Neurobiology and psychotherapy: an emerging dialogue

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Purpose of review

The paper outlines the beginning dialogue of neuroscience and psychotherapy by reviewing neurobiological research relevant for therapeutic concepts, presenting recent neuroimaging studies on psychotherapy effects, and discussing some conceptual problems.

Recent findings

Research into neuroplasticity, the role of explicit and implicit memory systems, early attachment processes, as well as the biological underpinnings of mental disorders has considerably influenced psychotherapeutic concepts, shifting the emphasis to implicit learning in the therapeutic relationship. Recent neuroimaging studies have also demonstrated that psychotherapy significantly changes functions and structures of the brain, in a manner that seems to be different from the effects of pharmacotherapy. These results as summarized in the paper give rise to some conceptual issues which are finally dealt with. It is argued that neurobiology may be helpful in assessment before therapy, but that psychotherapy is essentially based on its subjective and intersubjective dimension that cannot be turned into an 'applied neuroscience'.

Summary

The interplay between neuroscience and psychotherapy holds interesting prospects for the future, but also implies some pitfalls which are mainly due to reductionist approaches to the mind–body problem, suggesting caution about unrealistic expectations toward a 'neuro-psychotherapy'.

Keywords

neurobiology, psychotherapy, memory, attachment, mind–body problem

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Abbreviations

CBT cognitive-behavior therapy
PET positron emission tomography

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Introduction

Following a long period of mutual neglect, contemporary neuroscience and psychotherapy have entered a new stage of their relationship. With growing sophistication in its methods, neuroscience has started to identify neural correlates not only of mental disorders but also of therapeutic changes. The traditional dualism of psychological and somatic psychiatry seems no longer tenable, since even fleeting emotions or thoughts have been shown to leave their traces in the brain. This offers two diverging paths for psychiatry. On the one hand, neurobiology will claim hegemony over psychological approaches, implying some kind of reductionism which holds that all psychological states are 'really' brain states. Mental disorders should then be regarded as nothing other than chemical imbalances, and psychiatrists should not treat individuals, but their brains. On the other hand, psychological psychiatry could turn the tables and demonstrate that the formation of the brain is inseparably connected to a person's environment and life history. In this view, the brain may only be properly understood as a social and historical organ, along the lines of a 'social neuroscience' [1] or 'neurophenomenology' [2,3]. This would potentially integrate analyses of biological, psychological and social determinants of mental disorders into a coherent framework that would even stimulate psychotherapeutic theory and practice.

The following review tries to contribute to such an integrated perspective by outlining (1) the influence of neurobiological research results on psychotherapeutic theory; (2) the evidence for neurobiological effects of psychotherapy; and (3) some conceptual and methodological problems of a 'neurobiologically informed' psychotherapy.

Influence of neurobiological research results on psychotherapeutic theory

There are several areas of neuroscience that are of special interest for psychotherapy, above all recent research into memory and neuroplasticity, as well as the exploration of neurobiological underpinnings of attachment and intersubjectivity.

Neuroplasticity and memory

The investigation of neuroplasticity has added new insight to our understanding of therapeutic change. As we currently know, growth and differentiation of the brain are not only determined genetically, but also by its continuous interaction with the environment. This epigenetic formation of the brain does not end in early childhood: There is a life-long re-mapping of cortical networks according to the individual experience, including the de-novo generation of neurones in the adult hippocampus, as proven recently [4]. Neuroplasticity is a prerequisite for any enduring change in behavior, cognition, and emotion, which is the focus of psychotherapy. In order to produce lasting effects, psychotherapy should arrive at restructuring neural networks, particularly in the subcortical-limbic system which is responsible for unconscious emotional motivations and dispositions. 'Insight' or 'appeal' reach only corticohippocampal structures, which correspond to conscious memory and cognition, but have only very limited effects on the motivational system [5,6].

Memory research is directly relevant for the processes of learning and change that are dealt with in psychotherapy. Of particular importance is the distinction established by cognitive neuroscience between two memory systems [7,8]: procedural (implicit) memory encompasses all automatic performances, unconscious dispositions and nonverbal habits of behavior, whereas declarative (explicit) memory records single experiences for later recall. Both are based on different sets of neural structures: procedural or implicit memory involves, among others, the basal ganglia, cerebellum and amygdala; declarative memory is mainly located in the temporal lobe, especially in the hippocampus and connected cortical structures [9]. Since the implicit memory system also contains stored patterns of bodily and emotional interaction which are prereflectively activated by subtle situational cues (e.g. facial expressions, gestures, undertones, atmospheres), it is crucial for the patient's relationships as well as for the therapeutic process.

Developmental research, attachment, and the roots of empathy

In this context, further important results come from developmental research into memory and learning. Mother–infant interaction research has shown that procedural learning and the cerebral mapping of interaction patterns are fully developed in infants aged 3–4 months [10]. By unconscious processing of affective information, their implicit memory system is already capable of extracting prototypes and rules from repeated experiences. Thus procedural 'schemes-of-being-with' [11] are acquired that organize the child's interpersonal behavior, and which will later be transferred to other environments whether these are congruent with the early experiences or not. Thus implicit memory also serves as the link between deficient early interaction experiences, dysfunctional bonding patterns and disturbed affect regulations, which play a decisive role in most mental disorders. These convergent results from developmental and neurobiological research have confirmed, on the one hand, the role of the unconscious as emphasized by psychoanalysis. On the other hand, this implicit unconscious is quite different from the dynamic unconscious due to repression, defence, anxiety, or conflict, which Freud conceived as the predominant form [9]. Neuro-developmental research has also shown that childhood amnesia is not the result of a repression during resolution of the oedipal complex, but corresponds to late maturation of the declarative memory system [12]. Thus neurobiological findings have in part contradicted central assumptions of psychoanalytic metapsychology.

The 'biological turn' of psychology has also drawn renewed attention to John Bowlby's [13] attachment theory of social bonding. Supported and expanded by animal research on disturbed neurophysiologic homeostasis following early deprivation [14,15], Bowlby's theory may serve as a psychobiological model for the social development of the brain. There is growing evidence that the attachment system is a central organizing system in the brain of higher social mammals, allowing infants to use their parents for regulating their inner states until their own psychoneurobiologic functions become mature and autonomous. As Amini and colleagues have pointed out, the developing nervous system consists of 'open homeostatic loops' which require external regulation or 'tuning' from others [14,16]. On the phenomenological level, this corresponds to the shared states of 'affect attunement' [11] or 'dyadic states of consciousness' [17] of mother and infant. These early attachment experiences are internalized and encoded as procedural memory, thus establishing secure and stable bonds to others. Conversely, attachment deficits may result in disorganized behavioral repertoires and deficient 'body micro-practices' [18•], as well as an impaired physiologic capacity for self-regulation of stress and affects [9,14]. These findings highlight how deeply human sociality is weaved into the physiological structures of the body.

The intersubjective nature of the human brain is underscored by the discovery of a neural mirroring system in the premotor cortex and other areas of the brain, obviously serving as the neurobiological correlate of action understanding, nonverbal communication and empathy [19,20]. Mirror neurons discharge both when an action is performed and when a similar action is observed in another individual. They seem to represent a system that matches intentional behavior of others to one's own action experience, and in this way they form a link of mutual understanding through bodily simulation or resonance. Recently, 'pain neurons' activated by pain observed in others have also been found in the cingulate cortex [21]. Though not having direct applicability for psychotherapy, the concept of a mirror matching network supplies strong evidence for what the phenomenologist Merleau-Ponty [22] has called 'intercorporality': there is a sphere of bodily sensibility and mutual resonance which we share from the beginning with others as embodied subjects. To become aware of these prereflective processes going on during verbal exchange may enhance therapeutic effectiveness.

Consequences for psychotherapeutic concepts

These convergent influences of various research results, though still at an early stage, have already changed the overall framework of psychodynamic approaches and other psychotherapies considerably. The established role of procedural memory and emotional learning, the implicit nature of early acquired relational patterns, the crucial importance of attachment, intercorporality and empathy, in contrast to a decreasing role of repression and declarative memory, have shifted the emphasis from insight-oriented, interpretative or cognitive techniques towards procedural and emotional learning. Alteration of implicit memory patterns presupposes their activation as 'enactments' in the therapeutic process. Accordingly, Stern and other members of the Boston Process of Change Study Group [23,24] have developed a therapeutic model centered on 'now-moments' in the interaction which represent a particularly striking convergence of procedural relearning and insight. Cognitive-behavioral approaches increasingly emphasize the role of the therapeutic relationship [25].

Psychotherapy may thus be regarded as a new attachment relationship which is able to regulate affective homeostasis and restructure attachment-related implicit memory [14,26]. In this view, the core of therapeutic interaction lies in the affective communication mediated by bodily resonance, undertones and atmosphere much more than by symbolic language. Thus it is not so much the explicit past that is in the focus of the therapeutic process but rather the implicit past which unconsciously organizes and structures the patient's 'procedural field' of relating to others. Psychoanalyst Peter Fonagy even denies that the recovery of explicit memory or removal of repression is key to therapeutic action: 'Psychoanalysts should carefully and consistently avoid the archaeological metaphor' ([27], p. 220). In sum, the growing emphasis on implicit relearning in psychotherapy supports the present, experiential aspects of the therapeutic relationship as agents of change. Moreover, it argues against affective neutrality of the therapist, which would deprive the new attachment relationship of its actual operative dimension [14].

Neurobiological effects of psychotherapy

With increasing influence of neurobiological paradigms on psychotherapy, the question arises whether psychotherapeutic effects may also be demonstrated on the neurobiological level. Procedural relearning in psychotherapy should be expected to influence the structure and functions of the brain by altering synaptic plasticity and gene expression [28,29]. There is growing evidence for a modification of gene expression by emotional experiences [26]; for example, tender touch activates the expression of an 'immediate early gene' which promotes cellular processes of growth and maturation ([30], p. 14f). Of course, psychotherapeutic effects will be more dependent on long-term changes in pathophysiological patterns of the brain which may, for example, be shown by neuroimaging studies.

An exemplary positron emission tomography (PET) study was carried out by Baxter *et al.* [31] and later replicated by the same group [32], showing that in obsessive–compulsive patients both successful cognitive-behavior therapy (CBT) and imipramine treatment lead to a similar reduction in over-activation of the rostral caudate nucleus. In the meantime, a number of imaging studies have produced similar results. In PET studies of depressive patients, Brody *et al.* [33] and Martin *et al.* [34] found decreases in prefrontal lobe activity following interpersonal psychotherapy and antidepressant medication. Furmark *et al.* [35] and Paquette *et al.* [36•] reported normalized frontal metabolism after successful CBT treatment of social and spider phobia, respectively, and concluded that CBT is able to functionally 'rewire' the brain. In spite of some methodological shortcomings (mainly small and heterogeneous sample sizes), these studies support the hypothesis that different disorders show more or less characteristic changes of regional brain activity that may be normalized by psychotherapy. Finally, in a more sophisticated PET study of depressive patients, Goldapple *et al.* [37•] found differential target areas of successful CBT versus drug treatment: the medial frontal and cingulate cortex with CBT, and limbic-subcortical regions (brainstem, insula, subgenual cingulate) with pharmacotherapy. According to the authors, this means that CBT interventions should focus mainly on modifying dysfunctional cognitions, leading then to an alleviation of vegetative symptoms and inhibition, whereas pharmacotherapy should take the opposite course.

The latter study seems particularly interesting as it suggests different primary targets of action in these disparate treatments: psychotherapy seems to be mainly based on cortical 'top-down' mechanisms, and pharmacotherapy on subcortical 'bottom-up' mechanisms [37•]. This would correspond to a concept of the brain as an organ of transformation [38,39], which may be addressed by input on different hierarchical levels and translates it in both directions. The transformation runs 'top-down' in the one case, that is from subjective experience of meaning and interaction to the neurochemical level –

mental acts change the brain; and it runs ‘bottom-up’ in the other case, that is from pharmacological effects on subcortical transmitter metabolism to a change in subjective mood and cognition. Such a bidirectional concept is also supported by the results of the Mayberg group [40], showing mainly cortical (‘subjective’) effects of placebo in contrast to subcortical-limbic and brainstem effects of fluoxetine in major depression. In another study, the authors found a similar reciprocal cortical versus limbic affection in normal sadness and depression [41]. This points out that there is no separation, but rather a mutual transformation of psychological into biological processes and vice versa, brought about by the brain.

Transferred to etiology, this concept suggests that the simple bottom-up explanation of mental disorders as products of genetic or neurophysiological determinants is inadequate to the causal complexity involved. A more promising alternative would be a two-layer model of disease as suggested by Mundt [42]: a basic organic dysfunction or vulnerability (as manifested in an instrumental, emotional or interpersonal deficit) may lead to an emerging and more complex mental disorder, implying individual responses to a given life situation, coping mechanisms, or maladjustments such as avoiding or aggressive attitudes. This two-layer concept is well established, for example for Borderline personality disorder or schizophrenia [43–46]. However, it still suggests a linear (mainly bottom-up) causality. From a more complex perspective, the final disorder should be regarded as the product of a circular causality of subjective, neurophysiological, environmental and social influences continuously interacting with each other. Circular models involving negative feedback loops of primary symptoms, emotions, cognitions and social interactions have already been developed for depressive or anxiety disorders [25], as well as in systemic family therapy. In these circular interactions, the brain acts as a mediating, translating organ or a ‘relay station’ [38], not as the monolinear cause.

On this basis, the dualistic distinction between somatic therapies acting on the brain and psychological therapies having elusive, purely subjective effects is no longer tenable. Instead, a complementarity of approaches is required, using medication to target basic symptoms or temperamental dispositions such as impulsivity and affective instability, and psychotherapy aiming at changes in the patient’s implicit relational patterns, attitudes and behavior [26]. Even if there is often a common final pathway of symptom reduction, psychotherapy cannot be replaced by medication, for we do not have any biochemical means to change the maladaptive dispositions of interaction and behavior that have led to a disorder, and may lead to relapse in the future. Such dispositions are only accessible to change by new and repeated experiences, that is emotional, verbal and interpersonal processes of learning that over time are ingrained into brain structures [38].

Towards a ‘neuro-psychotherapy’?

So far the interplay of neuroscience and psychotherapy has been described in such a way that seems to offer the chance for a fruitful dialogue. The final section discusses some principle problems and pitfalls that may prevent a premature euphoria regarding a ‘neuro-psychotherapy’.

Methodological limitations of the neurobiological approach

First, we have to be cautious with the interpretation of neurobiological findings. While neuroimaging procedures can be very useful tools, they also have a number of limitations that need to be taken into account [47•]. Of course these glittering images do not show the real brain in action, but are merely visualizations of statistical analyses, based on subtraction of larger numbers of images, with problematic correlation to morphological brain structures [48]. Thus, they are much more scientific constructs than images of ‘the brain’. In addition, it is not at all certain that the clinically important phenomena actually correspond to those that show up most colorfully in the images [49•]. These could also result from inhibitory or compensatory activity in certain areas secondary to a basic dysfunction in others.

A more fundamental problem is the static view to which we are seduced by imaging single states of the brain. These methods on their own tend to turn lived experience and dynamic processes into thing-like objects. Such a view, however, is inadequate to describe the temporal and spatial structure of mental life as a being in the world. On the phenomenological level, there is nothing like isolated ‘mental events’ as assumed by neuroscience; consciousness exists only embedded in the world and in the temporal process of life [50•]. The same applies at the biological level: the mind is based on the continuous interaction of the brain with the organism, and of the organism as a whole with the environment [38]. It is not located in any one place but is distributed among the brain, the body, and the environment. Such an extended view of the mind has recently been advocated by Clark and Chalmers [51,52].

Psychotherapy in particular is an interpersonal process based on circular transference–countertransference relations that cannot be grasped from an individual perspective. It implies a mutual creation of meaning which is not a ‘state in the head’ but arises from the ‘between’, or the system, of patient and therapist. Neurobiology, however, is focused on single brains, as yet far away from the intricacies of intersubjectivity. A 'before–after paradigm' applied in imaging studies so far may be helpful for ascertaining effects or constraints on the substrate level, but fails to account for what is really going on during sessions. Psychotherapy has moved a long way from the traditional one-person psychology to focusing on the moment-to-moment interaction between patient and therapist. This progress should not be sacrificed on the procrustean bed of a single-brain neuroscience.

Incompatibility of first and third person approaches

The most basic problem that a cooperation of neurobiology and psychotherapy faces is the incompatibility of both approaches. Psychotherapy mainly deals with emotions which are the core of our subjective experience; it works in the dimension of intuition, atmospheric perception and empathic relationship, that is in the first and second person perspective. The biological paradigm, by contrast, uses means to objectify brain functions from a third person perspective. Subjective and intersubjective experience as such is not accessible to neuroscience in principle. Nor has it, by its very nature, anything to say about intentionality, that is the meaning which events and persons have for an individual. However, these dimensions are what psychotherapy is all about. Learning to know oneself has been its supreme goal since antiquity; however, even the existence of a self is questioned by today's neuroscience: it seems to get lost in the 'jungle of synapses' [53,54]. The phenomenological and methodological gap between physical processes and the level of experience is not easily overcome.

Even if one subscribes to an ontological monism of mind and brain, still an epistemic and methodological dualism of first and third person approaches seems inevitable. Research into the neural substructures alone, without considering the psychosocial level of meaning and context which in turn shapes the brain and its functions, will never provide a sufficient explanation for the manifestation and course of mental disorders [55]. This argument is even more valid for the complex processes going on between two persons and their brains during therapy. An integrated framework for these approaches could be based on systemic or circular causality models of biological, psychological and social processes, with the brain acting as an organ of transformation and translation. But even such a 'social neuroscience' framework [1], implying naturalistic and hermeneutic approaches alike, is still far from a unified science of the mind. At present, a dialogue of the competing paradigms seems more appropriate than a premature attempt at unification. In our scientific discourse, we are only just beginning to emulate the mutual translation of the levels of matter and meaning which the brain itself has achieved for thousands of years.

De-stigmatization versus de-personalization

Finally, a major ethical problem raised by neuroscience concerns our conception of mental illness. Biological psychiatrists often argue that it is de-stigmatizing for the patient to learn that his disorder is merely due to faulty transmitter metabolism. Focusing on impersonal brain mechanisms may disburden the patient or his relatives from inadequate feelings of guilt and responsibility. Psychological analyses by their very nature could potentially lead to blaming the person, whereas in the biological model only the body has to be searched for etiologies.

But should we really regard a mental disorder as something from which there is nothing to understand or learn? Granted, psychotherapy may put a burden on patients, but only insofar as it holds them capable of insight, autonomy, coping and maturation. It addresses their will to change, their responsibility for themselves, their search for meaning and identity even in their illness. In contrast, a reductionist biological concept of mental life may gradually lead to a self-alienation: in the wake of a popularized neurobiology, we are beginning to regard ourselves not as persons having wishes, motives or reasons, but as agents of our genes, hormones and neurones. The use of 'brain language' is increasingly permeating our self-conception. Consequently, our problems and sufferings are no longer considered existential tasks that we have to face, but results of malfunctioning neuronal circuits and hormone metabolism. Thus a recent article in *Nature* already envisages a 'commitment pill' for men with attachment deficiencies [56]. The President's Council on Bioethics [57•] has outlined the perils of a medicalized society, using chemical means for erasing unpleasant memories, tempering restless children, brightening moods and altering basic emotional dispositions.

Of course, psychotherapy may rightly argue that it influences brain structures as well. Some psychotherapists already start to redefine their work enthusiastically as a biological therapy which successfully re-programmes or re-wires the brain [36•,58]. But as therapists, we still talk to the patient, not to his synapses. Psychotherapy does not have to 'prove' its effectiveness by neuroscientific procedures; there is enough evidence for this from outcome research, based on the experiences of patients. To regard neurobiology as the 'real thing' to be targeted by psychotherapy means to devaluate the lived and shared reality of the therapeutic encounter which is the actual source of change.

Conclusion

The dialogue between psychotherapy and neurobiology has just begun. On both sides, all kinds of positions are still to be found, from fervent antagonism, scepticism or indifference to enthusiastic endorsement of some future 'neuro-psychotherapy' or 'neuro-psychoanalysis' (the name of a new journal). Thus Kandel welcomes the possibility of monitoring the process of psychotherapy by neuroimaging methods [59]. Grawe [25] has already developed a 'general psychotherapy' based in large part on neurobiological premises, including connectionist and systems theory; a similar approach is endorsed by Caspar [48,60]. On the other hand, psychotherapy has for a long time proven effective without being informed by neurobiology. The studies of brain changes caused by psychotherapy are still preliminary and require further replication. The action mechanisms of psychotherapy at the neural level are largely speculative at this stage [26]. All that may be said is that, owing to the translating function and plasticity of the brain, psychotherapy works by changing minds and neural networks at the same time.

Before long, this could change; neuro-biological models may then serve to improve the design of, and clarify the constraints for, psychotherapeutic interventions. A recent hint at future options is the finding that the activity level of the anterior cingulate gyrus of depressed patients predicts subsequent treatment response to selective serotonin reuptake inhibitors [61]. This could be transferred to assessments before psychotherapy: gaining a fuller picture of biological substrates of mental disorders may allow treatment plans to be formulated and help to decide what kind of therapy to apply [62]. In treating the sequelae of psychological trauma, for example, it is important to know if there are permanent changes not only in psychological functioning but also in brain structures [47•]. Thus the interplay of neuroscience and psychotherapy could be fruitful not only on a conceptual, but also on a practical level.

It would certainly be an illusion, however, to expect that the complex interpersonal processes occurring in the course of psychotherapy could ever be completely described by brain physiology. Neurobiology may well help to evaluate the chances and constraints of therapy; but when it comes to the subtleties of interaction and transference, practicing psychotherapists will always rely on their experience and intuition. As Nemiah rightly argued, 'we are ourselves the instrument that sounds the depth of the patient's being, reverberates with his emotions, detects his hidden conflicts, and perceives the gestalt of his recurring patterns of behavior' ([63], p. 465). No brain scan will ever be superior to this instrument. Moreover, the level of meaning, temporality, existence and self-knowledge essential for every intensive therapeutic encounter is in principle beyond the reach of neurobiology. Therefore, psychotherapy will never turn into applied neurobiology; its main foundational sciences will remain psychology, hermeneutics and the humanities in general.

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