SEROTONIN, VITAL AFFECTS AND PSYCHOTHERAPY – THEORETICAL BACKGROUND AND PRELIMINARY FINDINGS

Psykoterapi- och handledningsforskning i dialog: En nordisk konferens och nätverksbyggande. 21-22, oktober 2011, Stockholm
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Serotonin, vital affects and psychotherapy

Contents of the lecture

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7. Conclusions – what follows from including biological dimensions to psychotherapy research?
Motto:

- When psychotherapy and neuroscience meet, a frame for their interaction, or a grammar, has to be developed
- It does not exist, it has to be created
Theoretical background

- The relationship between serotonin and psychotherapy is part of a more general relationship of the mind and the brain

- The relevance of neuroscience to psychotherapy: a complex and disputed area

- The hard problem – how the mind can arise from neurophysiology (John Searle)

- The soft problem – how the mind and brain covary – how does the brain change when the mind changes
The primordial mind as an image of the state of the body

- The ego is first and foremost **the body ego** (Spinoza, Freud, Chasseguet-Smirgel)
- The body ego forms a basis for **automatic self-observation** at a psychophysiological level
- **The clinical body ego** - tuning to bodily feelings and sensations – how do you feel, how are you?
The primordial mind monitors the non-verbal state of the body and brain in the pleasure-pain axis (Sigmund Freud, John Hughlings Jackson, William James and others)

The bodily sense of being is monitored on a moment-to-moment basis

The background feeling - prevalent behind the consciousness (Damasio)

The bodily self-consciousness has an intrinsic connection with the object world via the sensory channels

The body and brain functions are thus imbedded in our non-verbal self-image
Freud and epistemology of science

- "...to establish psychology on foundation similar to those of any other science, such, for instance, as physics"

- "Reality will always remain 'unknowable'. .... We have discovered technical methods of filling up the gaps in the phenomena of our consciousness, and we make use of those methods just as a physicist makes use of experiment"

Freud in the "Outline of Psychoanalysis", 1940, SE 23: p. 196-7:

In the perspective of Freud’s epistemology, we can legitimately study the possible biological changes that may parallel the clinical effects of psychotherapy
From epistemology to clinical reality

- In clinical reality, psychotherapy needs its own concepts, theories and methods, like the natural sciences need their own theories and methods.

- The natural sciences stand on empirical verification.

- Psychotherapy stands on subjective reality, psychological interaction and hermeneutics.

- For becoming true psychology, the body ego has to acquire a personal, human "face", i.e. a personal identity:

  - Me as the owner of my mind
Clinical, ontological autonomy of psychotherapy

- The therapeutic couple creates a unique relationship between two individual personalities on the basis of their respective conscious and unconscious psychological work they bring to the relationship.

- Psychotherapy manages well without knowledge in neurobiology. Work in the consulting room is not based on data from neuroscience.

- The (possible) neurobiological effects of psychotherapy represent an unintentional biological benefit, a kind of added value that derives from the work in the clinical relationship.
Freud on clinical autonomy and biology

- "We have found it necessary to hold aloof from biological considerations during our psychoanalytic work and to refrain from using them for heuristic purposes, so that we may not be misled in our impartial judgement of the psycho-analytic facts before us.

- But after we have completed our psychoanalytic work we shall have to find a point of contact with biology; and we may rightly feel glad if that contact is already assured at one important point or another."

- *Freud S: The claims of psychoanalysis to scientific interest. 1913, S.E. 13:164-190.*
Eric Kandel on clinical ontological autonomy


- "When it comes to mental function, however, biologists are badly in need of guidance. It is here that psychiatry (in which he included psychoanalysis) as guide and tutor of its antidiscipline, can make a particularly valuable contribution to neurobiology."

- "Psychiatry and psychology can illuminate and define for biology the mental functions that need to be studied if we are to have a meaningful and sophisticated understanding of the biology of the human mind."

- This is the principle of clinical ontological autonomy of psychotherapy
Eric Kandel on neurobiology of psychotherapy


- The effects of psychotherapy should be observable in changes in brain function

- **Psychotherapy** - like any significant learning experience - can regulate the activity of the DNA in nerve cells

- Psychotherapy does not change the DNA code but may regulate its expression, i.e. it can activate or silence the DNA
Brain imaging studies of outcome of psychotherapy

- Today, more than a dozen studies have been published that demonstrate changes in brain activity as a function of psychotherapy
  - See reviews by Roffman et al (2005), Linden (2006), Beauregard (2009)
  - Psychotherapy can reduce the pathological increase, or decrease, of brain activity in depression, the phobias and obsessive compulsive disorders
  - The effects of psychotherapy on brain are partly similar and partly different from the effects of psychopharmacological treatment
# Studies on psychotherapy outcome using brain imaging

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Psychotherapy and the serotonin function

- The majority of brain imaging studies focus on brain networks and their changes in relation to psychotherapy.
- Only a few studies have been done on molecular effects of psychotherapy, e.g. on serotonin.
- Studying serotonin function in psychotherapy is of particular interest.
- It enables monitoring how non-verbal affects of primal consciousness (body ego) change in relation to the neurobiology of serotonin.
- It also enables comparison between the effects of psychotherapy and psychopharmacology.
Serotonergic System
"Serotonin is part of an exceedingly complicated mechanism which operates at the level of molecules, synapses, local circuits, and systems, and in which sociocultural factors, past and present, also intervene powerfully."

Serotonin and the primal consciousness

- There are serotonin-rich nuclei (raphe) in the brain stem that participate in the regulation of the all-over activity level of the brain (well-being, arousal, sleep-wake cycle)

- The influence of serotonin spreads all over the brain

- In the brain, serotonin is involved in the regulation of mental pain and endurance of feelings of frustration and anger

- Serotonin plays a major part in the symptoms of depression
Psychotherapy and serotonin

- Serotonin synapses play a part in the regulation of emotion and affect

- **Well-functioning serotonin synapses** enable feeling of the emotions, i.e. the subjective sense of having affects

- **Reduction of available serotonin** is likely to bear a relationship with the freezing of affects
Psychotherapy and serotonin...

- **Painful affects** of loss and adversity are warded off by the affect of freezing.
- Serotonin reduction may be involved in the internal, physiological mechanism of warding off painful affects.
- **Restoration of serotonin** levels in the synapses may have a connection to revitalization of affects, also the painful ones.
Psychotherapy and serotonin…

- The first studies on serotonin and psychotherapy were conducted at the Department of Psychiatry, University of Eastern Finland (Kuopio) in the late 90’s and early this millennium
Baseline

A

[123I] nor-b-CIT distribution volume ratio in midbrain

B

p = 0.0002

Controls (n = 19)  Patients with MDD (n = 29)

A male depressed subject, with traits of personality disorder, showed normalization of SERT during one year of psychotherapy whereas an untreated control case with similar symptoms had no follow-up SERT changes (Viinamäki et al. Nord J Psychiat 1998)

In a female patient with anxiety and depression the reduced SERT level increased to a normal range during one year of psychotherapy. Her clinical recovery was delayed, however, with six months from SERT normalization (Saarinen et al. Am J Psychotherapy 2005)
Psychotherapy and serotonin...

- A naturalistic sample of depressed subjects (n=18) with six months of dynamically oriented, supportive psychotherapy (1x week)
- A trend of SERT improvement as a function of clinical improvement, however, with an inverted U-shape curve
- Some subjects seem to improve without a SERT change
- In some subjects, SERT and clinical symptoms deteriorated
Fig. 1 Change in $[^{123}]$-beta-CIT specific binding in the midbrain in relation to decrease in HRSD total score in depression ($R^2 = 0.403; p < 0.02$). A second degree polynomial was used in data fit.
Atypical depression

- A comparison of atypical (n=8) and classical depression (n=11)
- One year of dynamic psychotherapy 2x week
- Clinical recovery in both groups
- SERT improvement in atypical subjects
- No SERT change (or even a slight decrease) in subjects with classical symptoms

Hamilton 21 scores, atypical scores and serotonin transporter densities before and after one year of psychotherapy

Major depression (n=11)
- Hamilton 21: 22.18 (7.45) 10.64 (7.00) p<0.003
- Atypical score: 5.18 (2.86) 5.18 (4.85)
- SERT midbrain 1.20 (0.13) 1.14 (0.18) p<0.20

Atypical depression (n=8)
- Hamilton 21: 19.13 (3.94) 12.50 (6.84) p<0.02
- Atypical score: 12.25 (6.45) 7.63 (6.46) p<0.02
- SERT midbrain 1.12 (0.14) 1.25 (0.17) p<0.019
Fig. 1. Midbrain SERT before psychotherapy.

Fig. 3. The change in midbrain SERT levels during psychotherapy.

Limitations of the study

- Small number of subjects studied
- Controversy on the validity of the diagnosis of atypical depression
- Fluctuation in the timing of the examinations
- No active comparison group
Strengths of the study

- Drug-naïve, first-episode depressive subjects
- Similarly trained, experienced psychotherapists
- Robust one-year stability of SERT (1.27±0.11 vs. 1.27±0.14) in the comparison group of healthy subjects - suggesting that the SERT changes are not due to the variability of the method
Conclusions

- Serotonin is relevant for the biology of normal human interaction and does not pertain only to psychopharmacology.

- Psychotherapy like any affectively significant human interaction may give rise to physiological changes (in serotonin and other physiological functions).

- Serotonin may be involved in the regulation of the general vitality of the mind.

- It also participates in the processing of conflicts at the level of higher brain organizations (prefrontal-limbic).
Conclusions…

- **Decrease in serotonin** transmission in depression is not necessarily irreversible - with likely differences between subgroups of depressive subjects

- **Serotonin transmission may recover before clinical symptom remission** - revitalizing of affects may increase anxiety

- Our findings are supported by a recent PET study, which showed psychotherapy-related increase of serotonin receptors that was not found in control subjects with antidepressant medication (Karlsson et al. 2010)
Conclusions…

- Biological dimensions of psychotherapy do not require special attention within the clinical autonomy of the therapeutic couple.

- The main matter is to keep in contact with the affects of the patient – and the therapist!

- In the psychotherapeutic interaction, physiology automatically takes care of itself.
Conclusions...

- In depressed patients, clinical tuning to the bodily level of affects is crucial.

- The affects felt in the body bring psychotherapy close to the intimacy of mental life and the instincts of the subject – and thereby to the functions of both the mind and the brain.

Toward Molecular Psychotherapy of Depression?

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