

PSYCHOANALYSIS AND NEUROIMAGING: FIRST FINDINGS
FROM THE HANSE-NEURO-PSYCHOANALYSIS STUDY

Anna Buchheim (University of Innsbruck, Institute of Psychology)
Horst Kächele (International Psychoanalytic University Berlin)




University Ulm/ Innsbruck

- Prof. Dr. Anna Buchheim (Project Coordination)
- Prof. Dr. Horst Kächele
- Dr. Henrik Kessler
- Dr. Daniel Wiswede
- Lenka Staun
- Dr. Roberto Viviani

University Heidelberg

- Prof. Dr. Manfred Cierpka
- Michael Stasch

University Magdeburg

- Prof. Dr. Thomas Münte

University Bremen

- Prof. Dr. Dr. Gerhard Roth
- Dr. Peter Erhard
- Prof. Dr. Georg Bruns

University Kassel

- Dr. Svenja Taubner

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REVIEW ARTICLE

Neuroimaging and the functional neuroanatomy of psychotherapy

JOSHUA L. ROFFMAN*, CARL D. MARCI, DEBRA M. GLICK,
DARIN D. DOUGHERTY AND SCOTT L. RAUCH
Department of Psychiatry, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA

ABSTRACT

Background. Studies measuring the effects of psychotherapy on brain function are under-represented relative to analogous studies of medications, possibly reflecting historical biases. However, psychological constructs relevant to several modalities of psychotherapy have demonstrable neurobiological correlates, as indicated by functional neuroimaging studies in healthy subjects. This review examines initial attempts to measure directly the effects of psychotherapy on brain function in patients with depression or anxiety disorders.


Method. *Fourteen published*, peer-reviewed functional neuroimaging investigations of psychotherapy were identified through a MEDLINE search and critically reviewed. Studies were compared for consistency of findings both within specific diagnostic categories, and between specific modalities of psychotherapy. Results were also compared to predicted neural models of psychotherapeutic interventions.

Results. *Behavioral therapy* for anxiety disorders was consistently associated with attenuation of brain-imaging abnormalities in regions linked to the pathophysiology of anxiety, and with activation in regions related to positive appraisal of aversive stimuli. In studies of major depressive disorder, *cognitive behavioral therapy* and *interpersonal therapy* were associated with markedly similar changes in cortical-subcortical circuitry, but in unexpected directions. For any given psychiatric disorder, there was only partial overlap between the brain-imaging changes associated with pharmacotherapy and those associated with psychotherapy.

Conclusions. Despite methodological limitations, initial neuroimaging studies have revealed convergent and mechanistically sensible effects of psychotherapy on brain function across a range of psychiatric disorders. Further research in this area may take advantage of emerging neuroimaging techniques to explore a *broad range of psychotherapies*, with the ultimate goal of improving clinical decision-making and treatment.

Neurobiology of psychotherapy in Depression (2011)

- 9 studies:
 - *Cognitive Behavioral Therapy*, 4 (FDG-PET, SPECT, fMRI)
 - *Interpersonal Psychotherapy 2* (FDG-PET, SPECT)
 - *Behavioral Activation Therapy* for Depression, 1 (fMRI)
 - *Psychodynamic Psychotherapy*, 1 (atypical Depression) (SPECT)



Changes after therapy, baseline

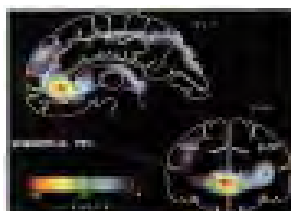
	Therapy	N	Method	Results
Martin et al. (2001)	IPT 6 weeks	13	SPECT	↑ basal ganglia ↑ PFC
Brody et al. (2001)	IPT 12 weeks	14 pat 16 contr	FDG-PET	↓ PFC ↑ inf. temporal ↑ Insula
Goldapple et al. (2004)	CBT 20 sessions	17	FDG-PET	↓ PFC ↑ limbic

Changes after therapy, fMRI

	Therapy	N	Method	Results
Siegle et al. (2006)	CBT	14	fMRI Words	vACC predictive of response
Fu et al. (2008)	CBT 16 weeks	16 pat 16 contr	fMRI faces	↓ amygdala, ant. hippocampus ↓ ACC-sup. fr. gyrus

Paradigms I

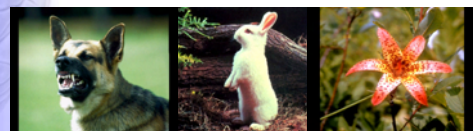
Baseline metabolic activity or perfusion



Drevets et al., Nature 1998

Paradigms II

Standard stimuli in functional neuroimaging of emotion



A Meta-Analytic Study of Changes in Brain Activation in Depression

Paul B. Fitzgerald,^{1*} Angela R. Laird,² Jerome Maller,¹ and Zafiris J. Daskalakis³

¹Alfred Psychiatry Research Centre, The Alfred and Monash University Department of Psychological Medicine, Commercial Rd Melbourne, Victoria, Australia

²Research Imaging Center, The University of Texas Health Science Center San Antonio, San Antonio, Texas

³Centre for Addiction and Mental Health, Clarke Division, Toronto, Ontario, Canada
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Emotional activation studies			
Carli et al., 2004	15/15	fMRI	Response to happy and sad facial (patients versus controls)
Goebel et al., 2005	18/18	fMRI	Response to sad or happy compared with neutral facial (patients versus controls)
Kirsch et al., 2005	12/12	fMRI	Response to concurrent happy or sad memory prompts and facial expressions (patients versus controls)
Kumari et al., 2003	6/6	fMRI	Response to positive negative facial caption pairs compared with neutral (patients versus controls)
Lawrence et al., 2004	9/11	fMRI	Response to happy and sad facial expressions of differing intensity (patients versus controls)
Surguchov et al., 2005	16/14	fMRI	Response to happy and sad, compared with neutral, facial expressions (patients versus controls)

Development of the Stimulus-Material?

- How to capture unconscious and individual material relevant for psychoanalytic psychotherapy?

Research Question

- Hanse –Neuro- Psychoanalysis- Study
- First study on neural correlates of change in patients with major depression during psychodynamic psychotherapy
- Longer observation time (15 months)
- Assessments of individual core conflicts in significant relationships and attachment representations
 - Dysfunctional interpersonal conflicts (OPD)
 - Attachment related conflicts (AAP)
- Sponsored:
 - Hanse Institute of Advanced Studies, Delmenhorst
 - Universities Ulm, Heidelberg und Magdeburg
 - IPA, Köhler-Stiftung
- In cooperation with the Sigmund-Freud-Institute (Prof. Leuzinger-Bohleber: FRED Study)

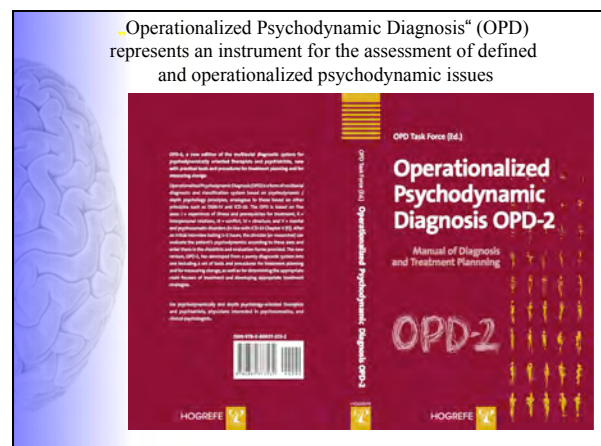
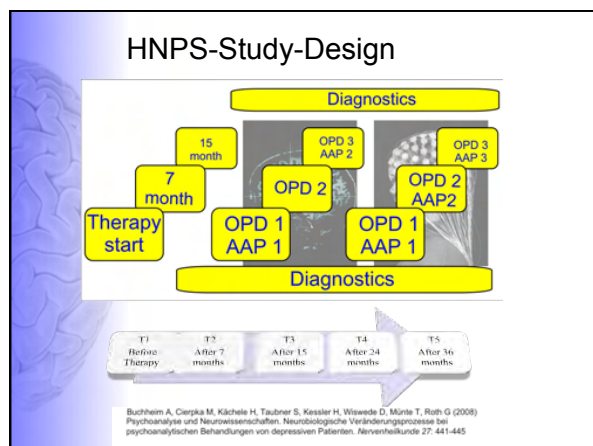
Recruitment

- 20 very experienced psychoanalysts in Bremen
- 20 patients with recurrent Major Depression
- 20 matched controls (age, education, sex)
- Psychoanalytic Psychotherapy: 2-3 sessions per week

Sample

	Patients (N=20)	Controls (N=20)
Age	39.2 (12.7) 20-64 years	37.1 (11.6) 21-64 years
Gender	16 f + 4 m	16 f + 4 m
Education	middle: 7 high: 12	middle: 4 high: 16
Diagnosis (SCID-I)	5.5 MDE (m) Onset 19 years (m) 50% comorbid anxiety disorders	No psychiatric history

Experiments	<ul style="list-style-type: none"> fMRI functional Magnetic Resonance Imaging EEG Electroencephalography
Interviews	<ul style="list-style-type: none"> SCID I/II AAI SPC HSCS OPD AAP Structured Clinical Interview DSM-IV Adult Attachment Interview Scales of Psychological Capacities Heidelberg-Structural-Change-Scale Operationalized Psychodynamic Diagnosis Adult Attachment Projective
Questionnaires	<ul style="list-style-type: none"> SCL 90 BDI DEQ ERQ LEAS Reading the mind in the eyes Symptom Check List Beck Depression Inventory Depressive Experience Questionnaire Emotional Regulation Questionnaire Levels of Emotional Awareness Scale



OPD-Paradigm

The diagram illustrates the OPD-Paradigm as a sequence of cognitive states and actions over time. It is structured as a staircase pattern with four rows of boxes. The first row contains four boxes, the second row contains three, the third row contains two, and the fourth row contains one. Each box contains a text prompt. To the left of each row, a time interval is indicated: 7.5 sec for the first row, 7.5 sec for the second, 7.5 sec for the third, and 7.5 sec for the fourth. The sequence of prompts is as follows:

- Row 1: "and try to think about nothing", "Then I feel empty and listless", "and try to think about nothing", "but he reacts inadequately."
- Row 2: "Try to get the head clean", "That is often too close for them, so they retreat", "Try to get the head clean", "you react to the other driver."
- Row 3: "Please try to relax", "Therefore I do a lot for them.", "Please try to relax", "you were very upset about this"
- Row 4: "Think of your safe place", "I wish to be accepted by others", "Think of your safe place", "the other driver made a mistake"

Below the diagram, four labels are positioned: "Relax" under the first box of the first row, "OPD conflict" under the second box of the first row, "Relax" under the first box of the third row, and "Traffic sentences" under the last box of the first row.

Open Access Society for Neuroscience

Individualized and Clinically Derived Stimuli Activate Limbic Structures in Depression: An fMRI Study


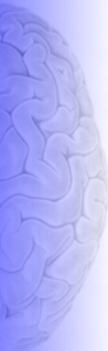
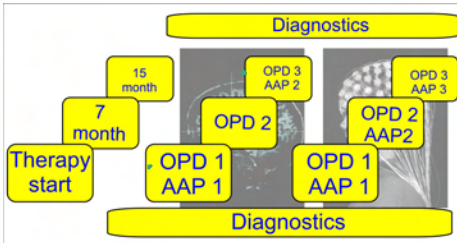
Henrik Kessler^{1,2,3,*}, Svenja Taubner^{1,3}, Anna Buchheim¹, Thomas F. Münte⁴, Michael Stasch⁵, Horst Kächele⁶, Gerhard Roth^{1,3}, Armin Heinecke⁶, Peter Erhard⁷, Manfred Cierpka⁸, Daniel Wawrode^{1,10}

*Helmholtz Institute for Advanced Study (Department of German, 2 Department of Engineering, Medicine and Psychology) University of Ulm, Ulm, Germany; 3Department for Social Therapy, Department and Center of University of Kassel, Kassel, Germany; 4Institute of Psychology, University of Frankfurt, Frankfurt, Germany; 5Department of Neurology, University of Magdeburg, Magdeburg, Germany; 6Institute of Psychology, University of Würzburg, Würzburg, Germany; 7University of Jena, Jena, Germany; 8University of Würzburg, Würzburg, Germany; 9State Research Institute, University of Bremen, Bremen, Germany; 10Bielefeld University, Bielefeld, Germany; 11Department of Psychiatry, University of Bonn, Bonn, Germany; 12Department of Speech Psychology & University of Jena, Jena, Germany

Results: Increased hemodynamic responses in the anterior cingulate cortex, medial frontal gyrus, fusiform gyrus and occipital lobe were observed in both patients and controls when viewing individualized stimuli. Relative to control subjects, patients with depression showed increased hemodynamic responses in limbic-paralimbic and subcortical regions (e.g. amygdala and basal ganglia) but no signal decrease in prefrontal regions.

Conclusions: This study provides the first evidence that individualized stimuli derived from standardized clinical interviewing can lead to hemodynamic responses in regions associated with self-referential and emotional processing in both patients and limbic-paralimbic and subcortical structures in individuals with depression. Although the regions with increased responses in patients have been previously reported, this study enhances the ecological value of fMRI findings by applying stimuli that are of personal relevance to each individual's depression.

Design

Therapy start

7 month

15 month

OPD 1 AAP 1

OPD 2

OPD 3 AAP 2

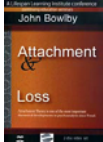

OPD 3 AAP 3

Diagnostics

Diagnostics

Attachment and Depression

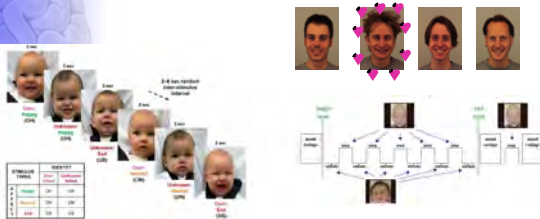
- Attachment theory (Bowlby, 1980) developed in part to explain the origins of depression due to loss



- Internal representations of the self as unlovable and of attachment figures as unloving/untrustworthy

fMRI and Attachment

- Visual individual stimuli (pictures, faces) or passively presented scripts
 - (e. g. Bartels & Zeki 2004, Nitschke et al. 2004, Strathearn et al., 2009)



- Examination of social attachment (maternal or romantic love) mostly in healthy samples

Attachment measure using attachment pictures and assessing attachment representations?

Adult Attachment Projective Picture System (George, West, Pettm 1999)

8 Projective Pictures
7 Attachment Scenes + Neutral Warm-up

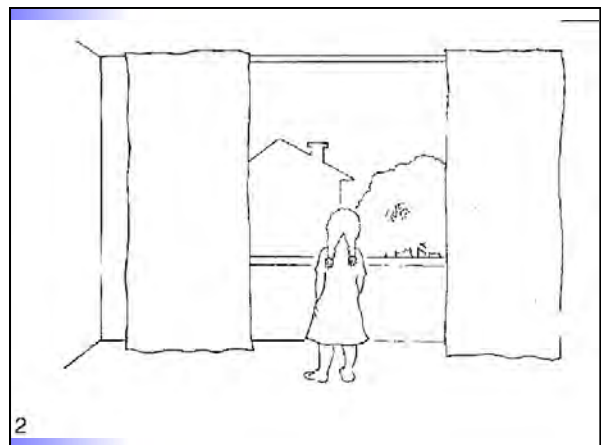
Dyadic

- Departure
- Bed
- Ambulance

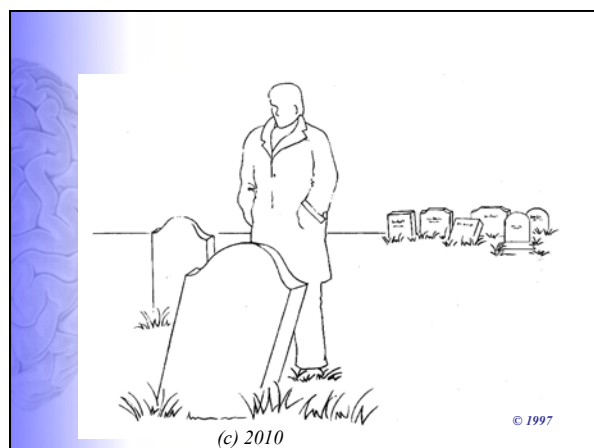
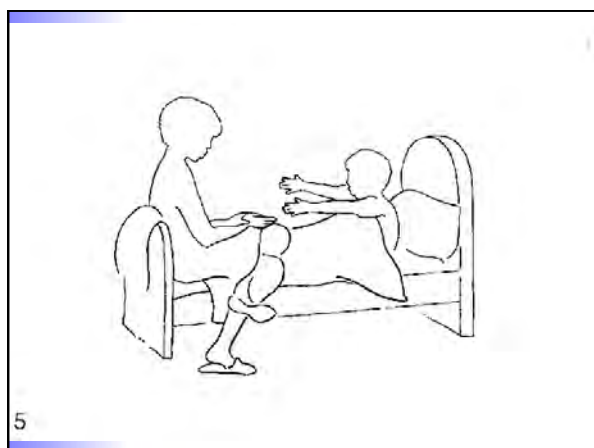
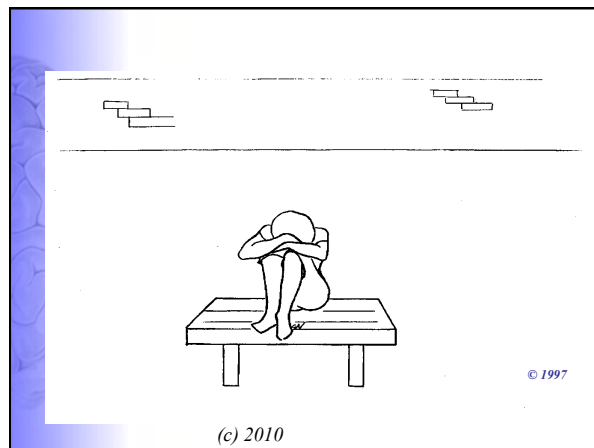
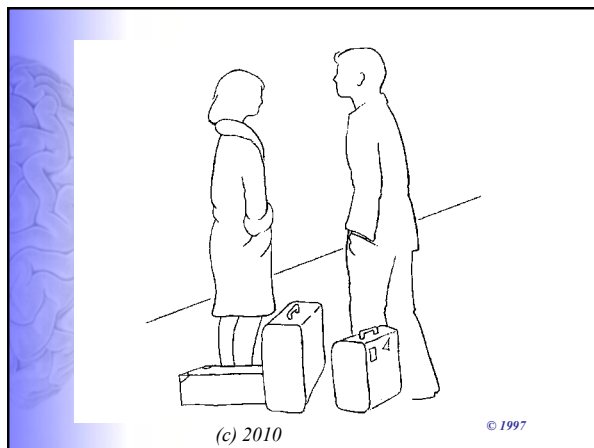
Alone

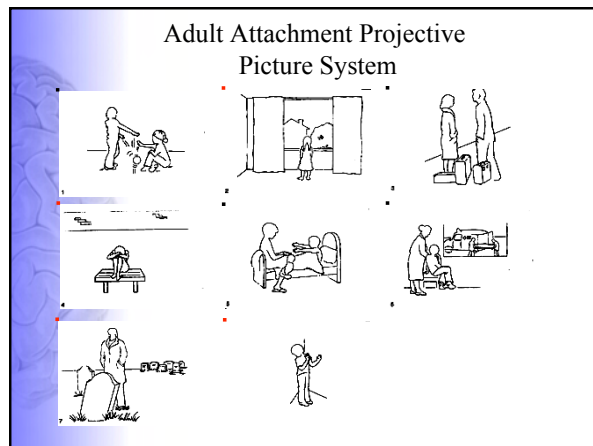
- Child at Window
- Bench
- Cemetery
- Corner

© George, West, & Pettm (1997)



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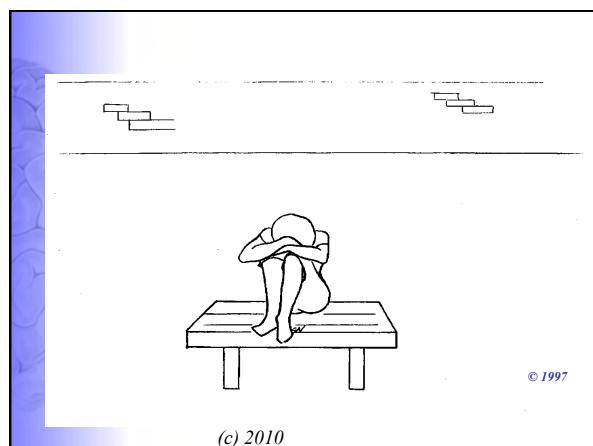




AAP Classification System

George & West, 1999, 2012
www.attachmentprojective.com

- Agency of Self
 - Internalized secure base, capacity to act
- Relationships with Others
 - Connectedness: The story character is connected to others in a behavioral system relationship = attachment-caregiving, friend-peer, romantic-marriage
 - Synchrony: Goal-corrected partnership = sensitive care or mutual enjoyment (Bowlby, 1969)
- Defensive Processes
 - patterns of deactivation, cognitive disconnection (ambivalence), segregated systems (attachment fears) in all attachment stories



Unresolved versus Resolved attachment status

Unresolved (disorganized)	Resolved (organized)
<p>„She is very desperate, wants to withdraw herself from the world, she is very frightened, is deserted by someone. What happens next? She is frightened and helpless, and wants to take her life. She sits there for ever, I really don't know.“</p>	<p>„A women is desperate, feels bad, had a fight with a friend, sits on a bench to be alone, she is very frightened about the future. What happens next? She thinks about the fight and how it came to that fight. She gets up after a while and is trying to get in contact with the friend to talk about everything“</p>

AAP Validity

George & West (2012), Buchheim & George (2011)

- Sample = 144 adults (18-64; 100 women, av. 36 yrs., 44 men av. 26 yrs.); Canada (51%) + US
- Interjudge reliability: 4 groups (F, Ds, E, U)
 - Judges 1-2, 90% ($\kappa = .85$)
 - Judges 1-3, 85% ($\kappa = .79$)
- Concurrent validity \square AAI (George, Kaplan & Main, 1984/1985/1996)
 - concurrent reliability: 4 groups
 - 90% ($\kappa = .84$)
- Discriminant validity
 - No significant differences among AAP classification groups on verbal intelligence or social desirability

Adult Attachment Projective Picture System

George et al. (1999); George & West (in press)

Feasible for an experimental setting:

- AAP in an fMRI environment
 - Buchheim, Walter et al. 2006, Psychopathology;
 - Buchheim, Walter et al. 2008, Psychiatry Res: Neuroimaging
- AAP and Oxytocin
 - Buchheim, Heinrichs, Gündel, 2009, PNEC

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Procedure in our study

- Assessment of AAP interviews
- Extraction of relevant sentences including defensive markers like
 - deactivation, preoccupation, traumatic dysregulation
- Presentation of these core sentences together with the AAP pictures



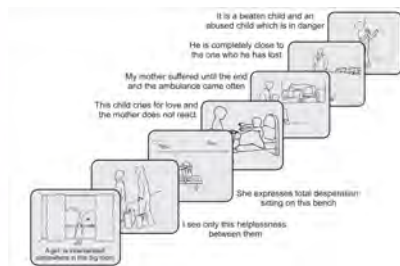
Cemetery: Unresolved

This man is standing in front of the grave of his wife and he visits her to tell her how much he feels deserted. The grave looks strange and it must be very cold. He is completely close to the one who he has lost. He has no idea what to do next and is lost in thoughts. He is very desperate and feels helpless. He will stand there for a long time.

Cemetery: Unresolved

*This man is standing in front of the grave of his wife and he **visits her to tell her how much he feels deserted**. The grave looks strange and it must be very cold. **He is completely close to the one who he has lost**. He has no idea what to do next and is lost in thoughts. **He is very desperate and feels helpless**. He will stand there for a long time.*

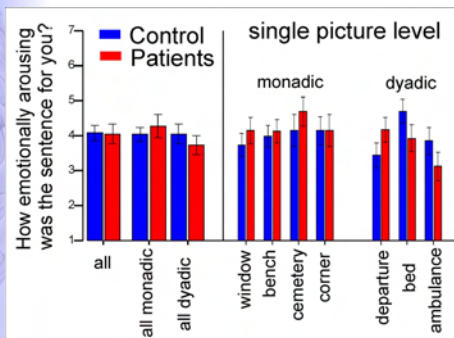
Attachment Paradigm



„Contrast“ to the relevant personalized sentences

- **Neutral Sentences**, describing the environment only:
- There are three suitcases
- There is grass around the tombstone
- Two curtains right and left

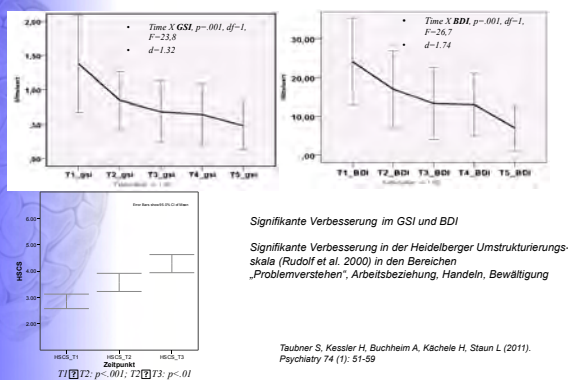
Emotional arousal



Results

- Clinical improvement including change of attachment representations
- Neural response to attachment stimuli after 15 months of psychodynamic psychotherapy
- Correlation between clinical and neural response

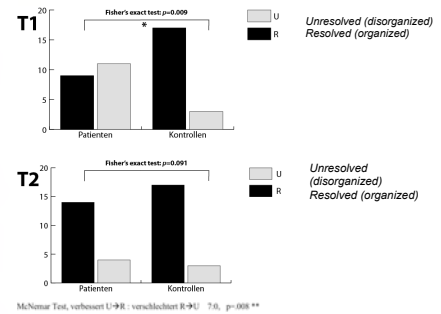
Change of symptoms and structure



Cemetery T2: Resolved

Oh this person is sad. He is standing in front of the grave of his wife. She is dead since many years. **What is he thinking or feeling?** Yeah, he misses her still a lot. Maybe he is crying, feels alone. It looks like that its winter, he is cold, has his hands in his pockets. He remembers what they shared together, thinks about her. Pause – **What is happening next?** He will stand there for a little while, he is still sad, but then he goes home and tries to distract himself, maybe he meets someone.

Change of attachment status after 15 months of treatment



Buchheim et al. (2012) Bindung, Psychotherapie und Bildgebung: Einblick in eine neurowissenschaftliche Studie zur psychoanalytischen Psychotherapie bei chronisch depressiven Patienten.
In: Böker H, Seifritz E (Hrsg) Psychotherapie und Neurobiologie: Ein Blick in die Zukunft. Huber, Bern

Studies relevant for our hypotheses

Changes after therapy, fMRI

	Therapy	N	Method	Results
Siegle et al. (2006)	CBT	14	fMRI Words	vACC predictive of response
Fu et al. (2008)	CBT	16 pat	fMRI	J amygdala, ant. hippocampus
	16 weeks	16 contr	faces	J ACC-sup. fr. gyrus

Hypotheses

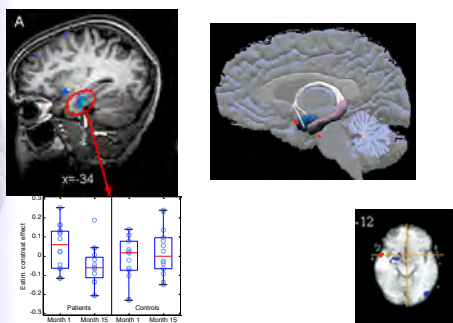
- Normalization of emotional reactivity indexed by changes in the amygdala-anterior hippocampus region
- Changes in prefrontal areas such as the ventral anterior cingulate cortex

Changes in Prefrontal-Limbic Function in Major Depression after 15 Months of Long-Term Psychotherapy

Anna Buchheim^{1,2}, Roberto Viviani^{1,2}, Henrik Kessler^{3,4,5}, Horst Kächele^{6,7}, Manfred Cierpka⁸, Gerhard Roth⁹, Carol George¹⁰, Otto F. Kernberg¹⁰, Georg Bruns¹¹, Svenja Taubner^{12,8,2}

¹ Institute of Psychology, University of Innsbruck, Innsbruck, Austria, ² Department of Psychiatry and Psychotherapy, University of Ulm, Ulm, Germany, ³ Institute for Advanced Study, Bonn, Germany, ⁴ Department of Psychosomatic Medicine and Psychotherapy, University of Ulm, Ulm, Germany, ⁵ Department of Psychiatry, University of Bonn, Bonn, Germany, ⁶ International Psychoanalytic University, Berlin, Germany, ⁷ Institute of Psychosomatics, University of Bonn, Bonn, Germany, ⁸ Department of Psychology, University of Bonn, Bonn, Germany, ⁹ Department of Psychology, University of Bonn, Bonn, Germany, ¹⁰ Department of Psychology, University of Bonn, Bonn, Germany, ¹¹ Department of Psychology, University of Bonn, Bonn, Germany, ¹² Department of Psychology, University of Bonn, Bonn, Germany

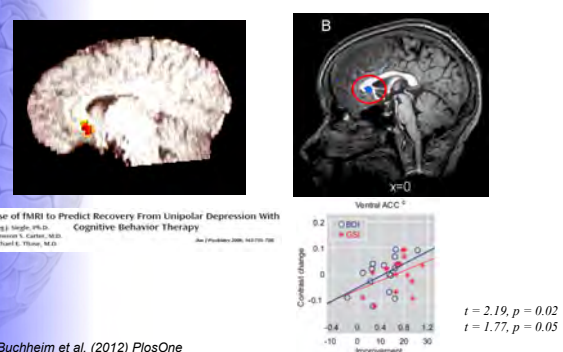
Interaction time x group personal versus non-personal stimuli



Buchheim et al. (2012) PlosOne

Fu et al. (2008) Biol Psychiatry 64: 505-512

Interaction time x group personal versus non-personal stimuli



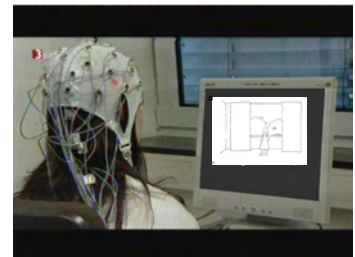
Buchheim et al. (2012) PlosOne

Summary

- First study documenting behavioral (including attachment narratives) and neural changes in chronically depressed patients during psychodynamic psychotherapy
- Signal associated with processing personalized attachment related material varied in patients from baseline to endpoint, but not in healthy controls.
- Patients showed a higher activation in the left anterior hippocampus/amygdala, subgenual cingulate cortex before treatment and a reduction in these areas after 15 months
- This reduction was associated with improvement in depressiveness specifically in the subgenual cingulate cortex

Outlook

AAP and OPD paradigms were also used in an EEG-Setting. Ongoing analysis



Thank you for your attention!

