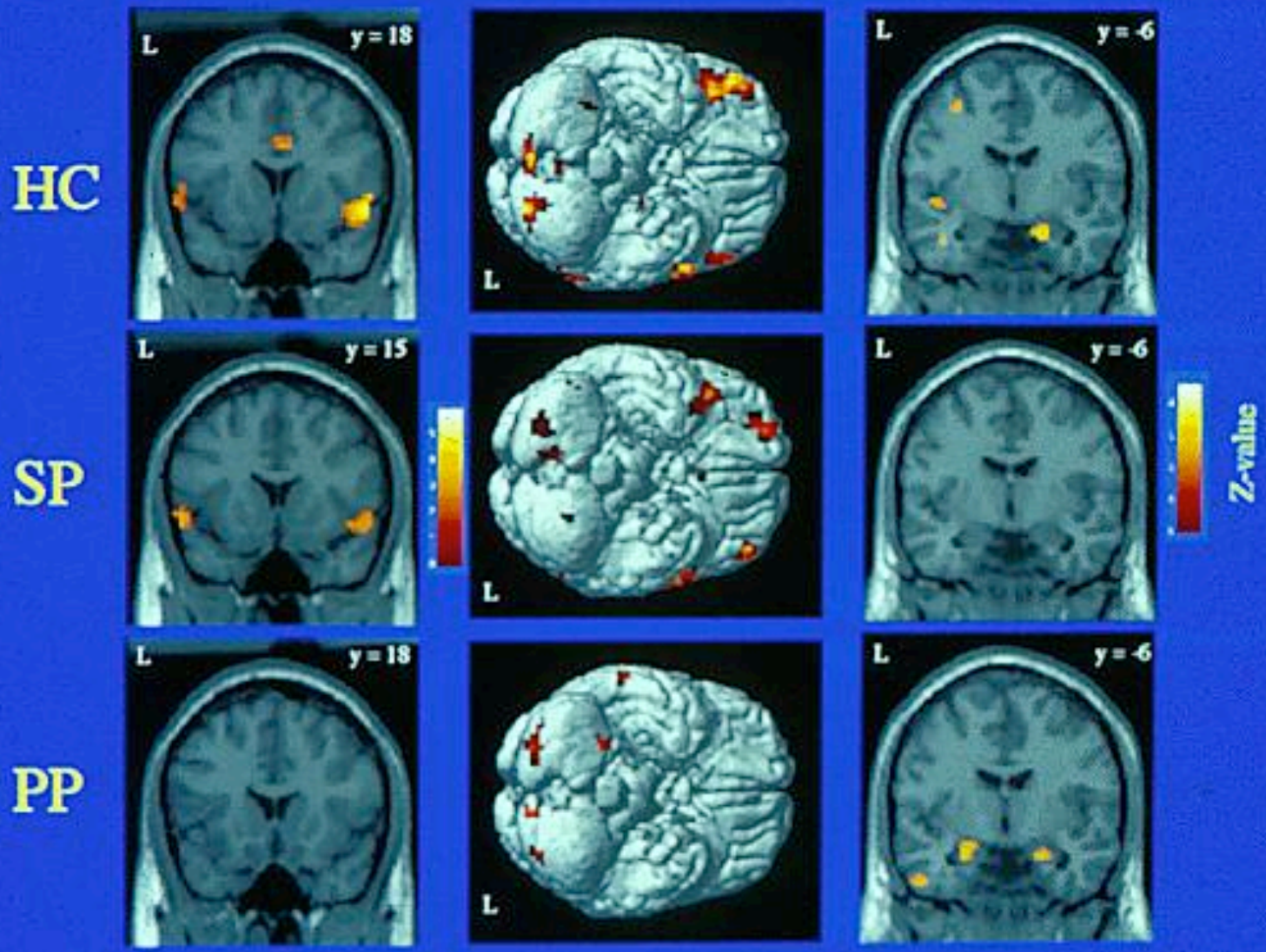


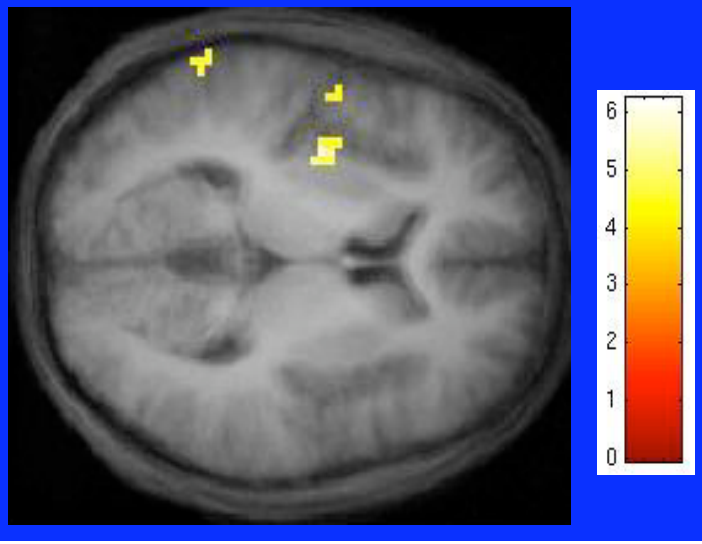
Fig 4. Behavioural results of subject FM

Acquisition CS+/CS-

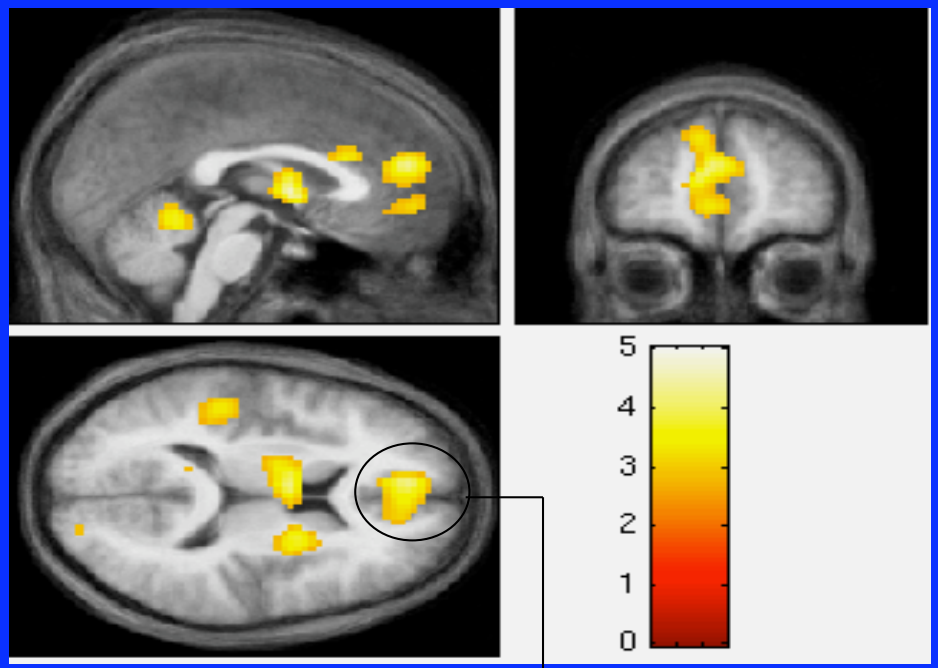


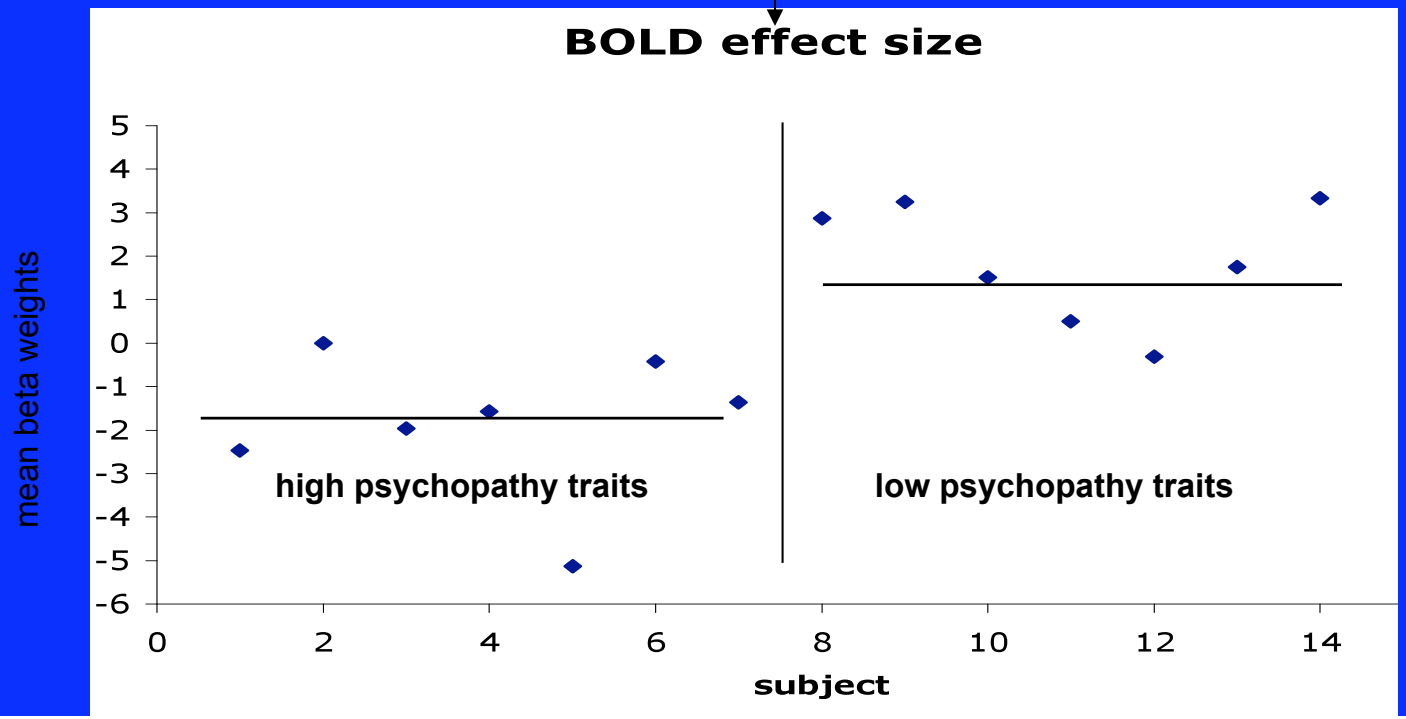
Birbaumer et al., Arch.Gen.Psychiatry (2005)

Aggressionsstudie: Bestrafung



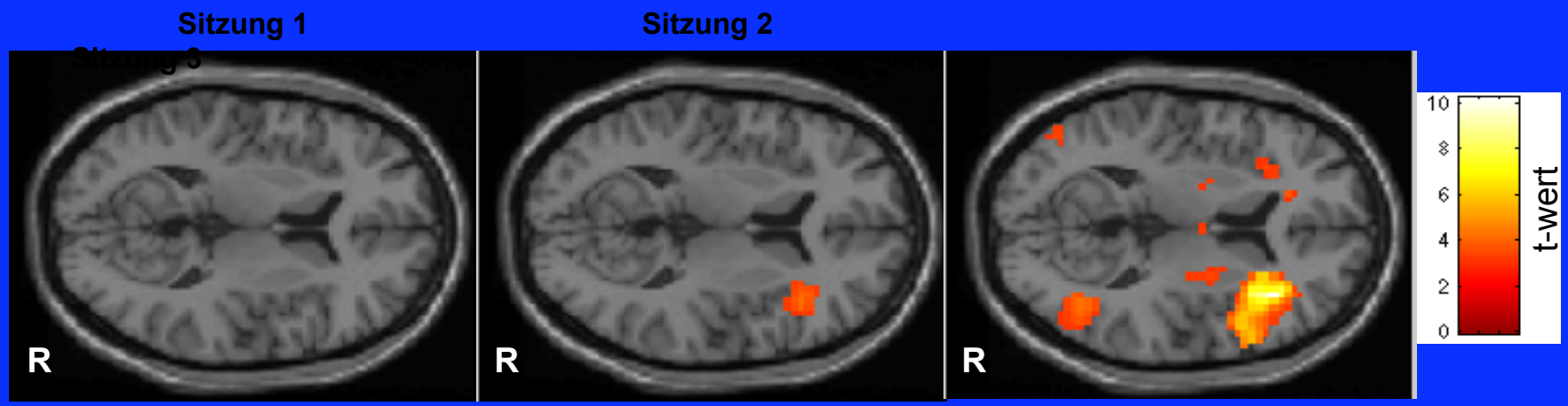
Guilt in low versus high psychopathy trait





Veit et al (2008)

Near Infrared Spectroscopy (NIRS) for
Operant Training of Cerebral Oxygenation



fMRI-BCI-Training of BOLD-Increase in the Right Anterior Insula
Caria et al, Neuroimage 2007

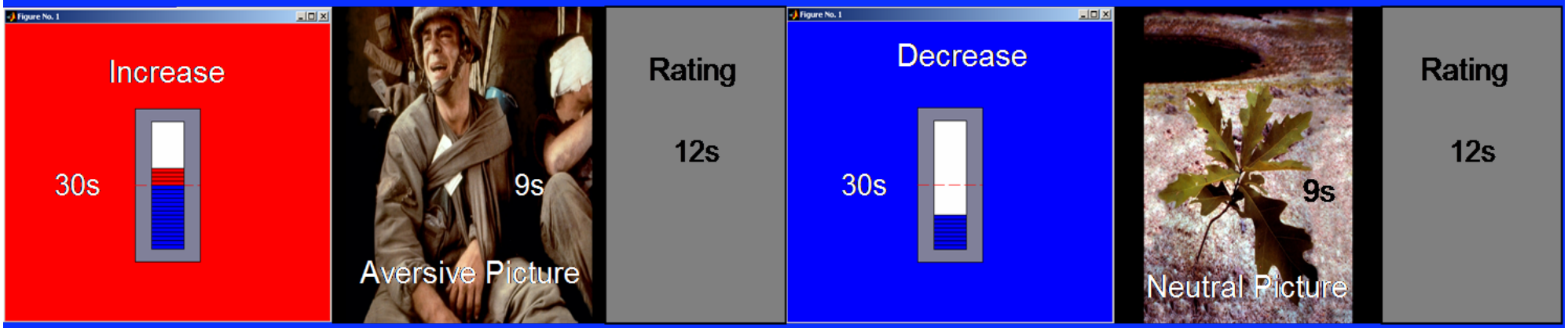
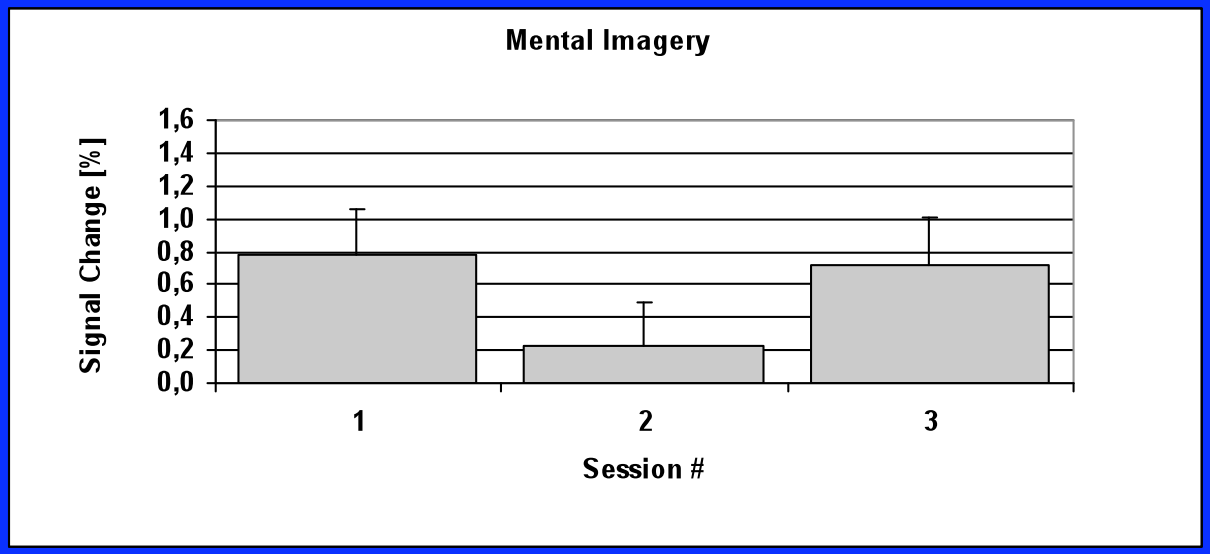
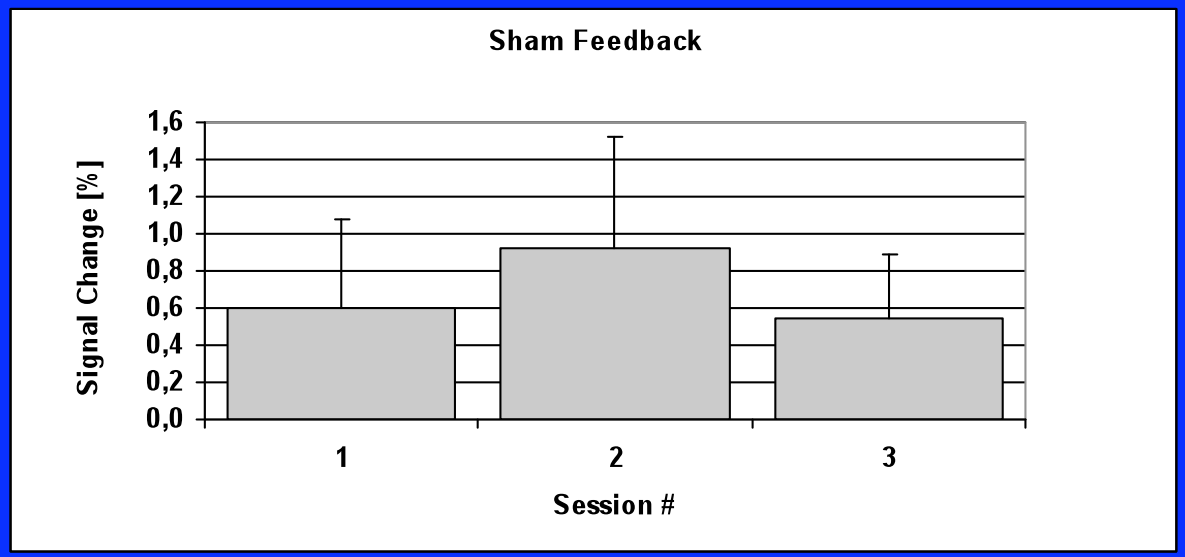


Figure No. 1
Increase
30s
9s
Aversive Picture
Rating
12s
Figure No. 1
Decrease
30s
9s
Neutral Picture
Rating
12s

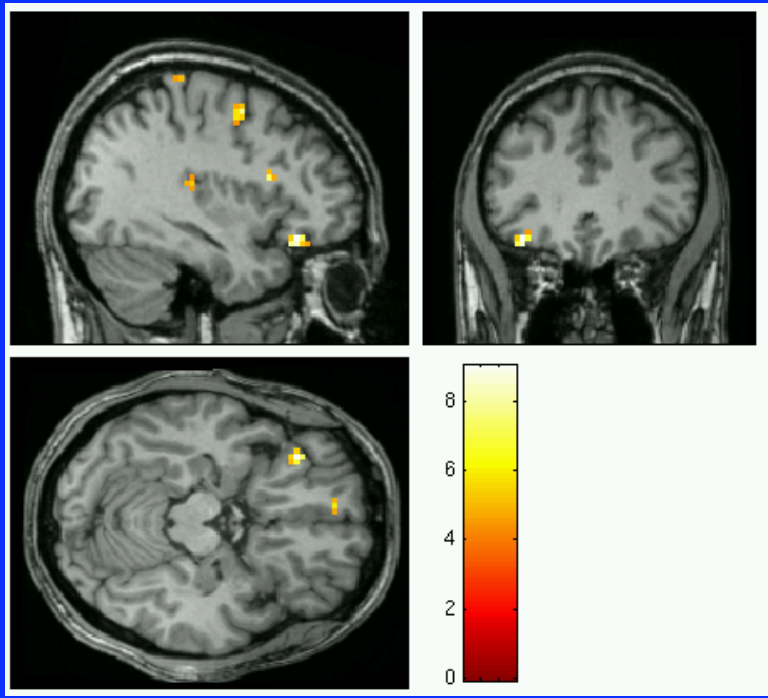


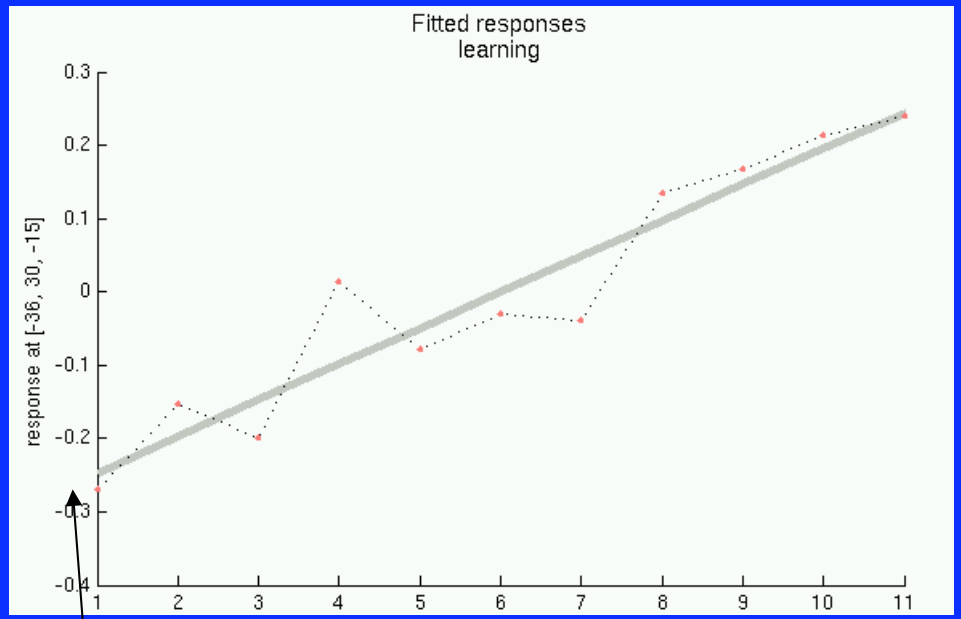


Caria et al, submitted

Psychopaths

Linear increase of activation over time in the left insula



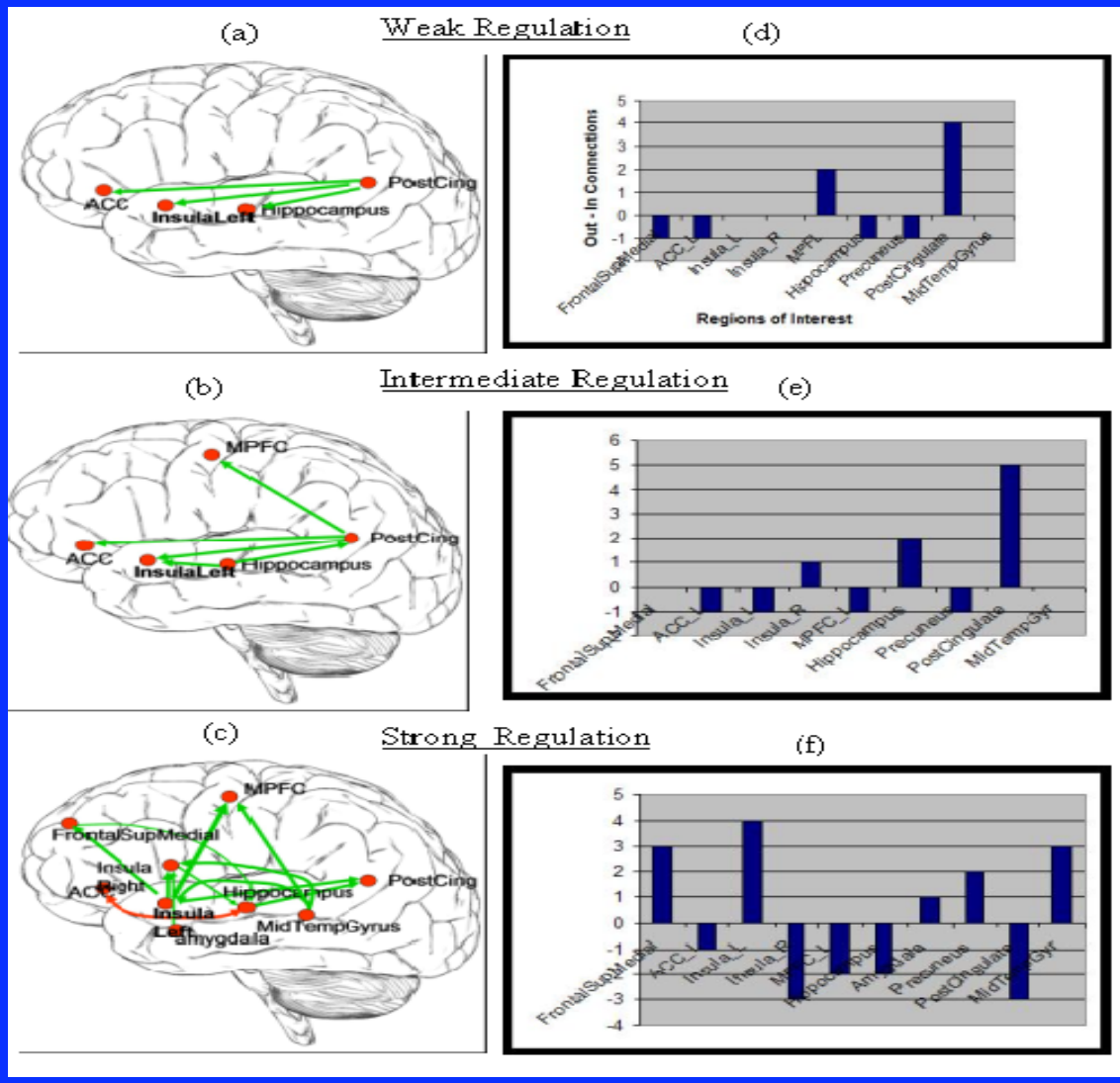


Session

Mean corrected values

Caria et al submitted

Functional connectivity changes due to training



Figures (a)-(c) show directed influence maps (DIMS) and figures (d)-(f) show the bar charts of the causal flow (CF; defined as the net difference between outgoing and incoming connections) in the brain regions (the emotional network) involved in the self-regulation of insula. Figures are arranged from top to bottom in terms of their increasing strength of regulation: from weak regulation (top), intermediate regulation (middle) to strong regulation (bottom). It is clear that as the strength of regulation increases, the number of directed influences in the emotional network also increases as shown by the DIMs. During strong self-regulation, many regions in the emotional network, including medial prefrontal cortex (MPFC), right insula, anterior cingulate cortex (ACC), amygdala and posterior cingulate cortex are seen to become connected with insula. The CF diagrams of the weak regulation shows that the activations at this stage are driven predominantly from the posterior portion of the brain (especially by the posterior cingulate cortex) and that the causal flow in the left insula is close to zero. However, with increasing strength of regulation, insula and the anterior regions of the brain seem to drive the network activation to a greater extent as shown by their increasing causal flow.

Fun lojter hofenung wer ich noch meschuge.

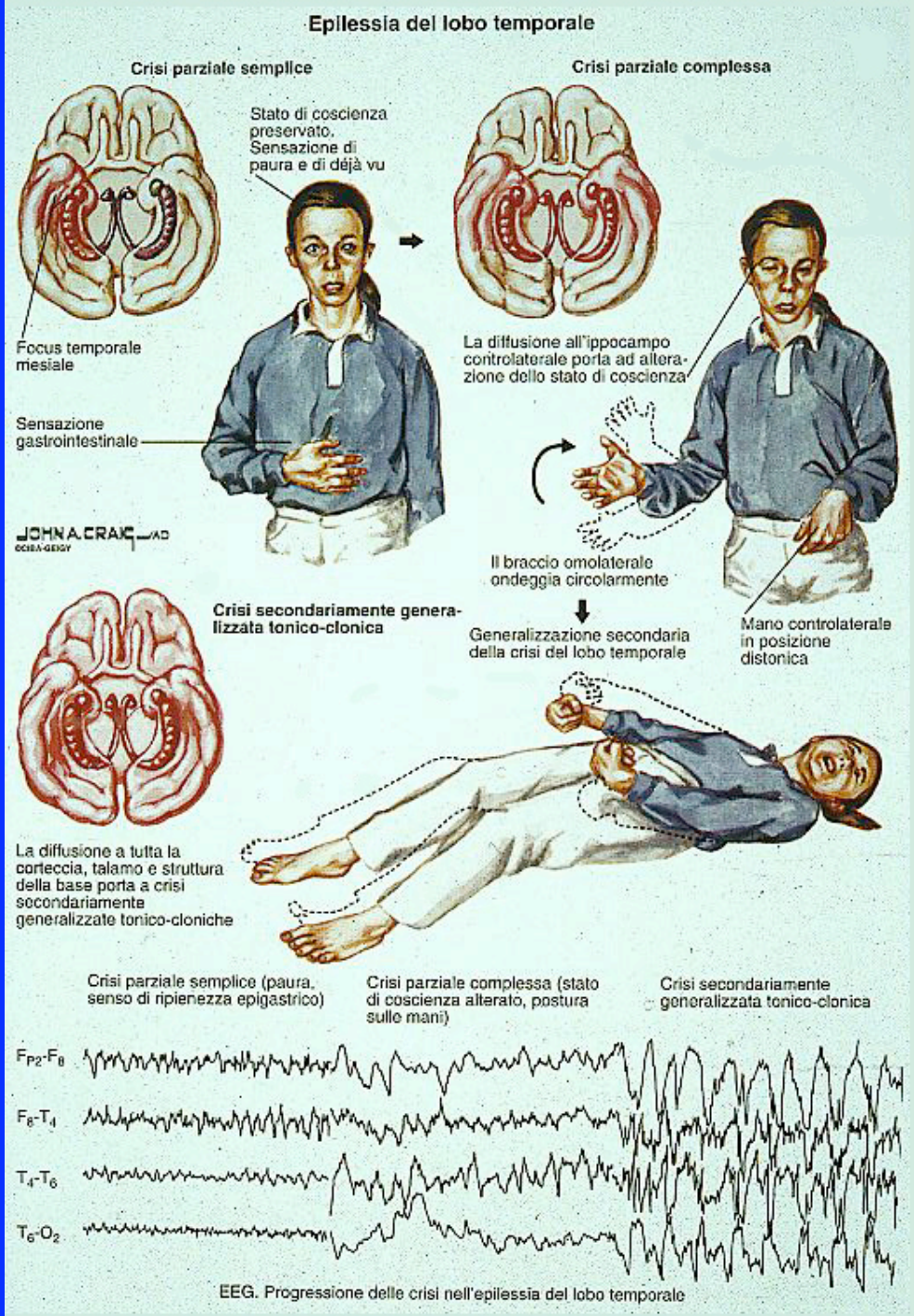
Vor lauter Hoffnung werd‘ ich noch verrückt.

I am mad of hope.

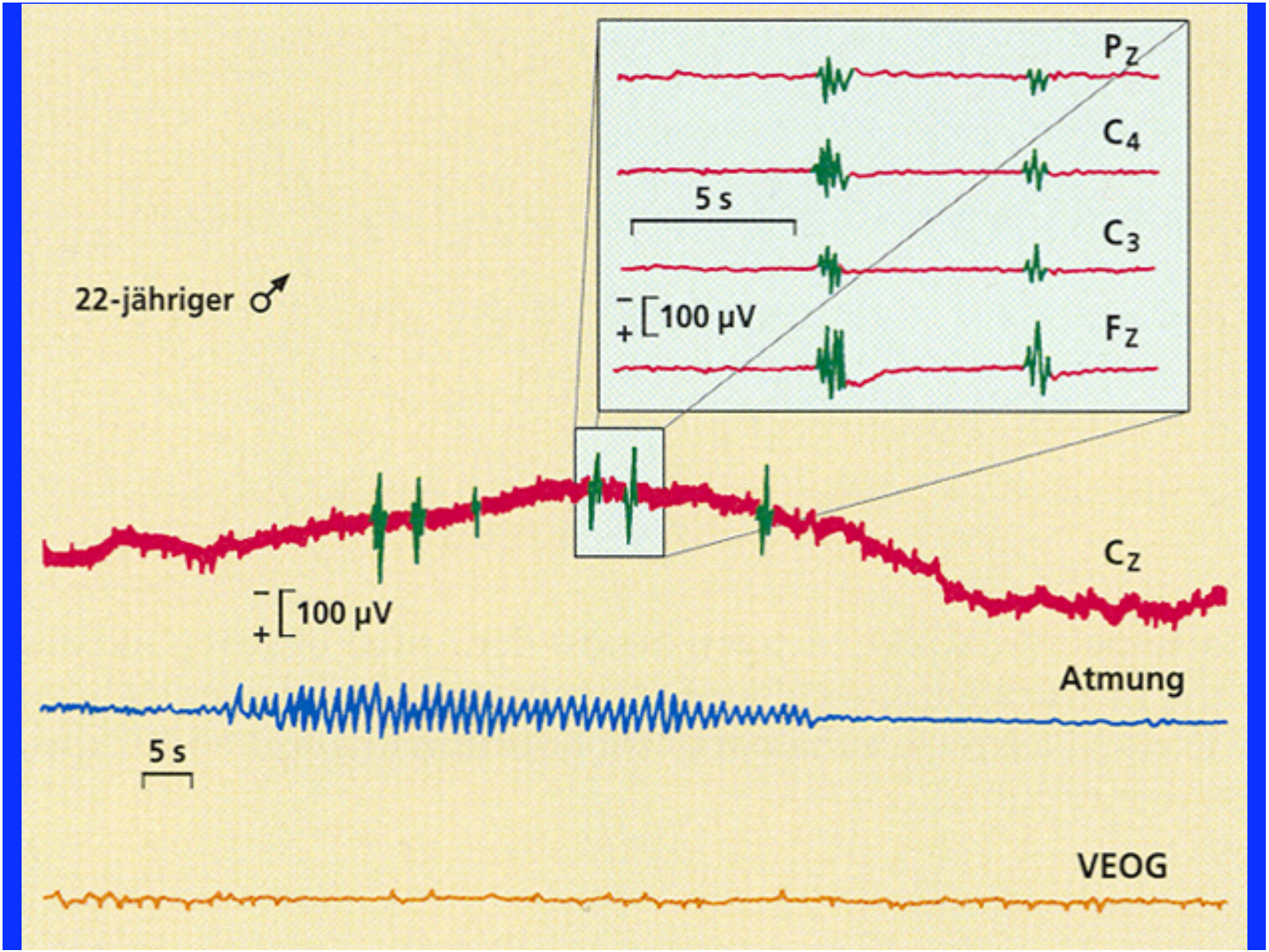
Jiddish Saying

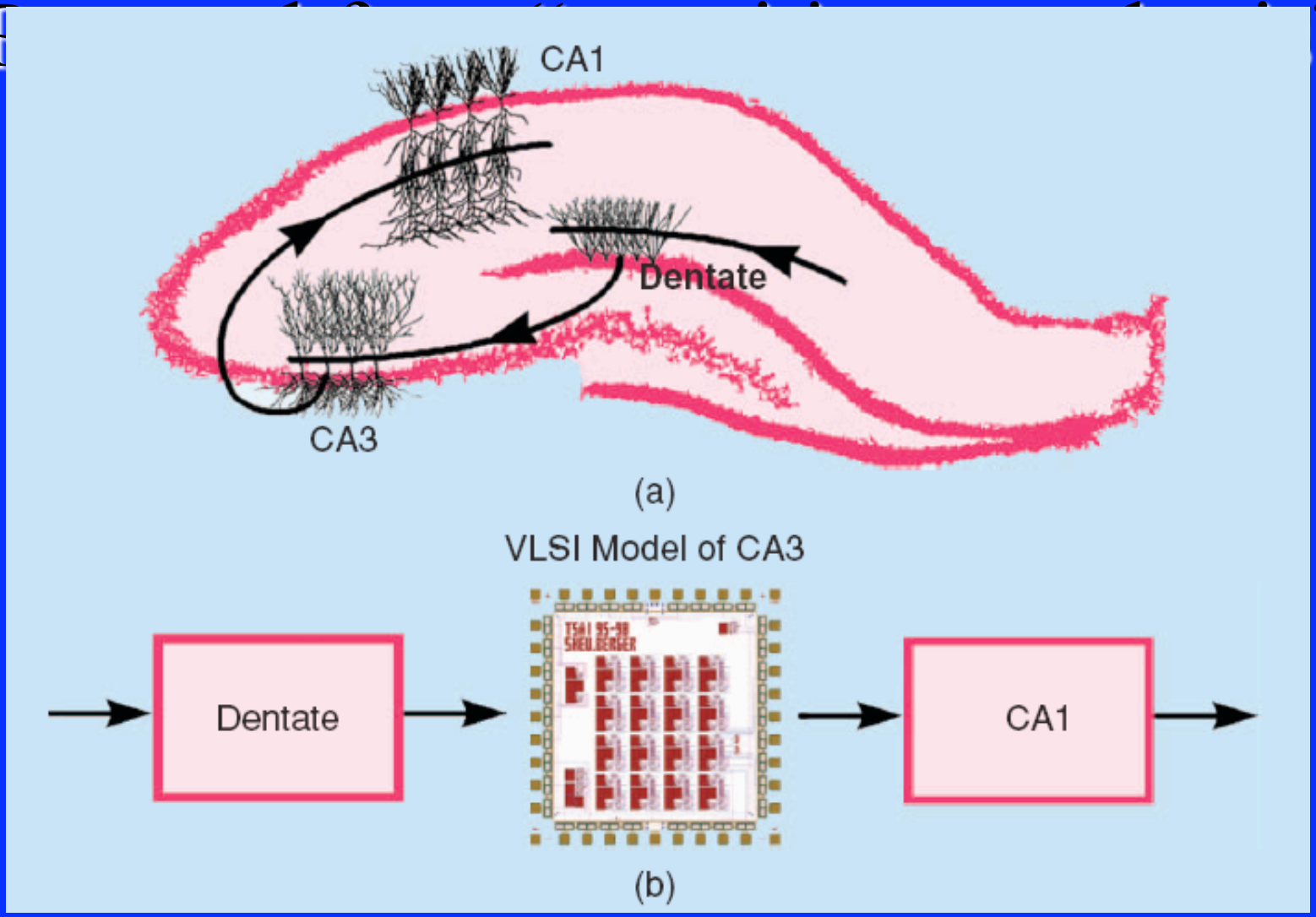
Supported by

- Deutsche Forschungsgemeinschaft (DFG)
- National Institutes of Health (NIH), NINDS
- Bundesministerium für Bildung und Forschung (BMBF),Bernstein Center for Computational Neuroscience
- European Research Council (ERC)
- Motorika, Cesarea, Israel
- European Union, Marie Curie Program



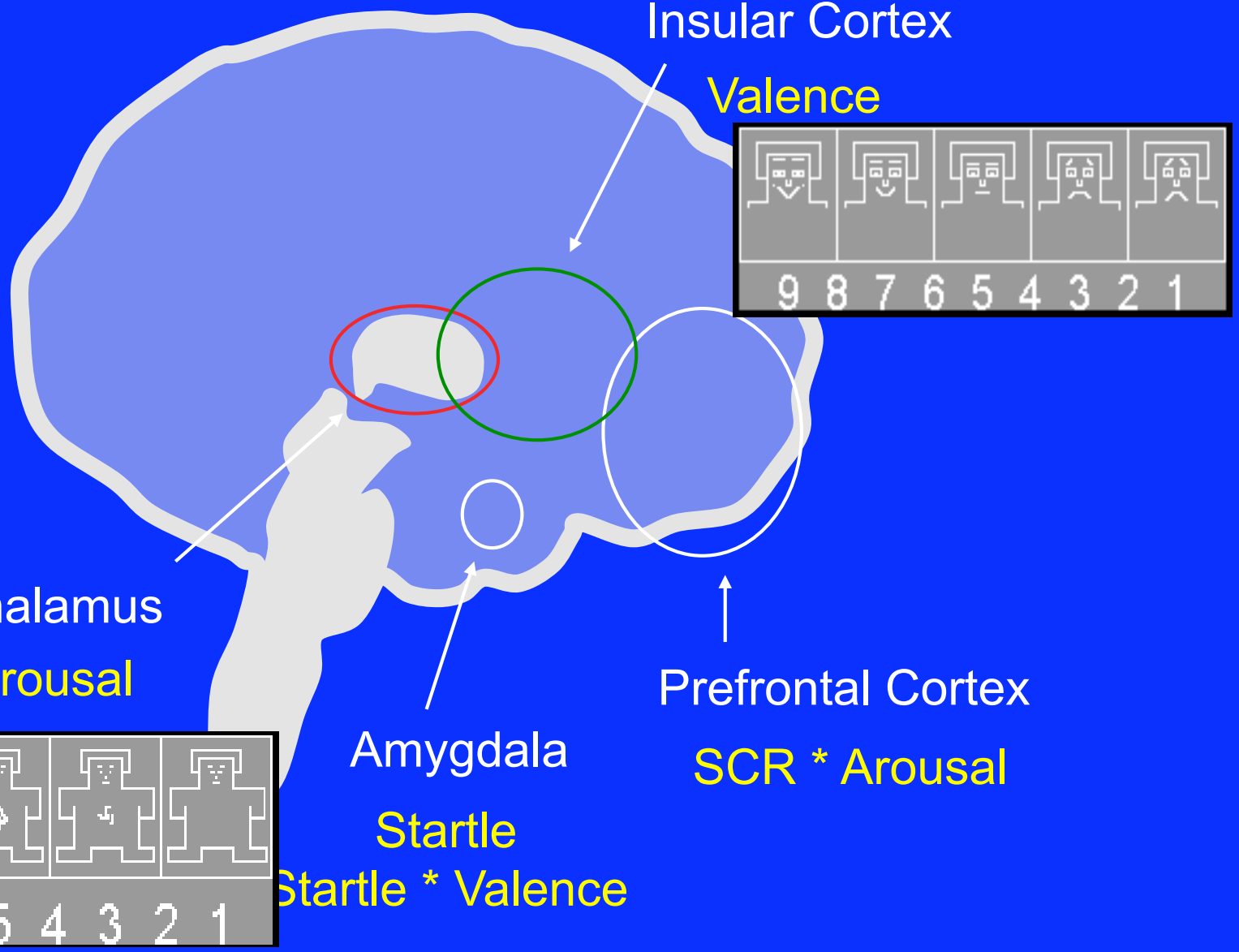
EEG. Progressione delle crisi nell'epilessia del lobo temporale


22-jähriger ♂
P_Z
C_4
5 s
C_3
100 µV
F_Z
C_Z
100 µV
Atmung
5 s
VEOG

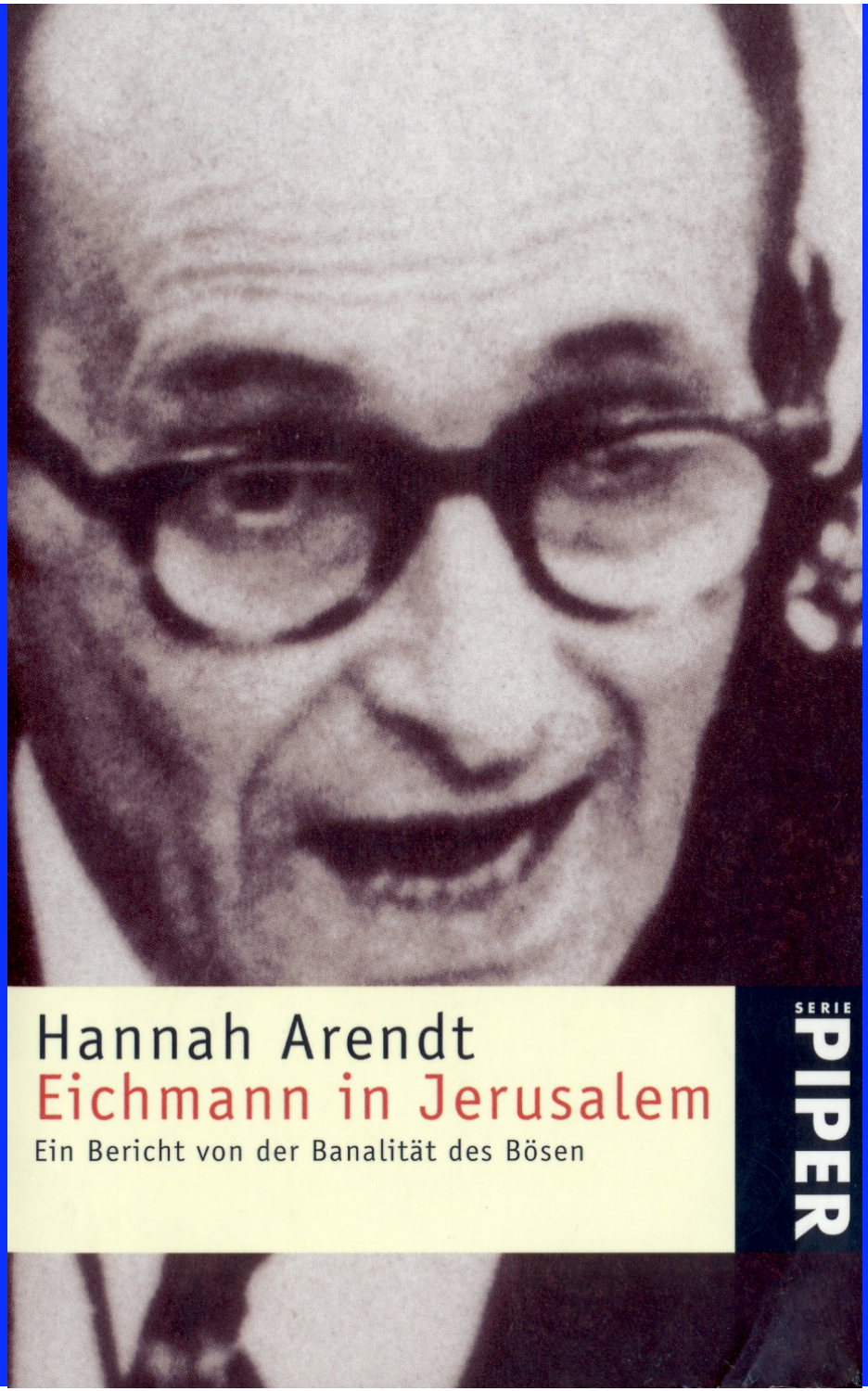


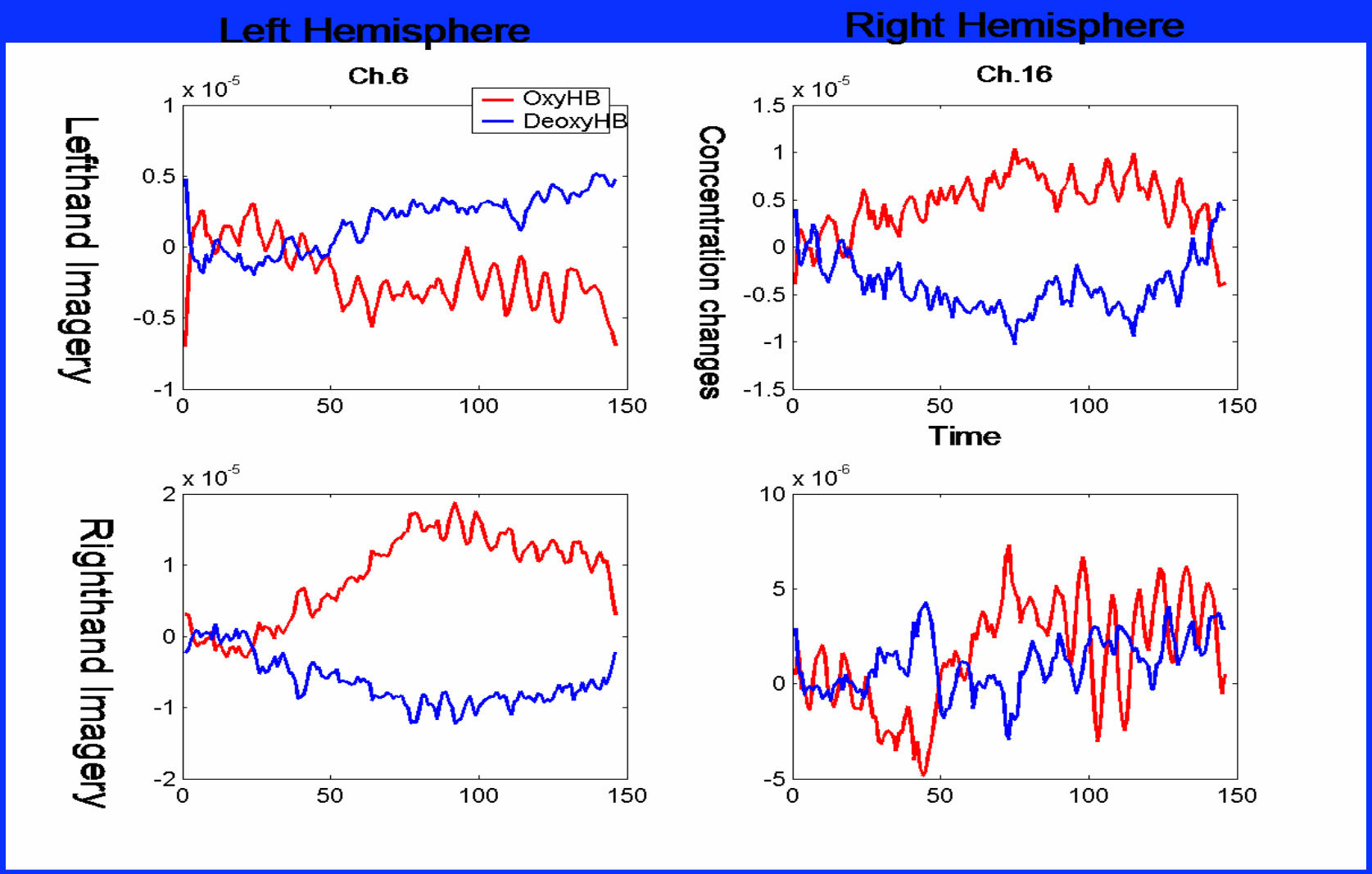
Berger et al, *IEEE Eng Med Biol Mag* 24, 30-44 , 2005

Emotional Processing in the Brain



Anders,et al.Human Brain Mapping(2004)

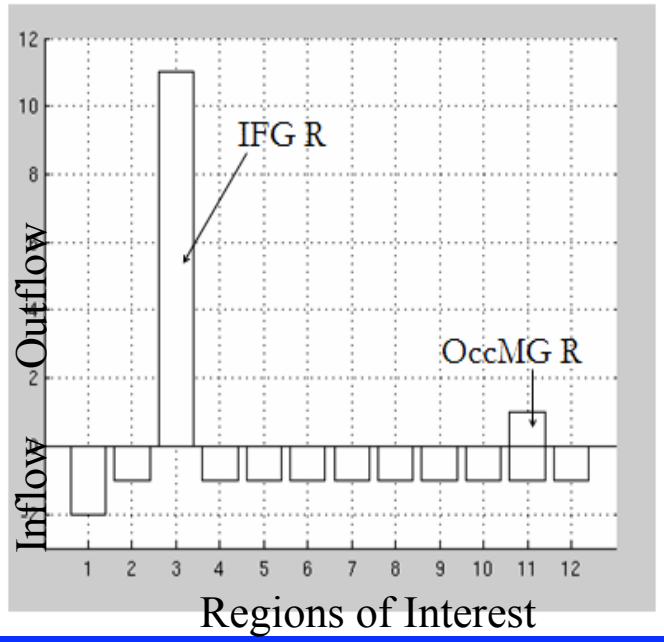

Hannah Arendt
Eichmann in Jerusalem
Ein Bericht von der Banalität des Bösen
SERIE
PIPER

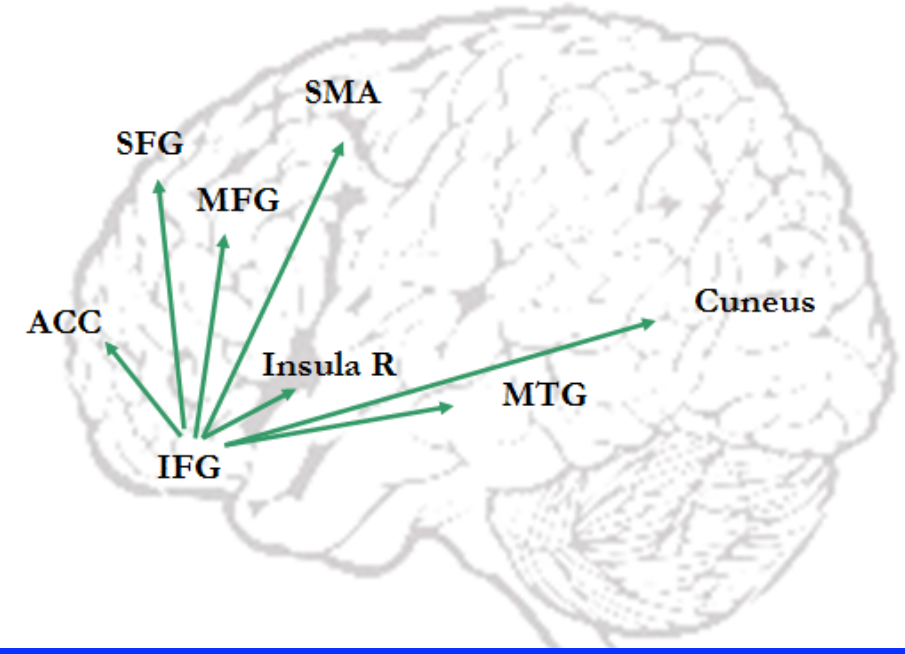


Sitaram et al., Neuroimage 2007

Functional connectivity changes induced by BCI training in schizophrenia

Weak /early insula regulation session

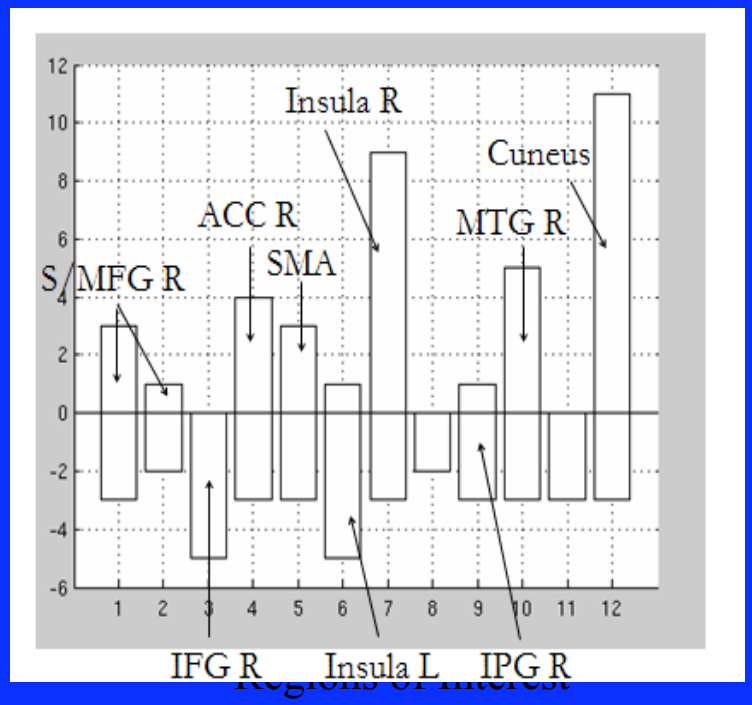


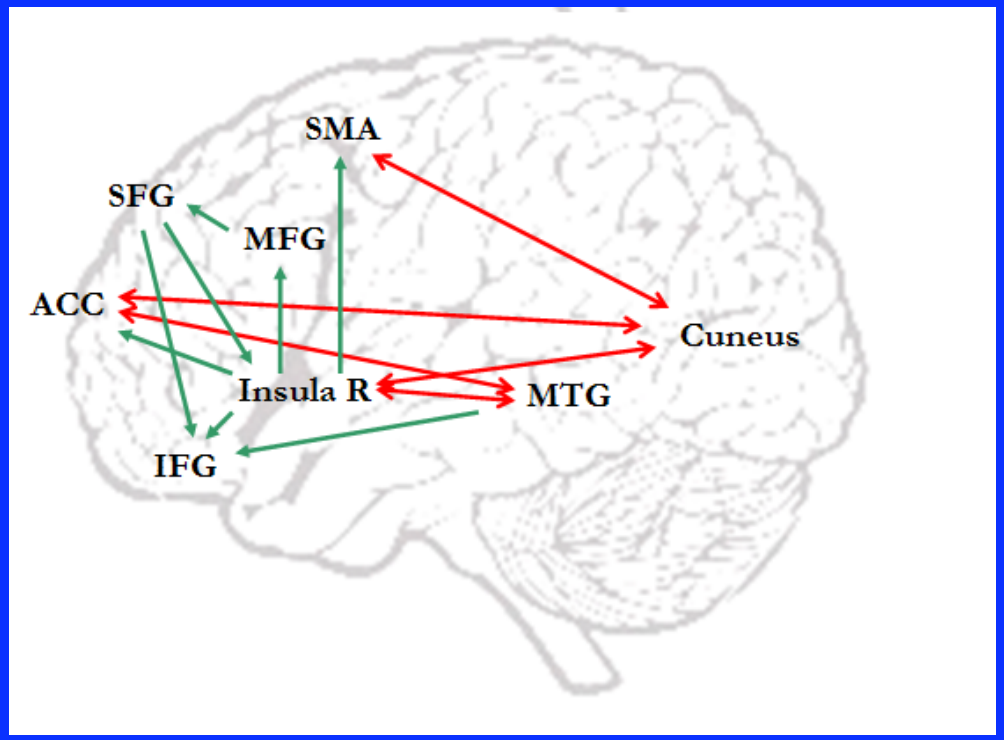


. Functional connectivity form subject FM in a weak/early regulation session.
The figure show the bar chart of the causal flow: outgoing (+) and incoming connections (-) in the network involved in regulation, and the respective direct influence map.

Functional connectivity changes induced by BCI training in schizophrenia

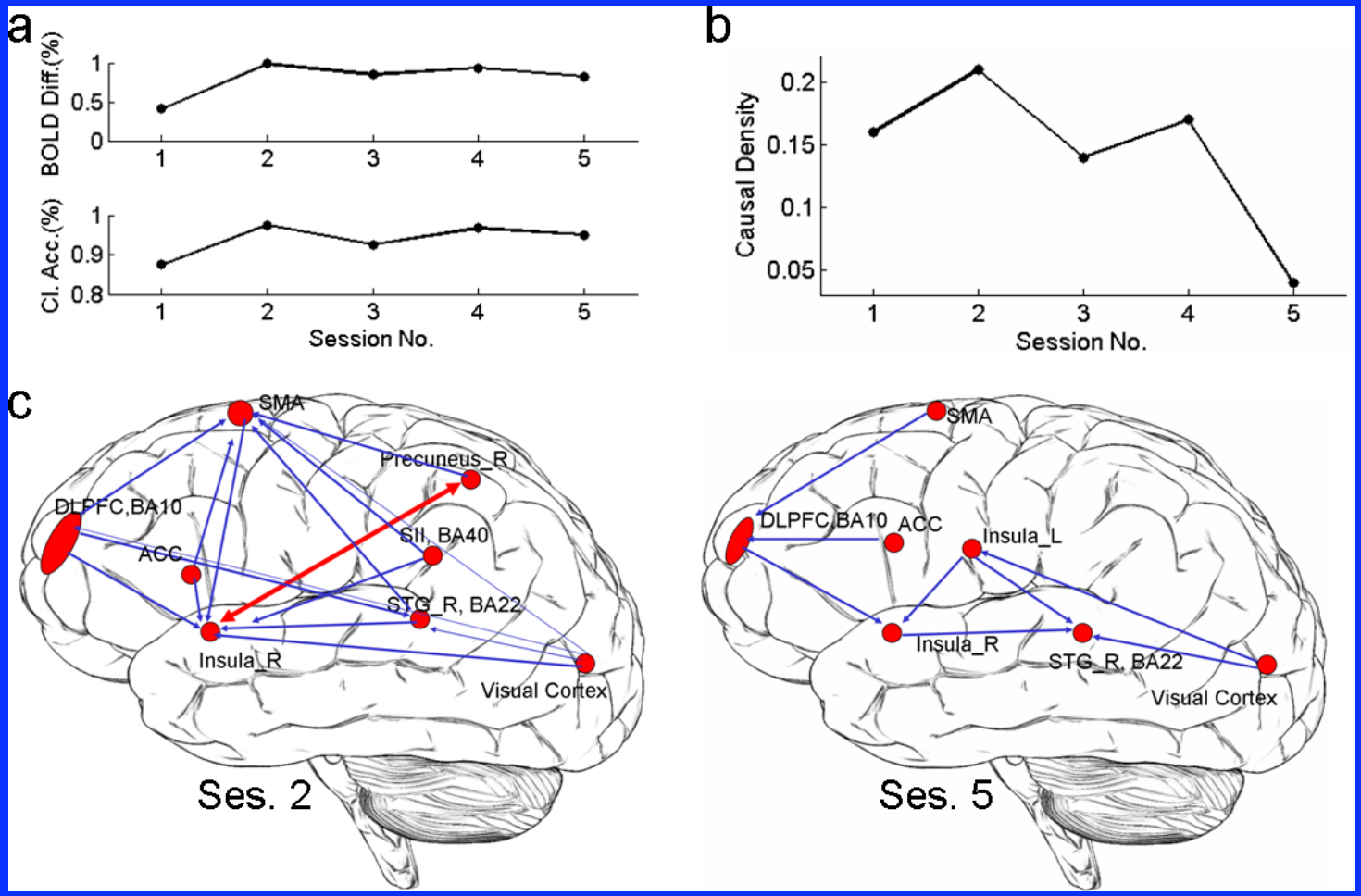
Strong/late insula regulation session





. Functional connectivity form subject FM in a strong/late regulation session.
The figure show the bar chart of the causal flow: outgoing (+) and incoming connections (-) in the network involved in regulation, and the respective direct influence map.

Causal Densitiy Maps Change with Training Time: Increase during Initial Training Phases - Decrease during Late Training Phases



Sitaram & Birbaumer, submitted

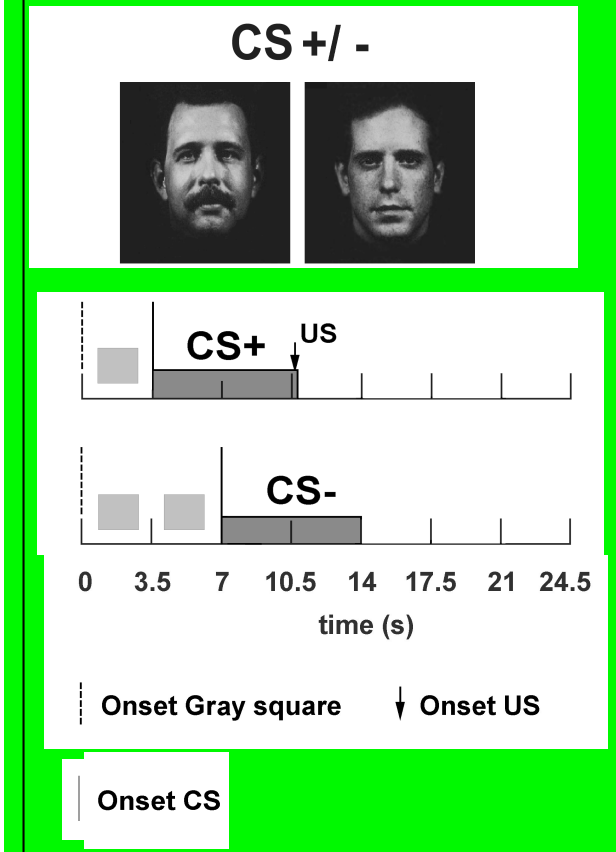
Instrumental Aggression and Psychopathy

- **Protective Factors**
- Female
- Classical Fear Conditioning
- Rewards for Empathic Behavior
- Genes and Perinatal Hormones (i.e.Oxytocine, Androgens)
- Strong Involvement of Parents in Education
- Consequent Educational Style
- Models for Emotional and Cognitive Self-Control
- Intelligence and Success in School
- Socio-economic Status Average
- Enriched Social and Physical Environment

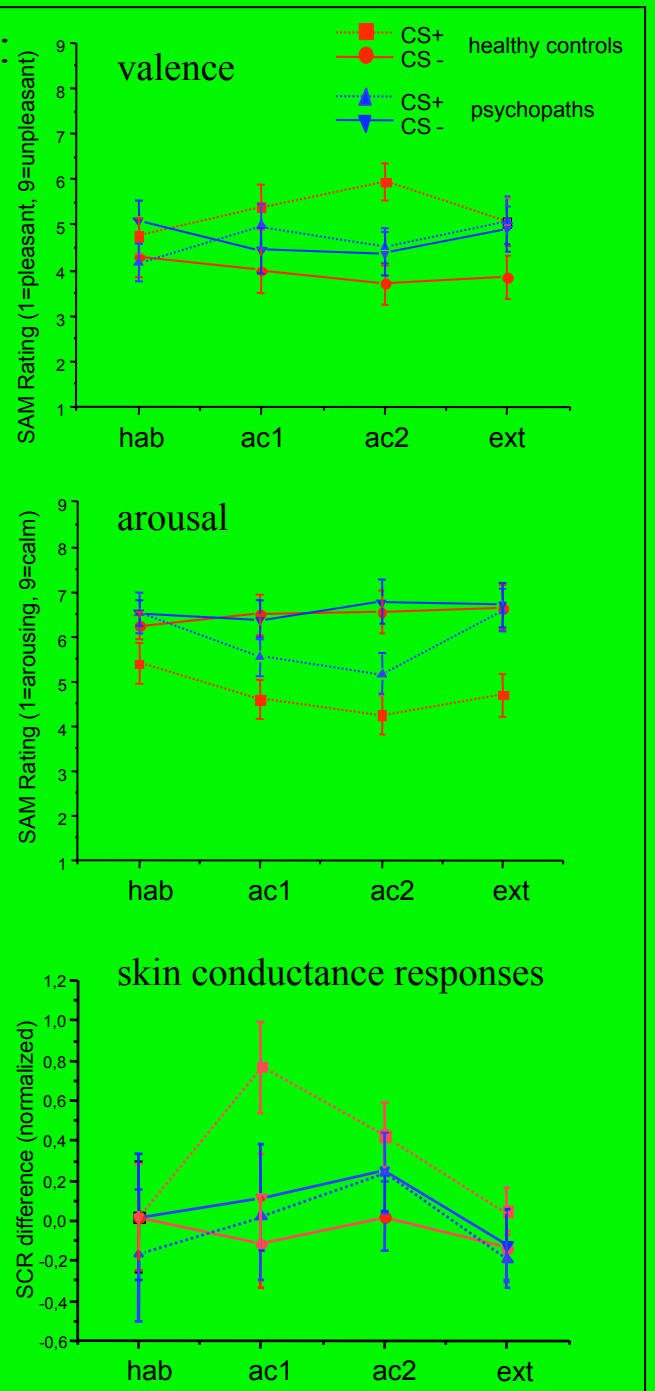
- **Risk Factors**
- Male
- Deficient Classical Fear Conditioning
- No Reward for Empathic Behavior, Reward for Instrumental Aggression
- Genes and Perinatal Hormones (i.e.Oxytocine, Androgens)
- Young, Single and Poor Mother
- Chaotic Home Environment
- Early Physical and /or Sexual Abuse
- No Models for Emotional and Cognitive Self-Control
- Low Intelligence, Failure in School, Attention Deficit Disorder and Hyperactivity
- Excessive Television, Aggressive Computer Games, Aggressive Pornography
- Sensation Seeking, Monotonous Environment, Sensitivity to Boredom
- Alcohol and Drug Abuse

Fig. 1:

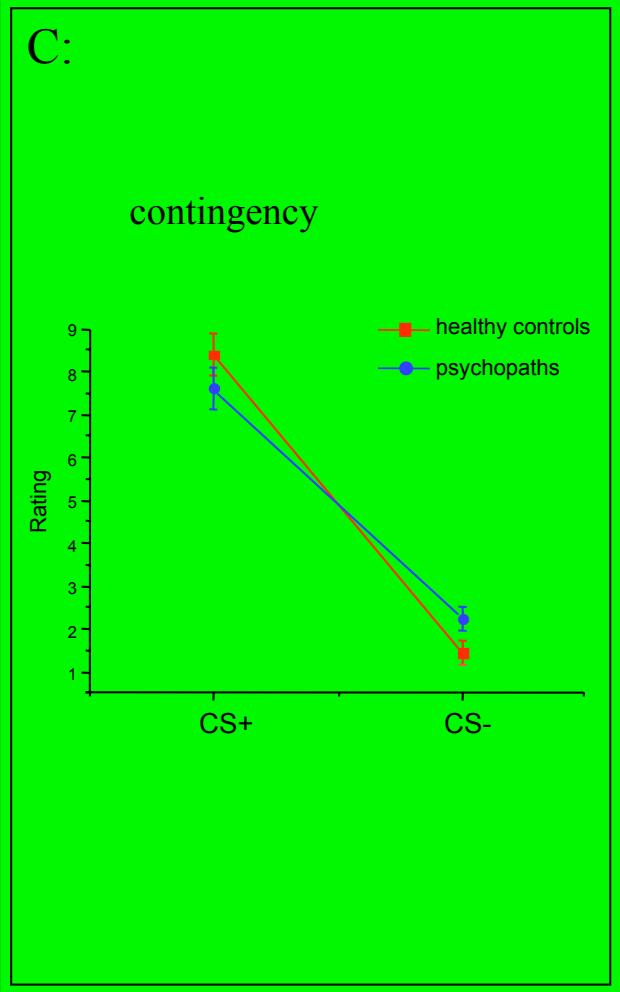
A:



B:

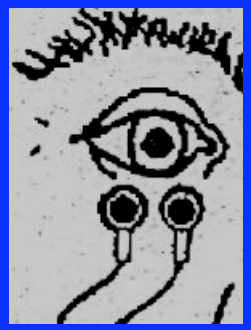


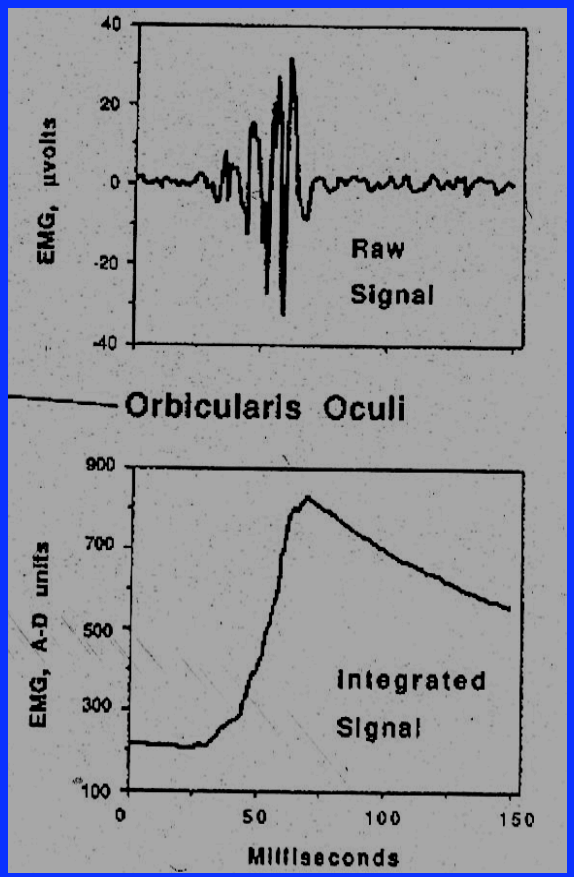
C:

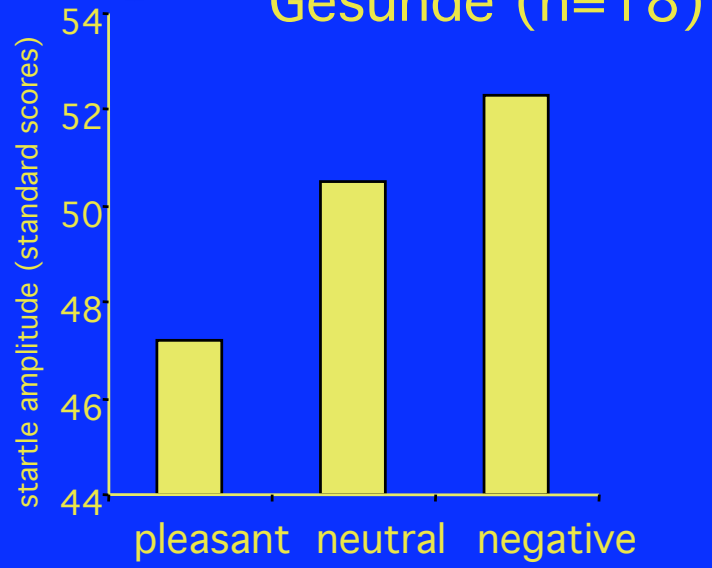


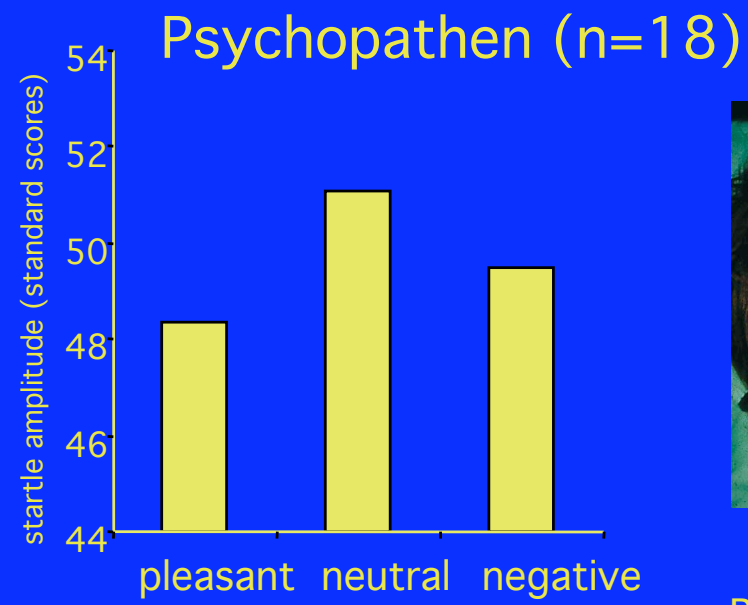
Birbaumer et al. Arch. Gen.Psychiatry (2005)

Startlepotenzierung und prim. Psychopathie:



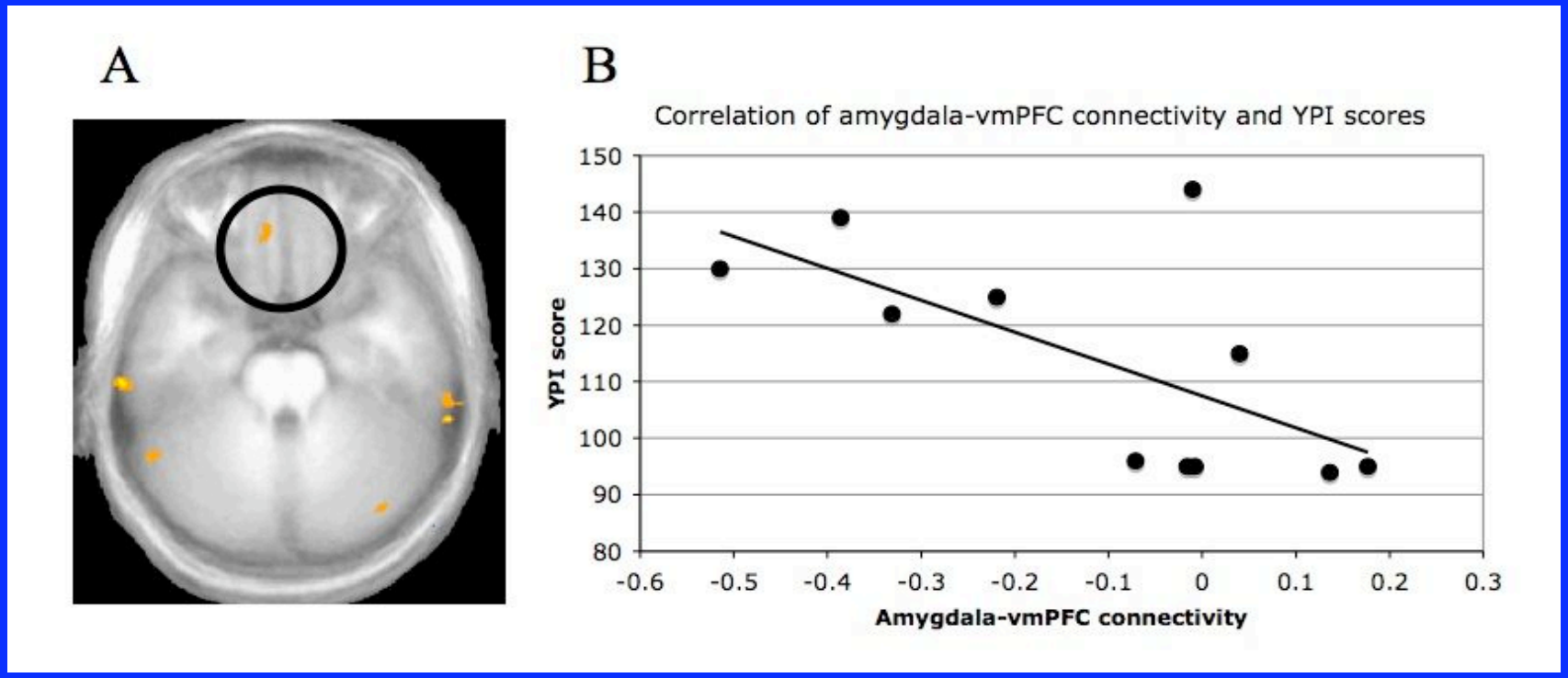






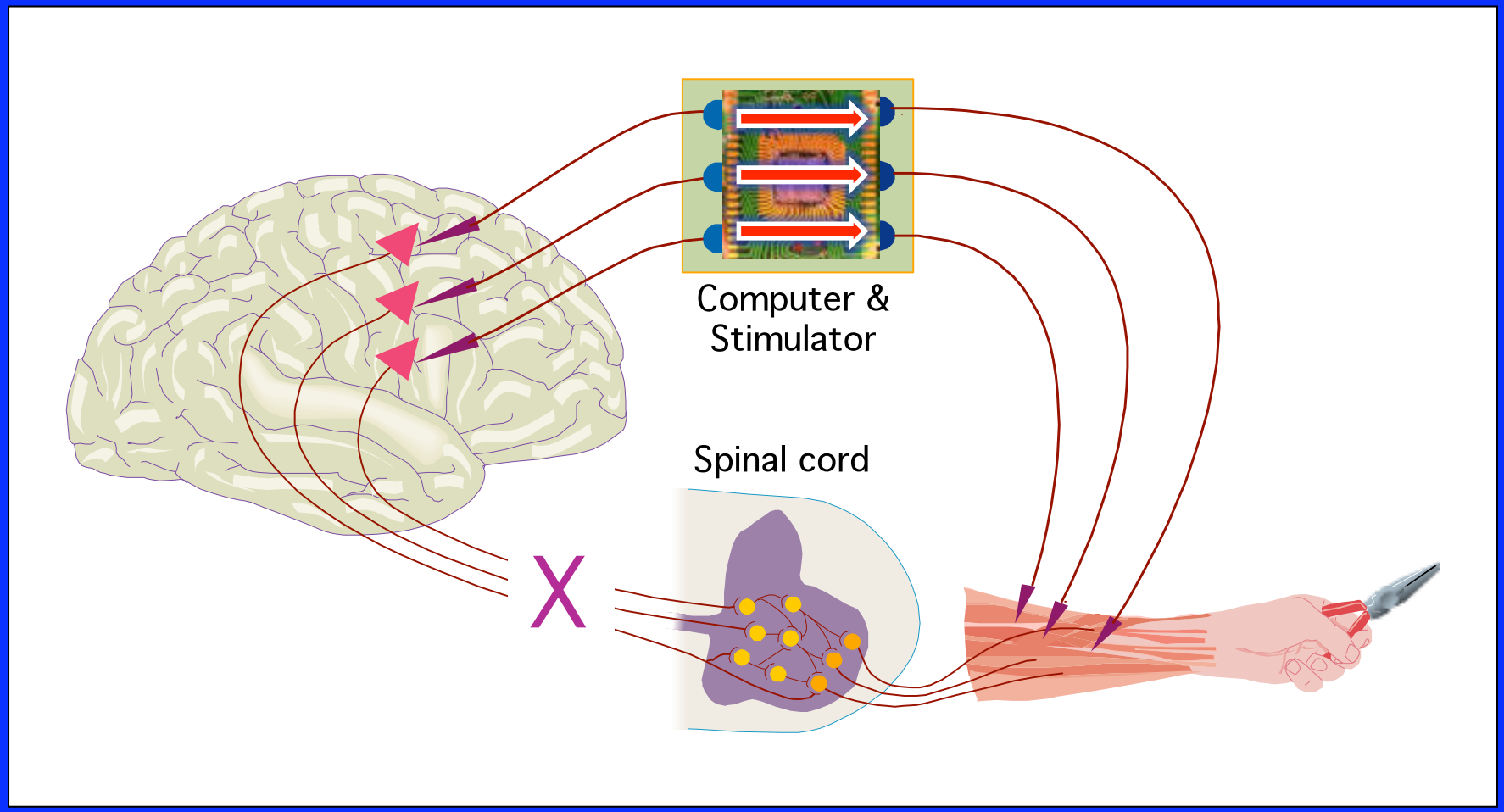
Patrick, Bradley, Lang, 1993

Decreased connectivity in callous adolescents to fearful faces between Amygdala and vmPFC

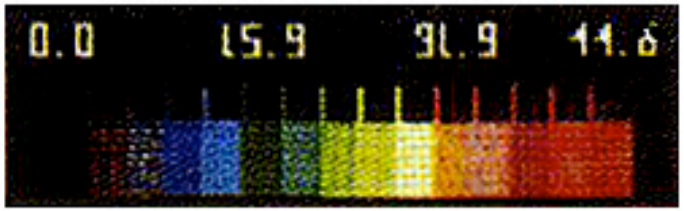


Marsh et al. Arch Gen Psychiatry (in press)

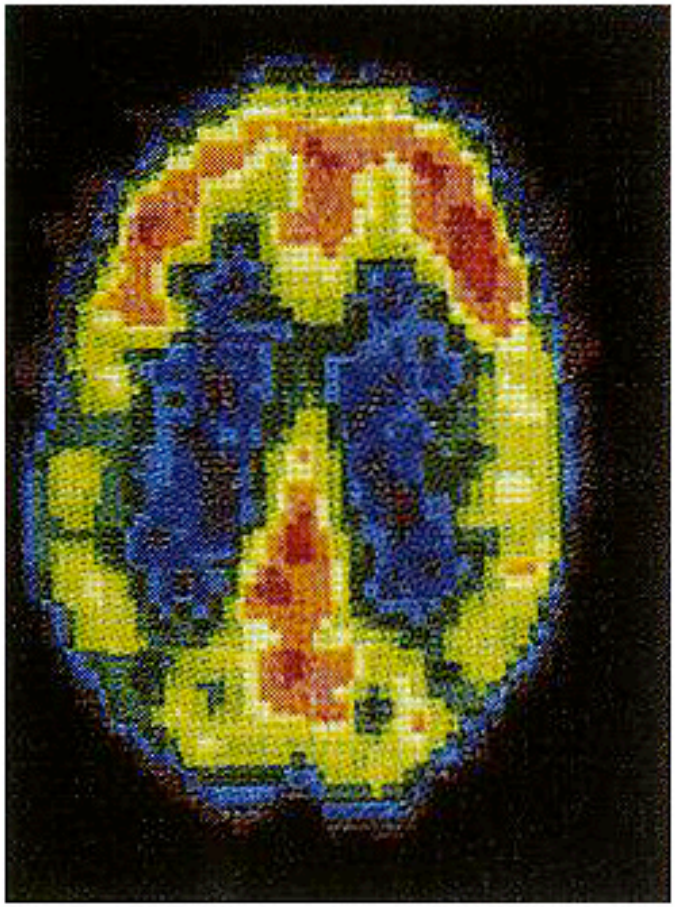
Recurrent BCI allows cortical cell activity to control muscle stimulation

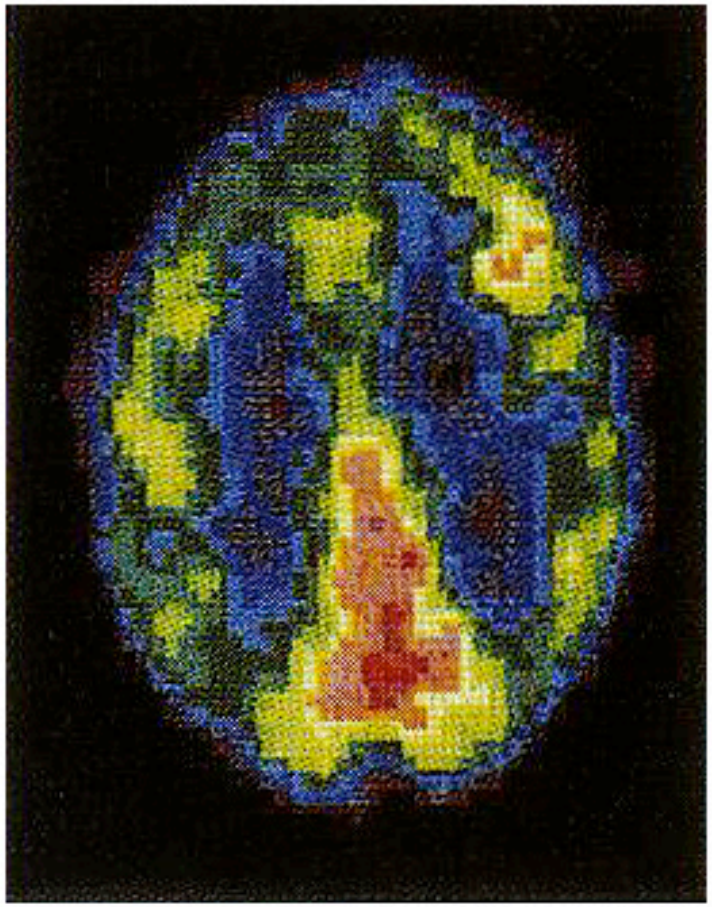


1. Utilizing muscles is more natural than prosthetic arm
2. Chronically implanted circuit will allow relearning



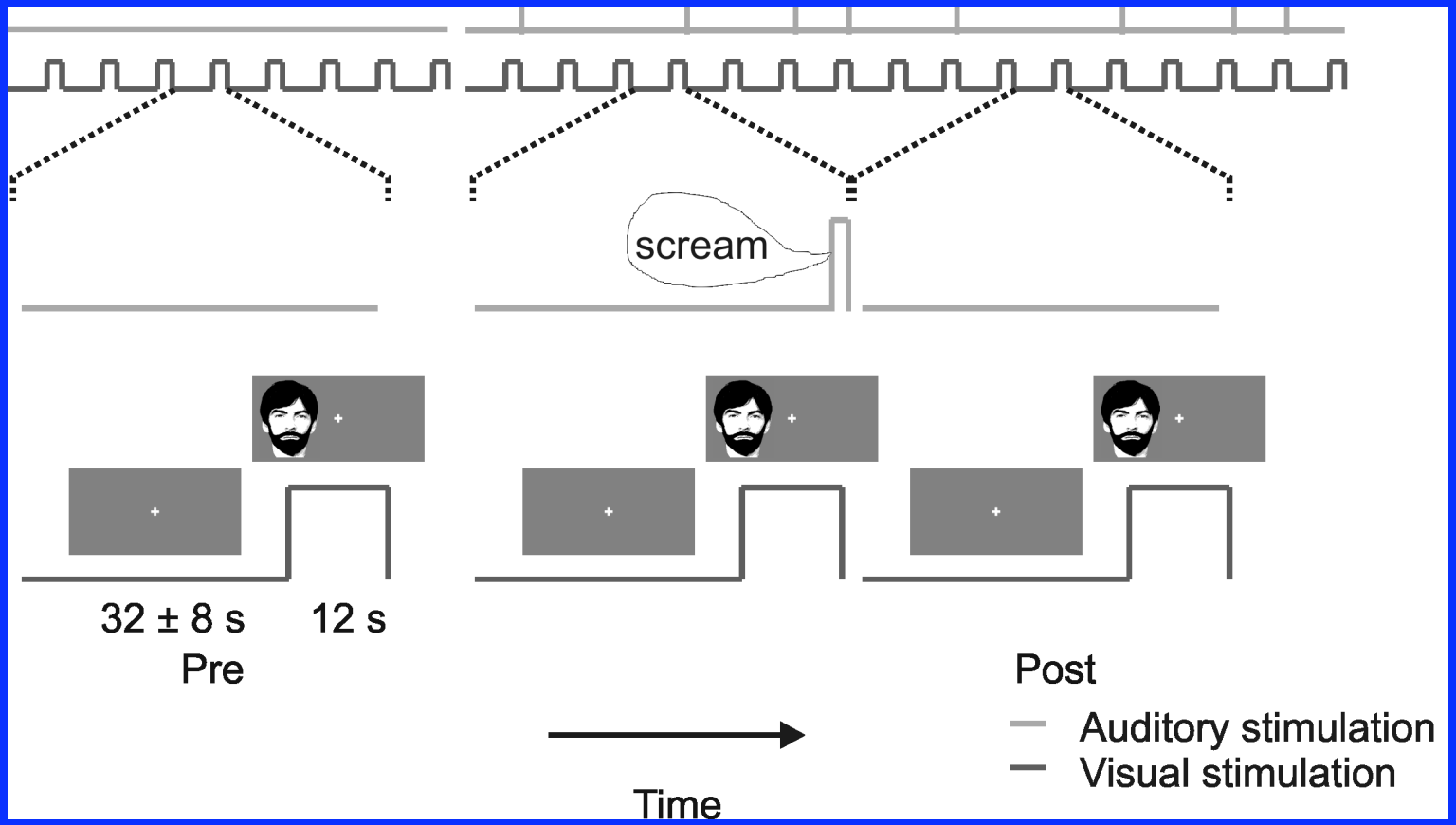
Raine, 1992





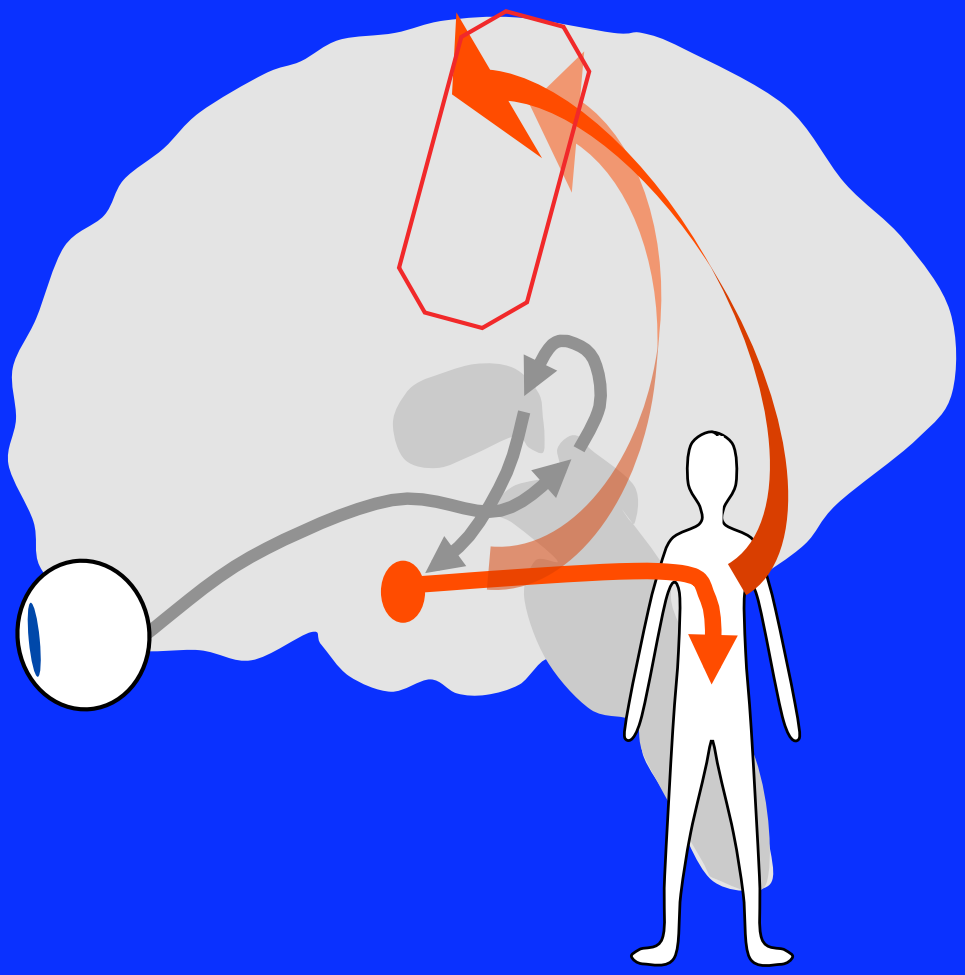
Murderous mind? A PET scan reveals less activity in the prefrontal cortex of a convicted killer (right) than in that of a nonviolent control.

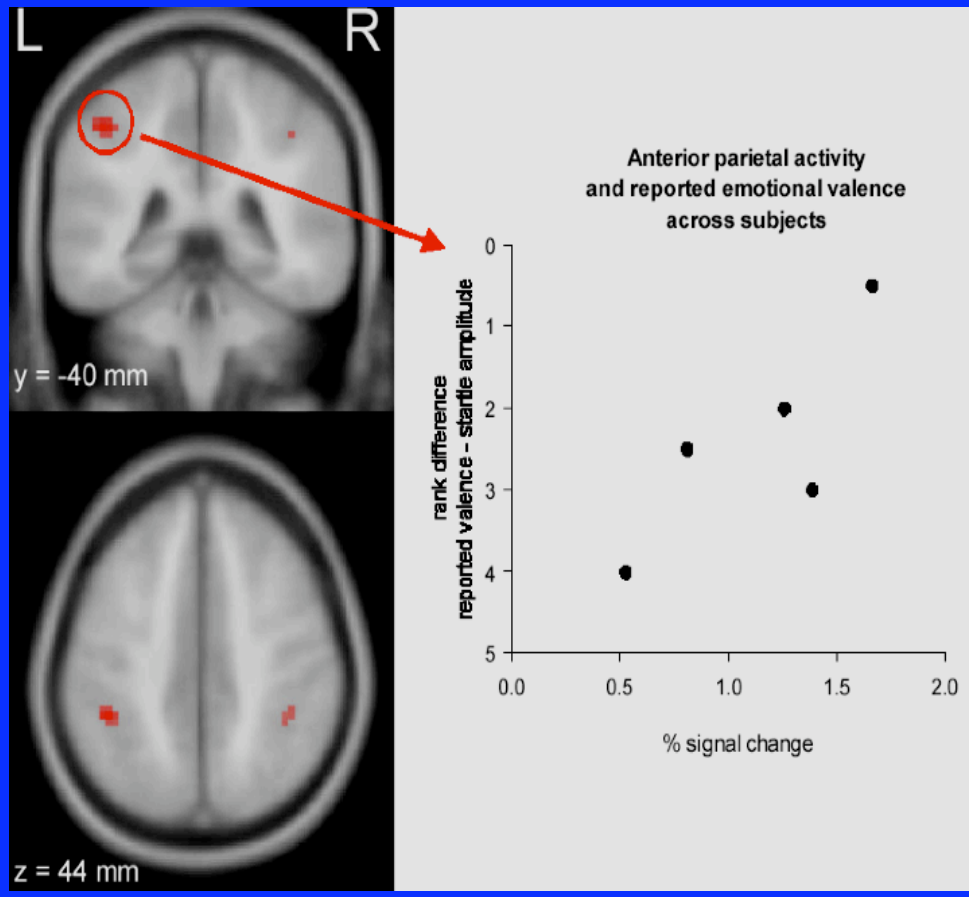
Angrilli, Birbaumer et al, Brain 1996



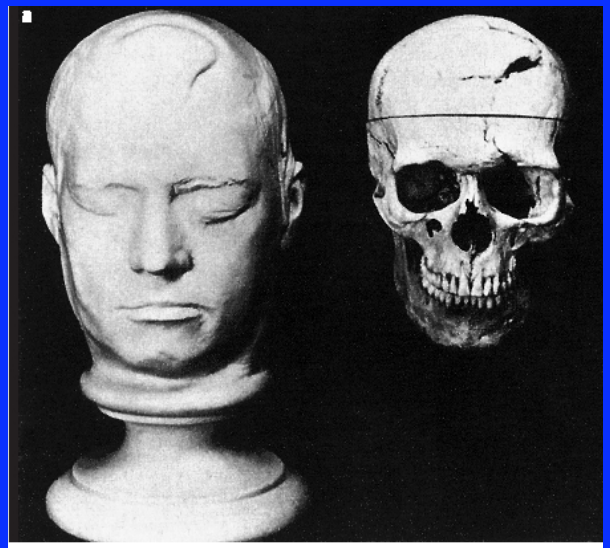
Anders, Birbaumer et al. 2004 Nature Neurosci.

„Somatic marker“ and blindsight





Anders, Birbaumer et al. Nature Neurosc. 2004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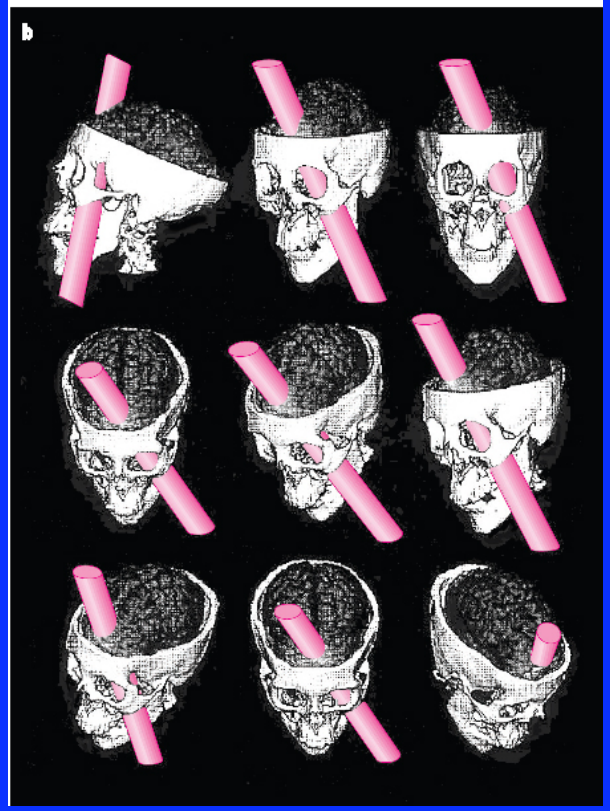
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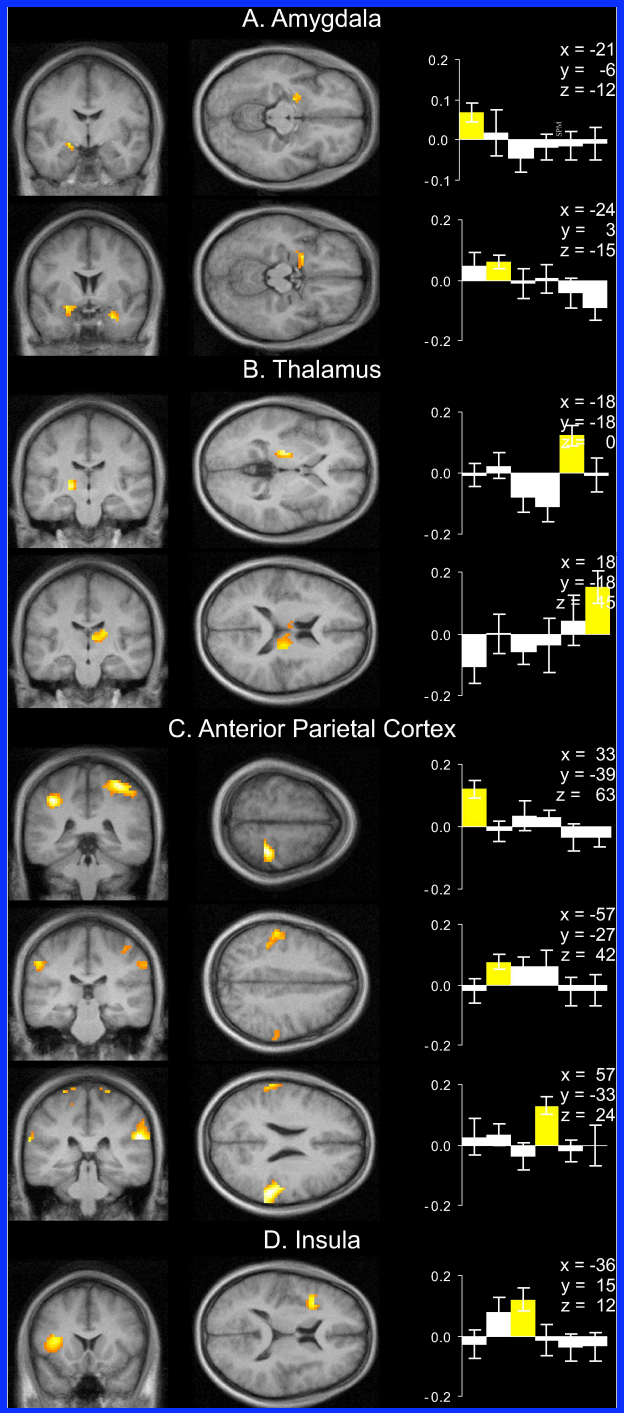


startle

startle x valence

skin conductance x arousal

arousal

startle

startle x valence

skin conductance

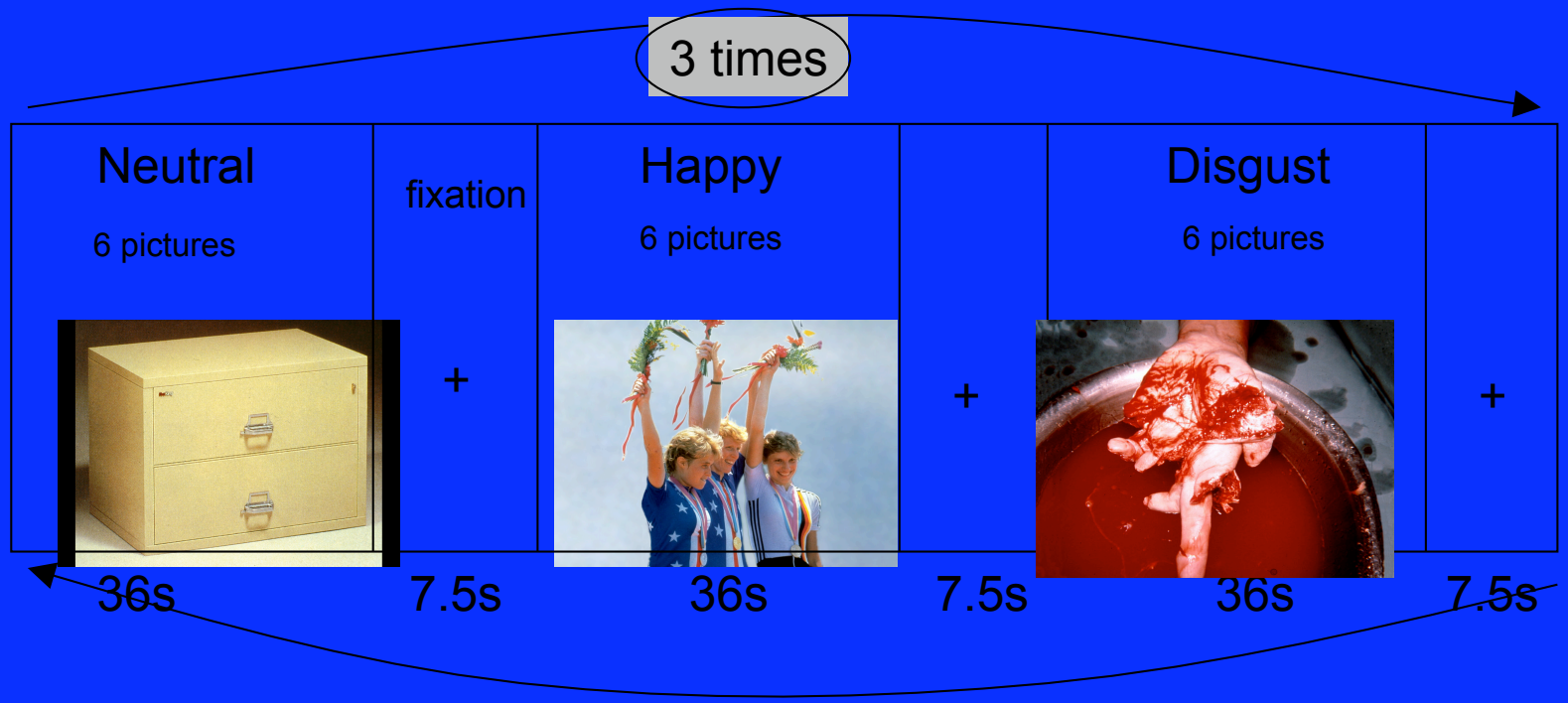
valence

Anders et al. 2004 Hum.Brain Mapping.

Experiment Stage 1 in detail

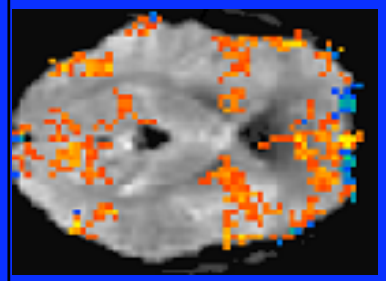
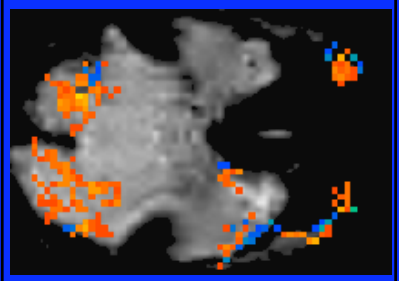
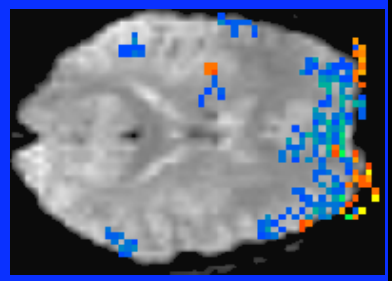
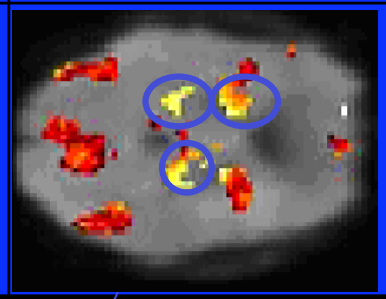
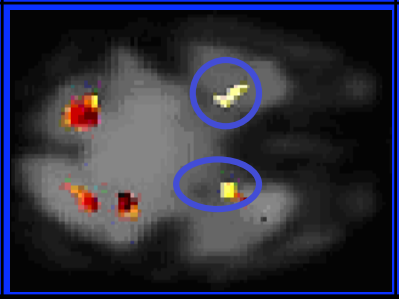
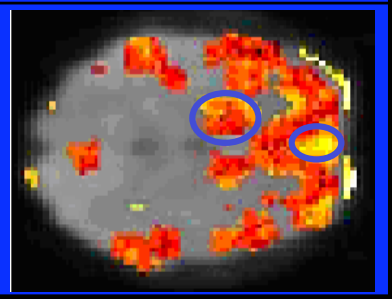
Group (a): Experimental protocol for Emotional Pictures

Each run has the 3 blocks of emotional stimuli presentation alternating with a fixation cross.



- 6 pictures will be presented in each block of emotion
- Each picture will be shown for 6s
- Students should attend to each picture without moving their head/body
- During the fixation blocks students should count down from 100..1

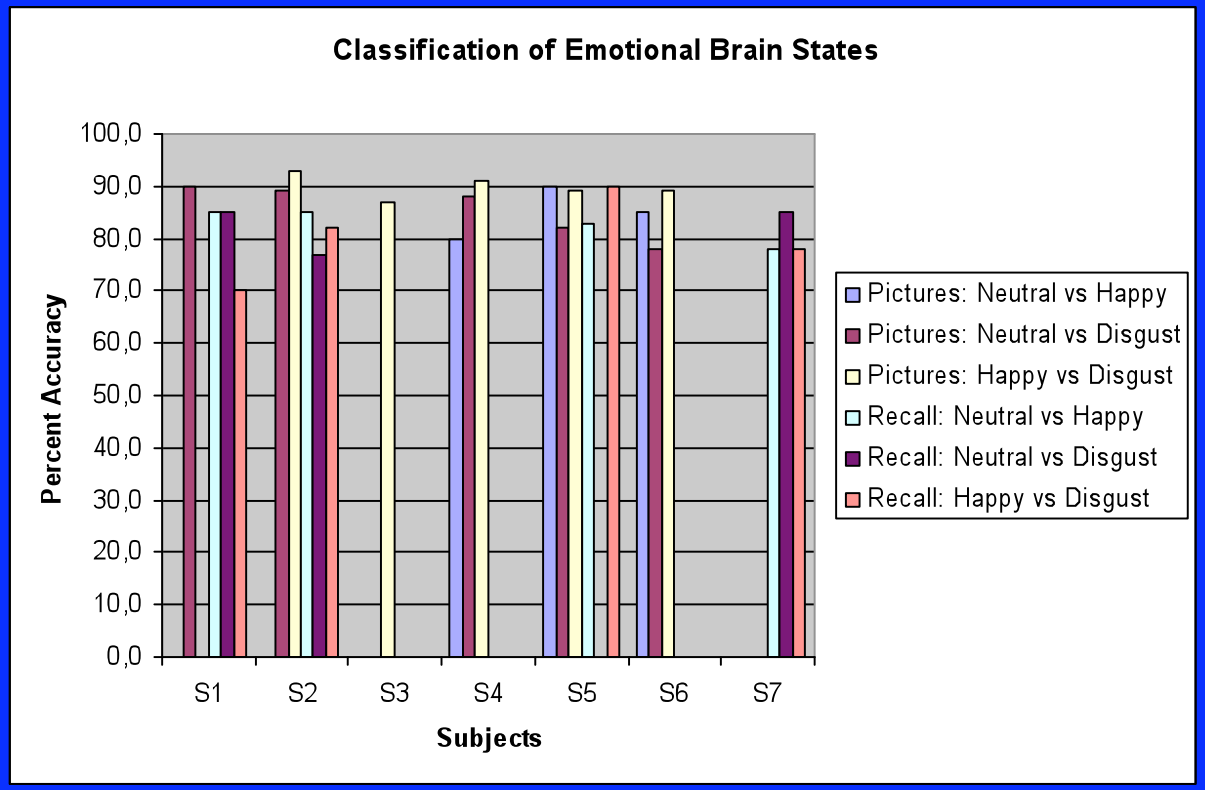
Comparing Univariate & Multivariate Methods for a single subject

	Happy vs Neutral	Disgust Vs Neutral	Disgust Vs Happy
Univariate (GLM)			
Multivariate (SVM)			

White/Yellow regions indicate voxels of highest discrimination between emotional states

Notice the different activation clusters that SVM uses for discrimination of emotional states. These area might possibly code spatiotemporally code for the brain state in a way that the voxelwise GLM is not sensitive to detect.

Classification Accuracy

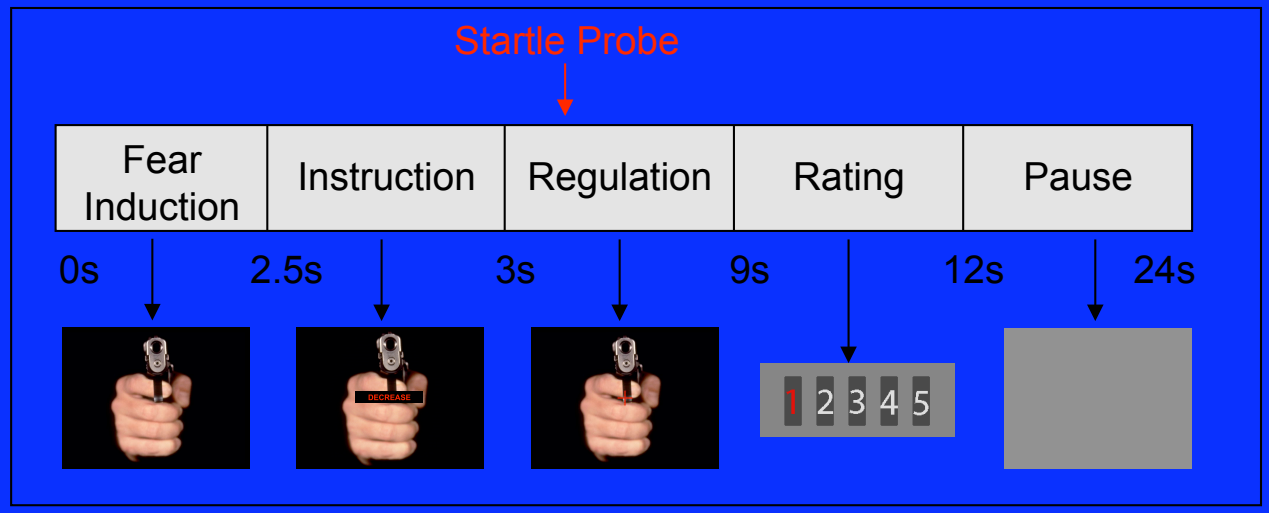


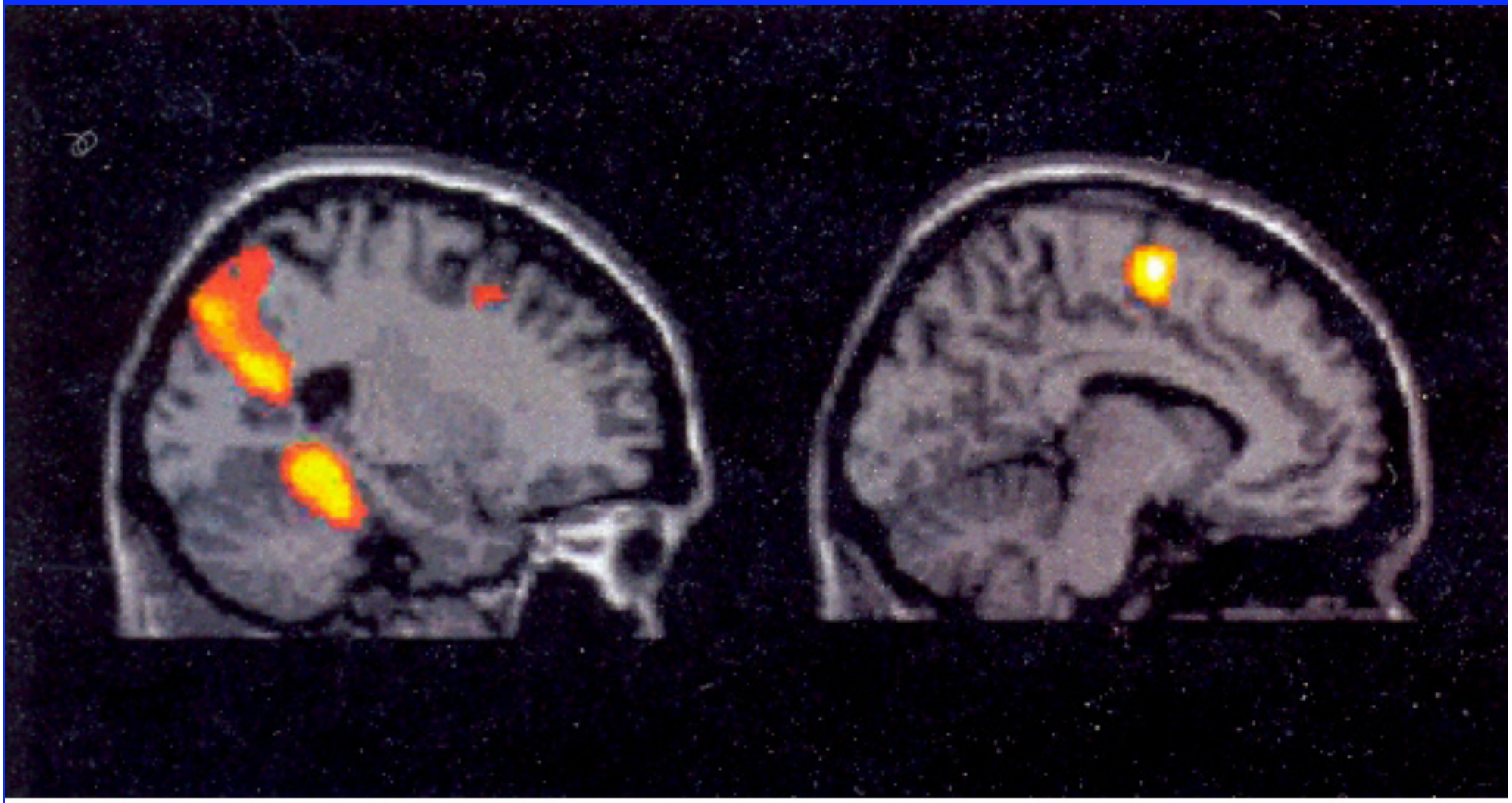
from Miltner et al

Exzessive instrumentelle Aggressivität, Kriminalität und Psychopathie

- **Protektive Faktoren:**
- weibliches Geschlecht
- klassische Konditionierung von Furcht
- Belohnung für Empathie
- Genetik und perinatale Hormone (Oxytozin, Androgene)
- Involviertheit der Eltern in das Leben der Kinder
- konsequente Kindererziehung
- gute Modelle für Selbst- und Emotionskontrolle
- Intelligenz und Schulerfolg
- geordnete sozioökonomische Verhältnisse

- **Risikofaktoren:**
- männliches Geschlecht
- keine Furchtkonsitionierung
- keine Belohnung für Empathie, Belohnung für instrumentelle Aggression
- Genetik und perinatale Hormone (Oxytozin ↓, Androgen ↑)
- junge, alleinstehende, arme Mutter
- chaotische häusliche Umgebung und Missbrauch
- wenig Modelle für Selbst- und Emotionskontrolle
- geringe Intelligenz, kein Schulerfolg
- Aufmerksamkeits-/Hyperaktivitätsstörung
- Langeweile/Sensationssuche, eintönige Umgebung
- exzessives Fernsehen


Startle Probe
Fear Induction
Instruction
Regulation
Rating
Pause
0s
2.5s
3s
9s
12s
24s
DECREASE
1 2 3 4 5

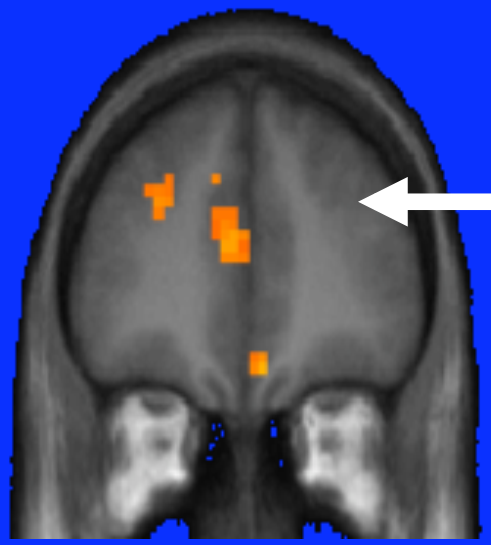


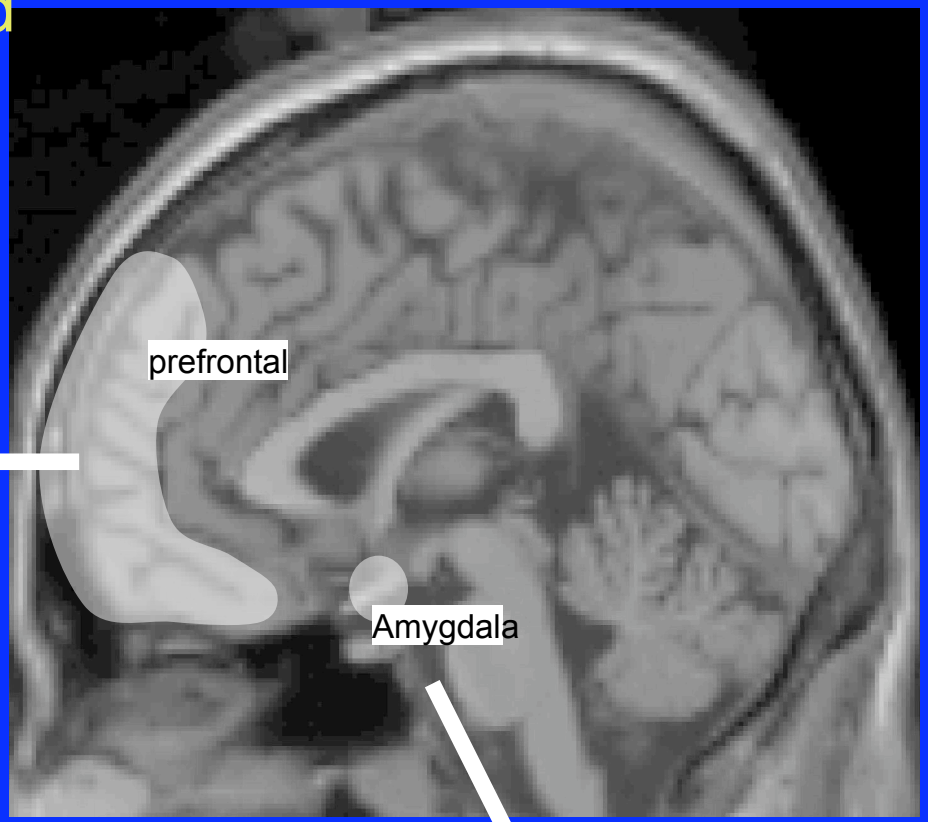
Imagining spatial navigation (left) and playing tennis.

Owen et al, Science 2006

Cognitive regulation of emotions

Increased acivity during up and downregulation

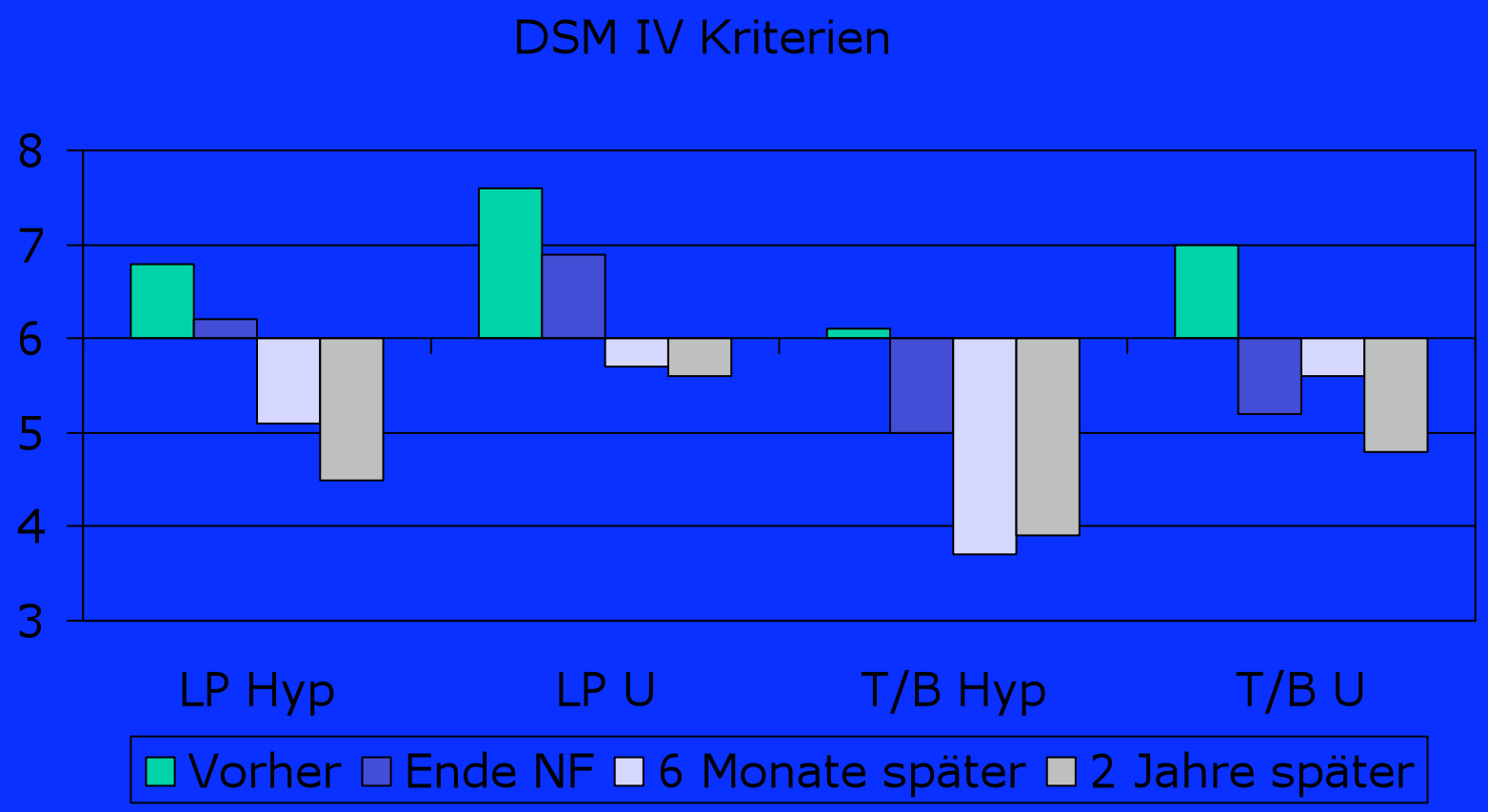




Increased activation during up-regulation
Decreased activation during down-regulation

Falk et al Human Brain Mapping 2007

Nachhaltigkeit



Gani, Birbaumer & Strehl, 2008

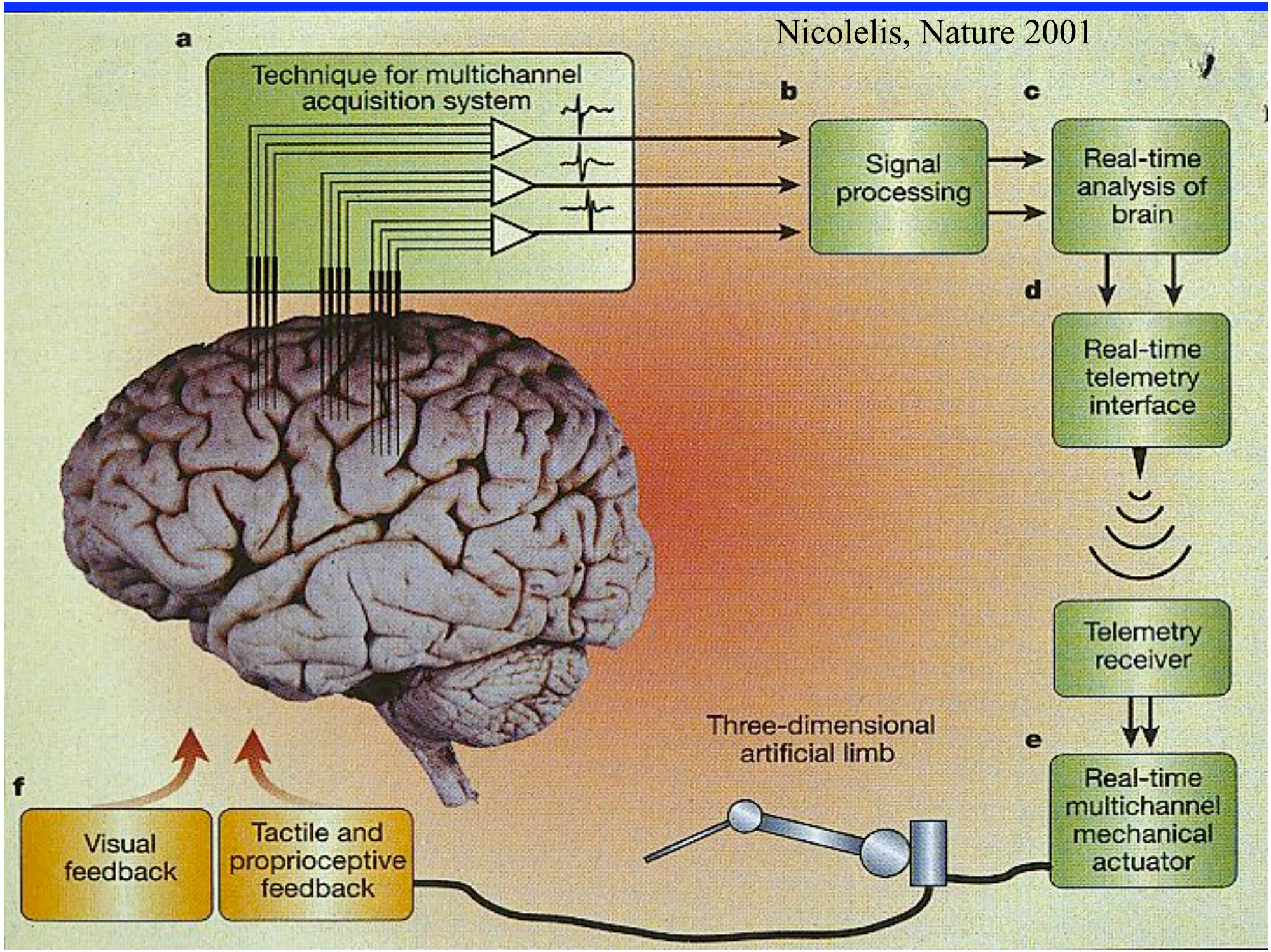
TU Graz, Medical Informatics 17.9.1999

Pfurtscheller,Neuper,Birbaumer,(2005)

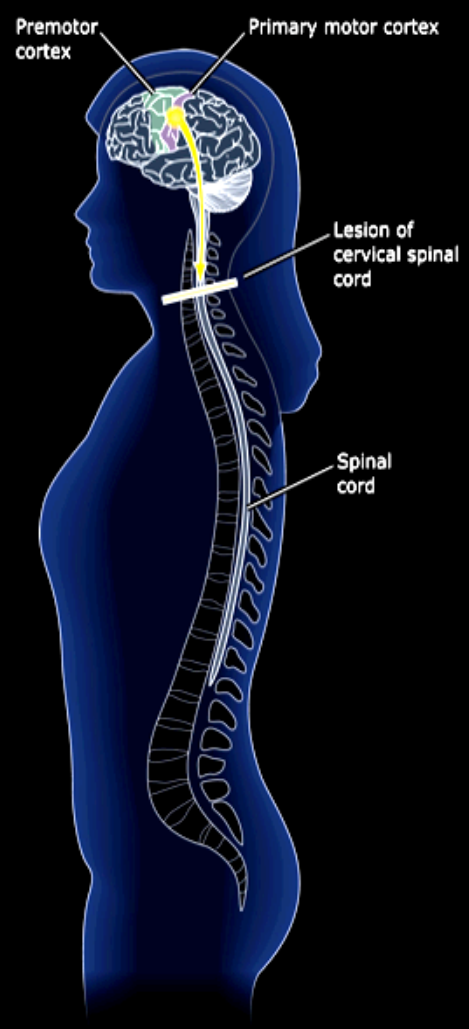
Trial	Letter Bank on the Screen	Response Type
1	ENIRSTAHDUGLCBMF	Selection
2	ENIRSTAH	Selection
3	ENIR	Non-response
4	STAH	Selection
5	ST	Non-response
6	AH	Selection
7	A	Non-response
8	H	Selection

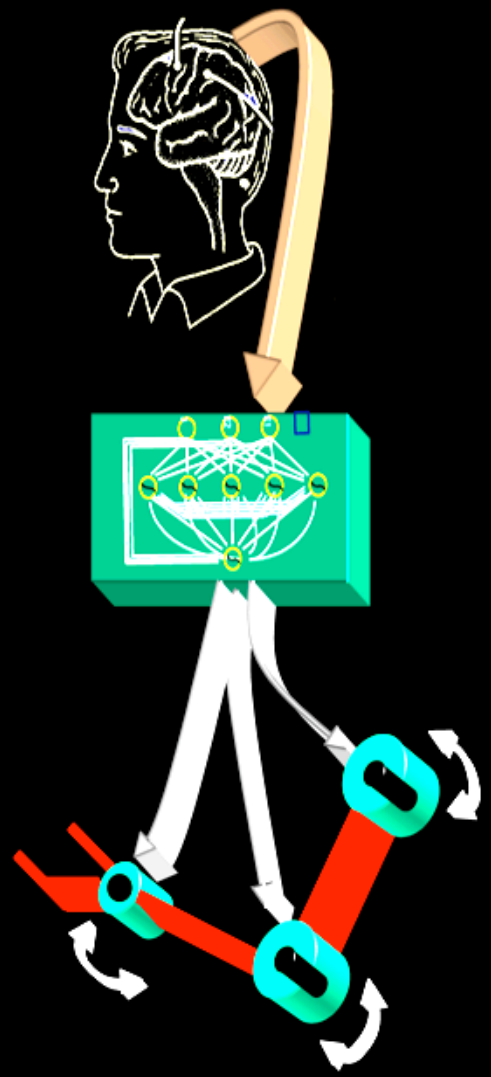
Perelmouter & Birbaumer, IEEE Biomed Engen (2002)

Nicolelis, Nature 2001



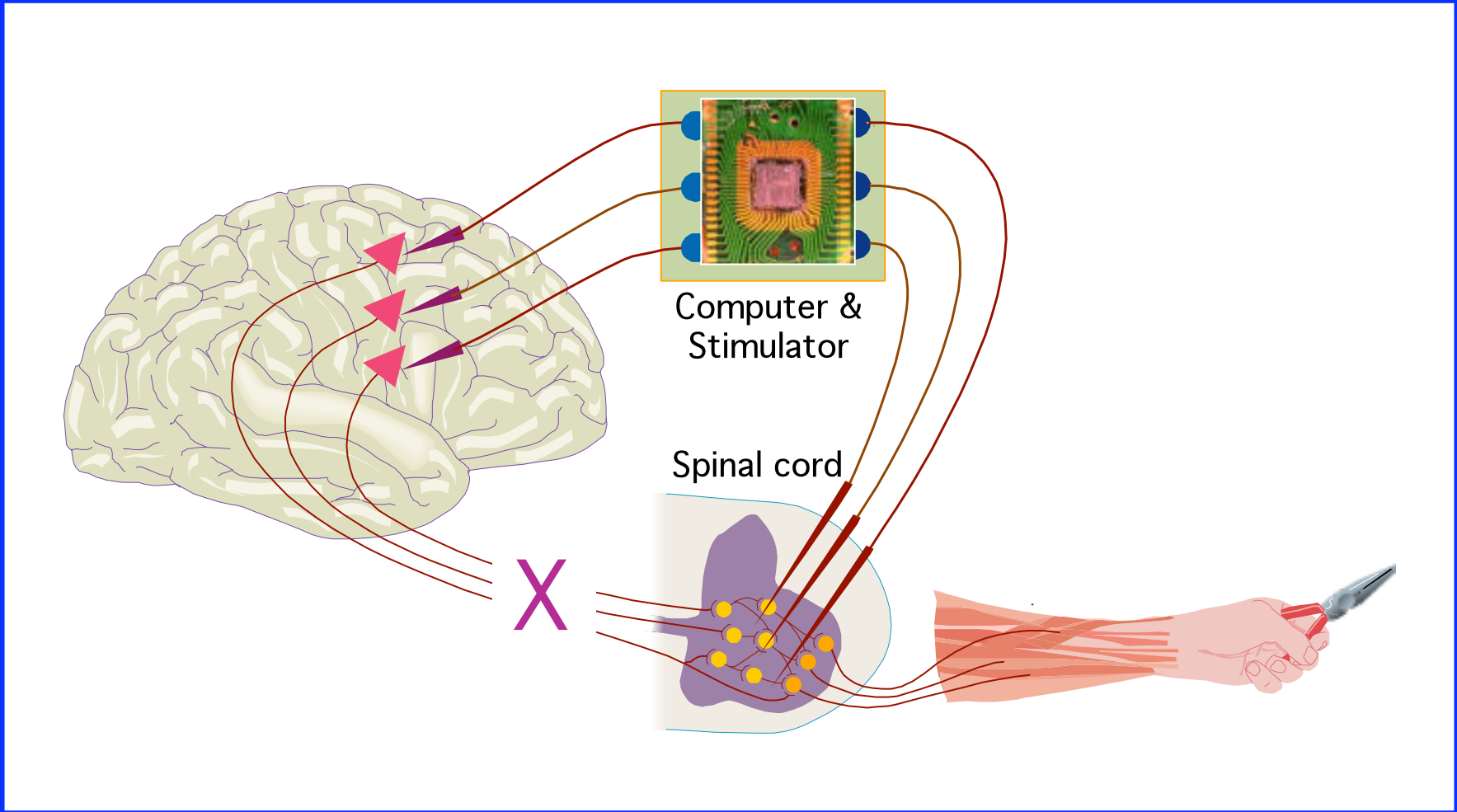
Cortical Neuroprosthesis for Restoring Motor Functions





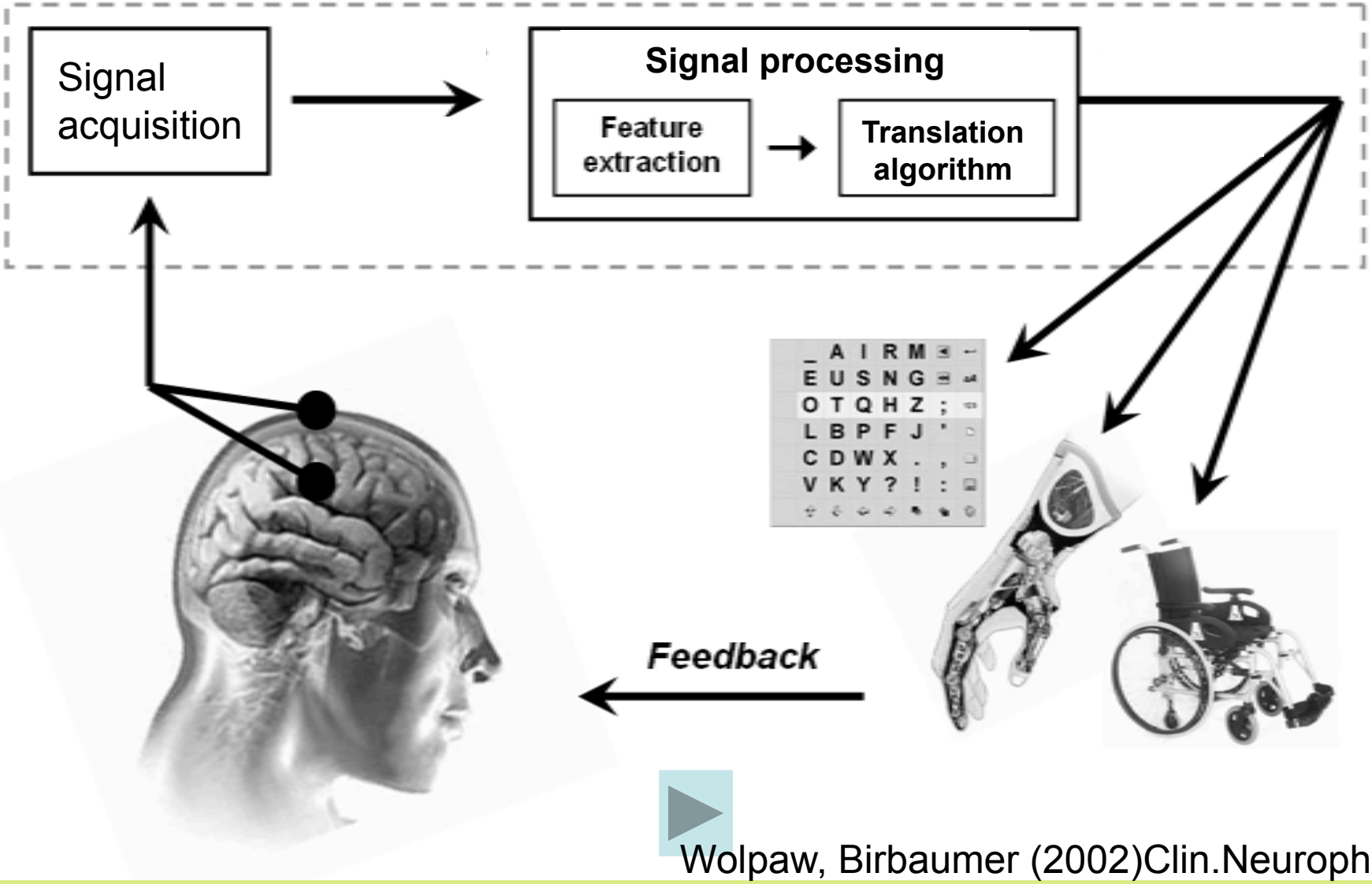
Nicolelis, Sc.American

Cortical activity could stimulate spinal cord



1. Stimulating spinal circuits recruits motor units in natural order
2. Spinal sites can evoke co-ordinated movements
3. Effect of implant will be integrated with any remaining spinal function

THE BCI SYSTEM

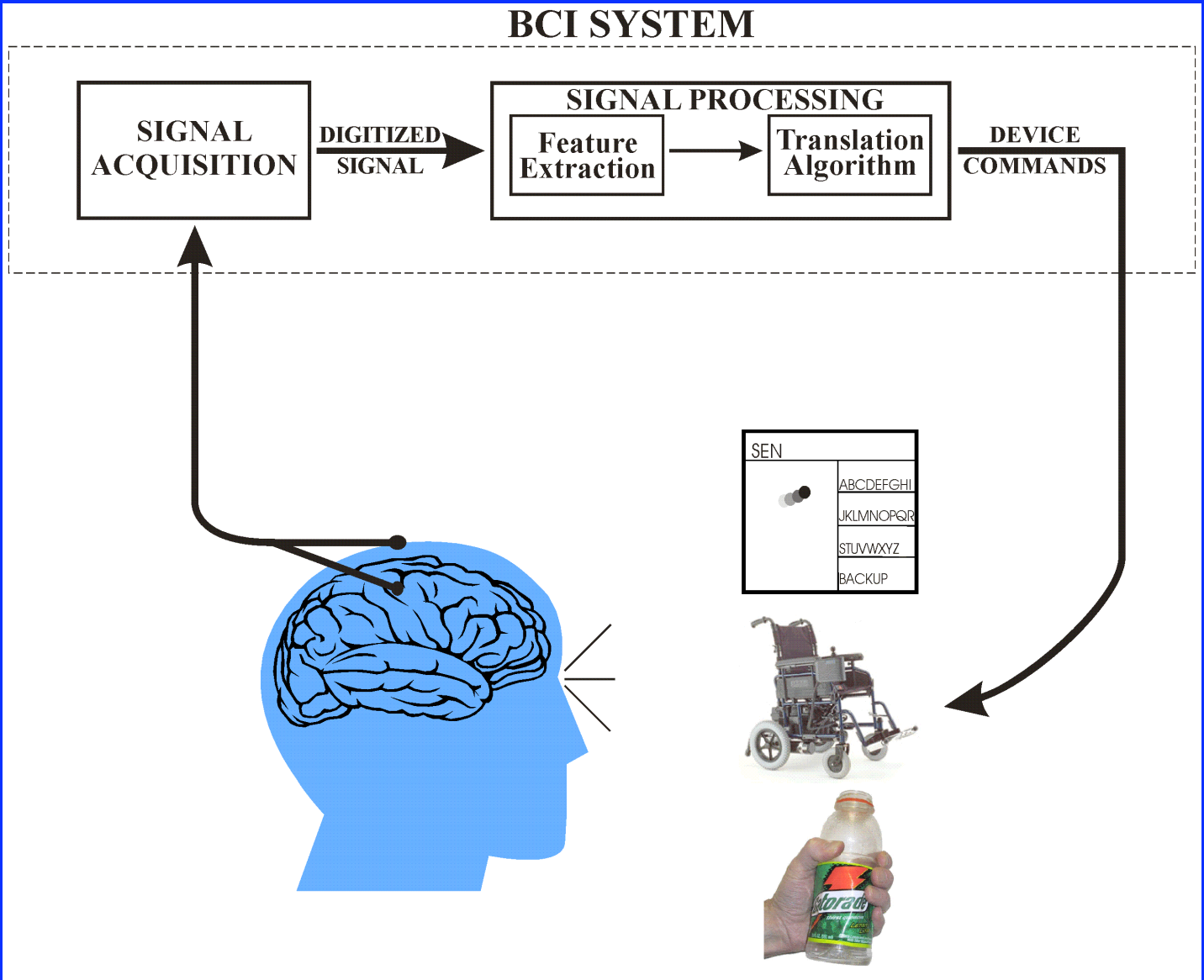


Wolpaw, Birbaumer (2002)Clin.Neurophysiol.

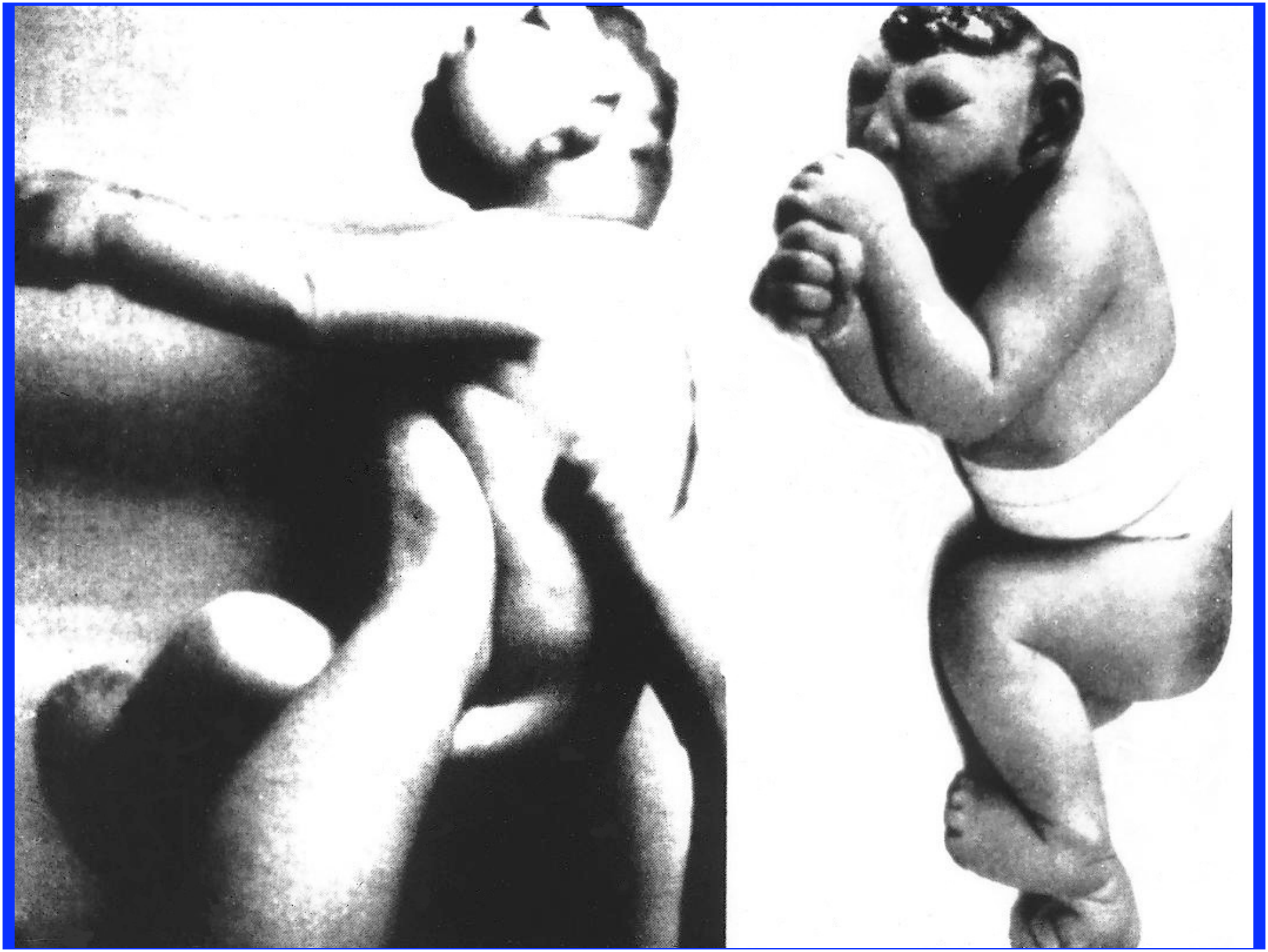
Es war gewissermassen schiere Gedankenlosigkeit – etwas, was mit Dummheit keineswegs identisch ist -, die ihn dafür prädisponierte, zu einem der grössten Verbrecher jener Zeit zu werden … wenn man ihm nämlich beim besten Willen keine teuflisch-dämonische Tiefe abgewinnen kann … Dass eine solche Realitätsferne und Gedankenlosigkeit mehr Unheil anrichten hat können, als alle in den Menschen vielleicht innewohnenden bösen Triebe zusammen genommen.

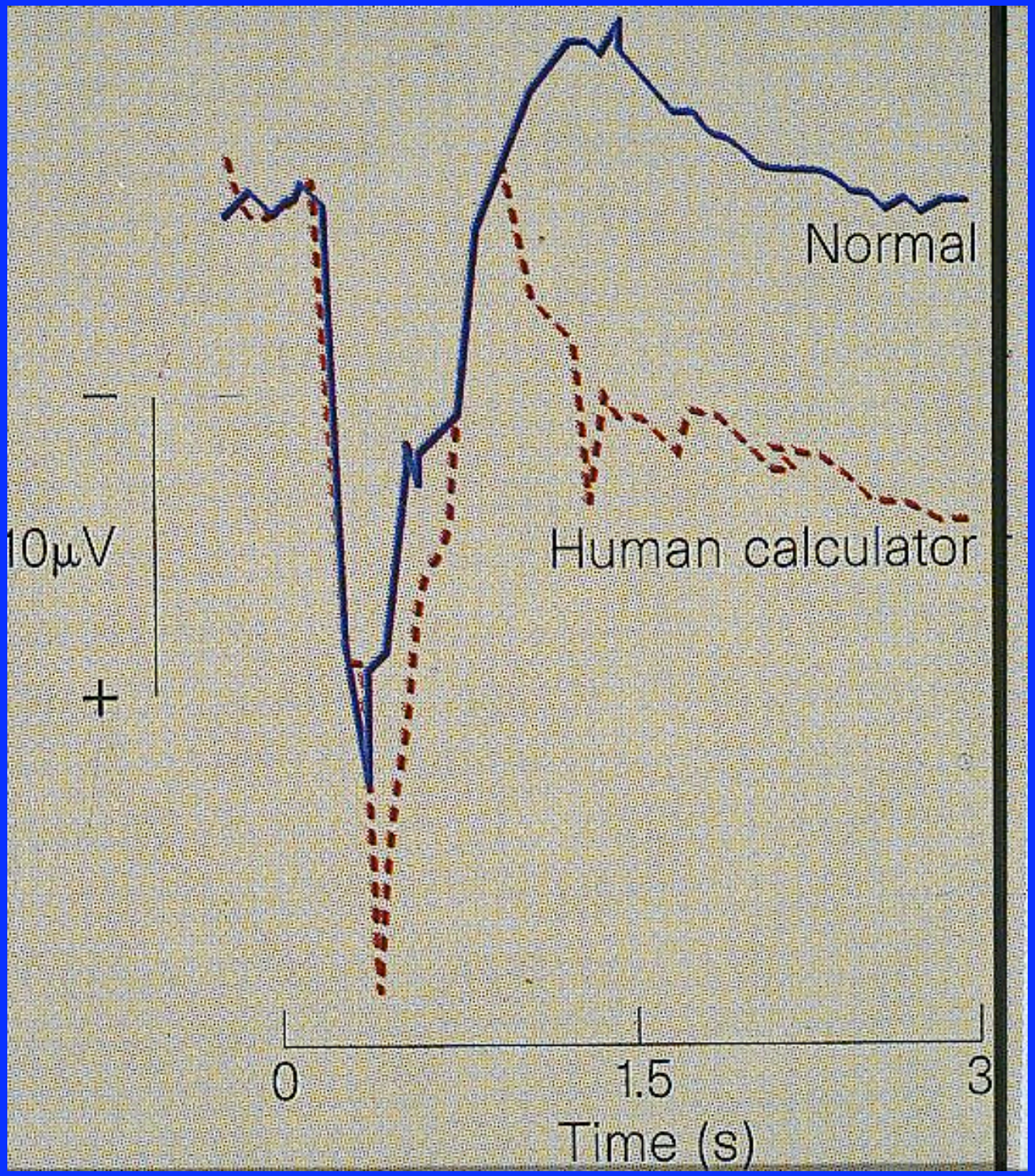
Hannah Arendt: Eichmann in Jerusalem

Brain-Computer Interface



Wolpaw, Birbaumer et al. Clin.Neurophysiol.(2002)




Normal
Human calculator
10μV
−
+
0
1.5
3
Time (s)

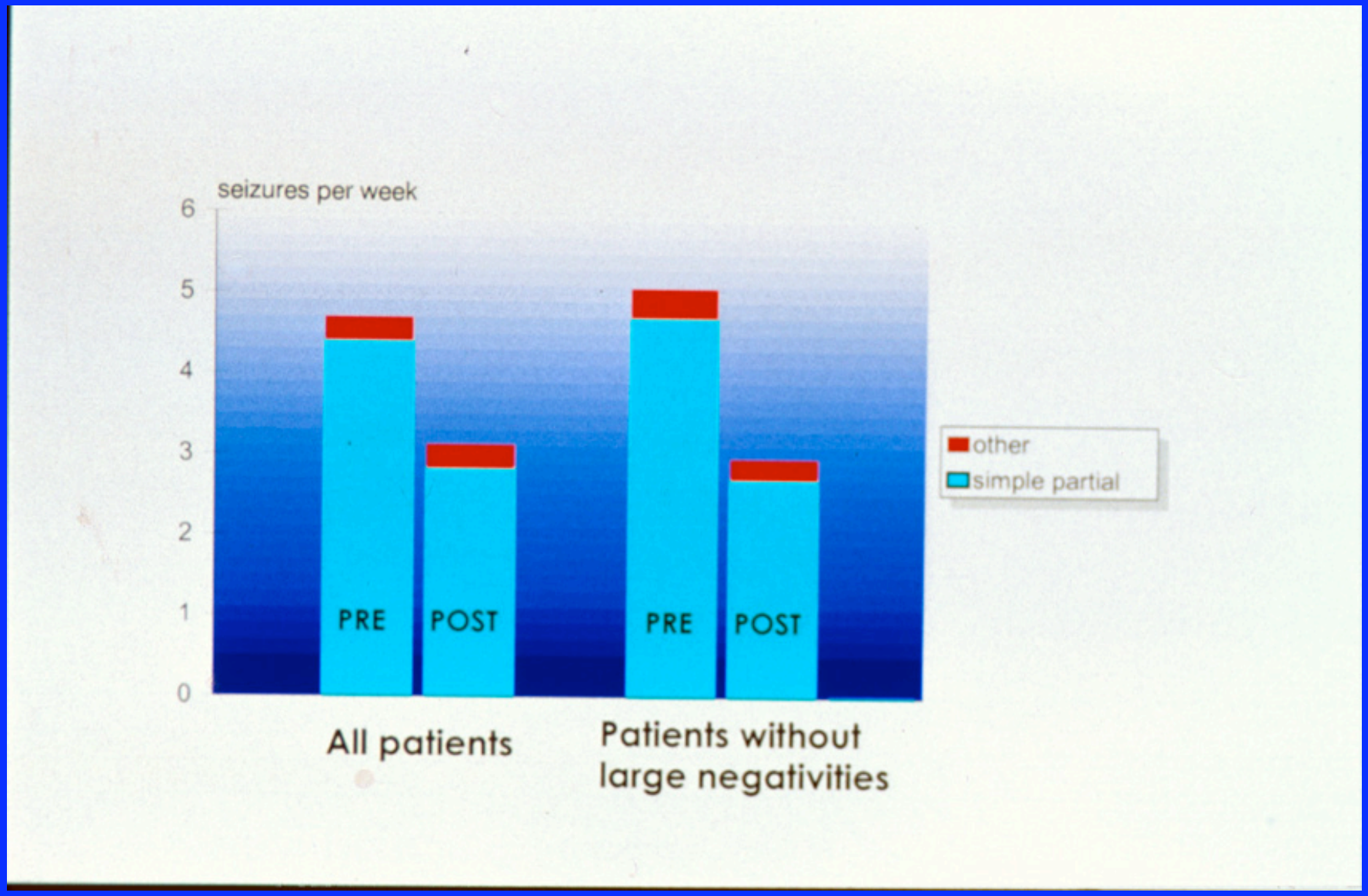
What happens to laughter
and to weeping, after
Their sound begins to wane?
What comes of the brain
After the thoughts depart?

Sandor Petöfi (1823-1849)

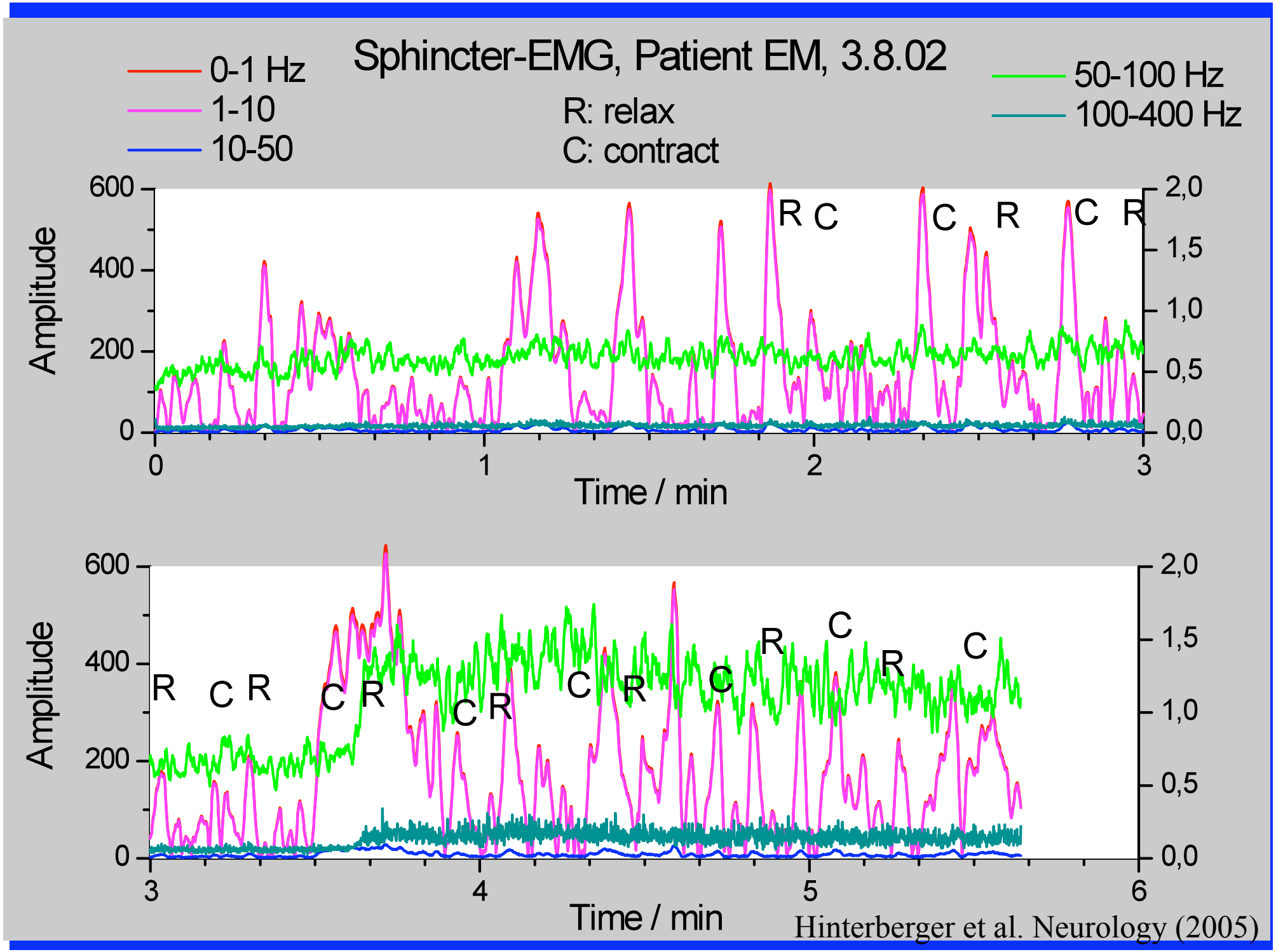
Through the frayed curtain at my window a wan glow announces the break of day. My heels hurt, my head weighs a ton, and something like a giant invisible diving bell holds my whole body prisoner.

Jean-Dominique Bauby: The Diving Bell And The Butterfly

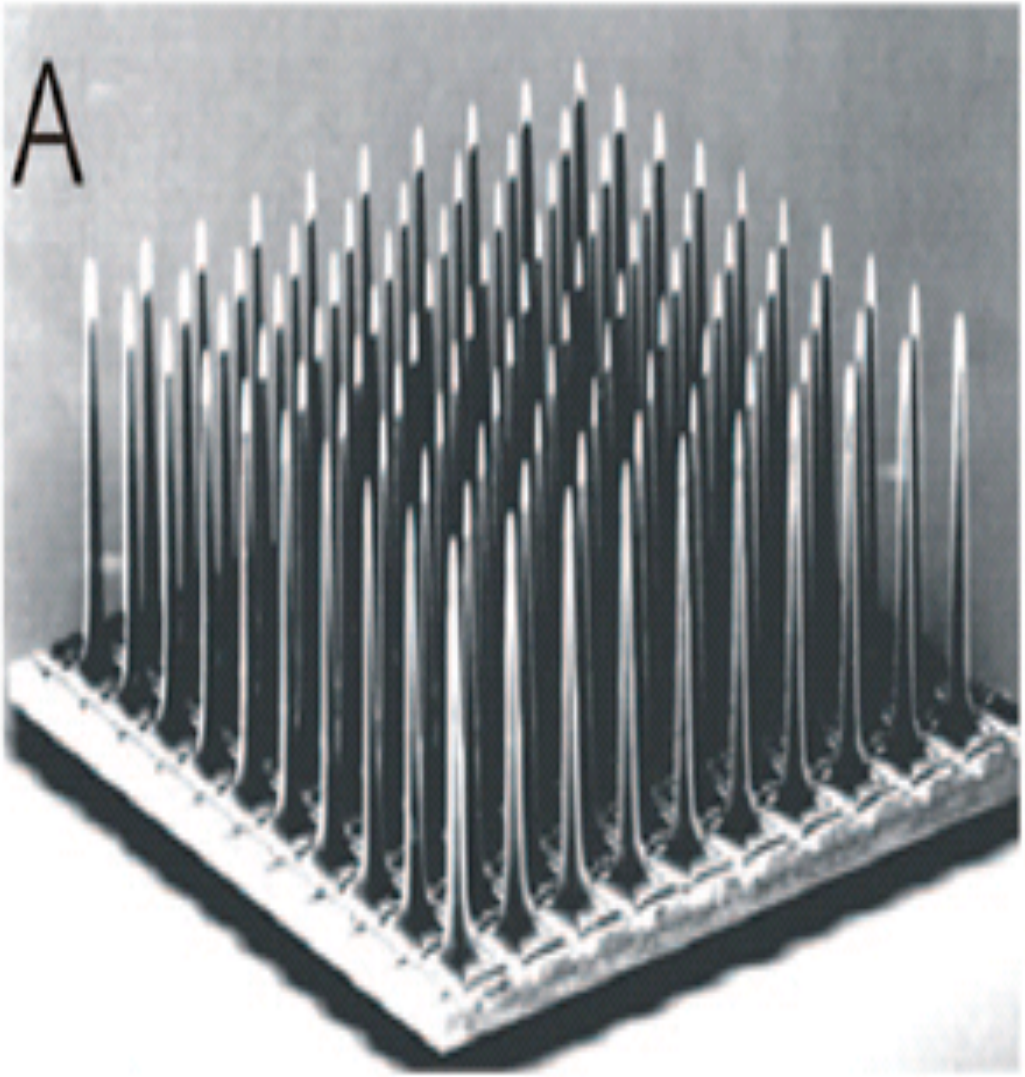

C
E

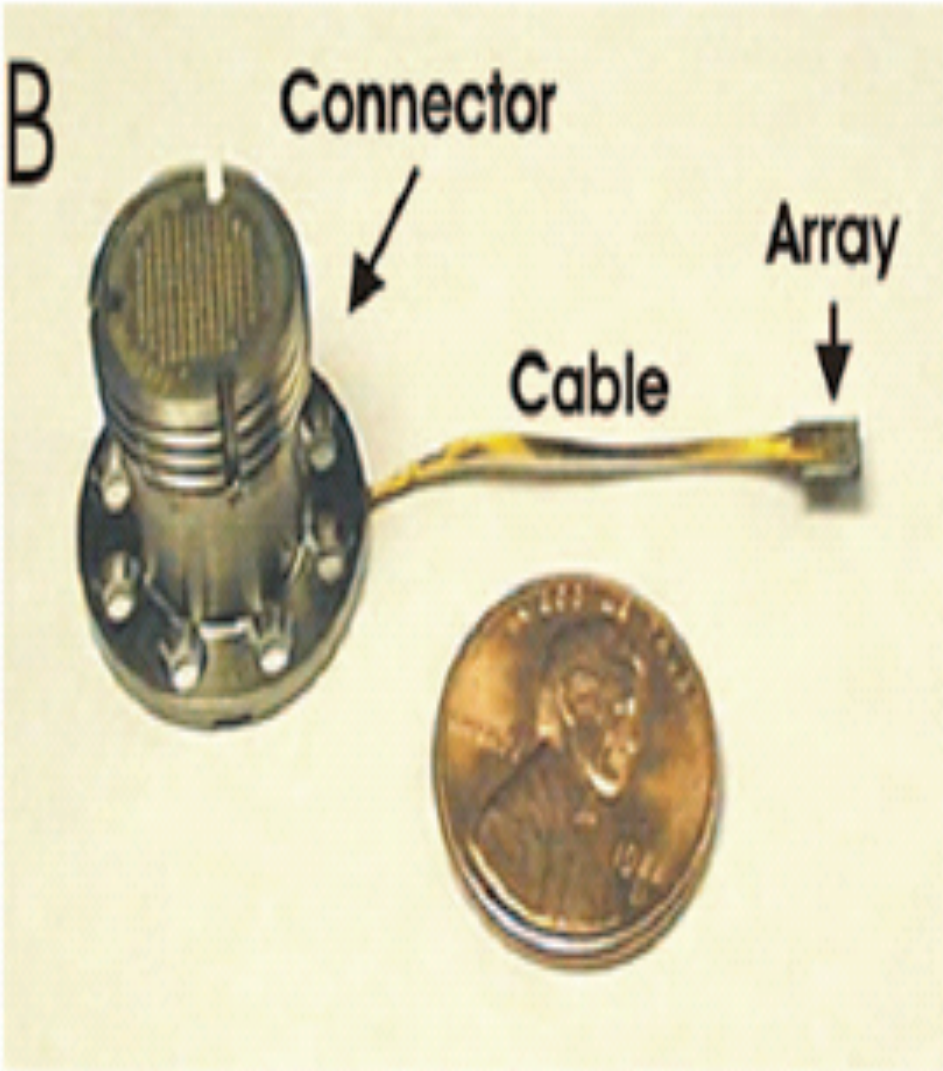


Kotchoubey et al., Epilepsia 2001



Hinterberger et al. Neurology (2005)

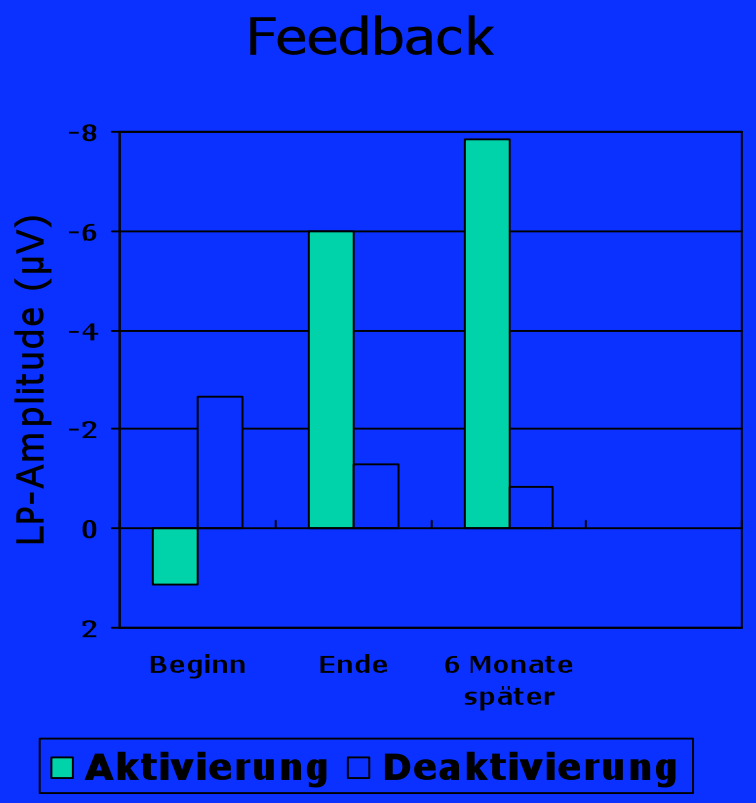


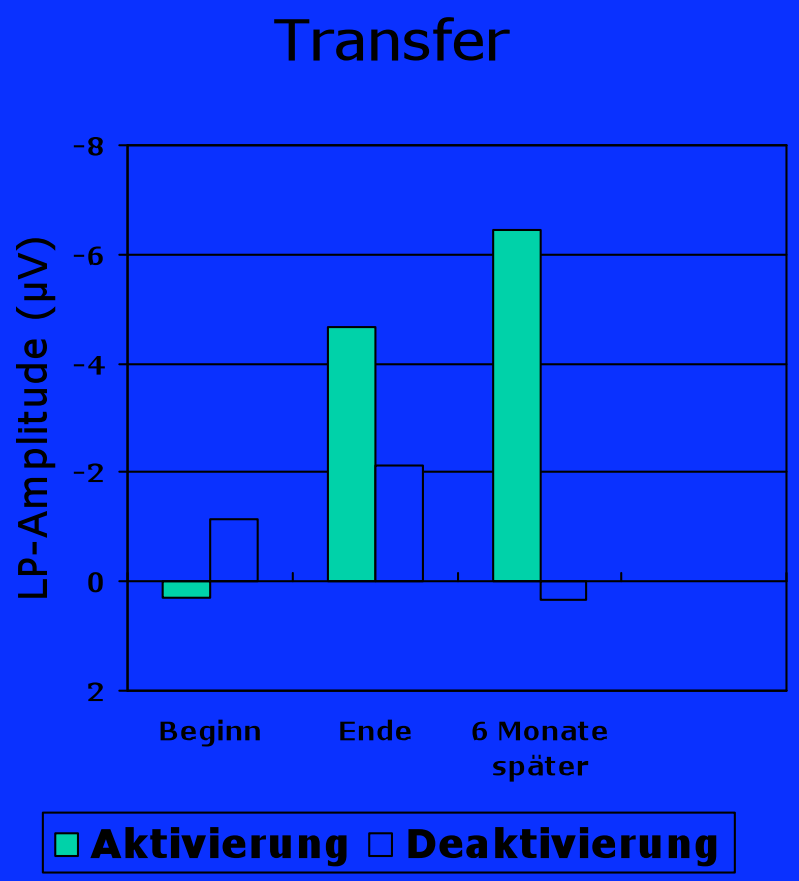


Hochberg et al, Nature 2006

Hochberg et al, Nature 2006

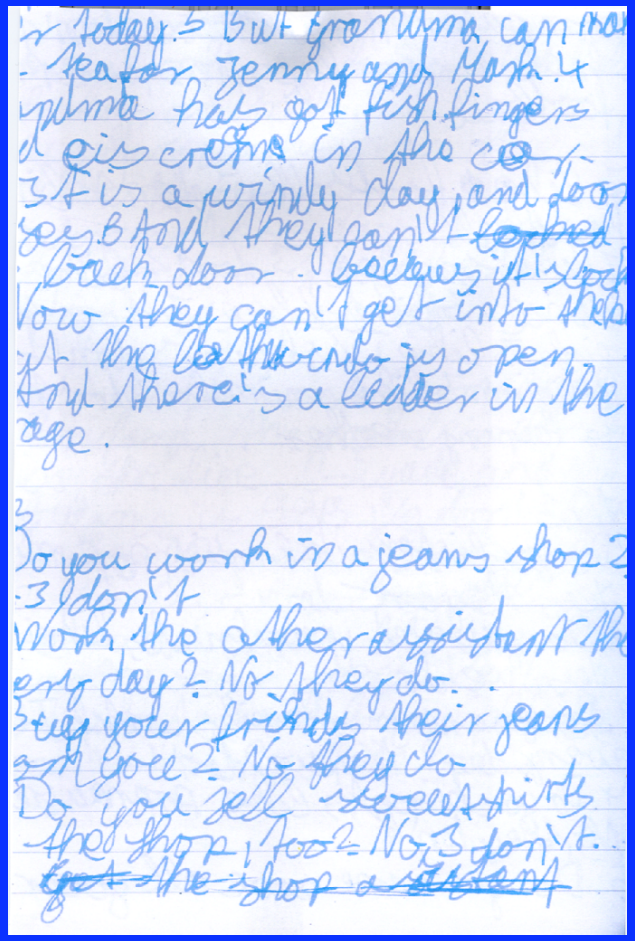
EEG Selbstkontrolle (LP-Gruppe)

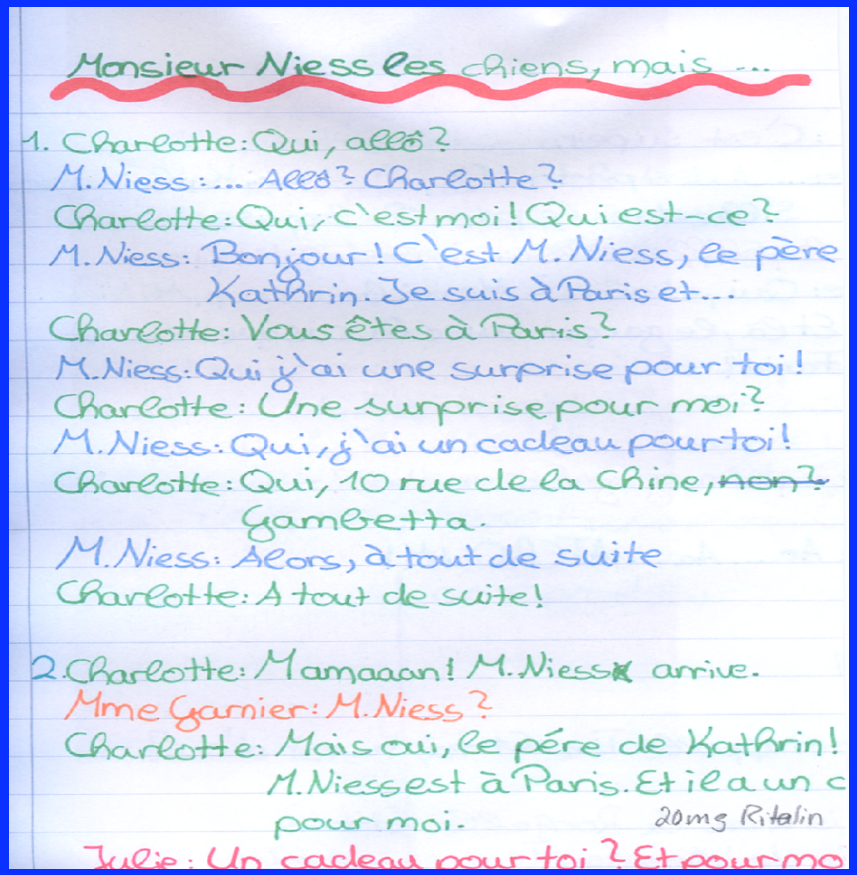




↳Aktivierung: signifikante Verbesserung (FB, TF)
↳Differenzierung: signifikante Verbesserung (FB, TF) *(Strehl et al., 2006)*

Feinmotorik





Ausriss aus Schulheft vor / nach LP-Training

Meta-Analyse

Efficacy of Neurofeedback treatment in ADHD: The effects on Inattention, Impulsivity and Hyperactivity: A meta-analysis. *(Arns, de Ridder, Strehl, Breteler & Conen, in press)*

N Probanden 718

N Studien 15, davon 2 RCT

Conclusion

"Neurofeedback in the treatment of ADHD can be regarded as clinically meaningful with

⇨ large effect sizes for Inattention and Impulsivity

⇨ and a medium effect size for Hyperactivity."

NIRS Experimental Setup

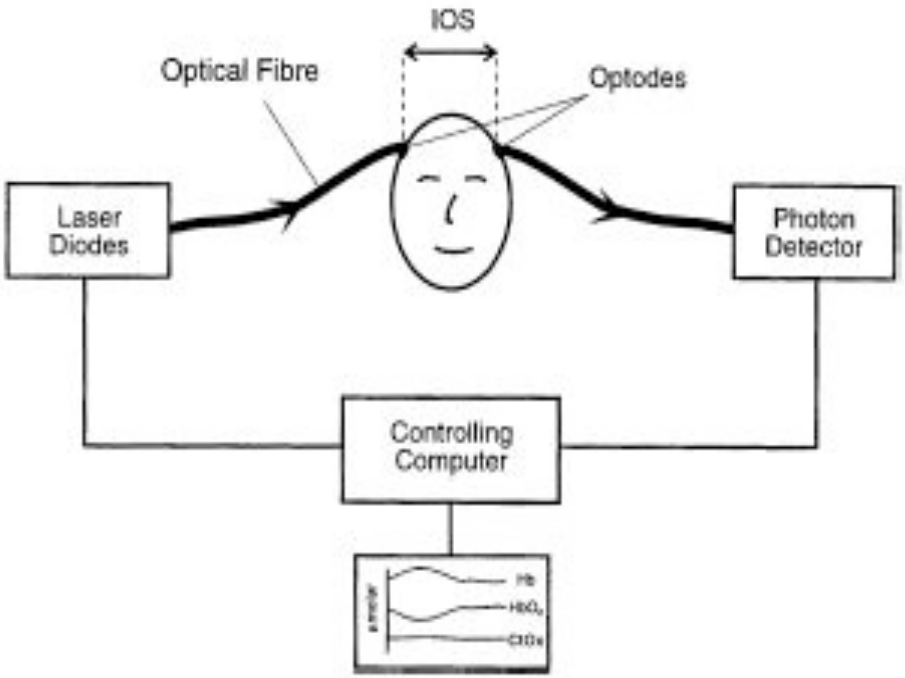


Figure 2 *Schematic of the experimental set-up for NIRS measurements across the head. In practice the optodes are rarely positioned directly opposite each other.*

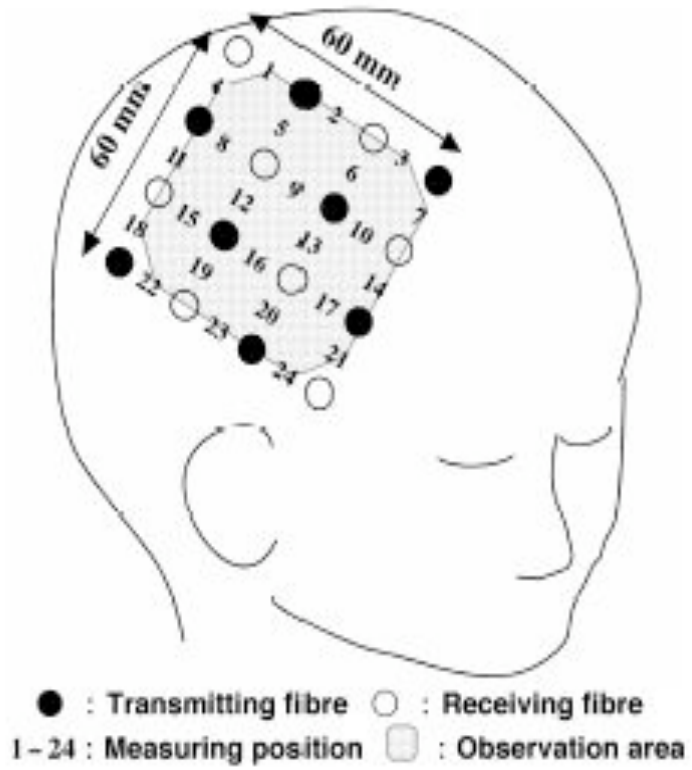


Figure 3 *Probe position on the neonate's head, and measurement locations, over the sensorimotor cortex.*