Neuropsychotherapy: Psychotherapy Methods and Their Effect

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Contents

G. Roth et al. (eds.), *Psychoneuroscience*, https://doi.org/10.1007/978-3-662-65774-4_14

The purpose of this chapter is to provide an introduction to a neurobiological perspective on psychotherapy. For this purpose, the previous development in the interaction of neuroscience and psychotherapy (research) will be considered and neuroscientific methods in psychotherapy research will be introduced. In addition, the major schools of therapy, such as behavior therapy and psychoanalysis, as well as cross-school concepts are considered and related neurobiological findings are presented as examples. Following on from this, implications of the neurobiological perspective for everyday therapeutic practice are explained. Finally, possible future perspectives of this field of research are outlined.

Learning Objectives

The readership, after working through this chapter, should …

… have developed an understanding of the development and interplay of neuroscience and psychotherapy (research).

… have received an overview of the scientific methods in the field.

… have become acquainted with the basic findings on the neurobiological foundations of both school-oriented and cross-school concepts.

… have gained a practical impression of the possible implications of neuroscientific findings for the application of psychotherapeutic methods.

14.1 Neuropsychotherapy: An Integrative Perspective

The following section provides a brief introduction to the topic with a view to the developments to date in the interaction between neuroscience and psychotherapy (research).

While neuroscience uses scientific methods to study the human brain, its structure and functioning, psychotherapy research, as a field of clinical psychology, is concerned with the mode of action of psychotherapeutic procedures, their effectiveness and the further development of psychotherapeutic methods for clinical practice. Thus, while on the one hand humans are viewed and studied as predominantly biological beings, on the other hand humans and their experience and behavior are understood and attempted to be changed predominantly as psychological phenomena. While the cradle of neuroscience is rather to be found in biology and medicine, psychotherapy research originates primarily in empirical psychology, more precisely: the subfield of clinical psychology and psychotherapy. The paths of neuroscience and psychotherapy research would therefore not necessarily have to cross. What both disciplines have in common, however, is that they focus on people and their mental processes and consider their adaptation to a changing environment. Another common feature is that both fields represent multidisciplinary research areas, i.e. scientists from many different disciplines, such as psychology, medicine, biology, computer science or mathematics, are involved and work on common research questions. Thus, it is not surprising that neuroscientific methods have become indispensable to research in clinical psychology and psychotherapy and, conversely, that psychological theories and concepts often inform neuroscientific research questions.

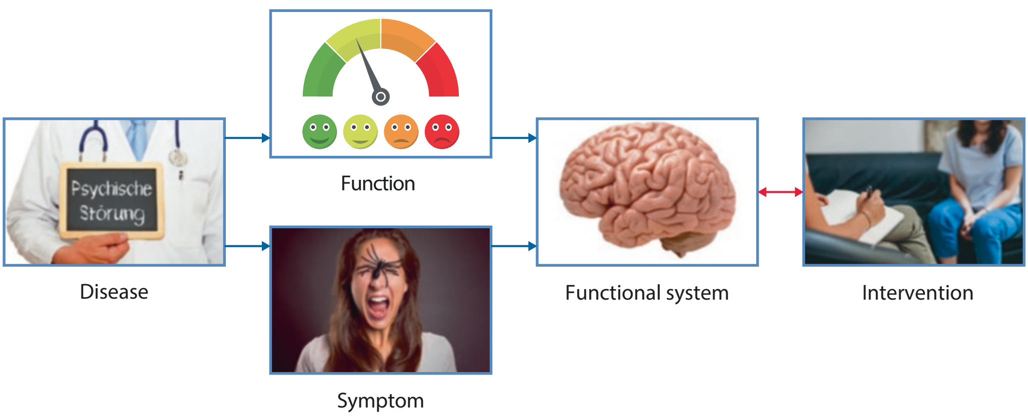
As an integrative concept, the neurobiology of the psyche or the so-called neuropsychotherapy has therefore clearly gained in importance in recent decades. Neuropsychotherapy is concerned with the application of the findings of neuroscience, i.e. from different sub-areas such as neurobiology and neuropsychology, to psychotherapy. The latter is based on empirical findings from psychotherapy research.

> The term neuropsychotherapy was coined primarily by the psychotherapist and psychotherapy researcher Klaus Grawe, who used it as the title of a book published in 2004 in which he argued for an integrative view of psychotherapy and for greater mutual promotion of psychotherapy research and the neurosciences (Grawe 2004).

This multidisciplinary and integrative approach is increasingly achieving important results in the field of the foundations of human learning and development processes. The most important example is findings on the neuronal plasticity of the human brain, which had long been considered clearly limited. Neuronal plasticity refers to the enormous capacity of the human brain to change throughout life through various neurobiological processes. This occurs in the context of a person's particular experiences and actions. Findings on lifelong neuronal plasticity therefore also underline the importance of therapeutic interventions for neurobiological changes in the brain of the person being treated. Gaining knowledge about brain changes that are associated with certain diseases or that are related to therapeutic interventions in the treatment process therefore represents a great hope for being able to help people with a mental illness as well and effectively as possible. The potential opportunities of looking at neuroscience and psychotherapy (research) from an integrative perspective therefore include several potentially useful aspects (► Box 14.1).

From a methodological perspective, findings from e.g. functional imaging add an intermediate step to the previous approach. If psychotherapy research usually wants to describe in more detail and understand how a specific symptom or function associated with a mental illness can be changed by a specific intervention, the neuroscience perspective adds the intermediate step of underlying changes in the brain (◘ Fig. 14.1).

In addition to the justified hopes, there are also justified doubts as to how great the added value of neurobiological findings for psychotherapy can actually be. This is mainly due to the fact that popular neurobiological studies, such as imaging studies, have so far mainly been able to make statements about overall samples. Predictions about clinically relevant parameters, such as diagnoses or expected treatment success, can hardly be made precisely or reliably for the individual with the methods available to date. Concrete translational implementa-



◘ **Fig. 14.1** Scientific investigation of the effect of therapeutic interventions. (© from left to right: DOC RABE Media, stas111, lassedesignen, danheighton, loreanto, each at ► stock.adobe.com) tions into clinical practice are accordingly still thin on the ground (Won and Kim 2018). It remains to be seen which methodological innovations can remedy this situation (see also ► Sect. 14.8).

From a more philosophical point of view, it is equally interesting to note that the study of the brain and its functions in particular, as an explanation for phenomena such as “the mind”, evokes astonishing scepticism. David Papineau, a contemporary philosopher, makes the comparison that we have little difficulty describing a clear, odorless, tasteless liquid by the word “water” and at the same time by the chemical structural formula “H_2O” (Papineau 1998). Both represent different approaches to the same phenomenon. It is incomparably more difficult for us humans to capture a feeling of “love” simultaneously by “neuronal activity in area X”, even though this is also not a substitution but the addition of a further level of description.

In this section we have taken a first look at the parallel development of neuroscience and psychotherapy (research). While both initially developed mainly separately from each other, these fields of research are now increasingly interacting with each other.

Box 14.1 Opportunities and Possibilities of an Integrative Perspective on Neuroscience and Psychotherapy (Research)

- Objectifying description of symptoms, which are by definition subjective in their clinical recording.
- Broadening the understanding of the development and maintenance of mental illnesses.
- Optimization of diagnostic procedures.
- Improving the effectiveness of known interventions.
- Further and new development of interventions based on neurobiological findings.
- Expansion of the possibilities of differential indications.
- Orientation of the therapist’s behaviour towards the best possible brain-biological conditions for change.

14.2 Neuroscientific Methods in Psychotherapy Research

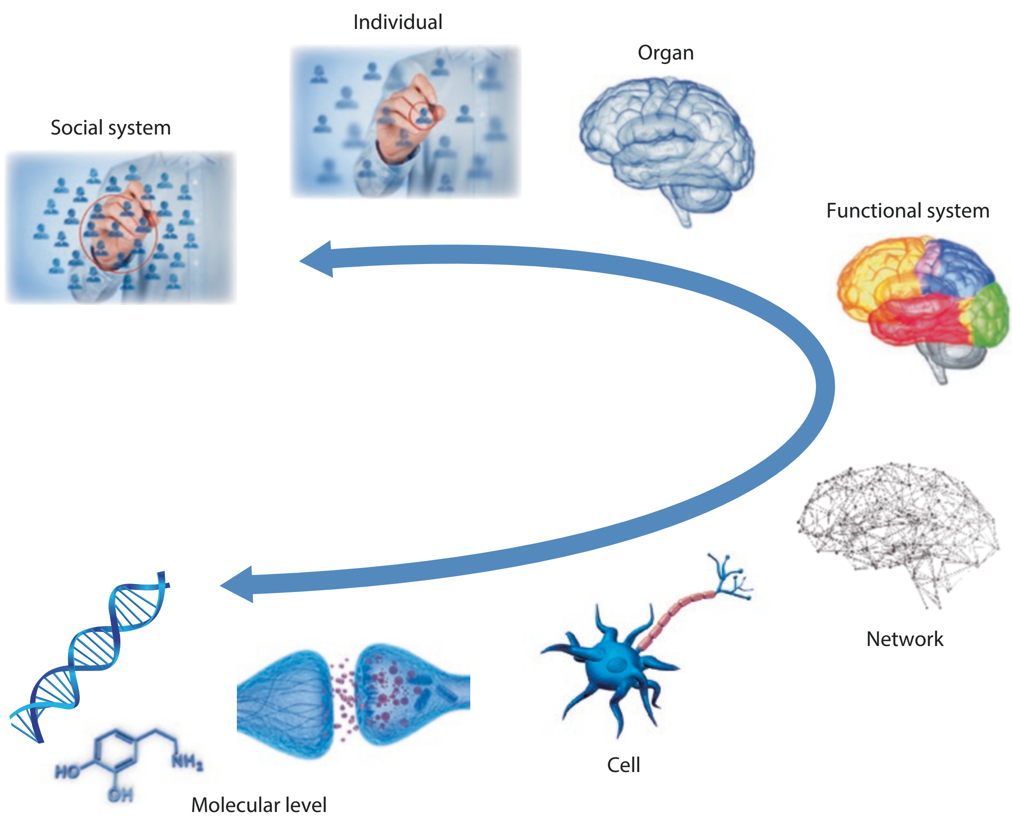
In order to be able to see and classify neurobiological psychotherapy research and its significance for the field as a whole, it is first important to explain and discuss the methodological peculiarities in this field of research by way of example. The aim is to create a basic understanding of the opportunities and limitations of the interlocking of neuroscience and psychotherapy research against the background of methodological conditions.

From archaeological finds of early Egypt it is known that man already performed surgical interventions on the human brain about 5000 years ago. Since then, man has tried to expand the understanding of this organ in our head with the possibilities available at the time. While in ancient times a strong interest in the brain and its processes prevailed, this clearly diminished over the Middle Ages, the understanding of the human brain continued to grow steadily in the further course of human history and reached a temporary peak with the great neurobiological findings of the nineteenth and twentieth centuries, such as the discovery of so-called long-term potentiation as a direct indication that experiences can change the activity of nerve cells. In recent decades and currently, this trend has continued, especially in the form of methodological innovations.

14.2.1 Methods of Neuroscientific Psychotherapy Research

The sub-fields of today's modern neuroscience, which deal with the changes in human experience and behaviour in the context of mental illness and their correlates in the brain, now use a wide variety of methods, with different strengths and weaknesses. These methods are also used to investigate the neurobiological basis of psychotherapeutic processes. Classical psychotherapy research focuses primarily on psychological and sociological methods to describe the changes in the individual or the social system, while neuroscience adds various neurobiological oriented approaches. Investigative methods such as electrophysiology, imaging, or so-called stimulation methods belong to macroscopic perspectives on the brain, while cell physiological, molecular biological, or genetic approaches, for example, aim to understand microscopic processes (◘ Fig. 14.2). Ideally, these different approaches complement each other to form an overall picture.

The available neuroscientific methods differ in their applicability to humans. Accordingly, mainly non-invasive methods are used in the field of neuroscientific psychotherapy research. These include various approaches which, with the help of technical devices, allow direct or indirect conclusions to be drawn about the activity of the brain.



◘ **Fig. 14.2** Different methodological approaches to the (neuro-)scientific study of humans. (© clockwise from top left: Jakub Jirsák (2x), ag visual (2x), tampatra, freshidea, vector_factory, dana_c, Alexandr Mitiuc, each at ► stock.adobe.com)

One example are the so-called electrophysiological methods, which measure electrical potentials or fields and can map changes in brain activity with temporal accuracy. These include *electroencephalography* (EEG) and *magnetoencephalography* (MEG). The advantage of both methods is that they can measure the activity of large cell clusters with high temporal resolution, whereas the spatial resolution is moderate. Therefore, these methods are particularly suitable for the analysis of successive processing steps in the brain. Methods that are primarily used to identify lesions in the brain, such as *cranial computed tomography* (cCT) or *structural magnetic resonance imaging* (sMRI), play little role in psychotherapy research. In contrast, all imaging methods that can depict functional changes in the brain are particularly relevant, such as *functional magnetic resonance imaging* (fMRI). This method is non-invasive, has good to very good spatial resolution and is widely available in Western countries, but has relatively poor temporal resolution. This group also includes the less widely used methods of *positron emission tomography* (PET) and *single photon emission computed* tomography (SPECT), which can measure molecular correlates of neurotransmission in addition to activation. In addition, *near-infrared spectroscopy* (NIRS) has a good temporal resolution but can only record small parts of the brain. Stimulation methods that can temporarily and locally influence brain activity, such as *transcranial magnetic stimulation* (TMS), *transcranial direct current stimulation* (tDCS) or *deep brain stimulation* (DBS), are also increasingly being used. These methods, some of which are invasive, have so far played only a minimal role in research into psychotherapeutic processes. Newer methods or further developments of the available procedures, on the other hand, are very interesting for psychotherapy research, such as the increasing analysis of fMRI data on the basis of network models and with a view to functional couplings (functional connectivities) as well as the recording of mechanisms on the basis of mathematical models in so-called *computational neuroscience*.

The use of microbiological or genetic approaches for questions in psychotherapy research has been rarer up to now. However, with regard to the modulation of peripheral physiological parameters by psychotherapy, such as stress-associated parameters, a correspondingly broad repertoire of peripheral physiological methods is used here.

Neuropharmacological approaches are also increasingly emerging in this field, i.e. the use of pharmacological modulation to augment psychotherapeutic effects. For example, the administration of D-CYCLOSERINE to accompany the cognitive behavioral treatment of anxiety disorders is being discussed in order to optimise the effect of psychotherapeutic interventions by modulating the glutamatergic system, but the data on this are still inconclusive (Ori et al. 2015).

14.2.2 Experimental Paradigms in Neuroscientific Psychotherapy Research

Different experimental paradigms are used to study the effects of psychotherapeutic procedures and specific interventions. Three main groups of paradigms can be distinguished:

- Paradigms with symptom provocation,
- paradigms to etiological models of a disease, and
- intervention paradigms.

Also used are so-called *resting-state* paradigms, i.e. measurements of brain activity under resting conditions.

■ Paradigms with Symptom Provocation

Paradigms with so-called symptom provocations examine the changes in the brain in connection with psychotherapy by comparing the changes in brain activity during targeted stimulation of the brain with a symptom-triggering stimulus before and after therapy. Examples include the neural processing of images of fear-inducing objects or situations in phobias (Paquette et al. 2003), auditory presented scripts of traumatic experiences in post-traumatic stress disorder (Lindauer et al. 2008; Malejko et al. 2017), or addiction-related stimuli such as images, smells, or sounds in people with addictive disorders (Owens et al. 2017). As can be seen from the examples, for methodological reasons this approach is particularly suitable when external triggers are present for the symptoms to be stimulated. It is more demanding to implement studies that refer to internal triggers, e.g. to trigger ruminative loops in depressive patients by means of certain thoughts.

Overall, symptom provocation paradigms are now widely used. For example, one of the first imaging studies on this topic (Paquette et al. 2003) showed in people with arachnophobia that the neuronal effects of confrontation with video sequences of spiders had normalized after a successfully implemented cognitive behavioral therapy. While the patients reacted to the spider videos before therapy with increased activity, especially in the dorsolateral prefrontal cortex and the parahippocampal area, which the authors interpreted as memory as well as self-regulatory activity, this was no longer measurable after therapy.

▪ Paradigms of Etiological Models of a Disease

Experimental paradigms on etiological models of a disease use knowledge about the development of a disease to stimulate an etiologically relevant functional system of the brain and to record its altered activity in the context of psychotherapy. For example, this approach can be found in studies on the neural processing of emotional stimuli in depression (Ritchey et al. 2011), on the processing of reinforcers in the brain's motivational system in addiction disorders (Balodis et al. 2016), on action control and its neural correlates in obsessive-compulsive disorders (Nakao et al. 2005), or on changes in prefrontal activity related to working memory functions in schizophrenia (Kumari et al. 2009). The latter study was able to show, for example, that patients with schizophrenia improved significantly with cognitive behavioral therapy (vs. *treatment as usual*) and that this clinical improvement was associated with increased dorsolateral prefrontal activity in a working memory task (Kumari et al. 2009). This example also illustrates well that experimental paradigms for etiological models often do not focus on symptom-related phenomena, such as hallucinations or delusions in schizophrenia, but rather on cognitive or emotional functions, which are regarded as a kind of basic dysfunction within the respective disease.

▪ Intervention Paradigms

So-called *Intervention paradigms*, on the other hand, examine changes in brain function in a therapy-like situation using a targeted intervention. This is found, for example, in the study of effects of clinical hypnosis on pain perception (Rainville et al. 1999) or in the use of neurofeedback (Hohenfeld et al. 2017), i.e., real-time feedback on activity in a specific brain region and its modulation to be learned. As an example of the successful use of Intervention paradigms in neuroscience research, studies have now consistently shown that mindfulness-based interventions directly affect pain perception as well as associated neural activity, particularly in the anterior cingulate, insula, and dorsolateral prefrontal cortex (Bilevicius et al. 2016).

▪ Paradigms for the *Resting* Activity of the Brain (*Resting-State*)

The use of *resting-state paradigms* is based on the assumption that a typical response readiness of the brain can be described in the pattern of brain activity at rest, which can be used diagnostically (Kim and Yoon 2018) or whose change can be measured as a result of psychotherapy. For example, it could be shown by means of PET that metabolic changes in the resting-state activity of the brain occurred in people with depression after cognitive behavioral therapy, particularly in the hippocampus and dorsal cingulate (increase) and in various frontal regions (attenuation), and that this pattern differed from the changes that were observable in connection with the effects of antidepressant medication (Goldapple et al. 2004).

14.2.3 Research Designs in Neuroscientific Psychotherapy Research

Different research designs are used in neuroscientific psychotherapy research to answer the respective questions (◘ Fig. 14.3; Linden 2006).

The classic design comprises a pure pre-post comparison of neurobiological parameters, as shown here, for example, on the basis of an imaging examination before and after an applied psychotherapy (i.e., implementation of psychotherapy A in ◘ Fig. 14.3) and a comparison with regard to the respective response or non-response (Lueken et al. 2013). Differential study designs additionally compare psychotherapy with a possible other intervention, e.g. pharmacotherapy, or another form of psychotherapy (psychotherapy A vs. psychotherapy B). Designs that do not look at a form of psychotherapy as a whole, but rather seek to describe the neurobiological correlates of concrete partial aspects, effect factors, or interventions, are also becoming increasingly important. One of the reasons for this is that neuroscience has led to a growing realization that people and their brains are not structured analogously to diagnostic categories, cf. the so-called *Research Domain Criteria* (RDoC) initiative (Insel et al. 2010). Similarly, it is inconceivable to map a treatment according to a specific psychotherapeutic school, such as behavioral therapy or psychoanalytic psychotherapy, precisely in neurobiological terms, since a wide variety of elements and factors are interwoven in each case. Thus, it is only logical to limit questions about mechanisms and modes of action of psychotherapy in particular to concrete interventions or concepts and to consider them

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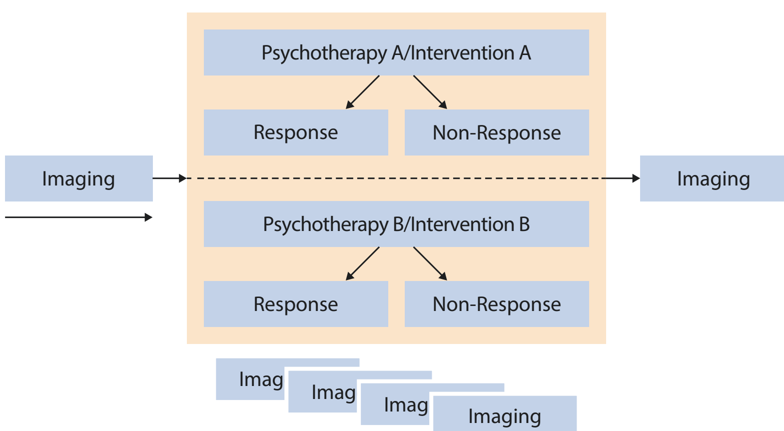
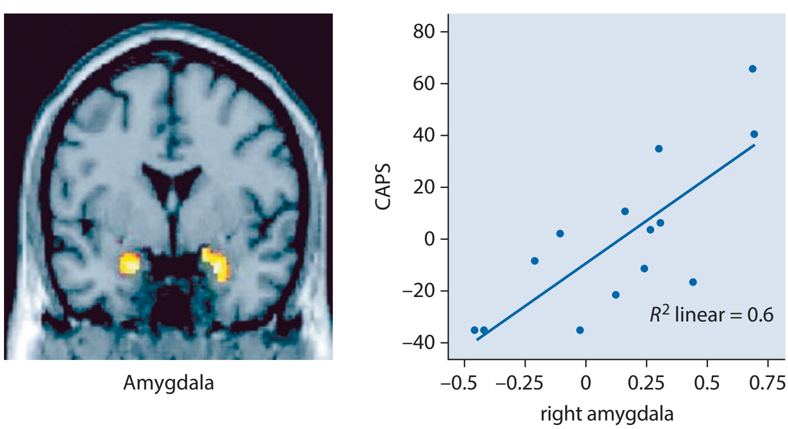


◘ **Fig. 14.3** Research designs in neuroscientific psychotherapy research differentially (Intervention A vs. Intervention B; Dörfel et al. 2014). It is also possible to identify neurobiological predictors of therapeutic success in order to use them in the sense of selective indication, e.g. testing of prefrontal functions under stress. Depending on whether a general prefrontal deficit or a situational/stress-related inhibition of functions is more likely to be evident, different intervention profiles can be defined. This type of investigation is also interesting for predicting the general responsiveness to a therapeutic intervention within a population. For example, a correlation between high responsiveness of the amygdala and ventral anterior cingulate to fearful faces before therapy and low response to cognitive behavioral therapy in posttraumatic stress disorder could be shown (◘ Fig. 14.4; Bryant et al. 2008).

Finally, with an appropriate study design, it is also possible to define neurobiological process variables and to collect these, such as via repeated imaging examinations parallel to the therapeutic process (◘ Fig. 14.3), which would make a process-oriented, adaptive indication possible on the basis of continuous feedback on the patient's brain functional changes in the process of therapy.

In this section we have looked at the methodological foundations of neuroscientific psychotherapy research. What people experience, what we perceive, feel, think and do can be scientifically described and investigated on different levels. Today's neuroscientific methods such as functional imaging offer the possibility to add further perspectives to our previous psychological and sociological perspectives and to watch the brain at work, so to speak. To answer the respective questions, neuroscientific psychotherapy research uses different experimental paradigms, including paradigms with symptom provocation, on etiological models of a disorder, intervention paradigms as well as resting-state measurements. These are used in the context of different study designs, which in turn allow various conclusions to be drawn, ranging from simple pre-post comparisons to the prediction of therapy effects.



◘ **Fig. 14.4** Amygdalae responsiveness to anxious faces before therapy is related to response to cognitive behavioral therapy for post-traumatic stress disorder (CAPS = Clinician-Administered Post-Traumatic Stress Disorder Scale, scale scores post-pre treatment). (Adapted from Bryant et al. 2008)

14.3 The Different Schools of Psychotherapy

In order to be able to look more closely at the results of neuroscientific psychotherapy research using examples, in the following section we will briefly look at the special features of the various schools of psychotherapy (behavioral therapy, depth psychology-based therapy, psychoanalytic psychotherapy, systemic therapy and client-centered (Rogerian) psychotherapy) and exemplify the most important core assumptions and postulated mechanisms of action.

If we look at the various schools of psychotherapy, it quickly becomes clear that they have developed out of different traditions and along different paths. In modern times, the classical schools of therapy are increasingly converging, yet they differ in their postulated mechanisms of action, which will be briefly presented here in the form of a tabular overview (Table 14.1).

In this section we have provided an overview of the characteristics of the different schools of psychotherapy (behavioral therapy, depth psychology based therapy, psychoanalytic psychotherapy, systemic therapy and client-centered (Rogerian) psychotherapy).

Table 14.1 Comparison of the major schools and directions of psychotherapy with a focus on a simplified presentation of the core assumptions and postulated mechanisms of action

Therapy school	Core assumptions and postulated mechanisms of action
Behavioral therapy	• Experience and behaviour have been learned to a large extent and can therefore also be "unlearned" or relearned • Promote understanding of the mechanisms of a problem through problem and condition analysis • Consideration of cognitions, i.e. thought patterns, or emotional and motivational processes that contribute to the problem • Behavioral exercises and alternative experiences help establish new behaviors, confront problematic stimuli (e.g., phobic stimuli), reinforce positive behaviors, and mitigate problematic behaviors
Depth psychology-based psychotherapy	• Focus on conflicts and developmental disorders that arise or are reactivated in the patient's current life situation • Suspected causes of this lie in childhood and adolescence, i.e. looking to the past for better understanding of the present • Interpretation of current statements and conflicts as an expression of an already long-lasting inner conflict in order to uncover dysfunctional coping strategies that are related to the disorder and the current problematic situation • Establishment of more mature processing and manifestations of unconscious conflicts in current life circumstances, especially in current interpersonal relationships
Psychoanalytic psychotherapy	• Unconscious factors influence our thoughts, actions and feelings, which can lead to inner conflicts • Fundamental conflicts acquired in childhood affect the therapeutic interaction (transference/countertransference) • Patients stick (resistance) to the previously used coping strategy (defence mechanism), even if it has led to problems • Unconscious return of the patient to the point of development at which the disturbance arose (regression) in order to bring about a new beginning in the protection of the therapeutic relationship

Table 14.1 (continued)

Therapy school	Core assumptions and postulated mechanisms of action
Systemic therapy	• It is not the patient who is the cause of the problems, but rather a dysfunctional system that is in dysfunctional homeostasis as a result of the index person's symptoms • Relationship processes contribute to the development and maintenance of problems • Metaphorical techniques (e.g. sculptures) reveal family constellations and social relationships; circular questioning and paradoxical interventions break the current constellation and push change process of the whole system
Client-centered (Rogerian) psychotherapy	• Person-centred, humanistic approach, i.e. the focus is on the person, not the problem • A person's hidden or hitherto socially unaccepted abilities are brought to light and patients are enabled to find independent solutions to problems • The positively experienced therapy relationship forms the basis for the development of the patient's potential, i.e. the therapist meets patients with appreciation, without prejudice and with understanding for their life contexts, genuinely and without expert attitude

14.4 Neurobiological Findings on the Effects of the Major Psychotherapeutic Approaches

The following are some concrete examples of previous studies on the neurobiological correlates of school-focused psychotherapies.

Already Sigmund Freud, whom we know as the founder of psychoanalysis and who was a neurologist by training, formulated the assumption in one of his early writings (Freud 1885) that mental states of suffering arise on the basis of changes in brain states. However, he himself did not explicitly pursue these theses during his life. Even the majority of today's psychoanalysts do not necessarily adhere to the vision of a neurobiological description of their activity. At the same time, famous personalities, such as the Nobel Prize winner Eric Kandel, argued that psychoanalysis had to face up to neuroscientific insights if it still wanted to play a productive role in the fields of psychiatry and psychotherapy in the future (Kandel 1998). Comprehensive studies on the effect of psychoanalytic therapies on neurobiological parameters as well as on long-term courses are still largely lacking (Abbass et al. 2014). With a focus on the neurobiological correlates of psychodynamic psychotherapies, for example, a study was conducted on the treatment of chronically depressed patients by experienced psychoanalysts. In addition to extensive clinical diagnostics with psychodynamic psychometric procedures designed to measure, for example, unconscious central conflicts or attachment representations, study participants were treated with a frequency of ≥2 therapy sessions weekly and examined over a period of 15 months by means of fMRI and EEG at two measurement time points. Neural processing of personalized attachment-related stimuli was found to change over time in the patients, showing increased activity in regions such as the left anterior hippocampus, amygdala, subgenual cingulate, and prefrontal cortex before treatment, which decreased after treatment and was associated with symptomatic improvement (Buchheim et al. 2012a, b; ◘ Fig. 14.5).

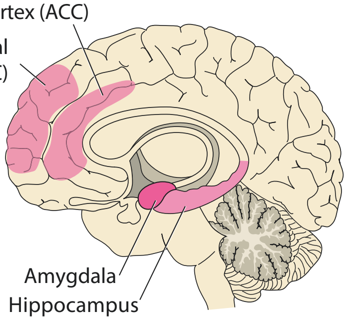


Fig. 14.5 Relevant brain areas in which a change was shown after psychoanalysis during the processing of attachment-relevant stimuli. (According to Buchheim et al. 2012a)

An investigation of the mechanisms of action of psychodynamic therapies is difficult, even with neuroscientific methods, due to the basic concept of Freudian theory, which defies empirical verifiability. Representatives of psychoanalysis argue that evidence of Freud's conceptualized unconscious has now also been provided outside neuropsychoanalysis (Doering and Ruhs 2015), e.g. in the form of the phenomenon of subliminal perception, i.e. perceptions of which we are not aware but which demonstrably exert an influence on our decisions (Berlin 2011). Thus, other neuroscientific findings can also be interpreted in terms of psychodynamic theory. Anderson et al. (2004), for example, saw hyperactivation of the dorsolateral prefrontal cortex combined with hypoactivation of the hippocampus in the process of "active forgetting" as analogous to repression, an important concept in psychoanalysis. Another important concept from the spectrum of methods of the psychodynamic school is free association. Indirectly, studies are also concerned with this, e.g. on the neurobiological basis of creativity and its connection with mental illness. Thus, it is argued that there might be a relationship between the resting-state activity of the brain (*default mode network*), which can be seen as an intrinsic function of the brain during free thought wandering, and free association as a therapeutic method, which is related to changes in activity in different frontal areas and parieto-temporal regions. Also, creative people showed more activity in association cortices during creative tasks and at the same time showed a higher likelihood of suffering from mental illness (Vellante et al. 2018).

Numerous studies now exist on neurobiological changes in connection with the other major school of psychotherapy, behavioral therapy (Linden 2006; Barsaglini et al. 2014; Lueken and Hahn 2016). This is also due to the fact that behavioral therapy emerged from empirical psychology and is correspondingly science-savvy. The following are some interesting examples of studies in this area: On the question of the neurobiological correlates of successful behavioral therapy, a fivefold repeated fMRI examination of people with borderline disorder—accompanying the course of a 12-week dialectical behavior therapy (DBT)—was able to neurobiologically map, that the affective hyperexcitability existing before therapy decreased during the experimental emotion induction in the MRI in the sense of a reduction of activity in the right anterior cingulate, in temporal and parietal cortices as well as in the left insula (Fig. 14.6; Schnell and Herpertz 2007).

Other researchers investigated, for example, at what point in the treatment of people with obsessive-compulsive disorder exposure therapy would be particularly promising, and also included neurobiological data. Using high-frequency logs of symptoms and repeated fMRI scans over an 8-week period, they were able to show in a single-case analysis that just before symptom reduction in the middle of treatment, the dynamic complexity of the data had increased, which can be interpreted as critical instability of the system that makes change processes more likely. The initially increased activity in the anterior cingulate when provoked with images that usually triggered compulsive

■ **Fig. 14.6** Examples of stimulus materials for the experimental induction of negative emotions. (From Schnell and Herpertz 2007)

actions in the patient (e.g., dirty laundry, etc.) decreased over the course of treatment (Schiepek et al. 2009).

The possibilities of differential comparisons (Furmark et al. 2002; Goldapple et al. 2004; Quidé et al. 2012; Barsaglini et al. 2014) are also interesting, i.e. to investigate in more detail whether psychotherapeutically mediated improvement of psychopathological symptoms is based on similar or distinct mechanisms as effective pharmacotherapy. For example, PET measurements have shown that cognitive behavioral treatment of social phobia, as well as treatment with the selective serotonin reuptake inhibitor citalopram, was associated with reduced responsiveness bilaterally in regions of the amygdala-hippocampal complex during symptom provocation (Furmark et al. 2002). It is possible that such similar effects are based on different neurobiological starting points. A common theory of differential mechanisms of action of different treatments for anxiety disorders and depression is that psychotherapy tends to address regulatory prefrontal functions (so-called "top-down" effects), whereas pharmacotherapy influences the functional networks involved by modulating the activity of subcortical structures (so-called "bottom-up" effects) (■ Fig. 14.7).

Imaging data have also been successful in identifying predictors of long-term outcome in people with depression. Depressed patients with initially lower activity in the subgenual cingulate and high amygdala activity benefited most from 16 h of cognitive behavioral therapy (Siegle et al. 2006).

In other therapeutic disciplines, the comprehensive use of neurobiological methods is not yet widespread, but is being discussed, for example, in systemic therapy (Schwing 2013). As the social neurosciences continue to grow, insights into the neurobiology of mental illness and its treatment are likely to become increasingly interesting for systemic therapists in the future.

In this section we have looked at exemplary studies of the neurobiological correlates of psychodynamic and behavioural psychotherapies in particular, and their results.

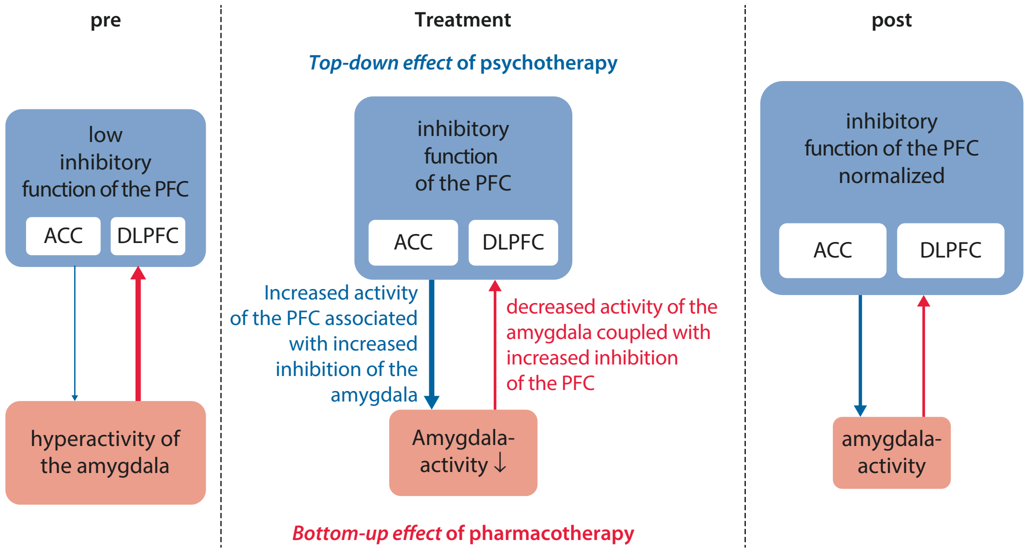


Fig. 14.7 Hypothetical model of brain functional changes in anxiety disorders and depression by different treatment approaches. Before treatment (pre), patients show overall increased amygdala activity and reduced inhibitory prefrontal activations. Different treatments lead to differential neurobiological effects in this model (treatment): psychotherapy (blue arrows) leads to an increase in inhibitory prefrontal activity, associated with reduced amygdala activity ("top-down" effect), whereas pharmacotherapy (red arrows) conditions a reduction in amygdala activity, associated with an increase in the inhibitory function of the prefrontal cortex on this structure ("bottom-up" effect). After treatment (post), the structures involved show a corresponding normalization of their function. *PFC* prefrontal cortex; *ACC* anterior cingulate cortex; *DLPFC* dorsolateral prefrontal cortex. (Adapted from Quidé et al. 2012)

14.5 Cross-School Methods and the Concept of General Mechanisms of Change in Psychotherapy

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This section will briefly explain integrative concepts of psychotherapy using the example of Grawe's model of general machanisms of change.

In addition to more school-focused approaches, there are now also cross-school approaches which assume common or similar factors of effect of successful psychotherapies regardless of the respective school. One of the most important models in this area is the concept of general mechanisms of change in psychotherapy according to Klaus Grawe (Grawe et al. 1994). According to this model, successful psychotherapy contains the general factors of effect regardless of the respective school (Table 14.2):

1. Resource Activation
2. Motivational/meaning clarification
3. Problem actuation
4. Problem solving/coping
5. Therapeutic relationship

Psychotherapies therefore work by improving psychological consistency. High consistency, synonymous with good possibilities for satisfying basic psychological needs (orientation/control, pleasure gain/unpleasure avoidance, attachment, self-esteem enhancement/stabilisation), contributes to protection against the development of psychological disorders. These arise in particular when psychological inconsistencies exist over a long period of time, e.g. because successful satisfaction of needs is blocked or

Table 14.2 General mechanisms of change in psychotherapy. (Grawe et al. 1994)

Impact factor	Explanation
Resource activation	Targeted use of the patient's existing strengths, abilities, interests, values, potentials, social relationships, etc.
Motivational/ meaning clarification	Promotion of insight into individual problematic patterns of experience and behaviour, problem contexts and conditional structures in connection with the illness
Problem actuation	Activation and making the problems in the therapy setting tangible, in order to make them accessible to a new experience in the therapy setting and in everyday life
Problem solving/ coping	Teaching skills for coping with problems and enabling coping experiences in the therapy setting and in everyday life
Therapeutic relationship	Establishment of a therapeutic interpersonal framework that enables a trusting engagement in the therapy and can serve as a basis for change processes

avoidance and approach goals motivationally interfere with each other. This leads to the assumption that therapeutically induced changes become possible when the therapy takes these psychological conditions into account and, if possible, also creates optimal conditions from a neurobiological perspective that enable and support the (re) construction of healthier processes and structures in the brain (Grawe 2000, 2004). For example, it results from this that therapy should be in the service of new, concrete and positive life experiences, i.e. the treatment of a problem should only contain limited interventions around the problem. Rather, it is essential for successful psychological change that important approach goals of the patients are in focus, i.e. that the therapist enables his or her patients as often as possible to experience perceptions that are relevant for the individual motivational goals and thus enable motivational learning, including the associated neuronal changes.

This section introduced an integrative concept of general mechanisms of change in psychotherapy, which can positively influence the course of psychotherapy independent of the respective orientation of the therapist or the school of therapy.

14.6 Neurobiological Correlates of General Mechanisms of Change in Psychotherapy

The following section presents some exemplary studies on the neurobiological correlates of general mechanisms of change in psychotherapy, such as the therapeutic relationship, resource activation, problem actuation and problem coping.

The physician, neurophysiologist and psychoanalytically trained Eric Kandel, who received a Nobel Prize in 2000 for his work on signal transmission in the nervous system, emphasized early on that we were faced with the fascinating possibility of using imaging methods to monitor the success of psychotherapy in the future. He argued that in the course of psychotherapy there is a change in gene expression in the neurons which, if the treatment is successful, also leads to structural changes in the neurons involved (Kandel 1979).

Basically, this is no surprise when we consider that our brain is an organ specialized in adapting to its constantly changing environment. Psychotherapy is based on these abilities of the brain to adapt to the respective environment and systematically shapes this environment according to psychological principles so that a process of change—i.e. a process of adaptation—comes about. That we do well to understand our brain as an organ of adaptation is now shown by numerous studies. Our brain changes greatly in the course of our life on a macroscopic and microscopic level. As we age, gray matter density decreases nonlinearly in most brain regions, particularly in dorsal-frontal and parietal association cortices. However, white matter volume, that of fiber connections between brain centers, continues to increase into older adulthood (Sowell et al. 2004). Structural imaging studies have also shown that volume in specific brain regions changes locally in response to our experiences. For example, London taxi drivers have higher volumes in the hippocampus, a central structure of human memory (Maguire et al. 2000). People who are newly learning to juggle show an increase in volume in regions of the brain associated with processing complex, visually controlled movements after just 3 months (Draganski et al. 2004). Contrary to earlier doctrines, the brain appears to exhibit a high degree of local structural plasticity in adult humans as well, depending on the demands of their environment. Changes in the organization of functional systems of the brain play an important role in connection with our experiences, which manifest themselves in the form of altered neurotransmission of a cell or synapse, changes in connectivities or synchronicity in a network, etc., and can thus be detected in functional imaging or electrophysiological studies, at least in principle. The brain can be conceived as a complex network that is in constant adaptation to its environment and may also exhibit features of self-organizing systems (Bassett et al. 2018; Takagi 2018).

Thus, if we assume that therapeutic changes are based on changes in the excitability of certain networks or systems in the brain, these changes take place primarily through processes such as priming/reinforcement, disuse/attenuation, and active inhibition. In this sense, the “extinction” of a fear response would consist in the establishment of an inhibitory or altered neural excitation pattern, whereas extinction in the sense of “forgetting” the relevant excitation patterns is unlikely to be relevant to psychotherapy. It is also likely that the brain can adapt to its environment differently under different conditions. Neuroscientific findings could therefore help to characterize the optimal conditions for change processes in more detail. The focus here is on neurotransmitters such as dopamine or serotonin (Heinz 2017). It is known that the activity of dopaminergic neurons plays an important role for the processing of reinforcers and thus motivational learning (Schultz 2016). Prosocial neuropeptides, such as oxytocin and vasopressin, which are released during sex or breastfeeding, for example, in turn promote dopamine release in the brain’s motivational system, thus promoting memory formation and strengthening social relationships (Vargas-Martínez et al. 2014). Neurotransmitters such as serotonin and norepinephrine modulate a person’s affective state (Young 2013). It is known that increased or prolonged release of stress hormones such as cortisol and adrenaline can lead to undesirable inhibition of neuronal activity and even to structural changes in the brain in the long term, such as in the context of traumatic experiences (O’Doherty et al. 2015).

At the latest since an improved investigation of emotional and motivational functions of the brain has been possible, the findings of neuroscience have become interesting for a deeper understanding of mechanisms of action in psychotherapies. If we follow Grawe's model of general mechanisms of change, then first of all there is the therapeutic relationship. On the one hand, it represents the basis for effective therapeutic action. On the other hand, the experience of a bond with other people also corresponds to one of our basic psychological needs. Neurobiological research has already shown that, analogous to the different, subjectively perceived qualities of interpersonal relationships, distinct activation patterns can also be mapped in the brain (Zeki 2007), e.g. in maternal vs. romantic love (Bartels and Zeki 2004), mediated, among other things, by differences in dopaminergic neurotransmission (Takahashi et al. 2015). The brain biological correlates of the sensation of unconditional love have also been considered (Beauregard et al. 2009), which is closest to the characteristic of unconditional appreciation in the context of the therapeutic relationship. Although the significance of unfavourable attachment experiences for the development of various mental illnesses is widely undisputed (Bora et al. 2009), detailed studies on the neurobiological correlates of a helpful therapeutic relationship are still lacking.

With regard to the general change factor of resource activation, a number of neurobiological studies can be cited that have examined the effects of approach behaviour, for example. This effect factor is closely related to the basic psychological need for pleasure/unpleasure avoidance. The well-documented negative influence of stress on learning and memory as well as associated neuronal processes (Schwabe 2017) suggests that people in states of subjective well-being are particularly willing and able to learn. The individually optimal conditions of a person's performance lie between respective under- or overload, cf. Yerkes-Dodson law (Yerkes and Dodson 1908). This means that the therapist's first task, also from a neurobiological perspective, is to create the most favourable initial conditions possible by understanding the patient's individual preconditions and motivational situation and supporting him or her in the development of his or her potential or enabling needs to be satisfied within the framework of the therapeutic relationship (cf. managing relationships motive-/need-oriented; Stucki and Grawe 2007). Only then would the conditions be optimal from a neurobiological point of view for a process of change. At the same time, these new, so-called corrective experiences within the framework of the therapeutic relationship will lead to an altered neuronal signature, which in turn will condition other expectations and arousal readiness of the brain in future situations. A whole branch of research investigates and substantiates various priming effects, i.e. context effects, and their neurophysiological correlates, both in the basal perceptual psychological domain, e.g. in subliminal priming (Elgendi et al. 2018) as well as with social psychological relevance (Molden 2014). However, the application of neurobiological methods to the psychotherapeutic context is still largely lacking here.

Neurobiological changes of therapeutic interventions that can be linked to the effect factor of motivational clarification could be considered, for example, in studies on the brain functional effects of psychoeducation. Although a positive effect of neurobiologically informed psychoeducation has been documented, especially on a reduction of stigma and help-seeking behavior of patients (Livingston et al. 2012; Han and Chen 2014), a neurobiological understanding of such interventions is still lacking.

With regard to the neurobiological correlates of change factors such as problem actuation and problem solving, it can be said that studies on the processing depth of emotions or on emotion induction on the basis of individual, i.e. personalized, stimuli as well as autobiographical information

(Cabeza and St Jacques 2007) are particularly interesting here, since these bring with them a corresponding emotional depth, liveliness and self-referentiality, which is also reflected in the underlying activation patterns. Commonly used in psychotherapies in this regard are techniques such as affect bridge work or imaginative overwriting (Holmes et al. 2007). In particular, the corresponding coping experience appears relevant for the satisfaction of the basic psychological needs for orientation/control and self-esteem stabilization/increase. In this context, studies on the neurobiological correlates of therapeutic interventions in patients with personality disorders from the so-called cluster B are also interesting. In disorders of this type, such as the so-called narcissistic or borderline personality disorder, the violation of the need for integrity of the self as well as self-esteem plays an important role in life-biographical development. On the psychological level, this manifests itself, for example, in changes in the competencies for affect regulation in interpersonally relevant situations, which therefore represents an important part of a behaviorally oriented psychotherapy for these clinical pictures. For example, in a functional imaging study of the neuronal processing of emotional stimuli, borderline patients initially showed increased responsiveness of the amygdala and insula, as well as increased orbitofrontal and insular activation compared to healthy individuals during attempts at conscious affect regulation (Schulze et al. 2011). Furthermore, it could be shown that these neuronal abnormalities regress during affect regulation after DBT therapy (Schmitt et al. 2016). In line with this, an increased responsiveness to negative social information in patients with borderline personality disorder was also associated with increased amygdala activity, which could be improved under intranasal therapy with oxytocin (Bertsch et al. 2013). Similarly, for people with narcissistic personality disorder, imaging techniques show that this patient group is particularly sensitive to experiences of exclusion, as evidenced by an attenuated response in regions of the so-called social pain network (anterior insula, dorsal and subgenual anterior cingulate) (◘ Fig. 14.8; Cascio et al. 2015).

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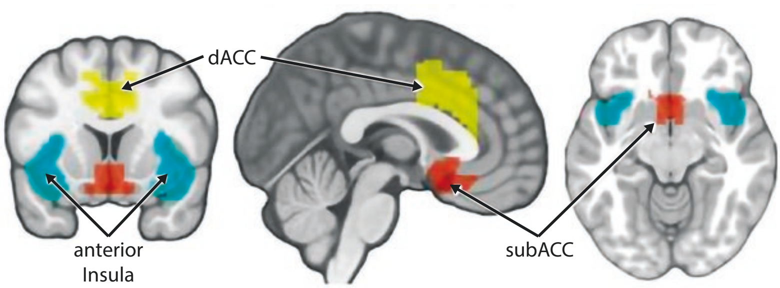
In this section, we have embarked on a search for neurobiological studies that allow us to better understand the general mechanisms of change in psychotherapy, such as the therapeutic relationship, resource activation, problem actuation, and problem coping experience. Despite interesting approaches of some studies in this field, further research on affective-motivational factors of therapy and their



◘ **Fig. 14.8** Illustration of the brain anatomical structures—anterior insula, dorsal (dACC) and subgenual (subACC) anterior cingulate—which are relevant for the so-called social pain network and which appear to be significant, among other things, in experiences of exclusion. (Adapted from Cascio et al. 2015) neurobiological correlates is necessary to further reveal the mechanisms of change in the therapeutic process and to create the best possible conditions for change also at the neuronal level.

Box 14.2 Implications of a Neurobiological Perspective on Mental Illness for Prac tice

- Complementation of a bio-psycho-social overall perspective.
- Health policy consequences, e.g. due to the extended objectifiability of psychotherapy effects.
- Adaptation of communication with patients.
- Influence on patients' and therapists' expectations of the therapeutic process.
- Promoting the destigmatization of mental illnesses.
- Influencing help-seeking behaviour.
- Stimulation of new approaches, especially for older patients.

14.7 Implications of Neurobiological Findings for the Development of Psychotherapeutic Approaches

In this section, we will present examples of the possible implications of neurobiological research for everyday therapeutic practice. For this purpose, we will look in particular at interventions that take into account and seek to induce changes in the motivational system in the context of mental illnesses such as addiction.

As fascinating and interesting as a more comprehensive knowledge of neurobiological correlates of successful psychotherapies, individual interventions or relevant mechanisms of change may be, this knowledge is only relevant from a therapeutic point of view if it can be translated into therapeutic action and thus serves to improve the care and treatment of people with mental illness. The neurosciences in particular, whose methods are often time-consuming and cost-intensive and in some cases invasive, must accept the question of what added value they provide for clinical practice, what benefit they have for society as a whole and for patients in particular (Walter et al. 2009).

Let us therefore first consider what significance an increasing collaboration between the neurosciences and psychotherapy research could have for society and the development of the field (► Box 14.2), before turning to concrete implications for therapists.

Opening up psychotherapy research to neuroscientific methods first of all complements the bio-psycho-social overall concept of the development of mental illnesses that predominates in medicine. Due to the extended objectifiability of psychotherapy effects or as an element of quality assurance, neuroscientific findings could also contribute to a strengthening of the argumentation for a more consistent provision of necessary resources for the psychotherapy of people with mental illnesses at the level of health policy. At the level of therapist or patient behaviour, opportunities lie in adapting communication between therapists and patients, e.g. in the sense of demystifying psychotherapy and promoting transparent information about the underlying mechanisms. Moreover, communication about the neurobiological basis of psychotherapeutic interventions is certainly directly beneficial for patients with a predominantly biological understanding of illness, which is most likely to be due to a change in patients' expectations of effects in the therapeutic process. The dissemination of knowledge about the neurobiological basis of mental illness and therapeutic interventions can also promote the destigmatization of mental illness and thus also have a positive effect on help-seeking behavior (Livingston et al. 2012; Han and Chen 2014). At the same time, it should be noted that a biological perspective on mental illness may also contribute to increased stigmatization by society under certain conditions, e.g., for people perceived as dangerous (Müller and Heinz 2013; Andersson and Harkness 2018). Last but not least, neurobiological findings, such as those on the lifelong high neuronal plasticity of humans, could lead to a further stimulation of therapeutic approaches for people in adulthood or for older patients in particular.

But what does all this mean for professionals in the help system and especially for therapists? As stated before, therapeutic conversations in familiar ways do not lead to long-term changes in the brain. From a neurobiological perspective, this means that the analysis of problems is on the one hand relevant, for example in the form of clinical or functional diagnostics, but on the other hand is only productive if it serves the preparation and targeted implementation of change interventions, i.e. enables new, alternative experiences of the person being treated. In order to achieve changes in experience and behavior, repeated, sustained activations of the specific networks are required, i.e., from a neurobiological perspective, it is helpful to direct the focus to thoughts, feelings, and behaviors that represent an approximation of the therapy goals, such as in the presentation of target states in behavior therapy or the so-called wonder question in systemic therapy. These must be relevant to motivational goals of the patient, otherwise it cannot be assumed that the self-referential network or the motivational network in the brain is activated. The latter, with the attribution of significance, ensures an increased attentional capacity for associated content, paves the way for behavioural impulses in this direction and promotes the memory consolidation of associated experiences (Schultz 2016). Thus, a simultaneity of processing problem constellations and activating approach goals in psychotherapy should be aimed at in order to stimulate a reconstruction of underlying brain biological systems. Finally, it should be noted that this important question of the concrete usability of the results from the neurosciences for everyday therapeutic practice is increasingly leading to the emergence of new works with a primarily therapeutic target group in addition to corresponding new textbooks and reference books (Eßing 2015).

We take a closer look at the concrete findings and their potential for implementation in practice for the research area of addictions as an example (Romanczuk-Seiferth 2017; cf. also ▶ Chap. 10): In the course of the development of an addiction, an initially positively experienced substance use becomes a habitual, automatic behaviour (Everitt and Robbins 2005; Seiferth and Heinz 2010). It is now well established from studies on the neurobiology of addictive disorders that the learning processes associated with the development of an addictive disorder are accompanied by neurofunctional changes in reward sensitivity and cognitive control. In addicted patients, it has been documented that there is an increased sensitivity of the brain's motivational system, the so-called meso-cortico-limbic reward system, to all addiction-associated contextual stimuli (Schacht et al. 2013), associated with a shift in attentional focus to addiction-relevant stimuli in the environment (Hester and Luijten 2014). At the same time, people suffering from addiction experience a hyposensitivity of the brain, i.e. a reduced responsiveness, especially in the so-called ventral striatum as a central region of the mesolimbic reward system (Wrase et al. 2007; Romanczuk-Seiferth et al. 2015), in the neuronal processing of common reinforcing stimuli, i.e. delicious food, sexuality, social contact, etc.

Furthermore, it is known that in the context of addiction there is also an altered neuronal activation in goal-directed behaviors

(Sebold et al. 2017) or in the cognitive control of behavioral impulses (Bickel et al. 2012). At the same time, patients find it more difficult to adapt their behaviour to changing reward contingencies, i.e. to relearn, which is associated with reduced connectivity between the ventral striatum and the prefrontal cortex (Park et al. 2010).

In principle, the communication of neurobiological knowledge, such as in the context of psychoeducation, therefore appears to be helpful for the treatment of addiction disorders, as it has been shown that shame and (self-)stigmatization are relevant barriers to the initiation of treatment (Wallhed Finn et al. 2014). It was also found that training of medical staff on this topic can contribute to a reduction of stigmatisation of people with addictions (Livingston et al. 2012). In addition, the findings on the impairment of relearning in addiction disorders, for example, can be communicated to patients in a relieving manner and thus serve to maintain motivation throughout the course of treatment.

However, direct therapeutic approaches can also be derived from the neurobiological findings on addictive disorders outlined above. One obvious approach is to reduce the motivational stimulus emanating from a substance or associated stimuli in the environment, as is found in clinical practice in strategies for stimulus control. However, the aim here is not to directly reduce the motivational stimulus, but to reduce the probability of occurrence of addiction-relevant stimuli, i.e. with a high motivational stimulus. It would therefore be interesting to consider newer therapeutic approaches that allow direct modulation of motivational stimuli. Similarly interesting are approaches that aim to weaken automated addictive behaviour. For this purpose, for example, a training was developed that weakens automatic approach tendencies to addiction-associated stimuli. This has been shown to be effective for reducing consumption or maintaining abstinence in smokers and alcohol addicted subjects (Kakoschke et al. 2017). On a neurobiological level, this can also be described, patients showed a normalization of the neuronal response to drug-associated stimuli in frontal and limbic areas through such training (Wiers et al. 2015).

Also relevant are measures to strengthen the executive control of addicts, as is already clinically common in rejection training or social skills training. Neurobiologically based therapy components in this sense are also methods that support a weakening of automated addictive behaviour, such as the use of observation tasks, diaries, behavioural analyses and traffic light systems to assess critical situations.

The aforementioned neurostimulation is sometimes used to modulate impulsivity or impulsive decision-making behavior in the context of addictive disorders. It could be shown that after stimulation of the dorsolateral prefrontal cortex via transcranial magnetic stimulation (TMS) in nicotine dependence, a higher ability to postpone reward as an aspect of (lower) impulsivity was detectable. However, this effect did not generalize to reduced cigarette consumption after treatment, so such treatments can so far only be helpful as an adjunct to demonstrably effective psychotherapy, such as cognitive behavioral therapy (Sheffer et al. 2013).

Particularly in view of the comprehensive adaptive abilities of our brain, therapy methods that focus on re-learning in connection with previous substance use and associated behaviour also appear to be useful and helpful, cf. application of exposure training in the field of alcohol/drugs.

Directly derivable from neurobiological findings is also the importance of therapy methods that aim at strengthening protective factors and reactivating the processing of alternative reinforcers, such as contact with people, sensual experiences, etc., as is sometimes found in therapeutic practice in so-called euthymic therapies or pleasure training. By means of exercises for perception with all five senses, the ability to enjoy is (re)strengthened and the brain is sensitized for the processing of these impressions—as an alternative to addictive behavior. It has been shown, for example, that when the motivational system is highly responsive to positive emotional stimuli, such as pictures of laughing people, etc., fewer severe relapses occur in the context of alcohol addiction (Heinz et al. 2007).

> In this section we have looked in more detail at the possible implications of neurobiological research for everyday therapeutic practice. To this end, we have taken a closer look at previous findings on the neurobiology of addictive disorders and discussed their possible significance for therapeutic action in the sense of neurobiologically informed psychotherapies.

14.8 Future Perspectives of Integrative Neuropsychotherapy

The following section will provide a brief concluding explanation of further relevant research perspectives and a general outlook.

For a better understanding of the development of severe mental illnesses, such as schizophrenia, great hopes have been and still are placed in the further development of genetic research. The combination of genetic information with neurobiological characteristics, as is the case with so-called *imaging genetics*, increases the probability of describing relevant endophenotypes of a disease and may continue to play a role as a research branch of human neuroscience in the future (Arslan 2018).

The identification of potential biomarkers of mental illness is of particular interest in terms of their usefulness for the future if they can be used to make predictions about the effectiveness of treatments or their sustainability. While the prediction of relapse seems to be of less prominent importance in other fields, it has traditionally played a major role in research on addictive disorders. Thus, there are now also individual findings on the neurobiological correlates of relapse in addiction disorders, e.g. on the importance of addressing the prefrontal cortex, which could be used to optimise current treatment strategies or for more selective indications (Moeller and Paulus 2018).

In a review article on the results of functional magnetic resonance imaging under *resting-state* conditions in panic disorder and social phobia (Kim and Yoon 2018), researchers were able to show that in people with panic disorder, in addition to changes in the *default mode network* and the medial temporal cortex, interoceptively relevant networks including the sensorimotor cortex were also relevant, while in people with social phobia, changes in connectivity in the so-called salience network were also evident. Such knowledge of overlapping and also distinct changes in brain connectivity at rest could be used to subdivide phenotypically different mental disorders, such as various anxiety disorders, into neurobiologically informed subgroups, which are suitable to better support the search for biomarkers and thus increase the chance of new therapeutic options. Accordingly, this could also advance the development of neurobiologically informed treatment programmes (Knatz et al. 2015). In this context, studies that allow us to directly modulate the brain neurochemically in people with mental disorders also appear to be of increasing interest: for example, it has been shown that intranasal oxytocin administration has a positive effect on the ability to process faces in people with autism (Domes et al. 2013). Overall, the therapeutic potential of neuropeptides and their neurobiological effects appear to be of growing interest (Lefevre et al. 2019).

The potential for translating existing neurobiological knowledge about relevant disease mechanisms into therapeutic action has also not been exhausted everywhere. For example, it can be argued that for eating disorders such as anorexia nervosa and bulimia nervosa, numerous studies on changes in the motivational system of the brain are available, but this knowledge has not yet resulted in concrete interventions that focus on modulating reinforcer processing (Monteleone et al. 2018).

Ultimately, the hope underlying all these approaches to the use of neurobiological knowledge in the therapy of mental illnesses is that, with the help of the knowledge gained, individual therapy decisions can be justified neurobiologically and predictions can be made about the possible prospects of success of a particular intervention on an individual basis (Ball et al. 2014). An important task for the future is therefore certainly to narrow or even close the gap between the findings from basic science and the practical application in everyday therapeutic practice. Individual statistical methods for bridging the gap between population-based research results and clinical practice appear to be very helpful here, e.g. on the basis of the application of machine learning approaches in so-called "*predictive medicine*" (Hahn et al. 2017). This includes methods that are intended to enable the prediction of certain characteristics, such as the presence of a mental illness, from other personal data at the individual level. For example, there are now several findings that can make predictions about the presence of an affective disorder at the individual level on the basis of people's brain-structural data using machine learning approaches and thus nourish the hope of being able to transfer results from neurobiological research directly into everyday clinical practice. At the same time, methodological considerations currently limit the generalizability and thus everyday applicability of these findings (Kim and Na 2018). However, the application of *computational* approaches in psychotherapy (*computational psychotherapy*) is also interesting with a view to expanding our understanding of mechanisms of action: For behavioral therapy approaches in particular, methods of mathematical modeling offer the opportunity to test existing hypotheses about how people make inferences from experience, how this is altered in mental illness, or how it is modified by therapy (Moutoussis et al. 2018).

Such approaches to predicting mental illnesses or the effect of psychotherapy are developing in close connection with the field of so-called "*precision*" or "*personalized*" medicine (Fernandes et al. 2017), which aims to implement treatment and prevention of illnesses taking into account the individual variability of a person with regard to genetics, environmental factors, lifestyle, etc. The aim of these approaches is to develop a new approach to the prediction of mental illnesses and the effect of psychotherapy.

Even though the present chapter focuses on the presentation of the possibilities of a neuropsychotherapeutic perspective, it is important to emphasize that from a scientific-methodological perspective, relevant critical aspects of the findings in this field need to be considered. For example, the results of neurobiological studies are rarely homogeneous; as a rule, there are heterogeneous findings on a specific question, which can be attributed to factors such as different methods and paradigms used, the size and selection of the samples studied, clinical characteristics of the population (comorbidities, duration of illness, etc.) and specifics of the therapy (type, duration, setting, intensity of interventions, etc.), and which limit the generalizability of the results accordingly (Walter and Müller 2011).

With the progress of neuroscience, its opportunities and limitations are also becoming the focus of a debate in society as a whole (Meckel 2018). In particular, the detachment of the techniques generated and the knowledge gained from an application in a clinical context deserve a detailed critical debate. Thus, it will be the task of today's society to decide for itself and future generations how far we want to commit ourselves to an optimization of the healthy brain, as is the goal, for example, in the field of so-called neuroenhancement. Or how far findings about us and our brain should be made usable as a basis for economic interests, as is already the case with so-called neuromarketing.

Last but not least, it would be highly interesting to understand in more detail the neurobiological changes that the therapist's brain undergoes in the course of the numerous therapy processes. As could be shown in experts vs. novices in a compassion mediation, experts show a neuronally enhanced sensitivity to emotionally-averse stimuli (Lutz et al. 2008). This may serve as an example of possible (neural) risks and side effects of being a therapist, which are certainly not yet approximately understood.

Overview

In this section we have looked at possible future aspects. These include the further development of genetic research in the sense of so-called "imaging genetics", the use of potential biomarkers of mental illness for predicting the effectiveness of various treatments or their sustainability, the description of neurobiologically informed subgroups of mental illness and the development of suitable treatment programmes, and the further development of methods for deriving results that can be used for individual therapy decisions, e.g. in the context of so-called computational approaches in psychotherapy. It remains to be seen whether the hopes placed in these future prospects will be fulfilled. In addition, from a scientific-methodological perspective as well as from a social-ethical point of view, relevant limitations of the field become apparent, which need to be discussed and taken into account.

Kurt Lewin, the co-founder of modern psychology, said, "If you want to truly understand something, try to change it" ► (► https://www.verywellmind.com/kurt-lewin-quotes-2795692, accessed 25 June 2019). Probably a joint, fruitful development of neuroscience and psychotherapy (research) has just begun.

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