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BRAIN, DEPRESSION
AND
PSYCHOANALYSIS

BRAIN RESEARCH
INSTITUTE
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GENERAL VIEW OF NEUROBIOLOGY ON MENTAL DISORDERS

Mental affective disorders such as anxiety disorders, depression, PTSD, bipolar disorders, as well as borderline personality disorder and antisocial behavior appear to have a common etiology:

- Genetic „load“, mostly gene polymorphisms related to the 5-HT and CRF-ACTH-cortisol metabolism
- Deficits in brain development, mood and stress regulation
- Early stress / psychotraumatization (neglect, physical or sexual abuse)
- Imbalance between cortical-cognitive and subcortical-limbic centers as well as between cortical and subcortical limbic centers
BRAIN AND DEPRESSION

**Functional Model:** Breakdown of cognitive control of subcortical activity (amygdala) by dIPFC (Cortical-limbic imbalance)

- Decreased activity: dorsolateral prefrontal cortex (*DLPFC, left blue*)
- Increased activity: *Amygdala (right red)*
An analysis of functional neuroimaging studies of dorsolateral prefrontal cortical activity in depression

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Meta-analysis: Fitzgerald et al. (2006 / 2008)

- dIPFC: hyper- as well as hypo-activation at rest and at emotional provocation are found.
- Role of amygdala unclear or unstudied
- No consistent model of neurobiological basis of depression so far!
Studies on the effect of antidepressants (mostly SSRI) and of psychotherapy (CBT, IPT – no PA) are even more inconsistent!
# Therapy effects on depression

<table>
<thead>
<tr>
<th>Study</th>
<th>Therapy, duration</th>
<th>Psychotherapy patients</th>
<th>Controls</th>
<th>Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Brody et al.</strong> (2001a)</td>
<td>IPT, 12 weeks</td>
<td>14 MDD</td>
<td>10 MDD, Paroxetine 16 HC</td>
<td>FDG-PET, resting state</td>
</tr>
<tr>
<td><strong>Martin et al.</strong> (2001)</td>
<td>IPT, 6 weeks</td>
<td>13 MDD</td>
<td>15 Venlafaxine</td>
<td>SPECT, resting state</td>
</tr>
</tbody>
</table>
Effect of psychotherapy on depression

**Intro**
- PFC (Goldapple et al., 2004; Brody et al., 2001a)

**Experiments**
- Ventral ACC (Brody et al., 2001a)
- Dorsal midCC (Goldapple et al., 2004)
- R posterior CC (Martin et al., 2001)
- R Basal ganglia (Martin et al., 2001)

**Perspective**
- Hippocampus (Goldapple et al., 2004)
- L temporal Cortex (Brody et al., 2001)
Problems with brain data

- Heterogeneity across studies
- More heterogeneity across subjects
- Unspecific, non-personal stimuli
The HNPS: Hanse Neuro-Psychoanalysis Study

„Neurobiological and psychometric changes in subjects with depression during psychoanalytic therapy“
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CENTRAL QUESTION:

DOES PSYCHOANALYTIC THERAPY CHANGE BRAIN RESPONSE?
Recruitment

- 20 experienced psychoanalysts of two psychoanalytic institutes
- 24 patients with chronic depression
- Comorbidity: 11 anxiety disorders, 1 eating disorder (SCID)
- 5 drop-outs
- 20 matched controls (sex, age, education)
The HNPS Study

• Beck Depression Inventory

The graph shows the distribution of Beck Depression Inventory (BDI) scores among subjects. The x-axis represents individual identifiers (e.g., A123, B456), while the y-axis represents BDI scores. There are two groups indicated: Kontrolle (blue diamonds) and Patienten (red diamonds).
• OPD – Operationalized Psychodynamic Diagnostics
  – Interview
  – Repetitive dysfunctional interpersonal relations
  – Central (unconscious) mental conflict
    → serve as basis for experiment
- Two control conditions: Relax situation and traffic stress situation (i.e. emotional but not conflict-related)
Individual sentences, derived from OPD

1. I wish to be accepted by others
2. Therefore I do a lot for them
3. That is often too close for them, so they retreat
4. Then I feel empty and lonesome
Experiments (2)

• AAP – Adult Attachment Projective
  – Presentation of 7 pictures – recording of answers
  → attachment representations
  – Critical sentences serve as basis for paradigms
  – Control condition: Neutral sentences describing scene
AAP Experiment

Intro
Depression
Experiments
fMRI
EEG
Perspective

15 month
7 month

AAP 2 Patient Control?
AAP 1 Patient Control
AAP 2 Patient Control
AAP 1 Patient Control

Therapy start
Results

All data presented here are obtained before onset of therapy (measurement point 1).
• Siemens Allegra fMRI Scanner (3 Tesla)
• Read sentences for three alternating conditions
  – Relaxation
  – Unspecific stress in traffic situation
  – OPD generated individual sentences
• 30 minutes presentation of sentences
• Knew sentences in advance
OPD prior to Therapy
----- effects of stimulation -----
OPD prior to therapy
--- effects of stimulation ----

Intro
Depression
Experiments
fMRI
Perspective
OPD prior Therapy
--- effects of stimulation ---

• Conclusion:
  – Increased ACC activation in both controls and patients, when exposed to person-relevant stimuli.

• But are there differences between groups?
OPD prior Therapy
--- effects of group x stimulation ---

Intro
Depression
Experiments
fMRI
Perspective

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OPD prior Therapy

--- effects of group x stimulation ---

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Intro

Depression

Experiments

fMRI

Perspective
In most cases, personally relevant (OPD) sentences evoke increased activity in a large number of cortical areas of patients.
At presentation of OPD sentences increased activity in right / bilateral amygdala in patients
Intro

Depression

Experiments

fMRI

Perspective

• Amygdala
  – processing of emotionally relevant information

• Posterior cingulate:
  – emotional processing word valence decision (Maddock, 2003, HBM)
  – auditory presentation of threat-related words (Maddock, 1997, Psych Res)
  – autobiographical memory retrieval (Maddock, 2001, Neuroscience)
  – ... but many other tasks....

• Sup. Parietal Gyrus
  – concerned with body image and spatial orientations
  – no good explanation yet.
EEG

- AAP and OPD also done while EEG is recorded
EEG-based methods

- Original EEG recording....
EEG based methods

- ... decomposed into frequency patterns (wavelet analysis)
EEG-based methods

• Why frequency analysis
  – coordination of distributed neural activity
  – Results from other patient groups
    • example: Epilepsia, Schizophrenia
EEG - first results: In patients, reduced cortical activity in the upper alpha-lower beta band
General Conclusion

• Worldwide first study to investigate neural correlates associated with psychoanalytical treatment in depression

• 19 patients and 20 healthy controls tested at
  – T1 (begin of therapy)
  – T2 (7-9 months), currently running,
  – T3 (15-20 months) will be finished by 2009

• Results presented are from
  – T1 (pre-treatment)
  – with two procedures (AAP and OPD)
  – and two methods (fMRI and EEG)
Summary fMRI

- Both, AAP and OPD,
  - used individually-tailored stimuli...
  - ... and found neural activations in areas important for
    - mentalizing,
    - self-reflection,
    - emotional processing,
    - social cognition,
    - autobiographical memory retrieval
    - conflict monitoring
Summary fMRI

• AAP:
  – Unresolved controls show more activity in an area involved in cognitive control of emotions

• OPD:
  – Patients show more activity than controls in areas previously shown to be hyperactive in depression (amygdala and putamen) when confronted with their dysfunctional interpersonal relations
Summary EEG results

• OPD:
  – Controls show specific activity in the upper alpha/lower beta band increasing from relaxation to traffic stress to OPD sentences.
  – Patients show deactivations in this band when confronted with their sentences

• AAP:
  – work in progress