Methods in brain imaging research

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Contents of the talk

1. Behavioural methods (”hearing tests”)
2. Animal models
3. Recording from single cells and cell populations
4. EEG and ERP
5. MEG
6. PET
7. MRI and fMRI
8. Optical imaging
9. Transcranial magnetic stimulation

Keep in mind …

- All research methods are limited
- The limitations differ between the methods
- All methods have ”The Best Question”, that is, the type of question that the methods answers with most accuracy and reliability
- When you have a question, you must choose the method accordingly
- When you have a method, you must choose the question accordingly

fMRI, PET

EEG, MEG

Warning!

- We know so little with brain imaging methods.
- The are many important questions related to music that can not be answered with brain research.

1. Behavioural methods

- Many types of questions related to sound features, qualitative and quantitative
- Very time-consuming when accuracy is required
- Different test types for different age groups, types of subjects, etc.
- Typically possible after age 5 years
- Also, respiration, skin conductance, muscle relaxation etc can be measured (”lie detector”)

Subjective and objective variables

- Subjective measures
  - Loudness estimation, pitch matching, judgments of “sound quality”, etc.
  - Require introspection
  - Subject to non-sensory biases
- Objective measures
  - Stimulus detection, discrimination
  - A measure of performance: There must be a correct answer.
  - Effects of bias can be separated from sensitivity using *Signal Detection Theory*.

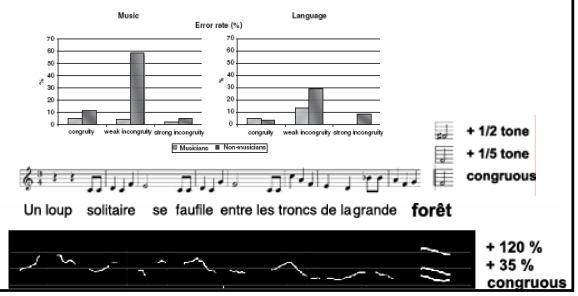
Example: loudness scaling

- Question: How is the perceived loudness of sound A related to the loudness of sound B?
- Possible study methods:
  - Magnitude estimation: Assign a number to theloudness of a sound
  - Magnitude production: Adjust the level of a sound to match a number
  - Ratio estimation: What is the loudness ratio of two sounds? (e.g. half, quarter, two, four, etc.)
  - Ratio production: Adjust the level of the second tone so that it is half/quarter/twice asloud as the first tone.

Question: How well do children notice changed pitches in music and speech? Does musicianship play a role here?

Children are asked to press the button when a melody or the prosody is ”wrong”. Musicians are more accurate in both tasks.

Moreno and Besson 2006



Head-turn method

- A puppet performance is ongoing on the right and is not related to the sounds.
- When the sounds are changed, a new performance is available for a very short time on the left.

Head-turn method

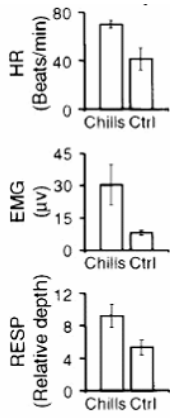
- If the baby notices the change in the sounds, she/he has time to see the 2nd show
- Statistical analysis of the results
- Question: can she/he detect the change?

Auditory preference method

- When the baby watches the screen, sound 1 is played
- When the baby looks away, silence
- When the baby looks again, sound 2 is played, etc.

Auditory preference method

- Statistical comparison of looking times
- Question: Which sound is preferred by the infant?
- Less than 4 months: familiar sounds, over 8 months, novelty



Bodily reactions to emotional music

- Each subject brings own music that elicits ”chills”
- Measurements are performed from heart rate, muscle tension and respiration rate (”lie detector”)
- Each measure shows a clear difference compared to ”chill-music” from other subjects

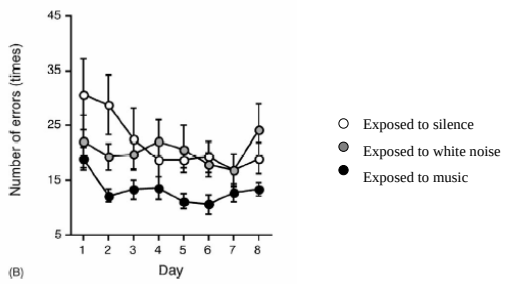
Blood & Zatorre, PNAS 2001

2. Animal models

- Monkey, rat and mouse are the most used animals to act as human models of hearing
- Monkey auditory system is very well known (but less well than the visual system)
- From animals, direct measurements from the brain are possible
  - Very accurate results in time and space dimensions
- Questions related to language and music are difficult to study

Question: Does music help mice to concentrate in a maze test?

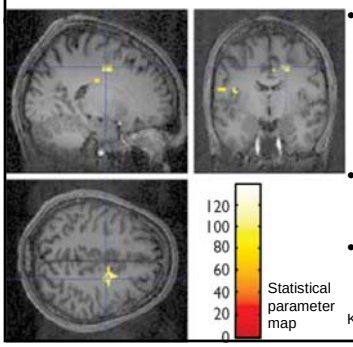
Mice who had been exposed to music during the second half of pregnancy were faster and made less errors in the maze. Chikahisa et al., 2006



3. Single cell recordings

- Available in humans during brain surgery and in planning phase of operations
- Typically patients are pre-operative epilepsy patients but sometimes also people suffering from severe mental illnesses or parkinson disease
- Catherine Liegeois-Chauvel from Marseille is the pioneer of this work in the field of music

Example: recognizing happiness and saddness in music

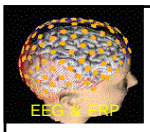


- Question: which parts of the brain are involved in recognizing happiness and saddness in music?
- Intracranial electrodes prior to brain surgery
- Orbitofrontal and cingulate cortices

Khalfa et al., 2005

4. EEG and ERP

- Electroencephalogram, event-related potentials
- Nowadays quite cheap
- Possible to do for all age groups starting from birth
- Comfortable for infants and children, adults, elderly people, patients, etc.
- Possible to move during the experiment, play a musical instrument etc.



ERP

- EEG is averaged into event-related potetials or ERP according to sound/event onset
- Temporally very accurate
- Direct measure of action in the nerve cells
- Best question: ”How does this *process** change in the brain if I change the task or the sounds?”

**process*= perception, memory, attention, ...

ERP in infants and neonates

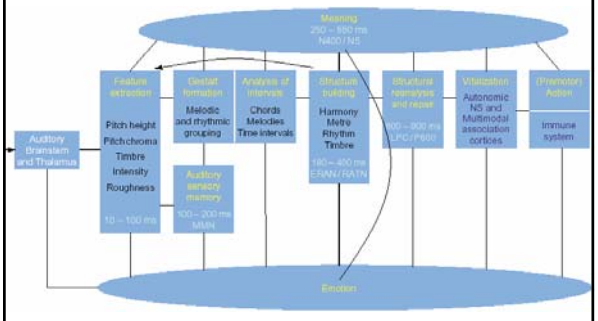
The more channels you have (up to 100), the better spatial accuracy you can achieve.

These **processes** can be studied

Sound onset	Sound selection	Attention
Expectancy	Comparison	Memory trace
Re-allocation of attention	Semantics	Error

These **ERPs** reflect the processes

Sound onset P50, N1	Sound selection PN, P300	Attention N1, PN, P3a, P300
Expectancy N1, MMN	Comparison MMN	Memory trace MMN
Re-allocation of attention P300,LDN,RON	Semantics N400	Error RON

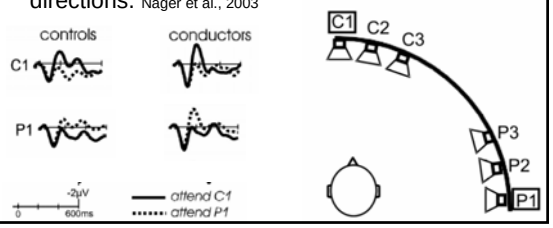


The neurocognitive model of music perception by Stephan Koelsch

Attention towards a direction

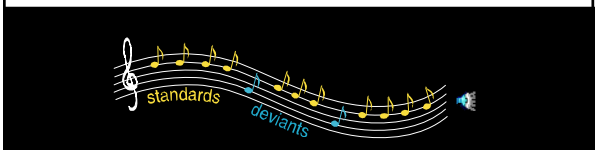
Question: How does attention towards a specific direction affect to sound processing in conductors?

Conductors can shut off sounds from the other directions. Nager et al., 2003



What is MMN?

- ERP to a change in a sound stream
- Reflects the action of the short-term memory
- First ”cognitive” response
- In infants, recorded during sleep
- Does not require attention



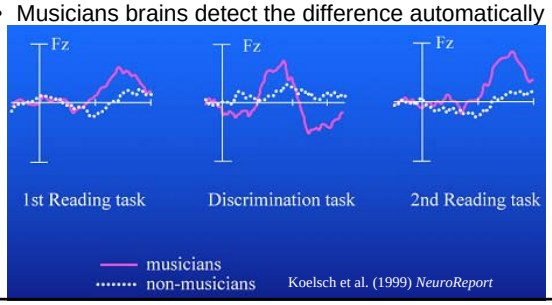
Memory trace

- Standard sounds automatically build up the memory trace
- A new sound is compared to the trace
- If a difference between the incoming sound and the trace is observed, MMN is elicited
- Amount of difference, speed of presentation

Näätänen&Winkler:The concept of auditory stimulus representation in cognitive neuroscience. Psych Bull vol.125 (2000)

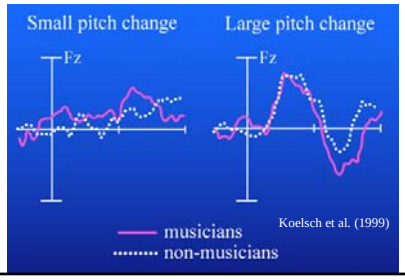
Minor changes in sound frequency

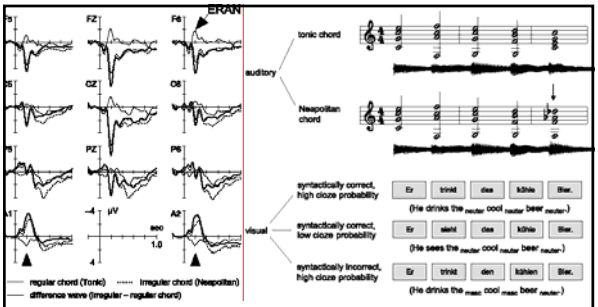
- ERP: G-major chord, sometimes slightly mistuned
- Musicians brains detect the difference automatically



More accurate perception

- ERP: G-major chord, sometimes slightly mistuned
- Musicians brains notice a smaller difference



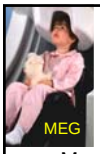


- Koelsch et al., 2006
- Brain responses to syntax errors in language and music

5. MEG

- Very similar to EEG and ERP
- Not available in all hospitals and research centers
- Possible to do for all age groups including fetuses

MEG



- Magnetoencephalography or MEG or ”magnetic EEG”
- The magnetic counterpart of EEG and ERP (ERF)
- Temporally very accurate, records directly the activity of neurons, can separate hemispheres well, has potential also for sound source location analysis
- Best question: ”How does this *process** change in the brain if I change the task or the sounds?” ”Do these two processes have the same locations in the brain?”

**process*= perception, memory, attention, ...

Child MEG

The child has to keep his/her head still during the recording.

Watching videos, laying down…

Infant MEG

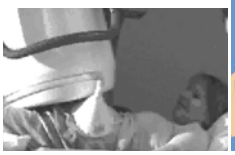
Infant-MEG

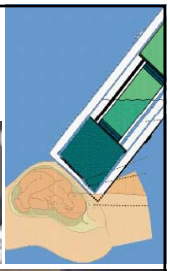
- Infants are recorded in MEG during sleep
- Simultaneous ERP and MEG is possible
- In MEG, only one hemisphere at a time with instruments dedicated to adults
- Best question: ”Is the infant’s brain so developed that we can see this *process* when we play these sounds?”

Fetal MEG

Neuromag-99

Flat-bottom MEG/MKG
BioMag Laboratory, Helsinki





SARA

SQUID Array for Reproductive Assessment

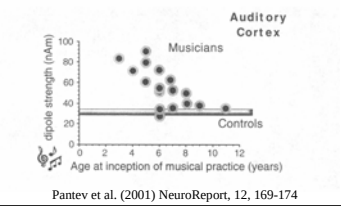
Little Rock
Arkansas USA

Fetal MEG

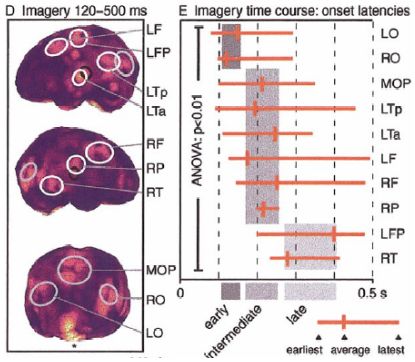
- ERP is not possible during the fetal period
- MEG is possible since the maternal tissues are ”invisible” to magnetic fields
- Completely safe
- Practically possible only when the head of the fetus is fixed (weeks 28 – 42)
- Best question: ”Can this *process* be observed in fetuses of this age?” ”How repeatable is it?”

ERF study of sound detection

- With MEG, ERF
- Musicians responses to sound onset are stronger
- Especially in those who started young



Pantev et al. (2001) NeuroReport, 12, 169-174



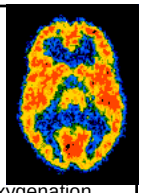
Schürmann et al.

Responses to imaging sounds from written notes

6. PET

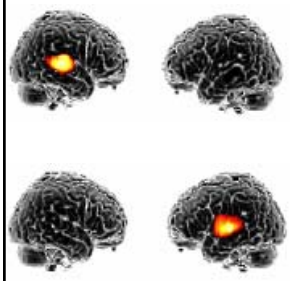
- Due to injection of radioactive substance, only one recording per male adult per year
- The use of PET is decreasing after fMRI was invented
- PET can also be used to track GABA, serotonin, etc etc.

PET



- PET = positronemissiontomography
- Picture of difference of brain blood volume, oxygenation, transmitter (GABA, serotonin, etc.) between two conditions (30 minutes)
- Quite accurate spatial resolution, temporal resolution 30 minutes
- Best question: ”Which *areas* in the brain are active in this task?” ”Which *areas* change their activity if I change the task or the sounds?” ”Is this transmitter important in this task?” ”Is there a difference in the activity of this transmitter between these two groups of participants?”

Right hemisphere is specialized to musical sound short-term memory



- PET study
- C-major vs c-minor: right hemisphere
- /o/ vs /e/: left hemisphere

Tervaniemi et al.

7. MRI and fMRI

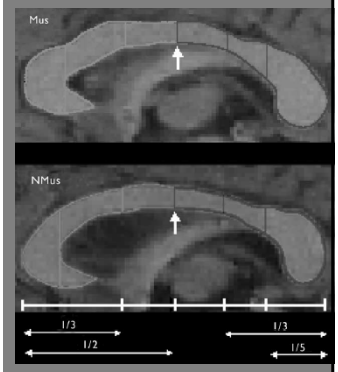
- MRI is structural imaging (”picture” of brain tissue)
- fMRI is functional imaging, this is what the public knows to be ”brain imaging”

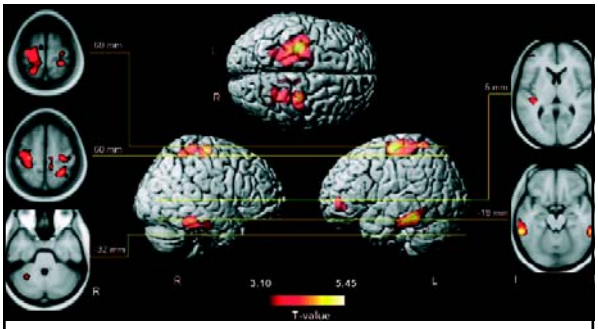
MRI

- MRI = magnetic resonance imaging
- Picture of brain tissue with different parameters emphasizing
  - Cortical structures, thickness etc.
  - White matter structures
  - White matter fiber directions
- Best question: ”Which *areas* in the brain differ in these two groups of participants?”
- Typically large groups are needed since there are large individual variations in brain structures

- Several studies show that the corpus callosum (connecting the left and right cortical areas) is larger in musicians. Corpus callosum is needed when a motoric task involves two hands, for example.

  Lee et al., 2003

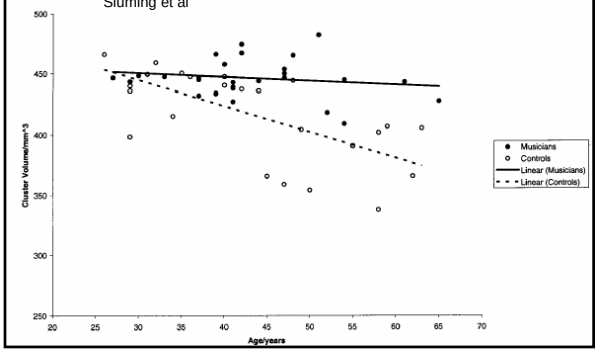




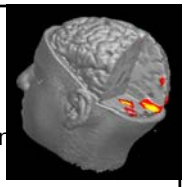
Differences in the thickness of cortex between musicians and non-musicians Gaser and Slaug

Temporal cortex thickness is lost with normal ageing. Musicians loose less thickness.

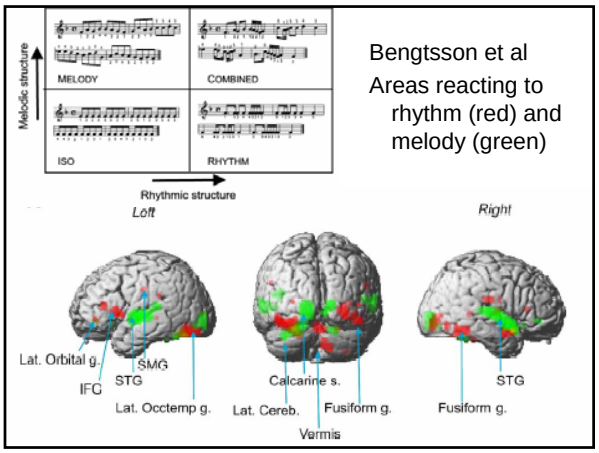
Sluming et al



fMRI



- fMRI = functional magnetic resonan imaging
- Picture of changes in blood oxygenation level
- Very accurate spatially (accuracy is only compromized close to large veins and arteries)
- Temporally less accurate: neurons -> oxygen
- Best question: ”Which *areas* in the brain are active in this task?” ”Which *areas* change their activity if I change the task or the sounds?”

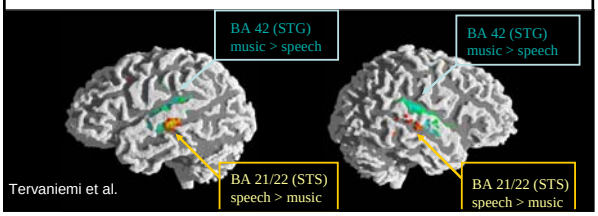


Bengtsson et al

Areas reacting to rhythm (red) and melody (green)

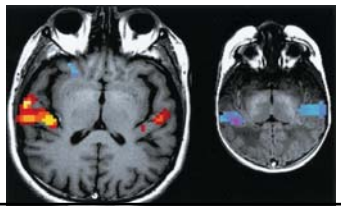
Areas specialized to musical sounds

- Both hemispheres react to speech and music
- More areas that react to music on the right
- More areas that react to speech on the left



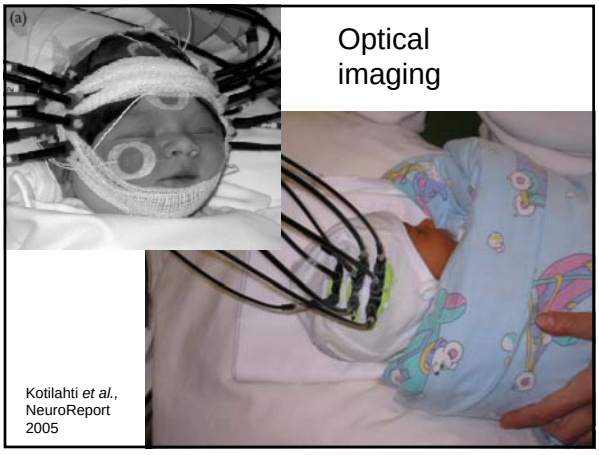
fMRI in infants

- In adults, BOLD (Blood oxygenation level dependent signal) increases in auditory areas when sounds are played. In infants it either increases or decreases Anderson et al 2001



8. Optical imaging

- The only method trying to combine neural activity measures and metabolic measures
- Pulses of near infra-red light are directed towards the brain
- Reflection, transmission and absorption of this light is measured
- These parameters depend on oxygenation of blood, and *may* also depend on neural activity



Optical imaging

Kotilahti *et al.*, NeuroReport 2005

9. Transcranial magnetic stimulation or TMS

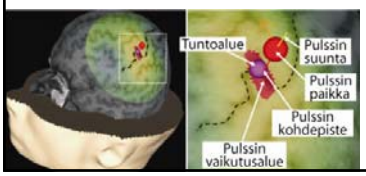
- Forces the brain to be active with very short electromagnetic pulses

Magnetic stimulation

- NBS = Navigated Brain Stimulation
- TMS = Transcranial Magnetic Stimulation
- Stimulation activates the brain below the coil
- Best questions
  - ”Which brain areas are connected together?”
  - ”How reactive is the brain tissue in this task?”
  - ”How important is this brain area in this task?”
- Only used in adults, which certain criteria (no history of epilepsy etc.)

Sensation

- Question: What happens to somatosensory sensation experience if the primary somatosensory area is not functional?
- If functionality is blocked between 50 and 200 ms after stimulation, sensation disappears



Hannula et al.