Universität Zürich[UZH]

KJPD

Functional imaging in cognition

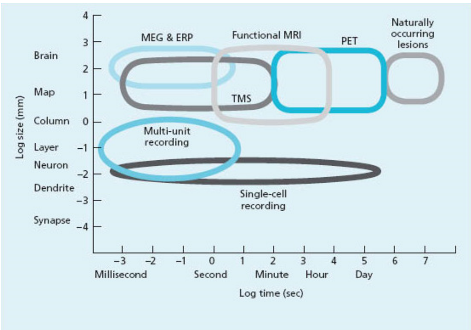
Silvia Brem

Slides: Thanks to Daniel Brandeis, Karin Kucian, Raffael Lüchinger
- http://psychology.uwo.ca/fmri4newbies
- http://www.fil.ion.ucl.ac.uk/spm/course/slides10-zurich/Kerstin_BOLD.pdf (Kerstin Preuschoff)

Überblick

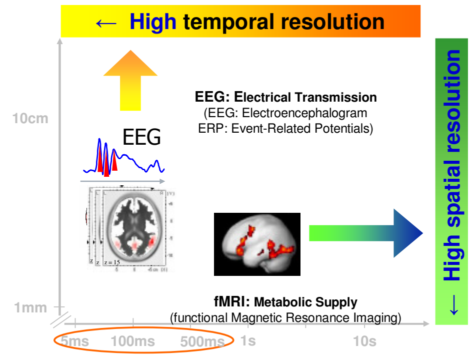
1. Forschungsbereiche und Methoden am KJPD
2. **Magnetresonanztomographie**
   - MR Physik
   - Funktionelles MRT
   - Beispiel Sprachverarbeitung
3. **Elektroenzephalographie**
   - EEG Grundlagen
   - Ereigniskorrelierte Potentiale
   - Beispiel Sprachverarbeitung
4. **Simultane Bildgebung**
   - Vor- und Nachteile
5. Diskussion

Spatial and Temporal Resolution



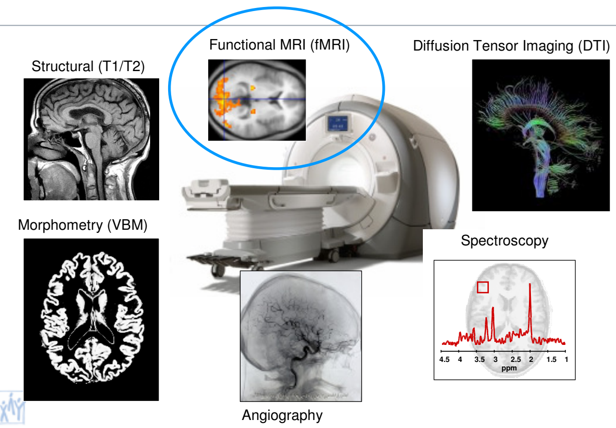
The Student's Guide to Cognitive Neuroscience by Jamie Ward, (2006) Psychology Press

Electrophysiology – Functional MRI



Magnetresonanztomographie (MRT)

Magnetic Resonance Imaging (MRI / MR



The principle of MR imaging

1. Place subject/material in a big magnet
2. Apply radio waves
3. Measure the emitted radio waves
4. Use magnetic gradients to encode space

After: http://psychology.uwo.ca/fmri4newbies and http://www.fil.ion.ucl.ac.uk/spm/course/slides10-zurich/Kerstin_BOLD.pdf

Magnetic resonance imaging (MRI)

MRI is based on the phenomenon of Nuclear Magnetic Resonance (NMR)

- The magnetic properties of atomic nuclei
- Can measure nuclei with odd number of protons/neutrons
- **e.g.** **1H**, 13C, 19F, 23Na, 31P

1H (proton)

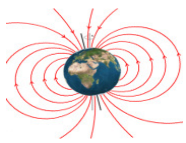
- Most important for MRI: abundant and high concentration in human body
- high sensitivity to NMR: yields large signals

Images: http://psychology.uwo.ca/fmri4newbies

Magnetic resonance imaging: Basics

Earth magnetic field:

0.00005 Tesla (=0.5 Gauss)

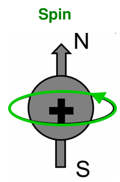


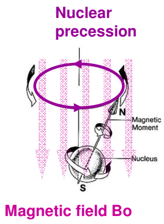
Magnetic fields in MR scanners:

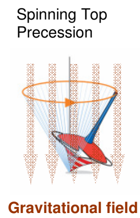
- 1.5 Tesla (T) = 15'000 Gauss
- 3T = 30'000 x Earth's magnetic field
- 7T = 70'000 Gauss…
- 20T (animals only)

Folie Dank an K. Kucian

Protons - Spins - Precession







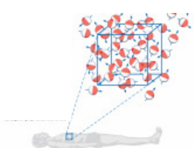
Spin: Protons (H+) rotate around their axis. Movement of the positive charge induces a magnetic moment

Precession: in a magnetic field spinning protons precess at a specific frequency

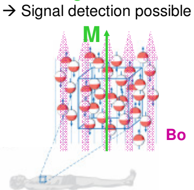
Images: http://psychology.uwo.ca/fmri4newbies; Magnete, Spins und Resonanzen, Siemens medical

1. Place subject in Big Magnet

No magnetic field:
→ No net magnetisation,
→ No signal



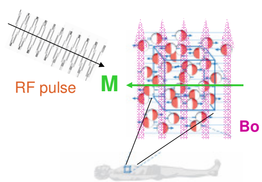
With magnetic field **Bo**:
→ **Net magnetisation**,
→ Signal detection possible

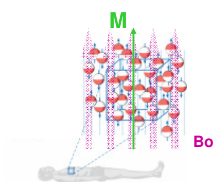


When you put a material in an MRI scanner, some of the protons become oriented with the magnetic field.

Images: http://psychology.uwo.ca/fmri4newbies; Magnete, Spins und Resonanzen, Siemens medical

2. Apply Radio Waves



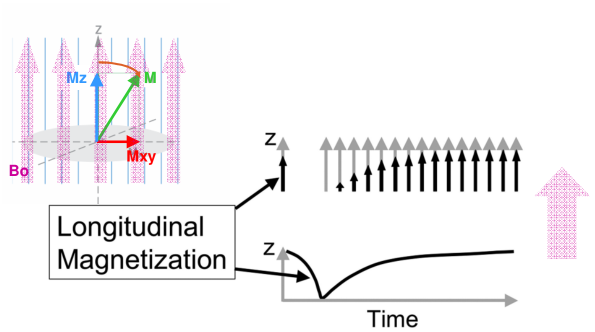


When you apply radio waves (RF pulse) at the appropriate (Larmour) frequency:
→ Protons **absorb energy** and change the orientation of their spins.

After you turn off the radio waves:
→ Protons return to their original orientation
→ **Emission of energy** in the form of radio waves.

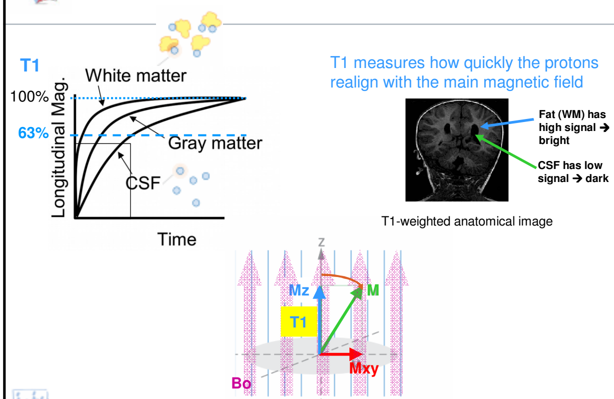
Images after: „Magnete, Spins und Resonanzen, Siemens medical" and http://psychology.uwo.ca/fmri4newbies

3. Measure emission of energy



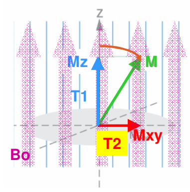
Pooley R A Radiographics 2005;25:1087-1099

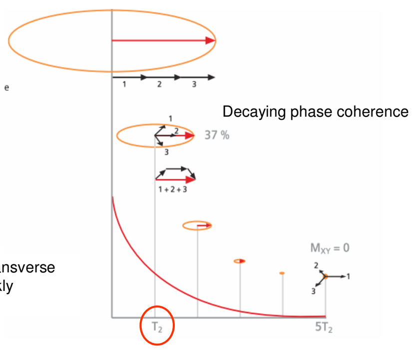
Measure Radio Waves in different tissues: T1



Which T1 is shorter, the one of water or fat?

Transverse relaxation: T2 or T2*

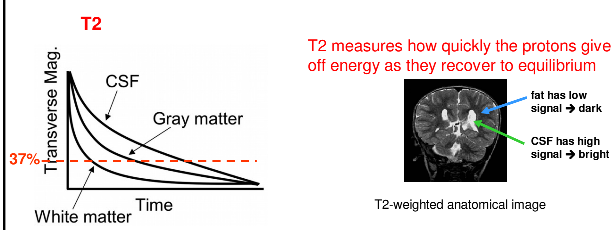




Initial **phase coherence** (transverse magnetisation) decays quickly
→T2

Images after: „Magnete, Spins und Resonanzen, Siemens medical“ and http://psychology.uwo.ca/fmri4newbies

Measure Radio Waves in different tissues: T2 or T2*



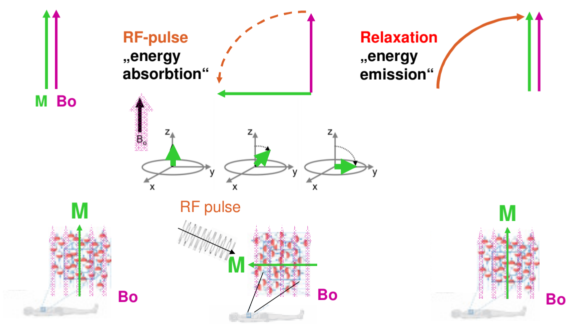
Which T2 is shorter, the one of water or fat?

Images: http://psychology.uwo.ca/fmri4newbies

T2* and magnetic susceptibility

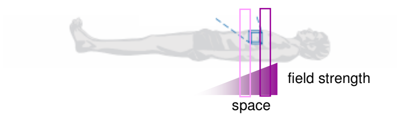
- Two factors contribute to the decay of transverse magnetization T2:
  1) molecular interactions → dephasing of spins
  2) local inhomogeneities of the magnetic field
  → T2* reflects the combined time constant
- **T2*** images are especially important for functional imaging because:
  - neuronal activations lead to small changes of T2* in the surrounding brain tissue that can be measured

Summary: Put in magnetic field – apply RF – measure RF…



Images: after „Magnete, Spins und Resonanzen, Siemens medical“ and http://psychology.uwo.ca/fmri4newbies

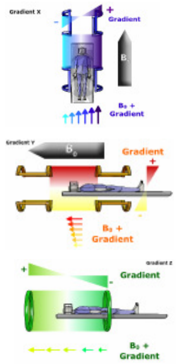
4. Use Gradients to Encode Space



lower magnetic field; lower frequencies | higher magnetic field; higher frequencies

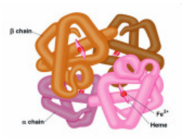
- Radio waves have to be the right frequency (Larmour) to excite protons.
- The frequency is proportional to the strength of the magnetic field (for H^+ in 1.5T → 63.87MHz).

→ When using gradients of magnetic fields, different frequencies will affect protons in different parts of space.



text: http://psychology.uwo.ca/fmri4newbies images: http://www.imaios.com/en/e-Courses/e-MRI/

Functional magnetic resonance imaging (fMRI)



- **Magnetic susceptibility** – the intensity of magnetisation of a substance when placed in a magnetic field
- **Oxygenated hemoglobin (Hb) is diamagnetic** (weak repulsion from magnetic field): no unpaired electrons and no magnetic moment
- **Deoxygenated hemoglobin (dHb) is paramagnetic** (weak attraction to magnetic field): unpaired electrons and magnetic moment

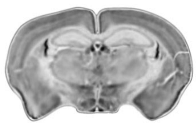
T2* and BOLD imaging

- T2* images are especially important for functional imaging because:
  - Neuronal activations lead to small changes of T2* in the surrounding brain tissue due to the changes in the amount of deoxygenated hemoglobin
  - Deoxygenated blood has a higher **magnetic susceptibility** (higher intensity of magnetization) within a magnetic field → causes spin dephasing → decay of transverse relaxation (T2*)
- **BOLD: blood–oxygenation–level dependent fMRI**

Deoxygenated Blood → Signal Loss

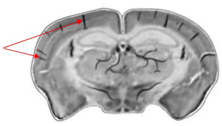
Rat brains

Oxygenated blood
(diamagnetic)
No signal loss…



breath only oxygen
(uniform texture)

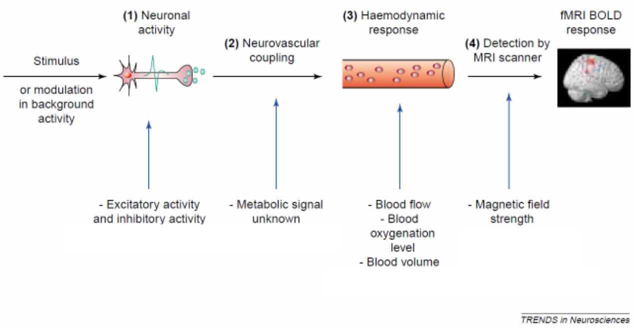
Deoxygenated blood
(paramagnetic)
Signal loss!!!



breath normal air
→ signal loss in vessels

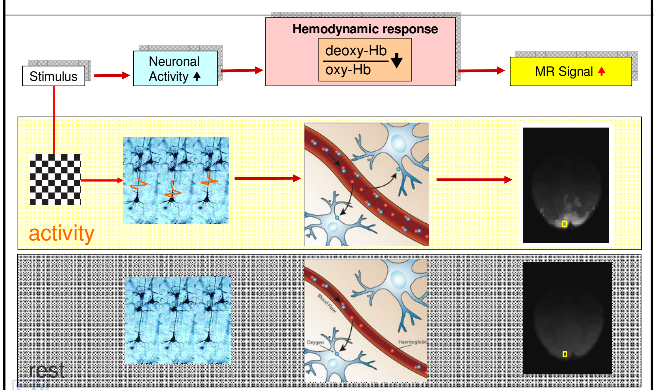
Images: Huettel, Song & McCarthy, 2004, Functional Magnetic Resonance Imaging. After Ogawa et al. 1990

BOLD (blood-oxygenation-level dependent) Imaging



Arthurs & Boniface, TRENDS in Neurosciences Vol.25 No.1 January 2002

The BOLD is a relative signal!



The BOLD time course

BOLD:
- Slow (~25s)
- Regional variability
- Interindividual variability
- Sometimes initial dip

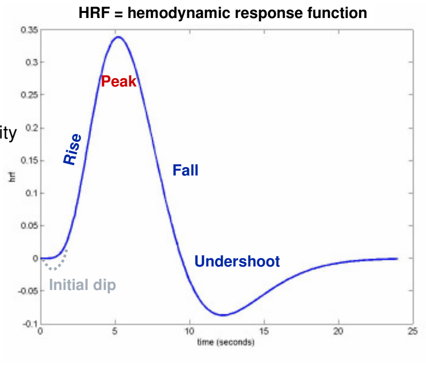
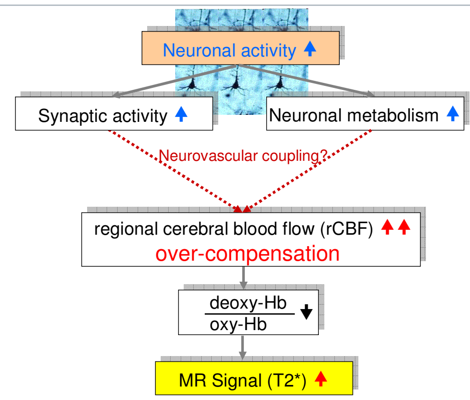


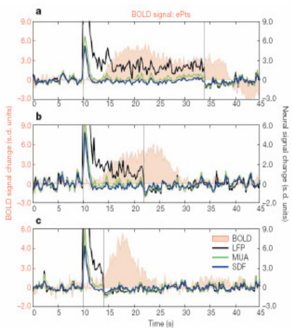
Image: http://www.math.mcgill.ca/keith/BICstat/

fMRT BOLD – neurovascular coupling

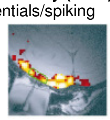


Neurovascular coupling: What does the BOLD response reflect?

Combined electrophysiological/ fMRI study in monkeys (Logothetis et al. 2001) compared:



- **Local Field Potentials (LFP),** reflect the summation of post-synaptic potentials
- **Multi-Unit Activity (MUA)** reflects action potentials/spiking

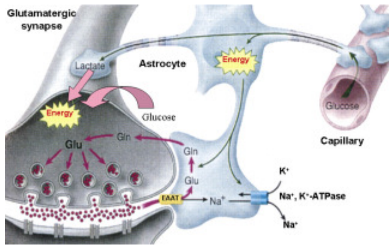


→ BOLD activity is more closely related to LFPs than MUA and thus **represents reflects the incoming input and the local processing** in a given area rather than the spiking activity

Logothetis et al, Nature 2001

Energetic consequences of postsynaptic activity

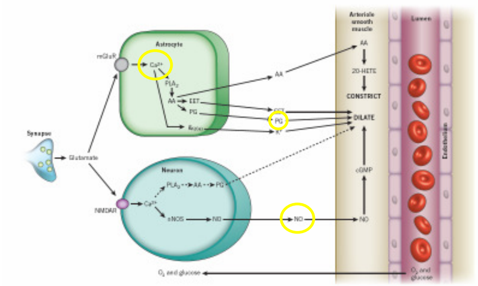
- Action potentials at pre-synaptic cell
- Glutamate release
- Open ion-channels on post-synaptic cell
- Re-uptake of glutamate by astrocytes triggers glucose metabolism



- Pump ions out of cell again to restore ionic gradients uses energy (50-75% for glu re-uptake) and oxygen
  →Postsynaptic responses seem to be the dominant energy consumer (Attwell et al. TINS, 2002)
  → **How does the energy and oxygen need affect the regional cerebral blood flow**?

Blood flow maybe directly driven by excitatory postsynaptic processes: Forward control of blood flow

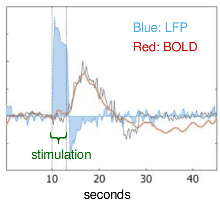
- BOLD results from postsynaptic Ca^{2+} increases at glutamatergic synapses
- Nitric oxide (NO) and prostaglandines (PG) couple synaptic activity to rCBF increases



Attwell et al. 2010, Nature

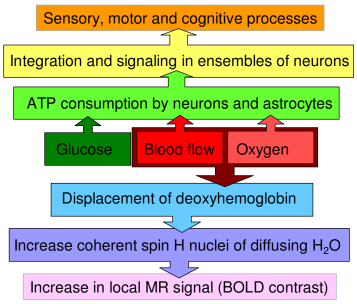
Summary: The BOLD signal

1. Represents a change in the dHb/Hb ratio in response to neuronal activity
2. Is an **indirect measure** of neuronal activity
   → the processes of neurovascular coupling are still debated
3. Is a **slow** measure (several seconds!)
4. Is assumed to reflect **mainly excitatory postsynaptic activity**



Logothetis & Wandell 2004, *Ann. Rev. Physiol.*

Summary: the BOLD contrast is an indirect measure of neuronal activity!



Scheme after: Huettel, Song & McCarthy, 2004, Functional Magnetic Resonance Imaging

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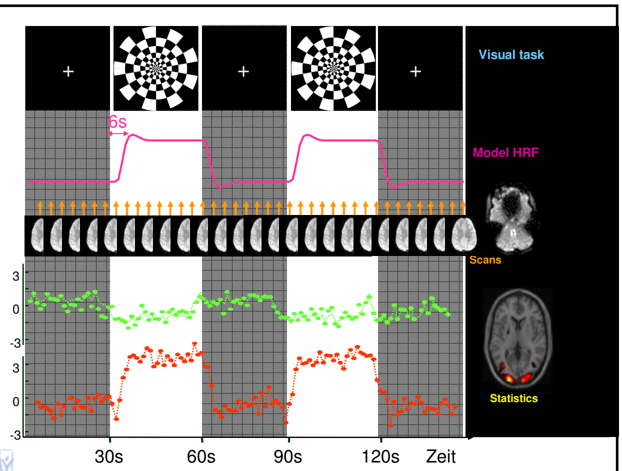
Functional imaging of cognition



Folie thanks to: K. Kucian

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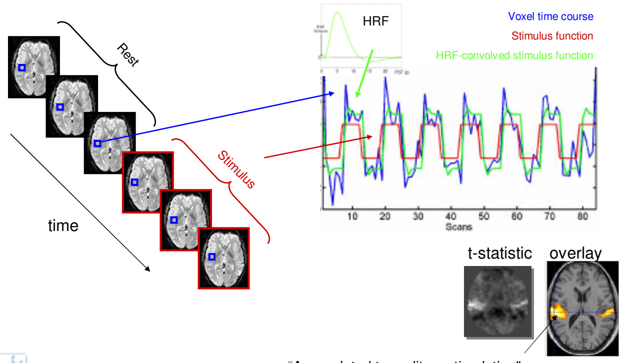
fMRI activation statistic



"Area related to auditory stimulation"

After: Prof. K. E. Stephan, Methods & models for fMRI data analysis

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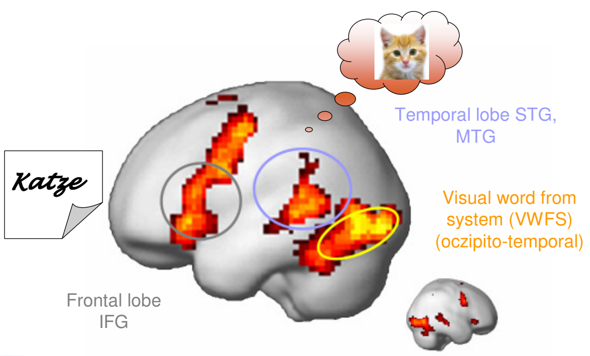
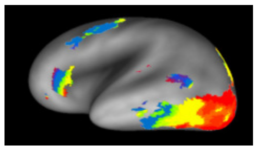
Spatial network of reading

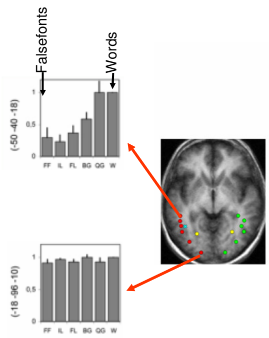


Visual word form system (VWFS)

The more wordlike the more anterior the activation in the left occipitio-temporal VWFS



Falsefont: \ɒſɔ۵\ɒʌſ



Vinckier et al 2007, Neuron

Electroenzephalography (EEG) and Event-Related Potentials (ERP)

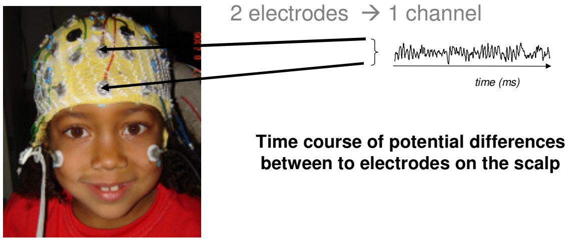
Scalp EEG: advantages and disadvantages

- ✚ High temporal resolution (milliseconds)
- ✚ Measures neuronal activity directly
- ✚ Non-invasiv (suited also for kids)
- ✚ Cheap

But:

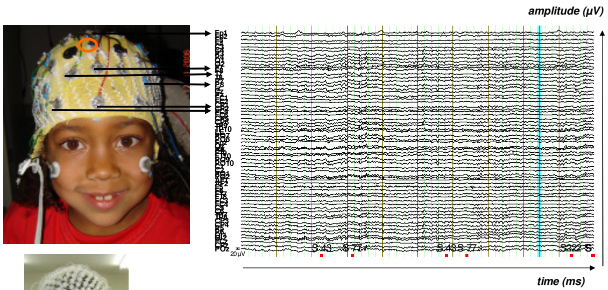
- Location of the source of activation can only roughly be estimated (low spatial resolution)

Electroencephalography



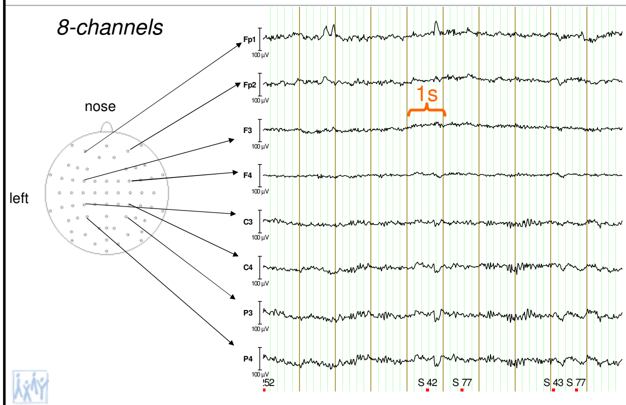
Time course of potential differences between to electrodes on the scalp

Multi channel recording

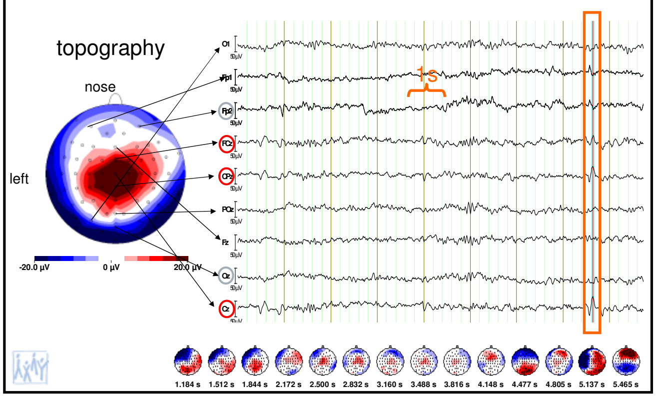


Often one reference electrode and many scalp electrodes (up to 256!)

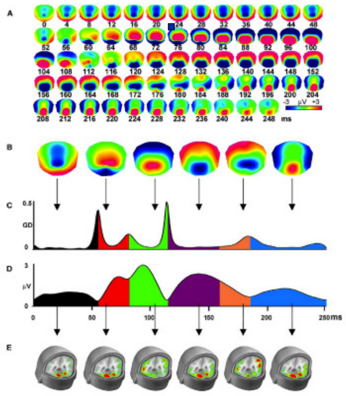
Time course (ms) – waveforms/ curves



Potential field distribution at a specific point in time: topography – maps - landscapes

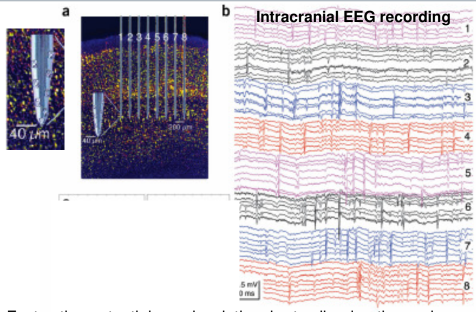


Microstates – defined by stable topographies



Michel et al. 2004

What is measured by the scalp EEG?

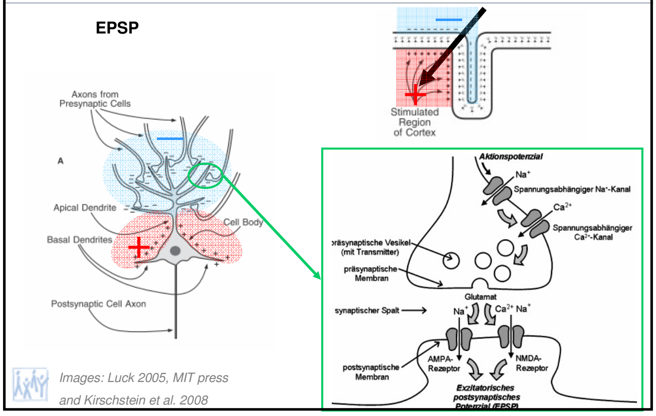


Fast action potentials are local: the short spike duration makes summation unlikely and spike amplitudes fall off rapidly (limited spatial spread) → neglectible for scalp EEG

Slow postsynaptic potentials (LFP) are more widespread→ EEG

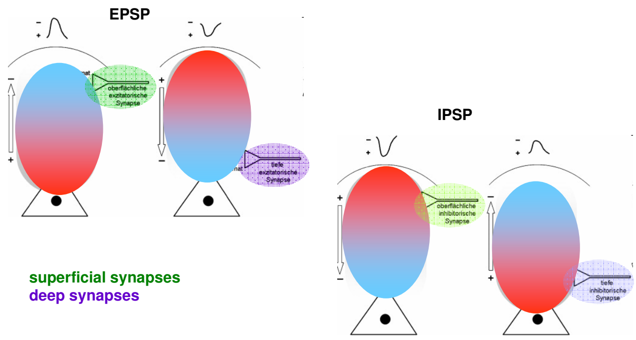
Buzsaki, G. (2004). Nature Neuroscience, 7(5), 446-451.

Neurophysiological basics of scalp EEG: postsynaptic potentials



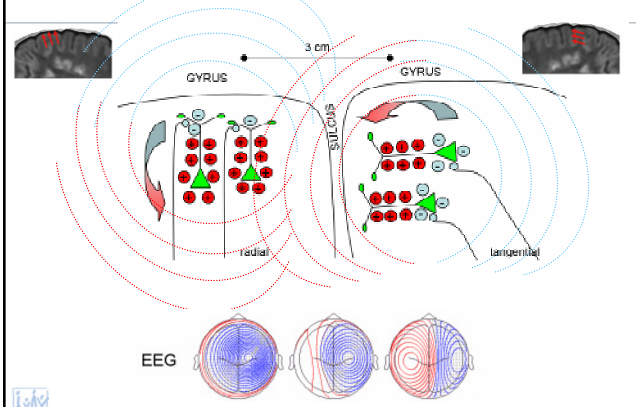
Images: Luck 2005, MIT press and Kirschstein et al. 2008

Excitatory and und inhibitory postsynaptic potentials



Images: Kirschstein et al. 2008

The scalp EEG measures summed activity

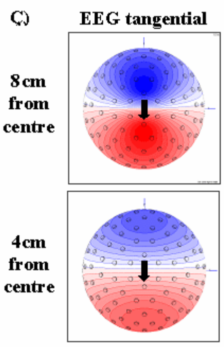


Brandeis et al (2009). From Neuronal Activity to Scalp Potential Fields. In Michel et al: Electrical Neuroimaging

EEG - maps and dipole sources

Superficial: 8 cm from centre

Deeper: 4 cm from centre



Superficial and deep sources contribute to the scalp EEG

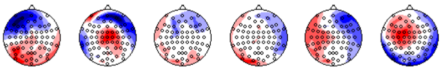
- Due to lower conductivity of the skull as compared to the brain tissue:
  → Superficial sources are attenuated more strongly

Hauk et al http://www.mrc-cbu.cam.ac.uk/EEG/doc/eeg_intro.shtml

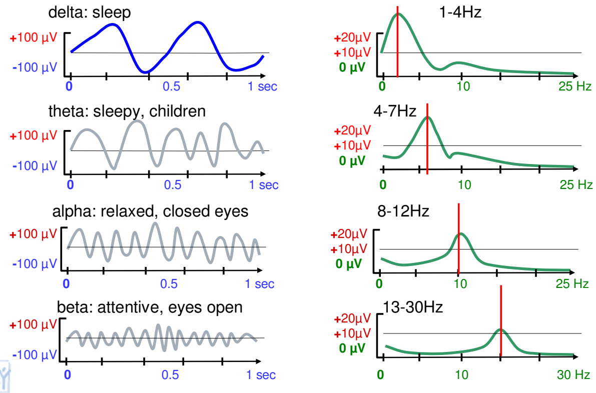
Basics of the scalp EEG

BASIS – neuronal mass activation

- Neighbouring neurons often share their orientation
- Neighbouring neurons are often simultaneously active
- Electric fields of neurons add linearly (additive, vectors)
- Polarization of extended brain regions makes scalp EEG-field
- EEG-fields are weak (typical: <100 µVolt)
- EEG-fields change rapidly (typical: 10Hz -> reversal every 0.05 s)
- EEG topography is determined through the active brain regions
- EEG time course reflects rapid information processing and state regulation



EEG: curves and spectra



Event-related potentials (ERPs) or evoked potentials (EP)

- Characteristic potential fluctuations with relatively fixed latencies and polarities in reference to an event
- Most often low amplitudes (1-20µV) and thus covered by the higher spontaneous raw EEG

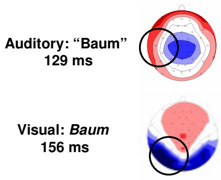
→ **Averaging of the EEG time-locked to the specific (external) event: Event-related activity**

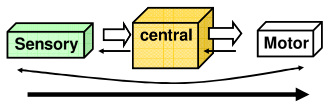
Early vs. late ERPs

Early Activity ~ 5-120ms: sensory (VEP, AEP, SEP), attention (filter)

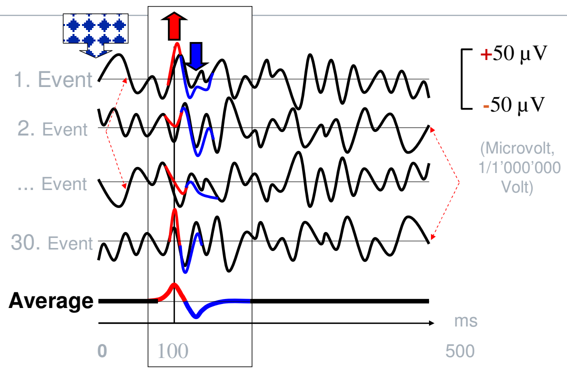
sensory memory (passive: mismatch negativity MMN), spezialization, expertise, plasticity, emotion

Late Activity ~ 200-600ms: attention-inhibition, resources (response set, working memory, preparation), language.



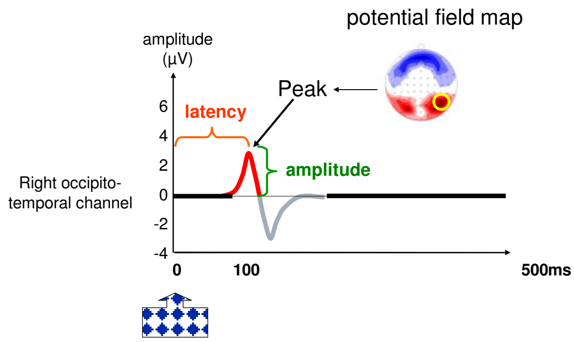


Event-related potentials "ERP"

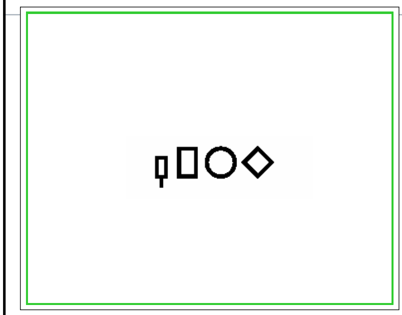


---- ERP (time and polarity locked activity to stimulus)

Nomenclature



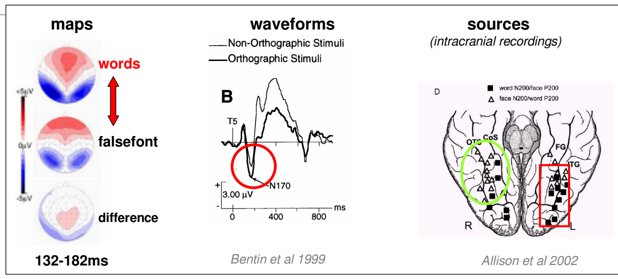
Testing implicit reading



conditions
- words
- falsefonts

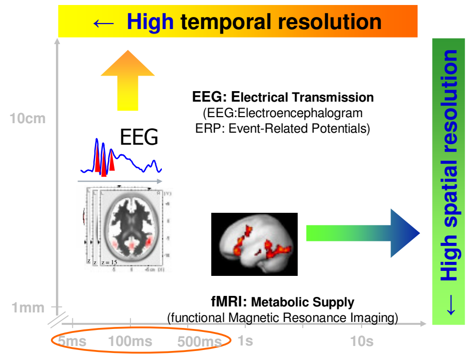
Task: Press button after immediate repetition of a word or falsefont string

ERP: Print sensitivity in adults



- Print specific activity after 170ms (difference between words and falsefonts)
- Implicit, automatic processing
- Source of the N1 in occipito-temporal cortex

Electrophysiology – Functional MRI



Combined EEG – fMRI imaging

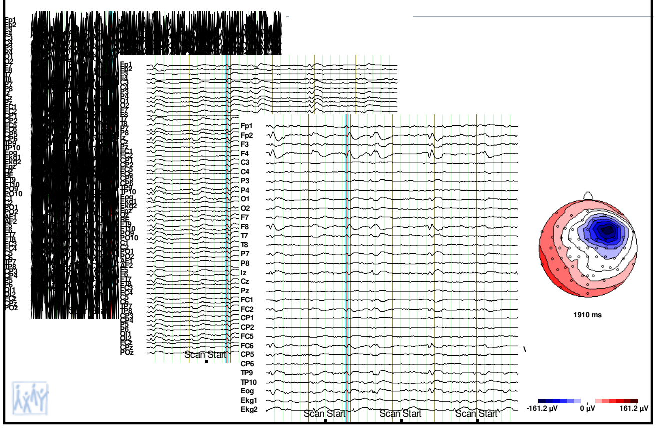
- **Sequential recordings**:
  - effects of task repetition
  - time consuming
  - different state (?)
  - different environment
  (different position, stimulation, …)

EEG – fMRI / fMRI – EEG

- **Simultaneous (concurrent) recordings**:
  - compatible equipment (safety!)
  - major artefacts (induced currents due to gradient switching and pulse artefacts) in EEG that need correction

Record EEG during fMRI

Simultaneous EEG- fMRI



Sequential ERP and fMRI study

Kindergarten children
ERP: 32, (♀ 17)
fMRT: 16, (♀ 13)

aged: 6.5y (±0.3j)

T1
Behaviour, ERP, fMRI

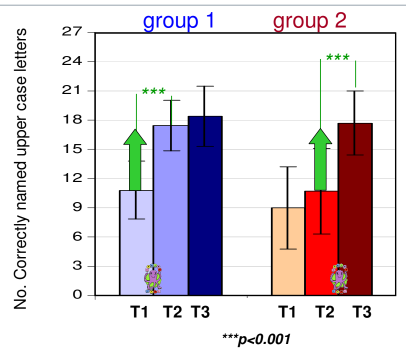
Training 1
(8 weeks)

T2
Behaviour, ERP, fMRI

Training 2
(8 weeks)

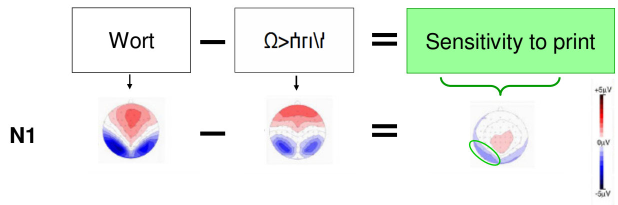
T3
Behaviour, ERP, fMRI

Training: Letter knowlegde

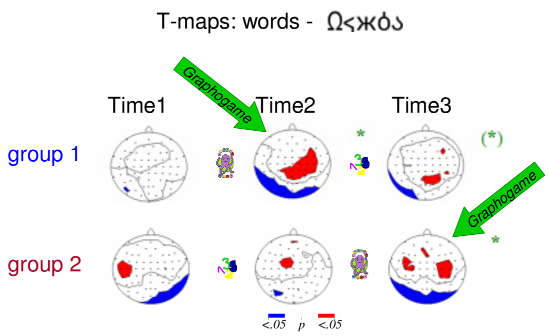


Brem et al. PNAS 2010

Example: Sensitivity to print processing

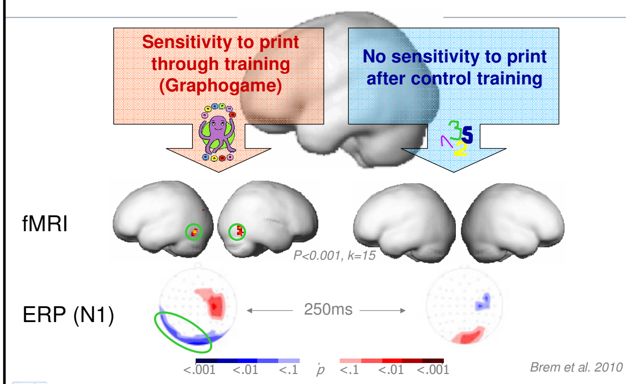


Training effects on N1 ERP



Brem et al. 2010

Converging EEG and fMRI results



Brem et al. 2010

Letter-speech sound correspondence training → specialisation to print

Thank you!