Neurobiology and Psychotherapy[1]

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Abstract

Body, brain and mind are all manifestations of one single organism, all mental processes are based on biological-neuronal processes and events. Advances in neurobiology have increasingly enabled decoding the correlates of psychological functions: the genetic conditions, brain processes from sensation to cognition and from emotion to empathy and social interaction. In the latter area, which is of decisive importance in psychosocial research, neurobiological investigations are in their very early stages.

Complex psychological functions are represented in networks; this renders it impossible to adopt simple reductionist approaches. Clinical phenomena, too, such as pain or depression are represented in neuronal networks. An abundance of neurobiological data validates (positively or negatively) psychological, psychotherapeutic or psychiatric theories or therapies. Such validation is indispensable. Currently, there are hardly any fundamentally new approaches to psychiatric and psychotherapeutic practice derived from neurobiological data. Psychological phenomena emerge from neurobiological processes. In view of their emergent nature, in the future we shall be in need of psychosocial approaches to understand such data in the sense of having to adopt methodological dualism (neurobiological versus psychosocial research methods).

Key words

Neurobiology – Brain Functions – Emotion – Psychotherapy – Psychosomatics

[1] Expanded version of the lecture given at the Congress in Innsbruck on 'Neurobiology and Psychotherapy' in July 2003.

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In his project on psychology, Freud had expressed his early hope that human experience would one day be based on neuro-biological foundations. A leap in this direction was enabled by knowledge gained on neuronal plasticity extending from principles regulating behaviour at the molecular level to those underlying complex functions. In the meantime, numerous pre-clinical and clinical investigations have adequately demonstrated the influence of experience and learning processes in early childhood on the structural maturation and function of the brain. In certain time periods during development characterized by increased neuronal and synaptic plasticity, psychosocial factors play an important role, leading to lasting alterations in brain functions (Braun & Bogerts 2001). These environmentally caused alterations (such as in cases of very severe deprivations) can be corrected only to a limited extent or only with great difficulty – primarily with psychotherapeutic measures.

There is a veritable explosion of results from neurobiological research so that it is hard to have an overview of the whole field. The number of journals dealing with the theme of neuro-biology, for instance, has increased at least 10-fold in the past 15 years and the number of studies, for instance using fMRI has increased from 50 to over 1000 per year (data from Med-line). The question how the network in the brain works in order to enable complex functions is gaining increasing attention. Imaging procedures such as PET, SPECT, fMRI, with all their advantages as well as limitations of temporal and spatial resolutions, are employed to investi-gate the most important psychological disturbances (anxiety, depression, compulsion, schizo-phrenia etc.). The fMRI signal, however, does not represent the entire cerebral activity; rather it provides a visual image of the input and intercortical processing and very little of the output (Logothetis 2001). Despite the fact that rapid advances in fMRI promise ability to map higher mental functions and their pathological deviations in the near future (Spitzer et al. 1998), functional associations are far from being clarified. A multimodal approach that includes cy-toarchitectonic maps, functional imaging and last but not least, functional neuro-anatomy (e.g. study of lesions) provides the overview that is necessary for an understanding of structure and function as a complex unit (Zilles 2002).

In his historical work 'Psychotherapy and Single Synapse' published in 1979 the Nobel laure-ate Kandel said that 'psychotherapy works at the same level as that we are investigating at present in order to understand the psychopharmacological interventions – the level of individ-ual nerve cells and their synaptic associations' (page 1028). Psychotherpay works in the sense that 'the effectiveness of existing associations between neurons changes and thus leads to an expression of new behaviour patterns' (page 1037). If psychotherapy alters the neurochemis-try and physiology of the brain and leads to new learning experiences and new behavioural

forms, then do we need a neurobiologically founded perspective of psychotherapy as Gabbard (2000) formulated it for a better understanding of psychotherapeutic measures with the help of neurobiological data or even for applying psychological treatment in a more effective fashion (Liggan & Kay 1999)? A satirical view point (adopted often enough) according to which ‘’everything is neurological or do you believe otherwise? ’’ needs to be avoided at all costs. For this purpose, in this issue, based on the current state of knowledge, we shall make a careful assessment of the possibilities and limitations of a neurobiological approach to psychological phenomena.

The Body-Mind Problem

Every discussion regarding the association between neurobiology on the one hand, and expressions of psychological experience in humans in the form of feelings, thoughts, behaviour etc., on the other, has to address the issue of the mind-body relation. Cartesian dualism separated man into two spheres, the brain and the mind, with the result that psychotherapy has to be considered as treatment directed to psychological disturbances, whereas medications are appropriate for treatment of biologically based disturbances. However, what we call mind can also be understood as the activity of brain – although the complex subjectivity of the unique individual is hardly to be reduced to neurochemistry and physiology. Psychological phenomena originate from the brain; in turn, however, subjective experiences influence the brain.

In contrast to Cartesian dualism that regards body and mind as being two different forms of existence (ontological dualism), the biopsychosocial model of today represents the theoretical framework for medicine and the relationship between body and mind (Engel 1977): Body, brain and mind are manifestations of a single organism. This organism is structured in a hierarchical fashion and they interact with each other via chemical and neural pathways. At every level there are emergent characteristics (the cell is more than a sum of its parts); thus intellectual and spiritual phenomena are emergent in character and arise from the complex brain (Goodman 1991, Damasio 2003).

The ‘easy problem’ of neuroscientific research is to detect correlates of psychological functions and consciousness. The ‘hard problem’ is represented by the question namely, how do psychological functions, in particular consciousness, originate from biological events and processes. According to the theory of emergent phenomena, mind arises from complex organisational forms of neurons – as water for instance has a higher form of organization than its atomic components. This, however, does not solve the mind-body problem; an analogy is being offered here, which leaves open the question of how mind arises from the body.

This mysterious leap – as Freud called it – from the soul to the body and from neuronal networks and maps to the soul, this mind-body problem is not yet solved and is likely to remain unsolved for a long time to come (Damasio 2003). One of the unexplained issues is the origin of consciousness and the so-called 'binding problem'- in other words, how does it come about that we have a unified total experience, a working together of differing networks and modules from which originates consciousness and an awareness of self, the awareness of 'I'.

If we follow up on this idea that the physical and the mental are not to be thought of as two different kinds of reality, but rather as two sides of a medal or as two different concepts representing the same object, these two conceptual systems require the use of different approaches to knowledge. Nobel laureate and brain researcher Sperry underlined the independence of the 'mental sciences'. "The events of inner experience, as emergent properties of brain processes, become themselves explanatory causal constructs in their own right, interacting at their own level with their own laws and dynamics … The results add up to a fundamental change … We now perceive a continuum." Sperry (1982).

'Mental' is thus a quality that cannot be described exclusively in neurobiological terms but comprise an independent area of knowledge and understanding. Neurobiological findings are the indispensable basis for further considerations, but they do not render psychological, psychotherapeutic and psychiatric research superfluous.

Methods of psychological investigations such as reports of subjective emotional experiences and introspection provide necessary and valid for opening up the psychobiological field for scientific investigation (Goodman 1991).

Foundations of Psychological Functions: Neuronal Networks[3]

In what follows, it is assumed that the reader is familiar with the key anatomical and functional facts about the central nervous system. For quick reference, the reader is directed to some books that give an overview of the whole field e.g. Fundamental Neuroscience (Squire et al. 2003) or Cognitive Neuroscience (Gazzaniga et al. 2002). There are of course several others of their kind available. For a brief overview of important functional associations that are necessary for an understanding of the brain, the reader of the journal is referred to Schuessler 1988, Schuessler 2002.

The human brain comprises 100 billion neurons and billions of associations between them. The basic construction of the brain is comprehensible; its functions, however, consisting of an almost infinite number of possible interactions, are incredibly complex. The characteristic

[3] Frequently used abbreviations: PFC prefrontal cortex, ACC anterior gyrus cinguli.

features of brain functions are dynamics of entry, connectivity, variability, plasticity, ability to categorize, and dependence on value.

Even if certain specific areas of the brain seem to be responsible for carrying out certain specific functions, these functions are not carried out exclusively in these or immediately surrounding anatomical areas. Neuronal connections form loops within the system and each component of this association makes an important contribution to functional integrity. Processes that appear to be quite simple such as control of movement demand a highly complex working together of very different brain structures. What appears to be a simple process, namely perception, processing of perception, signaling to the motor cortex and movement activated via the cerebellum will be seen, on a closer look, to be a highly complex one because of the feedback activities of the loops.

Since the brain is an information processing system organised for comprehensive and rapid adaptation, individual modules and networks and strands of information can be processed in parallel with each other.

The brain is organised in relatively independent functional modules or larger networks that work in parallel towards a globally functioning system. The brain is modular, its parts work independently of each other, it is a self-organising system with constant reference to and interaction with the environment. The structure is more or less hierarchical, although in part different levels of this hierarchy work independently and in part interact with each other in an up and down fashion (bottom to top, top to bottom). Psychological modes of function (behaviour, cognition, emotion etc.) constitute the structure of this network system and are – this gets more and more clear – distributed in the same modular way and structured hierarchically. The individual neuron is the basic building block, but the basic functional unit is the module (Szentagothai 1975). Parts of this modular system (with the size of the modules varying from a few to several million neurons) such as the visual system have been researched extensively. Modules bundle functions together into functional associations, namely the networks. Luria (1966) introduced the concept of functional systems in neuropsychology. Functional system means a working together of different parts, such as for instance the parts of the digestive system that work together in order to carry out a common function, namely digestion. Thus, digestion is not achieved by the stomach alone but only in cooperation with other parts of the digestive system. This holds true of the brain to an even greater extent. The aim of research is to identify and decipher these functional systems and networks with their modular structure, and to understand their interactions and their disorders, that is their dysfunction.

Neurons are building blocks of a module, which, however, are connected with other modules and subsystems at varying levels of hierarchy and integration. This means that functional systems (e.g. speech) are realized not by a single localized region of the brain but by a number of subcortical and cortical key points in a world of widely spread networks (perception of phonemes, word understanding, grammatic ability, naming, gesture, inner speech etc.). Memory, too, shows a similar network structure with various functions such as declarative or procedural learning (Schuessler 2002). There are relatively independent memory systems in the sense of a declarative (what we know about each other), a procedural (what we do with each

other) and an emotional memory (what we feel and what we have felt in the past). The network develops in different ways – the emotional-procedural system develops earlier than the declarative memory system (hippocampus) . This implies that habitual behavioural patterns in response to events are firmly established before the child develops the ability to remember and name these events with the help of his episodic and declarative memory system.

What are the consequences of this network model for neurobiology and an understanding of psychological disturbances?

Conclusions derived from a network model

- A lesion in a network can lead to functional disturbances if there are many tasks to be accomplished at the same time.
- A lesion in a network can remain 'quiet' under certain circumstances (parallel processing).
- One and the same function can be triggered through lesions in various regions of the brain if they are part of the network.

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This carries the clinical implication that there are no functional limitations that permit a conclusion about a specific lesion in an association cortex area and vice versa, namely that the presence of more than one functional disturbance does not necessarily imply the presence of multiple lesions.

Successful survival presupposes adequate automatic (unconscious) functioning of a series of modules, networks or systems: motivation, precise perception and assessment of the environment, regulation of the impulse of sexual aggressiveness, bonding with other human beings, initiation, organization and completion of goal-oriented behaviour as well as inhibition of improper behaviour (Schuessler 2002). These networks that guide our behaviour work both consciously and unconsciously. Unconscious processing and acting implies automatic choice of cognitive-emotional behavioural patterns appropriate to the given situation and require little or no effort for their activation.

Conscious processing, on the other hand, is voluntary and effortful and has less capacity at its disposal. Most behaviour occurs automatically and very fast, that is, unconsciously. Network-automated habits (habits that include also neurotic ones) recognized as not leading to achievement of goals, inappropriate or problematic can only be altered with a great deal of difficulty and even so, only when the person with such automated behavioural patterns becomes aware of these as such, is motivated to change them, is capable of accepting feedback about his behaviour without excessive defense mechanisms immediately coming into play and is ready to undertake efforts to change these automated behavioural patterns.

The sensory motor area, with its specific sensory-motor functions forms the foundations of the hierarchical organisation of the cortex. Higher order areas that develop later in the phylo- and ontogenetic evolution are responsible for complex and integrative functions reaching up to the highest level of this hierarchy, the pre-frontal cortex, which is dedicated to representation and carrying out of complex activities and interactions.

The entire prefrontal cortex (PFC) serves memory, planning and carrying out of complex actions. The orbital and medial parts of the PFC are very closely associated with processing of emotions. Functional breakdowns of orbital PFC lead to disorders of impulse, uninhibited behaviour and attention deficits (case of Phineas Gage). Breakdown of medial PFC leads to loss of drive. PET/fMRI show extensive activity of these parts of the brain in healthy people. The later region (the largest part of the brain in man) supports the temporal organization and processing of behaviour, speech and thought. Disorders affecting this area lead to inability to make plans and carry them out. The PFC matures after birth at two critical stages namely, in the second and fifth year of life. It develops further till the end of the second decade of life. The PFC plays a very important role in learning new things and in inhibiting habitual reactions which are inappropriate (Mesulam 1998).The orbital PFC inhibits behavioural patterns and autonomous reactions of fear and defense mechanisms; for instance, cardiovascular reactions (amygdala, hypothalamus) are muted by stimulation of the orbital PFC. Maturation of the PFC includes the gradual development of inhibitory control over stereotyped automatic behavioural patterns, inborn or acquired. Despite this roughly described organization of the brain, one cannot talk of a specific 'prefrontal' function since functions are quite comprehensive and furthermore, cannot be localized in discrete areas (Fuster 2001).

Cortical maps are dynamic constructs that are altered throughout life by environmental influences and learning experiences. The historical comment of Hebb (1949) that "neurons that fire together - wire together" is correct. Synaptic alterations – not molecules – are the causes of psychological disorders. Although the underlying basic brain structure is surprisingly very similar in all human beings, we feel and act in very different ways. The key to this individuality lies not in the global organization of the brain but in the fine adaptation of the underlying networks. About 50-70% of all genes found in the human body are active in the central nervous system (LeDoux 2002).

Learning from behavioural sequences activates pre-motor and lateral pre-frontal areas of the brain; with experience and constant repetition, activation moves to the subcortical structures (cerebellum, basal ganglia, thalamus etc.), is automated, and representation wanders to lower executive regions. What is stored there is then carried out one after the other in a linked-chain fashion. Automated routine behavioural patterns, however complex they may be, no longer require activation of the pre-frontal cortex and are fully anchored in subcortical structures. A rule of thumb is that a thousand repetitions are required for a new form of behaviour to become automatic (Gordon 2000).

"One neuron – one transmitter" is an exception in the central nervous system, since most neurons have at least one transmitter each and several neuropeptides with transmitter functions. Most neurons express almost all transmitter receptors with great differences in the number of receptors. The most frequent transmitter types are glutamate (exciting) and GABA (inhibiting). In humans, GABAergic neurons are highly developed in the cerebral cortex and are to be found mostly in interneurons, whereas glutamate is found mostly in projection neurons. The most important receptors and transmitters are metabotrophic, that is, they activate a second

messenger cascade, which in turn leads to complex changes in the cell including gene mutations (activation or deactivation). Transmitter changes lead to changes in the receptor density on the neuron with up (more receptors) or down (fewer receptors) regulations. A transmitter does not act on only one receptor but on several receptor types, although with varying specificity. In the brain, receptors are distributed regionally and in the brain layers they have a laminar distribution. Receptor patterns have a certain similarity although there is considerable quantitative variance.This simple basic fact makes it clear that a monofactorial approach is meaningless (depression = serotonin deficiency), because changes in a receptor lead to changes in all other receptors and vice versa.

The errors of a simplicistic-reductionist biological psychiatry (and pharmaceutical industry) must be met head on. It is an idée fix that simple biochemical deviations are at the basis of psychopathology or even of a psychopathological disturbance: ‘concerning oneself with symptoms or syndromes as if they were specific illnesses … or biological identities determinable by a laboratory test’ (Ross 1986). The ex juvantibus logic of working back from the effect of a medication (antidepressants increase serotonin) to the cause of a disturbance (depression = deficient serotonin) is a severe mistake since medications do not exclusively possess receptor-specific effects, but act on several areas of the brain and as a rule have an effect on very different psychopathological conditions. In a comparable situation, one would never dream of inferring aspirin deficit from the knowledge that aspirin alleviates headache.

Neurobiology and Genetics

A subtle interplay of genes, messenger substances and environmental influences regulates our behaviour. The limits of behavioural patterns are set by heredity, but within these limits there is room for endless variations. Even identical twins with 100% identical genetic material do not behave in identical ways. If we now consider the entire range of biopsychosocial interactions, it can be seen how complex behavior can be. Each human being creates his environment that corresponds to his predispositions, as a kind of an ecological niche. Parents give their children not only their genes, but also provide them with an environment that is adapted to the maternal and paternal heredity. In this environment, also non-genomic individual behavioural characteristics are passed on over generations (Francis et al. 1999). No doubt, behavioural characteristics are also genetically determined (genotype). Their expression (phenotype) is, however, influenced by developmental and environmental factors. This is true – on the basis of the complex genetic inheritance – especially of important psychological disturbances. In

his critique of biological psychiatry, Pam (1990) sifting through genetic studies, came to the conclusion that ‘inheritance of schizophrenia is not a scientifically established fact’.

The unravelling of the human genome is an extraordinary techical-scientific achievement. The most important knowledge gained, however, is that genetic activity is regulated and determined by the cellular environment. Signals from the extra-cellular environment, including hormones and neurotransmitters, regulate gene expression, and the potential for protein-gene and gene-gene interactions is almost endless. ‘The environment regulates the action of the genes, and genes influence the sensitivity of an organism to its environment via changes in the nervous system. These two causes cannot be separated in development’ (Wahlsten & Gottlieb, p. 178). Environmental factors determine the expression of specific genes and in turn, the proteins produced change the environment so that new genes are expressed. Thus there develops a self-organising process under the control of a continuous dialogue between the genome and the environment. This results increasingly in the formation of more and more complex structures. The additive model of gene + environment = phenotype must be given up and the answer to the question as to what determines behaviour is not simply nature or nurture, but rather that nature and nurture interact (Lewontin 1980). There are no genetic factors that can be described independently of the environment and no environmental conditions that can be described independently of genomic factors (Meaney 2001).

This interaction between genes and the environment occurs already in early stages as shown by Cooper and Zubek (1958) who investigated a brighter and a duller strain of rats growing up under different growth conditions. If both strains of rats grew up under the same normal conditions, there were marked differences between them (bright vs. dull) in the number of errors in a test. If they grew up in an enriched environment, even the genetically ‘duller’ gained enormous benefits. But when both strains of rats grew up in a miserable environment, they both demonstrated comparably poor results.

The extent to which environmental conditions (adverse experiences) influence the structure and function of brain becomes clear from preclinical, and increasingly also from clinical studies (McEwen 2000, Kaufman et al. 2000). The most important results are presented succinctly in the table below:

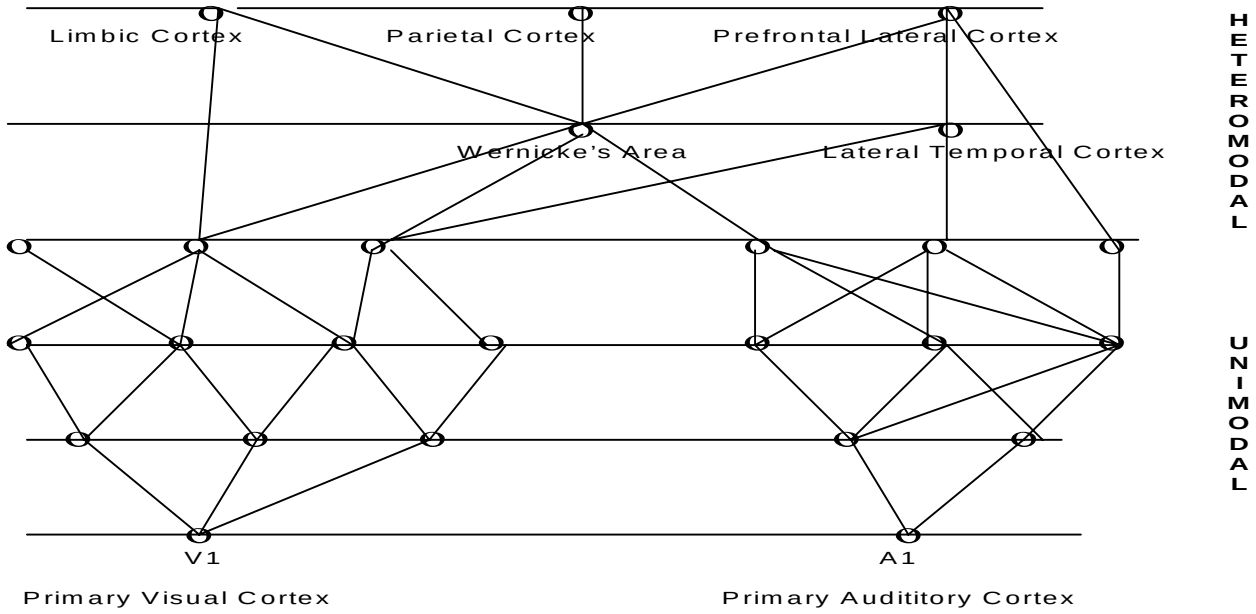
GENES and ENVIRONMENT

- There is no one-to-one correlation between genetic and personality factors.
- Since about 30,000 – 40,000 years there have been no major changes in the genetic material of man.
- Gene expression of complex characteristics is an advanced self-organising, interactive process; the regulation of gene expression and structural development are influenced considerably by external factors.
- About one-third of neuronal associations once established remain conserved, that means, the architecture of the cerebral cortex is influenced considerably by sensory signals (experience).
- Developments take place within specific time frameworks (Developmental phases).
- Brain continues to develop till late puberty (frontal brain)

From Perception to Cognition and Emotion

Mesulam (1998) has given us a 'State of the art' overview of the complex pathway that information travels, from perception to emotional-cognitive processing and then back again the influence on perception by a top-down feedback mechanism.

The process begins at the first synaptic level where the sensation is mapped in a primary dimension and processed. At the second synaptic level complex integration of perceptions are completed. The motivational-emotional influence and modulation of attentiveness are only of background importance at these two levels; however, the influence of these two factors steadily increases from level to level. The third and fourth synaptic levels have the comprehensive task of identifying and classification of patterns and objects such as faces, objects etc. In the diagram below it becomes clear that individual processing nodes have connection with nodes at the neighbouring level and the majority of these connections are reciprocal. Thus, there are endless possibilities of feed-forward and feed-back interactions. The identification of a face or a word is thus an achievement resulting from cooperation between several different synapses. The fifth and sixth synaptic levels comprise transmodal 'gateways' that have two interactive goals: they connect transmodal and unimodal brain regions to form a coherent global multimodal impression and they provide neuronal associations where multimodal convergence takes place.



The uni- and heteromodal regions are primarily responsible for perception and motor planning; as against this, the paralimbic (temporapolar-insular-orbitofrontal) and limbic (hippocampus, amygdala, olfactory cortex among others) regions channel, with their strong mutual interconnections to hypothalamus (the coordinator of homeostatic, autonomic and hormonal functions), emotions and motivation.

A network in the brain region reacting to painful stimuli was decipherd as the "***Pain Matrix***" (Peyron et al. 2000). This network confirms the key assumption of the Gate-Control-Theory that divides pain into three dimensions: the sensory dimension, the emotional dimension and the cognitive-evaluative dimension. The sensory-dicriminative dimension corresponds to the the lateral thalamus and somato-semsory cortex I and II, the insular cortex; the attention and cognitive dimension correlates with the posterior prefrontal cortex and the cognitive affective pain dimension is to be found in the ACC and orbitofrontal cortex. If a placebo is employed for modifying pain, the pain processing brain activity undergoes changes. In particular, placebo-elicited reaction is correlated with a marked activation of the orbitofrontal cortex and dorsolateral prefrontal cortex. These modules are connected with the midbrain regions (in which opioid receptors are anchored) so that the placebo effect is diminished when opioid-antagonists are administered (Wager et al. 2004). Observation of pain by a close partner (empathy) also activates a large section of this pain matrix, particularly the ACC, insula, prefron-

tal cortex, cerebellum and brain stem. Empathy, subjectively assessed to be high, correlates with higher fMRI-activation (rostral ACC, insula) (Singer et al. 2004).

Pain pathways do not run as a part of exteroceptive-somatosensory systems (touch), but rather as a part of the interoceptive pathway recently discovered by neuroanatomy, which projects hunger, thirst, visceral feelings, temperature and pain through afferent pathways (Lamina I) via thalamocortical switches, in particular in the insula and the anterior cingulum. The insular region appears today as the network section in which body identity is anchored as the feeling of subjective bodily existence. The interoceptive system is associated with autonomic functions carried out primarily via the anterior cingulum. To put it simply, the insular cortex can be described as the network of feelings pertaining to one's self and the anterior cingulum as the agent of autonomic motives (Craig 2002). Deciphering this pathway and its central network links represents a great step forward in psychosomatic medicine and understanding of somatoform disorders.

From Emotion to Empathy and Social Interaction

Emotions have occupied a central position in psychotherapeutic and psychiatric interest and work since a very long time. They are at the core of important disturbances (depression, anxiety. compulsion etc.). Emotions arise at the interface between an organism and its environment, they mediate between changing situations and behavioural responses (Krause 1998). Emotions are fundamental processing schemata, inborn or acquired, that enable a rapid assessment of situation and thus to actions. Emotions are complex reactions that, according to psychological-psychotherapeutic research, have different components (Krause 1998): the motor-expressive part (e.g. mimic), the physiological components (e.g. autonomic reactions), the rational components (readiness to act), perception of bodily correlates (perception of autonomic reactions) and naming and explanation of feelings in terms of its experienced perceptual and meaning structure. Emotions as subjective phenomena were alien to neurobiological research for a long time. It is only in the past 20 years that attempts are being made to understand their neurobiological correlates or to decode emotions in a neurobiological fashion. This implies at the same time a recognition and acceptance of subjectivity in neurobiological research! Similar to psychological research, emotions can be decoded neurobiologically as steps in processing, proceeding from the simple to the complex (according to Damasio 2003). Thus experienced emotions (feelings) are at the highest level, below them lie primary and social emotions, for the most part automatic and unconscious; the other side of the medal represents

drive and motive resulting from them. Emotions have been and continue to be the preferred subjects of functional imaging.

Phan et al. (2002) and Wager et al. (2003) have summarized the results of 55 methodologically sound fMRI- and PET studies of basic emotions of happiness, anxiety, anger, mourning and disgust in healthy volunteers between 1990 to December 2000 .

No region of the brain is activated by all emotional tasks (visual, auditory stimulation or remembering).

- The medial prefrontal cortex has overlapping tasks – independent of the nature of activation – during processing of emotions .
- Most often, fear leads to activation of the amygdala, mourning and sorrow to activation of the ACC (subcallosum) and happiness and disgust to activation of the basal ganglia.
- Memory of emotions and duties that demand additional cognitive performances activate the ACC and the insula.
- There is no clear lateralisation of emotions.

Imaging studies of emotions have not succeeded in identifying precise and specific structures associated with emotions, that is, in localising emotions; rather they have demonstrated that almost all emotions activate complex networks such the prefrontal region, amygdale etc.

Brain Structures Associated with Emotions	
Basal frontal brain Frontal cortex	Hypothalamus Amygdala Brain stem
None of these structures can by themselves trigger emotions. Emotions result from varying interplay between several areas of activity (emotional network).	

Let us look at the consequences of emotional disturbances as represented by imaging results (PET, fMRI). Imaging modalities reveal that psychotherapeutic procedures lead, as expected, to normalization of the previously altered activities of the dysfunctional system just as medications do. Evidence for changes caused in the brain as a result of psychotherapy was first provided by PET studies of Baxter and Schwarz (1985), in patients with compulsion disorders. In the meantime, additional results are available for social phobias (Furmark et al. 2002)

and depression (Brody et al. 2001). To what extent pharmacotherapy and psychotherapy impinge on different modules within the 'depression network' (e.g. psychotherapy primarily on the prefrontal region and antidepressants specifically on the subcortical region, Goldapple 2004) remains to be clarified further.

If we look at the results of functional neuroanatomy, neurobiology and imaging modalties together, it appears that depression, the most widely investigated disturbance, is a dysfunction of a comprehensive interacting network of connections between the cortico-striatal and cortico-limbic systems, a network that regulates mood and the associated motor, cognitive and somatic behaviour (Mayberg 2003).

One has to distinguish between a dorsal network region (neocortical and medial limbic elements that influence attention, cognition and impulse and a central network region (paralimbic, subcortical and brain stem regions in which the vegetative and somatic aspects are processed. Depression thus does not appear to be a local disturbance, but rather a dysfunction of one or more components, that is, a disturbance of interaction. There is a variety of evidence for this view.

- Induced mourning in the healthy leads to imaging results comparable to those found in individuals whose depression is in a resting state:
  - Increase of activity in the ventromedial cortex
  - Decrease of activity in the frontal region
- In depressed individuals, the findings correlate with the severity of depression; it normalised under different therapies (medications, psychotherapy):
  - Inhibition of overactivity in paralimbic regions
  - Normalisation of activity in frontal region

There are no specific ‚depression regions' in patients with neurological lesions; in cases of neurological diseases affecting different locations (e.g. stroke, Parkinson's disease), imaging studies reveal the above-mentioned pattern in the presence of depression.

These network concepts must be taken into consideration when assessing fMRI findings in relation to psychological disturbances. A local change (e.g. in the amygdala region) does not necessarily indicate a causal connection, but might be an expression of a change in another brain region so that the three 'Cs' must be kept in mind: Cause, Consequence and Compensation (Lewis 2000). Thus functional deviation might represent the cause of disturbance, but it can also represent the consequence

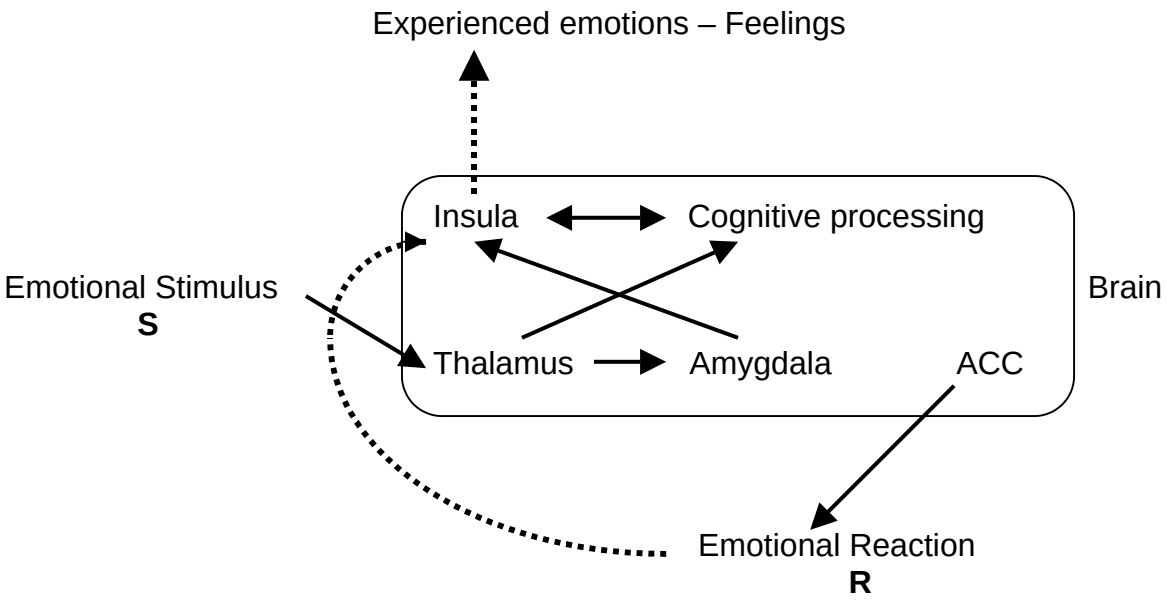
of a disturbance in super or subordinate brain regions (consequence of reciprocal connection between most of the regions) or it can also be an attempt at compensation aimed at restoring, at least partially, the disturbed functional equilibrium. This has been only inadequately taken into consideration during PET and fMRI investigations - mostly carried out in small numbers of patients - and this also explains why functional imaging has offered very little that is of concrete value in unraveling psychological disturbances (Fletcher 2004).

How are emotional stimuli processed and how do they trigger emotions? It is the old question: 'does the heart beat faster because we are afraid or do we feel afraid because our hearts are beating fast?' The answer seems to be that both are correct.

Gross perception triggers emotional reactions fast and immediately (as a rule unconsciously). The next step is a refinement of perceptual reappraisal and a motivational processing, particularly in the amygdala region and the frontal cortex. This is followed by emotional reaction and its cognitive processing (among others in the brain stem, hypothalamus, hippocampus and basal forebrain) and only finally does emotional representation with experienced emotions appear as the highest performance level with its characteristic features (somatosensory cortex and prefrontal cortex) (Adolphs 2003).

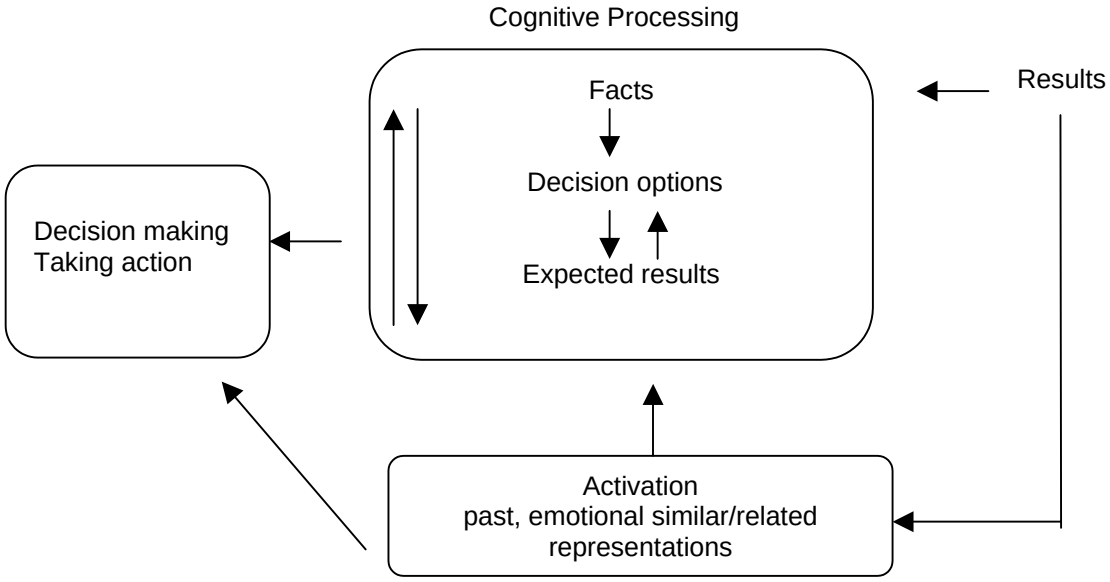
The following figure according to Morris (2002) illustrates this process.

Network of Emotions



The insula appears as the integrative sensory network section in which visceral, enteroceptive, gustatory, somatosensory, visual and auditory information are related to the corresponding mapping of feelings so that there is always a connection between a feeling and its bodily representation and vice versa. The amygdala has the task of communicating the automated reaction patterns of an emotion, that is, the vegetative responses. Feelings are mental representations of such processes (Damasio 2003).

Do we make decisions on the basis of cognitive processes or based on emotional processes or do cognitive processes influence the emotional ones and/or vice versa, (see theory of Lazarus of Primary Appraisal) ? In neurobiological research, some clarity is beginning to appear: decisions are reached both cognitively and emotionally; the two ways run parallel to each other. However, some decisions are reached only through the emotional pathway (consciously or unconsciously). These 'purely' emotional decisions (gut feelings) are often meaningful and highly valuable (Damasio 2003).



Only recently has neurobiological research, in cooperation with psychosocial researchers, attempted to go beyond the limits of primary and often automatically functioning emotions and started to investigate social behaviour with the emotions associated with it such as shame, guilt feelings, and social responsibility (Blakemore & Frith 2004, Adolphs 2003).

How can we understand what is going on in the minds of others, in what condition they are, what actions they perform and what feelings they experience? In brief, how does the ability to empathise originate? The first building block here was the description of 'mirror neurons' (Rizzolatti 2001). Mirror neurons were first described in experiments with apes. They are the ones that are activated in an observer when he perceives a specific movement made by the one observed. In principle, they are the same neurons that are activated when the observer himself makes a movement. Observation of emotions too in others automatically activates a representation of these emotions (including autonomic and somatic reactions accompanying this condition) in the observer. This is the basis of all studies so far on functional imaging in which processing of emotions is investigated. Emotion-filled faces, videos and stimuli are

presented and by a process of emotional contagion, the corresponding centres in the brain of the observer are activated.

Based on these results, Preston and Waal assumed in their Perception-Action-Model (PAM) theory that perception of an object or its condition calls forth a corresponding representation in the observer, which in turn triggers automatic and autonomic responses. Beside the different modules involved in their respective networks, the pre-frontal cortex has a decisive role to play (Preston & Waal 2002). Although this empathic occurrence runs an automatic course, it is under subjective control and is also deeply influenced by the context of the experienced and by experience of the observer in general.

Initial evidence for this theory is available. The methodologically elegantly carried out study on empathy in the face of pain (Singer et al. 2004) reported that there is activation of the pain matrix in those who experience empathy, as if they themselves were experiencing pain.

Relevance of Neurobiology for Psychotherapy and Psychosomatic Medicine

The fact that all mental processes have their foundations on neuronal processes is the starting point of all discussions on the significance of psychotherapy for neurobiology and of neurobiology for psychotherapy. Given the independence of the mental as a separate sphere, independence of research methods investigating these phenomena must also be acknowledged. Even if it is the case all psychological functions (including disturbances of these functions) have neuronal correlates, this would not be sufficient for a complete explanation of psychological phenomena in terms of neurological concepts. Since the psychological level represents a separate level of functioning, it will need to be explained at its own level, in terms of concepts applicable to this level.

Whether descriptions of neuronal correlates of psychological phenomena open up a possibility of offering a better explanation and contribute to a better understanding of psychological phenomena than if explanation of these phenomena were to be restricted to the framework of psychological concepts alone is at the present time anyone’s guess. One might cautiously express the view that there are as yet no signs of undoubtedly better explanations and thus better clinical-therapeutic possibilities resulting from neurobiological findings, although it must be admitted that the plethora of these findings makes it well nigh impossible to have an overview of the field.

Despite great hopes expressed by those pursuing basic research (identify depression, identify the anxiety gene etc), it would be wise to look at the matter a bit more soberly. Neurobiological research is yet to find appropriate ways and means to start investigating im-

portant elements of psychological disturbances – emotions, disorders of emotions and their social interactive context.

We must be warned from hastily taking over neurobiological concepts the validity of which is claimed to be established and applying them in psychosocial area. As a historical example, research on dreams may be mentioned. Based on the results of their dream research, Hobson and McCarley (1977) described dreams as lather, as expressions of activity of pontine brain stem mechanisms and in no way as expressions or source of higher order psychological functions, in contrast to the view point of psychoanalytic dream theories. Hobson presented this theory rather placatively at the annual meeting of the American Psychiatric Association in 1976. At the end, the question of whether Freud's dream theory was scientifically supportable was put to vote. Although at that time most psychiatrists were trained in psychoanalysis and were oriented towards this standpoint, the votes were unanimously against psychoanalysis. If the matter were to be put to vote today, almost thirty years later, the results most certainly will be exactly the opposite, based on our current knowledge about dreams and their psychological significance (cited according to Solms & Turnbull 2002).

Besides neurobiology, we need to have psychosocial theory and practice as independent scientific conceptualization. To avoid slipping into reductionist fallacies, a methodological dualism is necessary – an approach from psychosocial side as also from the biological side. Whether neurobiology and a psychosocial approach to psychological functions (psychiatry, psychology and psychotherapy) can team up together to form a comprehensive science of mind and brain is still wide open.

What now can be said about the advantages of an association between psychotherapy and neurobiology? For one thing, there is growing support for the biopsychosocial model, and increasing evidence for interaction between genetic, neuronal, somatic and psychological areas in basic research (some articles in the Zeitschrift für Psychosomatische Medizin und Psychotherapie' on this subject can be mentioned as examples).

In basic research there is accumulating evidence for psycho-somatic and somato-psychological interactions:

- Stressors of early childhood and their biopsychosocial consequences (see among others, Egle et al. 2002, Felitti 2002, Fuchs and Fluegge 2001)
- Pain research
- Psycho-neuroendocrinology (Uvnaes in print)
- Psycho-neuroimmunology (Schubert 2001, Schuessler & Schubert 2001)
- and Psycho-neurobiology of the central nervous system (Schuessler 2002)

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Confirmation of the biopsychosocial model

Neurobiological research not only supports the biopsychosocial model, but also validates (positively or negatively) different psychosocial theories. Whereas till recently several psychodynamic concepts such as the unconscious and defense mechanisms were considered dubious and unscientific (and therefore useless for application in practice), neurobiological research has confirmed their validity and also assigned them decisive significance and value (Schuessler 2002). Thus neurobiological research has to carry out the critical task of evaluating concepts and labeling them as unsupported and false or well-founded and correct. In this task (legitimization or umpire role according to Henningsen, 2004), neurobiology is comparable to developmental psychology, which, with its empirical results, made it possible to recognize several behavioural therapeutic and psychoanalytic theories as false, at least partially (Schuessler & Bertl-Schuessler 1992). Psychotherapeutic concepts, techniques and theories – if they are to be convincing to therapists, patients and third parties – must be in conformity with available biopsychosocial knowledge.

Different therapeutic approaches such as psychotherapy or drug therapy can achieve comparable psychosocial and neurobiological results since they intervene (probably in different areas of the brain; Mayberg 2003) in the complex neuronal dysfunctional network (e.g. depression). Treatment with medications and psychotherapy are thus not a matter of an either /or approach, but rather differing approaches that complement each other. The central questions that now arise are which form of therapy is meaningful for which patient, under what conditions and given by which therapist. As yet, little help for making decisions in these matters is forthcoming from neurobiology (biological marker).

Psychosocial changes take place within the interpersonal psychotherapeutic framework in explicit as also in implicit interactional, intersubjective processes between patients and therapists. These processes include working on cognitve and affective procedures, aiming at deactivating old negative patterns and establishing flexible and adaptive patterns of interaction. This presupposes destabilsation of habitual patterns and requires security (Boston Change Study Group 2002). Whether this enables translating the aim of psychotherapy in neurobiological terms, in terms of functional tasks and building up and expanding the influence of prefrontal cortex (Solms & Turnbull 2002) will remain as a partial description of the complex events and processes.

States of mind such as depression or anxiety can be changed both by drugs and psychotherapy. This is plausible from a neurobiological point of view. Alterations in the procedural-affective-cognitive networks (traits = personality features, lasting conflicts, habitual learning experiences) require a longer period of therapy before they can be anchored once again in

emotional-procedural networks. If neurobiological knowledge can support the view on learning that even simple activities such as bicycling require long learning periods, it becomes clear that complex interactional patterns and their changes will require a much longer period of time. Neurobiology of learning is thus the best lawyer for advocating longer psychotherapies the aim of which is to change not only states (such as short-term therapies of 10-20 hours), but also neurotic (procedural-affective) patterns.

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