Neuroethology: comparative fMRI

Attila Andics
1. fMRI
1. fMRI
2. dogs: why and how
3. dog fMRI studies
4. auditory dog fMRI studies
Anatomical imaging methods

from Posner & Raichle, Images of Mind
MRI vs. fMRI

MRI:
- High resolution (1 mm)
- One 3D volume

fMRI:
- Low resolution (~3 mm)
- Series of 3D volumes (i.e., 4D data)
Begining of MRI

1977: Az első MR kép az emberi testről

2 perc / voxel
4 óra / slice…
1990: Ogawa először talál összefüggést szenzoros ingerlés és agyi erek MR képe között (a BOLD jel felfedezése)
1992: Ogawa et al. és Kwong et al. először mutat be funkcionális képeket
First functional images

Flickering Checkerboard
OFF (60 s) - ON (60 s) - OFF (60 s) - ON (60 s)

Source: Kwong et al., 1992
fMRI boom

Friston, 2010, Science
Take a proton...

Páratlan számú protont vagy neutront tartalmazó atommagok
$^1\text{H}$, $^{13}\text{C}$, $^{19}\text{F}$, $^{23}\text{Na}$, $^{31}\text{P}$

$^1\text{H}$ hidrogén (proton)
  sok van belőle (5 x $10^{27}$ proton egy 70 kg tömegű emberben)
erős jeleket bocsát ki
Without magnetization

- Protonok orientációja: random
Protons in a big magnetic field

$B_0 \parallel M_z > 0$

$M_{xy} \approx 0$

Fentről ugyanez:

$M_z > 0$

$M_{xy} \approx 0$

Longitudinal magnetization $M_z$

Transverse magnetization $M_{xy}$

longitudinal axis

transverse plane
Add RF pulses... (excitation)

90°RF Pulse

$M_z \sim 0$

$M_{xy} > 0$

$B_0$

Fentről ugyanez:

Longitudinal axis

Longitudinal magnetization $M_z$

Transverse magnetization $M_{xy}$
Measure RF pulses... (echo)

- A protonok fokozatosan visszatérnek eredeti konfigurációjukba, eközben mérjük a kibocsátott rádiójeleket.
Measure RF pulses... (echo)

**TR, TE, T1, T2**

**Long T2**
- (e.g., CSF)

**Short T2**
- (e.g., fat)

**Long T1**
- (e.g., CSF)

**Short T1**
- (e.g., fat)

**Time to Repetition = TR (s)**

**Time to Echo = TE (ms)**

**Longitudinal Magnetization $M_z$**

**Transverse Magnetization $M_{xy}$**

**T1 relaxation:** milyen gyorsan rendeződnek vissza a protonok a fő mágneses tér mentén

**T2 relaxation:** milyen gyorsan fogy el a protonok pulzusból nyert energiája

**T1-weighted anatomical image**

**T2-weighted anatomical image**
Local activity increases...
Neuronal response

Physiological changes

Deoxyhemoglobin changes

BOLD signal changes
(BOLD = Blood-Oxygen-Level-Dependent)
The linear relationship between neural activity and BOLD signal
2. dogs: why, how?
Dog fMRI
The DOG model

• Evolutionary distance makes it EXCITING

• Social proximity makes it FAIR

• Cooperativity makes it DOABLE

The first non-human species to participate in non-invasive brain imaging experiments with no restraints

Andics A, Miklósi Á, 2018, Neuroscience & Biobehavioral Reviews
TRAIN DOGS TO BE HAPPY VOLUNTEERS IN THE SCANNER

• Step-by-step (lying, headphones, noise)

• Positive reinforcement (social and food)

• Model-rival training technique

• 5-20 sessions before scanner

• 5-9 sessions in scanner
Head motion during fMRI test
SOME CHALLENGES

• Training time limits subject pool

• Small brain, individual variation

• No standard fMRI preprocessing pipeline

• No standard nomenclature

• Air cavities in the head, susceptibility artefacts

• Press the button?
DOG BRAIN, HUMAN BRAIN

Andics A, Gácsi M, Faragó T, Kis A, Miklósi Á, 2014, Current Biology
**DOG BRAIN, HUMAN BRAIN**

<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chinese Crested</td>
<td>Golden Retriever</td>
</tr>
<tr>
<td>~2.3–5.4 kg</td>
<td>~27–36 kg</td>
</tr>
</tbody>
</table>

Coronal slice

3D-reconstruction

Axial slice

INDIVIDUAL VARIATION
CREATING AN MR-BASED DOG BRAIN ATLAS

Kálmán Czeibert
3. dog fMRI studies
Tóth et al. 2009 (abstract), 2011(thesis)

**Aims**
- Developing a method to scan conscious dogs
- Comparing images from conscious and sedated dogs

**Stimuli**
- Projected image of a treat
- Somatosensory stimulation

**Scanning**
Block design

N=2
Tóth et al. 2009 (abstract), 2011 (thesis)

Projected image of a treat

Somatosensory stimulation

n. caudatus

area sensorica contralateralis
Tóth et al. 2009 (abstract), 2011(thesis)

Findings
- Developed successful training methodology
- Comparable image quality from conscious dogs
- Activation in the nucleus caudatus both in response to the image of the treat and to the tactile stimuli

Conclusions
- Dogs can be trained to lie still continuously for 5-6 minutes in the scanner
- High quality images from unrestrained dogs
Aims
- Develop a methodology
- Determine which brain circuits respond differentially to human hand signals

**Stimuli:** two types of hand signals

**Scanning:** two runs, rewards given after „reward” trials (longest „still” period was 24 sec)
- Region of interest analysis vs. whole brain analysis

N=2
Berns et al. 2012 Functional MRI in Awake Unrestrained Dogs

Findings
- Successful functional scans with the proposed methodology
- Observed caudate activation in 2 dogs in response to the hand signal denoting reward versus no-reward

Conclusions
- Dogs are able to hold still in the scanner long enough (note: longest still period: 24 s)
- Findings are in line with the reinforcement learning literature
Motion thresholds

Berns et al. 2012
Aims
-Determine the replicability and heterogeneity of these results
-Report improvements in training, image acquisition, and analysis of fMRI data

Stimuli: two type of hand signals
Scanning: two runs, total of 40 trials,
Food reward delivered after „reward” trials
→ movement artefacts & fMRI

N=13
Berns et al. 2013 Replicability and heterogeneity of awake unrestrained canine FMRI responses
Findings
-8 of 13 dogs had a positive differential caudate response
-one dog was a negative outlier and was subsequently excluded from further analyses

Conclusions
-caudate responses in awake unrestrained dogs during fMRI are reliable and consistent
-20 repetitions seemed a good compromise between signal detection and habituation
Jia et al. 2014 Functional MRI of the olfactory system in conscious dogs

Aim
Compare the response of lightly sedated dogs and fully conscious ones to odorants of different concentrations

Stimuli: odor intensity (from single mixture)

Scanning: four runs, 5 min each

N=6 Labradors
Jia et al. 2014 Functional MRI of the olfactory system in conscious dogs
Jia et al. 2014 Functional MRI of the olfactory system in conscious dogs

Findings
-The olfactory bulb and piriform lobes were activated in both awake and anesthetized, the frontal cortex mainly in conscious dogs
-Differences regarding to odor intesity in the olfactory bulb, piriform lobes, cerebellum, and frontal cortex

Conclusions
-Device and proposed a training procedure for imaging conscious dogs in an ecologically valid setting
-Higher order brain structures were activated mainly in conscious dogs
Berns et al. 2015 Scent of the familiar

**Question**

Whether dogs’ response toward odors are based on species (dog or human), familiarity, or a specific combination of these

**Stimuli:** scents from familiar/unfamiliar dogs/humans + own scent

**Scanning:** two runs, each lasting about 7–14 min, 9 reward trials during each runs
Findings
- The OLF ROI was significantly activated to all scents (no difference between scents)
- CD ROI was not active to all scents, significant difference between the scents (familiar human)

Conclusion
- The caudate nucleus prefers familiar scents
Training
Human faces > Objects

[Diagram showing brain regions activated for different stimuli]
Peristimuli response

- **Human Faces**
- **Objects**

% BOLD signal change vs. Time from stimulus (s)

Visual Stimulation
Dog faces > Objects

[Graph showing neural activity compared to baseline with dog faces and objects]

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Dog Faces</th>
<th>Baseline</th>
<th>Objects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>12.25 s</td>
<td>7 s</td>
<td>12.25 s</td>
<td>7 s</td>
</tr>
</tbody>
</table>
Posterior – anterior pattern

**Visual:** Objects, dog faces, human faces

**Faces:** Dog faces, human faces

**Human faces**
4. auditory dog fMRI studies
Voice sensitivity in the human brain

Belin et al., 2000, Nature
Voice sensitivity in the primate brain

Figure 1  Auditory cortex regions preferring species-specific vocalizations in two awake monkeys.

Petkov et al., 2008, Nat Neurosci
RESEARCH QUESTIONS

- How do dogs (vs humans) process emotional vocalizations?
  - Voice area?
  - Cross-species emotions?

- How do dog brains process human speech?
  - What is said?
  - How is it said?
  - Who says it?
SPARSE SCANNING FOR AUDITORY EXPERIMENTS

Diagram showing STIMULI at 8 s, 2 s, and 10 s intervals. A graph illustrates BOLD signal over time from activity onset.
Dog brain, human brain
AUDITORY REGIONS

Auditory regions in dogs

Auditory regions in humans

VOICE AREAS IN DOG AND HUMAN BRAINS

HAPPY OR UNHAPPY?

Faragó et al., 2014, Biology Letters
VOICE PROCESSING IN THE DOG BRAIN

• The same auditory region is specialized for conspecific sounds in dogs and humans

• Dogs and humans use similar brain mechanisms to process vocal emotions

Andics A, Gácsi M, Faragó T, Kis A, Miklósi Á, 2014, Current Biology
SPEECH PROCESSING IN THE DOG BRAIN

WORD MEANING AND INTONATION

Appi!

Help!

Pomocy!

Segítség!

Yardım!

Membantu!

Siza!

Aiuto!
VERBAL PRAISE

• Signalled both lexically and intonationally

• Used in dog-directed speech as social reward

• Good understanding of primary reward regions

Russo and Nestler, 2013
MANIPULATING REWARD VALUE IN WORD MEANING AND INTONATION

<table>
<thead>
<tr>
<th></th>
<th>GOOD DOG!</th>
<th>good dog</th>
<th>AS IF!</th>
<th>as if</th>
</tr>
</thead>
<tbody>
<tr>
<td>Word</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intonation</td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

![Image of a dog and a person in a medical scan room]
**Word meaning and intonation**

**Conditions**

- Praise words, praising intonation \((Pp)\)
- Praise words, neutral intonation \((Pn)\)
- Neutral words, praising intonation \((Np)\)
- Neutral words, neutral intonation \((Nn)\)

**Acoustic variation of stimuli**

**Neural reward responses to verbal praise?**

**Which matters: what we say or how we say it?**

DOG AUDITORY REGIONS RESPONSIVE TO SPEECH

LATERALIZATION TEST

Right hemisphere bias for processing meaningful words

Auditory region processes acoustic cues of intonation, and is functionally linked to reward regions

PRIMARY REWARD CIRCUIT

Reward response if both word meaning and intonation fit

Human-analogue Processing of Meaning in Dogs

- Separation of word meaning and intonation
  - Lateralized processing of meaningful words, independently of intonation
  - Auditory region for intonation, independently of word meaning

- Integration of word meaning and intonation
  - Primary reward regions rely on both to process reward value of speech

- Evidence for lexical representations in the dog brain
  - Mechanisms? Speaker dependency?

SUBCORTICAL SHORT-TERM FMRI ADAPTATION REFLECTS INTONATION SENSITIVITY

Gábor et al., under review – POSTER #40 TODAY!
CORTICAL LONG-TERM FMRI ADAPTATION REFLECTS LEXICAL MEANING SENSITIVITY
ATTACHMENT-DEPENDENT PROCESSING

Gábor et al., in prep.
CONCLUSIONS

• Vocal social perception involves human-analogue neural mechanisms in dogs

• Linguistic representations in a non-primate mammal
  – Multilevel adaptation reveals a human-analogue hierarchy for lexical processing
  – Why only humans use words must be revisited

• Neural measures of how pleasurable a verbal praise is
  – Primary reward circuitry reflects what is said, how and by whom
  – Functional connectivity between auditory and reward regions

• Dog is a suitable model for comparative social neuroscience
FUTURE DIRECTIONS

- Voice vs face areas, spoken vs sign language
- Word learning, learning a new language, meanings in the brain
- Relate fMRI data to resting-state networks, sleep EEG, awake ERP
- Involve other species
Face processing in dogs
Olfactory fMRI?
References


