Disclosure

Name of Commercial Interest: GE-Healthcare
Type of Financial Relationship: Advisory board
Learning Objectives

• compare fMRI and intracarotid amobarbital test
• sensitivity / specificity of fMRI for lateralization and localization of language and memory
• prediction of post-operative cognitive outcome
• role of simultaneous EEG-fMRI
Role of fMRI in epilepsy

Presurgical evaluation / mapping of eloquent cortex:

- motor function ⇒ ECoG
- Language lateralization ⇒ Wada test
- Language localisation ⇒ ECoG
- Memory function ⇒ Wada test?
- Interictal epileptiform activity ⇒ depth recording
Role of fMRI in epilepsy

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<table>
<thead>
<tr>
<th>Task</th>
<th>dorso-lateral PFC</th>
<th>superior PFC</th>
<th>superior temporal</th>
<th>ventro-lateral temporal</th>
<th>ventral occipital</th>
<th>angular gyrus</th>
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<tbody>
<tr>
<td>Listening vs. rest</td>
<td>Bil</td>
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<td>Bil</td>
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<tr>
<td>Reading sentences vs. rest</td>
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<td>Bil</td>
<td>L&gt;R</td>
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<td>Object naming vs. rest</td>
<td>Bil</td>
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<td>L&gt;R</td>
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<td>Semantic decision vs. tone</td>
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<td>Word generation vs. Rest</td>
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Binder et al. Epilepsia 2002
“Atypical” language dominance

- epilepsy ~25%
- controls ~2%

Woermann et al, Neurology 2003
Janecek et al, Epilepsia 2013
“Atypical” language dominance

- epilepsy ~25%
- controls ~2%

High discordance between WADA / fMRI:

- Bilateral language representation
- Interhemispheric dissociation

Woermann et al, Neurology 2003
Janecek et al, Epilepsia 2013
“Atypical” language dominance

- Early seizure onset
- Vascular pathology

Interhemispheric dissociation:

- Left (temporal) focus
- Left handedness

Berl et al.,
Annals of Neurology 2013

Language Localisation: fMRI vs WADA

- Left temporal focus
- Early seizure onset; left (hemisphere) vascular pathology
- Left handedness
Prediction of post-op language: fMRI vs WADA

Sabsevitz et al., Neurology 2008
Janacek et al. Epi Behav 2013

Bonelli et al., Epilepsia 2012
• ATLR leads to seizure freedom in up to 70% of patients with medically refractory TLE
• ATLR may lead to memory impairment

Prediction of post-operative memory deficits: „holy grail“ of fMRI
Prediction of post-operative memory deficits „holy grail“ of clinical imaging

- ATLR leads to seizure freedom in up to 70% of patients with medically refractory TLE
- ATLR may lead to memory impairment
- Prognostic indicators for memory decline
  - preoperative memory performance
  - Structural MRI – hippocampal volume
  - Age at epilepsy onset
  - Language dominance on fMRI/ IAT
  - Functional MRI
Limitations of fMRI

- Noise
- Distortions/signal loss
- Subject movement

covert responses
temporal pole
patients > normals
## Limitations of fMRI

- **Noise**
  - covert responses
- **Distortions/signal loss**
  - temporal pole
- **Subject movement**
  - patients > normals

### Paradigm

<table>
<thead>
<tr>
<th>Neuroscience</th>
<th>Clinical fMRI</th>
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<tr>
<td>stimulus</td>
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<tr>
<td>performance</td>
<td>controlled</td>
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<tr>
<td>task</td>
<td>complicated</td>
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<td>baseline</td>
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<td>subtraction</td>
<td>specific component</td>
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<tr>
<td><strong>Subjects</strong></td>
<td><strong>Groups of</strong></td>
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<tr>
<td>healthy controls</td>
<td>vs</td>
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<tr>
<td></td>
<td><strong>Individual</strong></td>
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Limitations of fMRI

Richardson, Nat Neurosci 2004

Postoperative verbal memory change

Left-right hippocampal encoding activity difference

R² = 0.82
P = 0.00027

Neuroscience

Clinical fMRI

Subjects

Groups of healthy controls vs Individual patients

Paradigm

Neuroscience

Patients

stimulus

event

- event-related

blocked

performance

controlled

variable

task

complicated

Simple

Neuroscience

Clinical

fMRI

Subjects

Groups of healthy controls vs Individual patients
Limitations of fMRI

Richardson, Nat Neurosci 2004

- Noise
- Covert responses
- Distortions/signal loss
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Paradigm
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Neuroscience Clinical fMRI

Subjects Groups of healthy controls vs Individual patients

Postoperative verbal memory change

Richardson, Nat Neurosci 2004

\[ R^2 = 0.82 \]

\[ P = 0.00027 \]
memory encoding fMRI
Study Design

10 pictures  10 words  10 faces

ALARM

Post-scanning recognition test:
- outside scanner
- 60 min delay
- 50% novel items
- random

Button-press response:
Pleasant or unpleasant

Button-press response:
“old” or “new”

Powell et al, Neuroimage 2005; Bonelli et al., Brain 2010
Prediction of post-op memory deficits

greater ipsilateral anterior HC activation correlated with greater verbal memory decline

Encoding words vs change in verbal learning

Bonelli et al., Brain 2010
Prediction of post-op memory deficits

greater ipsilateral anterior HC activation correlated with greater verbal memory decline

greater ipsilateral (posterior) HC activation correlated with better verbal memory outcome

reorganisation within ipsilateral TL

Encoding words vs change in verbal learning

Bonelli et al., Brain 2010
post-op memory encoding fMRI
post- > pre-operative L TLE

correlation with verbal learning outcome

Bonelli et al., Brain 2013
Bonelli et al., Brain 2013

post-op memory encoding fMRI
post- > pre-operative L TLE

correlation with verbal learning outcome
Summary: memory encoding in TLE

- hippocampal connectivity: increased to posterior hippocampus → better outcome

- pre-op increased activity in posterior hippocampus: → better post-op outcome

- Pre > post-op activation in posterior hippocampus: → better post-op outcome

- Post > pre-op activation in posterior hippocampus: → poor post-op outcome
language fMRI: effect of seizures

After seizure cluster

Listening  Repetition  Semantic fluency  Phonological fluency

Right

Two weeks later

Left

No BOLD changes
Discordant
Some concordance
Entirely concordant

Chaudhary et al.
Brain 2012
EEG-fMRI: common effects of interictal discharges

Laufs et al, Neurology 2011
fMRI in Epilepsy: Summary

• Altered task-specific activations in TLE: intra-/inter hemispheric re-organization

• Seizures can disrupt networks partially and temporarily

• Evidence for common seizure-modulating site

• fMRI allows exploration of specific effects at network level, complementing neuropsychological assessment
Consider **WADA**, if

- fMRI is **not** possible (e.g. VNS, claustrophobia, LD,...)
- L TLE and R MTL pathology on MRI/EEG
- R TLE and L MTL pathology and R language dominance
fMRI in Epilepsy: Impact on Clinical Care and Practice

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- patient can perform task
- overt responses (microphone, decision-making,..)
- event-related, or bilaterally activating memory paradigms available in centers with experience in healthy controls
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Consider **fMRI**, if

- patient can perform task
- overt responses (microphone, decision-making,..)
- event-related, or bilaterally activating memory paradigms available in centers with experience in healthy controls

Consider **EEG-fMRI**, if

- patient has frequent inter-ictal discharges, or frequent focal seizures without significant movement
Prediction of post-op memory deficits

Hippocampal connectivity in left TLE

Task positive network: DLPFC, hippocampus
Task negative network: Precuneus, anterior cingulate

Blue arrows: Decreased connectivity intra hippocampus.
Red arrows: Increased connectivity to posterior hippocampus

Sidhu et al. in preparation