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Cognitive-Behavioral Therapy and Neuroscience: Towards Closer Integration

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Abstract

The aim of this review article is to provide an integrative perspective by combining basic assumptions of cognitive-behavioral therapy (CBT) with neuroscience research results. In recent years, interdisciplinary research in the field of neuroscience has expanded our knowledge about neurobiological correlates of mental processes and changes occurring in the brain due to therapeutic interventions. The studies are largely based on non-invasive brain imaging techniques, such as functional neuroimaging technologies of positron emission tomography (PET) and functional magnetic resonance imaging (fMRI). The neuroscientific investigations of basic CBT hypotheses have shown that (i) functional and non-functional behavior and experiences may be learned through lifelong learning, due to brain neuroplasticity that continues across the entire lifespan; (ii) cognitive activity contributes to dysfunctional behavior and emotional experience through focusing, selective perception, memory and recall, and characteristic cognitive distortion; on a neurobiological level, there is a relationship between top-down and bottom-up regulation of unpleasant emotional states; and (iii) cognitive activity may be changed, as shown by therapeutic success achieved by metacognitive and mindfulness techniques, which also have their neurobiological correlates in the changes occurring in the cortical and subcortical structures and endocrine and immune systems. The empirical research also shows that neurobiological changes occur after CBT in patients with arachnophobia, obsessive-compulsive disorder, panic disorder, social phobia, major depressive disorder and chronic fatigue syndrome.

Keywords: cognitive-behavior therapy, brain, neuroimaging, anxiety disorder, mood disorder

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Cognitive-behavioral therapies (CBT) are short-term, collaborative, problem-focused therapeutic methods aimed at reducing symptoms and improving the quality of life of people with emotional disorders. CBT has been refined, elaborated, and evaluated in numerous empirical studies (Clark & Beck, 2010). Due to having been rigorously tested, CBT is now considered an empirically-supported treatment for a variety of disorders, such as anxiety disorders, mood disorders, learning difficulties, sexual problems, and bulimia nervosa (Butler, Chapman, Forman, & Beck, 2006; Tolin, 2010). Recent research has shown that CBT may also be successfully applied in the treatment of more serious mental disorders, such as schizophrenia (Turkington, Kingdon, & Weiden, 2006) and bipolar disorder (Lam, Hayward, Watkins, Wright, & Sham, 2005).

Cognitive-behavioral therapies combine two different theoretical and therapeutic approaches resulting from two different, but complementary paradigms of human nature and psychopathology. One is the behavioral paradigm, based on the learning theory and models of experimental psychology. Its basic idea is that every behavior, either adaptive or maladaptive, has been learned. The other is the cognitive paradigm, which claims that mental disorders arise from altered cognitive processes, i.e., specific errors in information processing (Jokić-Begić, 2008).

Until recently, studies investigating CBT efficacy did not pay attention to the biological correlates of changes in patients' behavior and experience. Moreover, in the process of developing therapeutic interventions, cognitive-behavioral paradigm did not rely on the biological basis of mental disorders, despite the implied significance of neuropsychological processes and genetic influence (Beck, 2008). In recent years, interdisciplinary neuroscience research has increased our knowledge about the neurobiological correlates of psychological functions and changes resulting from therapeutic interventions (Beauregard, 2007; Frewen, Dozois, & Lanius, 2008). There are a rapidly increasing proportion of studies using brain imaging methods to investigate cognitive functioning, emotional experience and self-regulation, psychopathological entities, pharmacotherapeutic and psychotherapeutic effects, placebo effect, and other phenomena traditionally studied within psychology and psychiatry. These studies are based on non-invasive brain imaging techniques, such as functional neuroimaging technologies of positron emission tomography (PET) and functional magnetic resonance imaging (fMRI). PET and fMRI measure the metabolic activity within different regions of the brain, such as that indexed by glucose metabolic rate (PET) or blood oxygenation of vessels within the surrounding neural tissue (fMRI). The brain is scanned while it is at rest and then again after stimulation. During scanning, glucose or oxygen metabolism is measured in different brain regions. Metabolic activity in the brain regions that are activated by the stimulus differs from that at rest and is considered to indirectly reflect neural activity. By comparing brain metabolic activity in individuals with and those without psychiatric disorders, we may identify the functional neural circuitry by which they differ. Pre-post changes in the brain metabolic activity that occur during effective psychotherapeutic treatment can also be used to study the functional neural correlates of such treatment (Frewen, Dozois, & Lanius, 2008).

Cognitive-behavioral therapies are based on continual empirical testing of their effectiveness. Therefore, it is not surprising that, with the advent of brain imaging techniques, research efforts have refocused on finding the evidence of neurobiological correlates of the changes observed in patient's behavior and experience after CBT. Furthermore, CBT requires a detailed analysis of behavior, cognition, and emotions and a precise determination of the treatment goals, which allows us to hypothesize about neuroanatomical changes and functional processes occurring during particular brain activity. Thus, the number of empirical studies of CBT effectiveness measured through neurobiological changes is constantly increasing.

The main goal of this review is to contribute to an integrative perspective by combining some basic CBT hypotheses and neuroscience research results. The results of neuroscientific testing of basic CBT hypotheses show that (1) functional and dysfunctional behavior and experience can be adopted through life-long learning; (2) cognitive processes contribute to dysfunctional behavior and emotional experience through focusing, selective perception, memory, and recall, and characteristic cognitive distortion; (3) cognitive activity can be observed and changed. Finally, this article looks at the results of empirical research of neurobiological changes after CBT in patients diagnosed with different disorders.

Life-Long Learning

The basic CBT hypothesis is that people can continue to learn throughout their lives. Both functional and dysfunctional behavior is learned. Every behavior that is learned may be unlearned and replaced by other behavior that is more functional. CBT helps patients to learn and adopt new knowledge and skills, which will enable them to observe and change their own thoughts, behavior, and emotional states. After a successful therapy, patients may be expected to be more functional and have better subjective quality of life.

Do these changes in behavior and attitude have a neurobiological basis? In the 1970s, the adult brain was considered to be a strictly organized and fixed structure, with different brain regions responsible for different functions. However, this perspective has changed in the last 30 years. Research has shown that cortical networks in the brain change, including synaptogenesis, neurogenesis (Bjorklund & Lindwall, 2000), and programmed cell death, as a result of one's experience. The brain is characterized by neuroplasticity, or cortical remapping, which is a complex, multifaceted, and fundamental property of the living brain that allows it to adjust to the changes in environmental and physiological conditions and experience (Pascual-Leone, Amedi, Fregni, & Merabe, 2005). Individual connections within the brain are constantly being removed or recreated, which largely depends upon how they are used. One of the key elements of the human brain's ability to change through neuroplasticity is creation of interconnections between neurons based on their simultaneous firing over a period of time. This concept is captured in the aphorism, "neurons that fire together, wire together"/"neurons that fire apart, wire apart", which was articulated in more detail by Canadian psychologist Donald Hebb (Hebb, 1949). Long-term synaptic plasticity is believed to be the molecular basis of learning and memory (Clark & Beck, 2010; Kandel, 1998). It has also been established that learning accompanied by the development of new neuronal connections also leads to the development of new neurons (Gould, Beylin, Tanapat, Reeves, & Shors, 1999).

The impact of experience on neural and behavioral development depends on the timing, duration, and intensity of stimuli and biological vulnerability, resilience, potentiating risk factors, and protective effects (Gunnar & Fisher, 2006; Pollak, 2005). Research in neurobiology of learning and memory suggests that, after each new learning event, there is a necessary and sufficient change in the nervous system that supports the learning (for review, see Kleim & Jones, 2008).

Numerous neuroscientific studies provide the basis for the explanation of the principles of experience-dependent plasticity that governs learning (Kleim & Jones, 2008). Since cognitive-behavioral therapies are learning-based therapies, the changes brought about by therapeutic interventions are expected to occur according to the same principles. Furthermore, according to the cognitive-behavioral paradigm, dysfunctional patterns are adopted through learning. Thus, the adoption and manifestation of learned dysfunctional behavior can be explained by the same principles. Table 1 lists the principles of experience-dependent plasticity developed during the decades of basic neuroscience research (Klein & Jones, 2008), which could be useful in understanding the significance of learning for adoption and maintenance, as well as removal, of unwanted experience and behavior. The table shows examples of how individual principles may be applied to deviant behavior and how CBT may be used in interventions. Although the cognitive-behavioral paradigm had been developed before the plasticity of the brain was discovered, the compatibility of principles resulting from neuroscientific research and those resulting from CBT theory and practice is quite evident.

Table 1. Principles of experience-dependent plasticity (according to Klein & Jones, 2008)

Principle	Description	Abnormalities	Therapeutic intervention
Use it or lose it	Failure to drive specific brain functions can lead to functional degradation.	For the fear of being evaluated, the person avoid speaking in public, which leads to the loss of skill of speaking fluently.	Systematic omission of compulsive behavior will lead to its disappearance.
Use it and improve it	Training that drives a specific brain function can lead to an enhancement of that function.	Obsessive-compulsive symptoms spread and intensify in time.	Frequent practice leads to increasingly successful task performance.
Specificity	The nature of the training experience dictates the nature of the plasticity.	Elective mutism results from anxiety that occurs only in specific situations.	A person learns to discern the signs in the environment that cause anger in order to avoid impulsive reaction.
Repetition matters	Induction of plasticity requires sufficient repetition.	One panic attack can remain an isolated event, but frequently felt intensive anxiety followed by physical symptoms will lead to panic disorder.	A single exposure will not lead to solving phobia - multiple systematic exposures are needed.
Intensity matters	Induction of plasticity requires sufficient training intensity.	A single traumatic situation of high intensity is enough to develop intense anxiety.	Flooding technique elicits strong emotional states that my lead to significant symptom reduction.
Time matters	Different forms of plasticity occur at different times during training.	Vomiting in bulimia is volitional at the beginning, whereas later on, full stomach becomes a sufficient trigger for spontaneous vomiting.	Systematic desensitization with step-by-step exposure leads to the development of skill of facing.
Salience matters	The training experience must be sufficiently salient to induce plasticity.	Traumatic experience where a person feels helpless leads to the development of posttraumatic stress disorder (PTSD).	In the treatment of anxiety disorders, the person is exposed to the anxiety-inducing content; otherwise, the therapeutic effect will fail.
Age matters	Training-induced plasticity occurs more readily in younger brains.	Basic beliefs are adopted under the influence of early learning.	Behavior control treatment in ADHD is more successful if started at younger age.
Transference	Plasticity in response to one training experience can enhance the acquisition of similar behaviors.	Generalization of stimuli leads to fear of all dogs after an unpleasant experience with one dog.	After breaking one bad habit, it is easier to break other bad habits.
Interference	Plasticity in response to one experience can interfere with the acquisition of other behaviors.	Learning academic content is hindered by hypervigile attention in a child with ADHD.	Doing progressive muscle relaxation under conditions of exposure to frightening stimuli hinders development of anxiety.

The more some type of behavior is used, the more changes in the anatomy and functions of the brain occur, thus increasing the probability of the same behavior being used again. If an anatomical structure is increasingly used in some type of behavior, there will be competition for the available cortical space, which will be occupied by the most frequently used function (Jones, 2000). The evidence from the previous neuroscientific studies shows that brain activity and organization change after the treatment of obsessive-compulsive disorder (Schwartz, Stoessel, Baxter Jr., Martin, & Phelps, 1996), panic disorder (Prasko et al., 2004), phobias (for review, see McNally, 2007; Paquette et al., 2003; Straube, Glauer, Dilger, Mentzel, & Miltner, 2006), depression (Brody et al., 2001; Goldapple et al., 2004), post-traumatic stress disorder (Felmingham et al., 2007), tics and dyslexia (for review, see Beauregard, 2007; Frewen, Dozois, & Lanius, 2008).

Cognitive Regulation of Emotions and Behavior

There is evidence that a chronic inability to self-regulate negative emotions, such as sadness and fear, may play a pivotal role in the genesis of clinical depression, anxiety disorders, and other mental disorders (Davidson, Putnam, & Larson, 2000; Jackson, Malmstadt, Larson, & Davidson, 2000). According to the following CBT hypothesis, emotional reaction and behavior depend on cognitive processing in a specific situation. Each individual receives and processes data from the environment in his or her particular and unique way. In accordance with the perceived information, interpretation of its importance, understanding of causative relationships, and personal meaning ascribed to an event, an emotional reaction arises and influences the behavior. It means that the event itself has no "objective" meaning, but is perceived, interpreted, remembered, and evaluated in relation to oneself, in accordance with one’s own cognitive activity (Jokić-Begić, 2008). However, a person cannot respond to all pieces of information received. Information has to be filtered. According to cognitive psychologists, for something to be perceived at all, it has to be personally important, and this importance is based on previous experiences, i.e., memory. The perception-cognition-emotion sequence starts by paying attention to some internal and/or external stimulus, followed by assessment and emotional and behavioral reactions. Emotional response to a stimulus may be automatic (especially in case of threatening and dangerous events, when the process follows a perception-emotion-cognition sequence), but for most stimuli, a volitional cognitive evaluation is needed in order to develop an emotional reaction.

Cognitive therapy does not assume that cognitions cause mental disorders, but they play an important role in the development of disorders, assessment of social support, and recovery from the disorder (Živčić-Bećirević, 2003). Changing cognitive activity will lead to changes in emotional response and then in the behavior. During CBT, a patient learns how to self-regulate unpleasant emotions, which is essential for mental health (Beauregard, 2007). The techniques used include refocusing, cognitive restructuring, problem-solving and other techniques that in a rational manner alleviate unpleasant emotional states.

Is there neuroscientific evidence of the basic hypothesis that change in the cognitive activity results in the change of emotional dimension? From a neurobiological perspective, different regions of the brain are involved in emotion regulation processes. Generation and regulation of emotions involves interplay between two modes of information processing: automatic, reflexive, bottom-up and effortful, symbolic, and top-down processes (Clark & Beck, 2010; Wright et al., 2008).

Bottom-up processing is a primitive, automatic, effortless, implicit, and preconscious information processing dominated by the salient features of a relevant stimulus or situational cues and their schematic associations (Clark & Beck, 2010). Studies of emotional evaluation using fMRI have associated bottom-up processing with the amygdala (Wright et al., 2008). Traditionally, it was considered that bottom-up activity was automatic and not modulated by cortical structures (Whalen et al., 1998). However, this thesis has recently been questioned (Pessoa, 2005; Vuilleumier & Driver, 2007). Research shows that refocusing, explicit evaluation, and cognitive processing of emotional experiences leads to a more intense amygdalous response, subjectively stronger emotional reaction, and characteristic physical changes (Wright et al., 2008).

Top-down processing is slow, deliberate, explicit, and strategic form of rational processing that uses rule-based knowledge to guide the information processing system (Clark & Beck, 2010). A region frequently implicated in top-down processing of emotion is the orbitofrontal cortex (OFC) (Wright et al., 2008). Other regions implicated in top-down processing include the ventromedial prefrontal cortex (vmPFC) and anterior cingulate cortex (ACC) (Lane, Fink, Chau, & Dolan, 1997; Ochsner et al., 2004; Taylor, Phan, Decker, & Liberzon, 2003). Subcortical emotion generating structures and cortical emotion regulating structures interact in complex ways that result in behaviors that are indicative of the regulation of emotion (Ochsner & Gross, 2007).

Cognitive restructuring is the basic technique used to replace a dysfunctional manner of thinking by a functional one. From neurobiological perspective, it is the top-down regulation by which rational thinking leads to reduced emotional response and regulation of negative emotional states.

The results of studies of neurobiological changes have shown that CBT is associated with decreased activity in the amygdalohippocampal subcortical region (i.e., bottom-up processing) and increased activation in the frontal cortical regions (i.e., top-down processing) (Clark & Beck, 2010). Reviewing the neurobiology studies of psychotherapeutic changes, Linden (2006) concluded that CBT leads to reduced fronto-striato-thalamic activity in anxiety disorder, but the findings are less consistent for depression. Studies indicate that symptom improvement in anxiety or depression after CBT is associated with decreased activity in the amygdalohippocampal subcortical regions that involve bottom-up emotion processing and improved activity of top-down processes in the orbitofronatl cortex (OFC), medial prefrontal cortex (mPFC), and the ventral and dorsal anterior cingulate cortex (ACC). The ACC and mPFC are responsible for higher-order executive cognitive functions, which are primarily targeted during CBT (Ochsner & Gross, 2007).

Research findings related to the two regulatory mechanisms contributed to understanding why particular techniques have different therapeutic success. Previous comparative studies of pharmacotherapy versus CBT showed that their therapeutic success depended on the type of disorder, criteria of success, duration of follow-up, research methodology, and so on (Dobson, 2009). One of the explanations is that pharmacotherapy modifies the bottom-up regulation by influencing the subcortical transmitter metabolism and thus eliciting a change in subjective mood and cognition. On the other hand, psychotherapy influences top-down regulation by modifying the patient's implicit relational patterns and attitudes (Gabbard, 2000). Goldapple et al. (2004) found that drug treatment affects limbic-subcortical regions (brainstem, insula, subgenual cingulate), whereas CBT influences the medial frontal and cingulate cortex. This finding also explains the commonly observed lower relapse rate in clients undergoing CBT, whether or not combined with medications (Dozois, Bieling, & Patelis-Siotis, 2009; Segal & Gemar, 1999; Segal et al., 2006). Without the changes in top-down regulation elicited by new and repeated experiences, i.e., emotional, verbal and interpersonal processes of learning, there can be no permanent changes in behavior patterns (Fuchs, 2004).

Abelson, Liberzon, Young, and Khan (2005) aimed to determine the significance of cognitive factors in the regulation of physiological responses, but without inclusion of emotional states. The authors administered infusion of penagestrin, which activates stress axis subjectively manifested as a panic attack. They also administered a short-term cognitive intervention to help subjects attain a feeling of control over the situation when infusion was administered and instructed them how to reduce the feeling of stress and threat. Subjective degrees of stress and cortisol level were measured in specific time intervals before and after the infusion. The results showed that cognitive intervention influenced the cortisol blood level but not the subjective level of stress, that cognition had a significant influence on the endocrine system, and that relationship was not mediated by emotional states.

As opposed to other therapeutic approaches, CBT aims at removing the symptoms, improving the functionality, and achieving a generally more positive emotional state. Therefore, it is often criticized as being superficial, not insisting on "obtaining insight" into difficulties, and working on previous unpleasant experiences. Neuroscientific research, however, emphasizes the significance of positive emotional states as facilitators of a neurobiological change. New scientific research on neuroplasticity suggests that positive emotional states may trigger lasting, durable changes in the structure and function of the brain (for a review, see

Garland & Howard, 2009), which instantiate and promote further adaptive thoughts and behaviors. Therefore, CBT orientation towards creating a positive and optimistic atmosphere, which is attained by removal of symptoms, is neurobiologically justified.

Metacognition - Thinking about Thinking

Self-directedness on one's own body and mental activity, interpretation of what is observed, and the resulting emotional reactions may be either functional or non-functional. Individuals with emotional disorders have mistaken beliefs and wrong knowledge about their own thoughts and thinking processes, they are over-concerned with them, and often experience these thoughts and emotions as a reality that caused unwanted emotional reactions in them. The third CBT hypothesis says that cognitive activity may be observed and changed. By changing dysfunctional thinking, we can achieve the desired changes in the behavior and emotional response. Classic cognitive therapy was focused on producing changes in the thinking content and, consequently, in other aspects of functioning. Brain imaging studies confirmed that there are neural correlates of these changes, as described previously. However, more attention has recently been paid to the so-called metacognitive level, i.e., notions about and ways of controlling one's own cognitive processes. Metacognition often suggests conscious or volitional control of thoughts, memories, and actions (Shimamura, 2000). Metacognitive regulation involves attention, conflict resolution, error correction, inhibitory control, and emotional regulation. These aspects of metacognition are presumed to be mediated by a neural circuit involving midfrontal brain regions (Shimamura, 2000).

In order to influence this aspect of thinking, CBT successfully introduced new techniques directed at observing, exploring, and changing one's own thoughts and emotions (metacognitive therapies, mindfulness). A person is taught not to accept his/her thoughts and emotions as accurate reflections of reality, but as short-term, transitory mental events. An awareness of awareness itself allows the individual to consciously attend to thoughts, emotions, and action tendencies (Chambers, Gullone, & Allen, 2009) and to choose those that benefit the individual. Mindfulness involves a systematic retraining of awareness and non-reactivity, enabling the person to consciously choose adequate thoughts, emotions, and sensations rather than habitually reacting to them (Arch & Craske, 2006; Chambers, Gullone, & Allen, 2009).

Not only that these techniques proved effective in the treatment of different disorders (primarily depression, obsessive-compulsive disorder, generalized anxiety disorder, immunological states); they also aroused more far-reaching questions about the nature of mental processes. Neuroscientific findings indicate that changes occur in mental processes due to the changes in the way how one thinks about one's own thoughts. Mindfulness CBT is documented to have a positive effect on the hypothalamic-pituitary-adrenal axis and hormonal and immune system (Carlson, Speca, Faris, & Patel, 2007; O'Loughlin & Zuckerman, 2008). Mindfulness-based interventions have led to the changes in the brain electrical activity (increased left-sided anterior activation) (Davidson et al., 2003) and affective and cognitive processes (Arch & Craske, 2006; Chambers, Gullone, & Allen, 2009). The neuronal correlates of dispositional and trained mindfulness are reminiscent of those seen during pain control and placebo response (Stein, 2005). Studies of placebo effect show that beliefs and expectations may significantly shape neurophysiological and neurochemical activity in brain regions involved in perception, movements, pain, different emotional states (Beauregard, 2007). By changing the mind, we change the brain (Paquette et al., 2003).

Neuroimaging Studies of CBT Treatment of Various Disorders

Arachnophobia

Impressive are the studies of neurobiological changes that occur during arachnophobia therapy. One study (Paquette et al., 2003) included 12 clients with arachnophobia in whom fMRI scanning was performed a week before and a week after the CBT treatment. Healthy control volunteers (N = 13) were also scanned (once) while exposed to the same film excerpts. The CBT consisted of gradual exposure-based treatment to spiders and education to correct erroneous beliefs about this insect. The CBT approach was used, because previous research had shown that a short and intensive CBT treatment is a method of choice in the treatment of phobias. If we compare it with the principles of experience-dependence plasticity, we may see that such a therapeutic choice conforms to almost all principles. The clients met once a week over a 4-week period for intensive 3-hour sessions. In the first session, they were exposed to photographs of spiders, in the second session to movie-clips showing explicit pictures of spiders, in the third session to real spiders brought by entomologists, who also gave a lecture on these insects. In the last session, the subjects were asked to touch a tarantula. All phobic volunteers responded successfully (they were able to touch the entire series of pictures depicting spiders, the TV screen showing living spiders, and real spiders without reporting fear reactions). The fMRI results showed that, in phobic volunteers before CBT, watching these disturbing pictures of spiders was associated with significant activation of the right lateral prefrontal cortex (LPFC), parahippocampal gyrus, and bilateral visual associative cortical areas. For normal control volunteers, only the left middle occipital gyrus and the right inferior temporal gyrus were significantly activated. In phobic subjects, the LPFC activation possibly reflected the use of metacognitive strategies to self-regulate fear response, whereas the parahippocampal activation was possibly associated with automatic emotional response of fear leading to avoidance behavior and eventually maintenance of phobia (according to the principle: use it and improve it - the more avoidance is used, the more automatic it becomes). After successful completion of CBT, no significant activation was found in the LPFC and the parahippocampal gyrus. These changes indicate that CBT treatment may lead to adaptive changes in specific brain regions in individuals with anxiety disorders.

In another study (Straube et al., 2006), brain activation to spider videos was measured with functional magnetic resonance imaging (fMRI) in spider phobic (N = 28) and healthy control volunteers (N = 14). Phobic volunteers were randomly assigned to a CBT group (N = 13) and a waiting-list control group (N = 12). Before CBT, the phobic group differed from the healthy control group and among themselves in brain activity. Compared to control volunteers, phobic volunteers exhibited stronger responses in the insula and anterior cingulate cortex (ACC) when exposed to spider videos. CBT significantly reduced phobic symptoms in the CBT group, while no changes in the symptoms were recorded in the waiting-list control group. The scans after the treatment showed a significant decrease of activity in the insula and ACC in the CBT group in comparison with the waiting-list control group. These results indicated the importance of the insula and ACC in the development and maintenance of phobia.

Both studies showed changes in the brain regions after CBT treatments, although only a limited overlap in the identified neural regions was observed. Further studies are necessary to identify the regions that most reliably mediate the CBT effects of treatment of arachnophobia and other specific phobias.

Obsessive-Compulsive Disorder

Baxter et al. (1992) were the first to perform a neuroimaging analysis of neural effects of CBT on obsessive-compulsive disorder (OCD). Their results were confirmed and upgraded by the same research team (Schwartz et al., 1996). Recently published results of a study performed in Japan also confirmed previous findings (Nakatani et al., 2003), which showed a significant right-sided or bilateral reduction in the metabolic rate of the caudate occurring after CBT treatment for OCD symptoms. The percentage of change in the metabolic rate in the caudate correlated with clinical changes.

Schwartz has developed a CBT therapy for OCD clients on the basis of their clinical and research experience, taking into account the principles of neuroplasticity and CBT (Schwartz & Begley, 2002). The main goal of this treatment is to teach clients how to observe their obsessions as an accidental brain activity that should be responded to in a new and more adaptive way. The treatment always consists of the following 4 steps: relabel, reattribute, refocus, and revalue. The first step involves teaching patients to relabel the intrusive thoughts and urges as the symptoms of OCD disorder. In the second step, patients are encouraged to reattribute the bothersome and persistent nature of the symptoms to 'false messages' coming from a dysfunctional brain. The goal of the first two steps is to change the relationship toward OCD symptoms, which may result in intensification of the feeling that the person has a choice of what to do after the symptoms penetrate into the consciousness. In the third step, patients learn to change behavioral responses while the uncomfortable intrusive thoughts and urges are still present. In the fourth step, patients come to revalue the intrusive thoughts and urges as much less important and noteworthy, and the fear and anxiety associated with them gradually disappear. A very important aspect of this treatment is mindfulness, i.e., perceiving one's own thoughts and feelings as short-term events that reflect OCD rather than reality. Thus, a stronger distinction is created between the experience of the self and that of the OCD symptom, thus increasing the feeling of having a choice after an obsessive thought or urge first appear. The individual learns to control one's own thoughts. According to the authors, the treatment success in the sense of reducing symptoms is present in approximately 80% of clients, which makes it the most successful therapeutic approach in the treatment of OCD. PET scans before and after the therapy showed the following results. Before treatment, there were significant correlations of brain activity in the right hemisphere between the orbitofrontal gyrus and the head of the caudate nucleus and the orbital gyrus and the thalamus. These correlations were significantly reduced after effective treatment.

These results suggest that a prefronto-cortico-striato-thalamic brain system is involved in the mediation of OCD symptoms. Importantly, these results show that psychotherapy may produce significant changes in brain activity.

Panic Disorder

Prasko et al. (2004) used a neuroimaging study to investigate the effects of CBT on panic disorder. Patients with panic disorder (N = 6) were included in a 6-week group CBT treatment, which consisted of psychoeducation about the disorder, cognitive restructuring, training in diaphragmatic breathing and relaxation, *in vivo* exposure, and problem solving. Panic Disorder Severity Scale (PDSS) testing and PET scanning were performed before and after the treatment. After the treatment, the PDSS scores were significantly reduced. The PET scans after the treatment showed increased metabolism in the left inferior and right middle frontal cortex, left insula, right precuneus, right posterior cingulate cortex, left middle and superior temporal cortex, and middle and superior parietal cortex. These results were consistent with the suggested mechanisms of change in CBT for panic disorder (e.g., altering problem-solving capacity and emotional processing). It may be speculated that intensified metabolism in the left insula would partly reflect an increase in parasympathetic (relative to sympathetic) tone (Craig, 2005), as manifested in the increased ability to 'feel at ease' within their physical body and surrounding environment as a result of the CBT intervention (Frewen, Dozois, & Lanius, 2008). These results suggest that effective CBT can positively alter brain metabolism in individuals with panic disorder.

Social Phobia

In the study performed by Furmark et al. (2002), 18 middle-aged subjects with social phobia were allocated into three equal groups as follows: CBT, antidepressant pharmacotherapy (Citalopram), and waiting-list. PET scanning was performed before and after the treatment (12 weeks) during an anxiety-provoking public speaking task. Specifically, 20 minutes before the scanning, participants were asked to prepare a short speech about a vacation or travel experience and, while being scanned, performed this speech in the presence of at least a six-person audience while being recorded by a portable video-camera. The anxiety level was assessed by Spielberger State-Anxiety Inventory and 100-point Subjective Units of Distress scale. Both treatment groups showed a significant decrease in the psychometric parameters of anxiety after treatment, which was not observed in the control group. CBT and pharmacotherapy groups achieved equal decrease in the level of anxiety after 12 weeks. In the CBT group, a reduced blood flow was observed bilaterally in the amygdala, hippocampus, periaqueductal gray and anterior and medial temporal cortex, while increased blood flow was noticed in the right cerebellum and the secondary visual cortex. In contrast, no significant changes in the cerebral blood flow were observed in these areas in the waiting-list control group. The only difference between the treatment groups was increased blood flow in the right thalamus observed only in the pharmacotherapy group. These results led to a conclusion that reduced fear of public speaking was associated with the decreased activity of the amygdala. Additionally, reduced activity in the hippocampus and medial temporal lobe may be associated with a perceived lower need to consolidate the post-treatment public speaking experience as a threatening situation that should be avoided in future, because these structures are associated with fear conditioning and emotional episodic memory (Frewen, Dozois, & Lanius, 2008).

Major Depressive Disorder

CBT is a method of choice in the treatment of depression (Clark & Beck, 2010). Goldapple et al. (2004) investigated the efficacy of CBT treatment using a neuroimaging study design. Their study included 14 patients involved in 15-20 session CBT treatment. During the treatment, patients learned to use several behavioral and cognitive strategies aimed at combating dysphoric mood and reducing automatic reactivity to negative thoughts and attitudes. Behaviorally, patients were asked to increase the frequency of pleasant events in their lives. Between the sessions, the patients were asked to record negative automatic thoughts and to test their interpretations and beliefs via behavioral experiments. Before and after therapy scores on the Hamilton Depression Rating Scale (HAM-D) and PET scans were compared. All patients showed a significant reduction in the symptoms of depression on the HAM-D. In the CBT group, Goldapple et al.

(2004) found pre-treatment vs. post-treatment increases in metabolic activity within the hippocampus/parahippocampal gyrus and dorsal cingulate cortex. Decreases were also found in the dorsalateral and ventrolateral prefrontal regions, orbital frontal regions, posterior cingulate, inferior parietal regions, and inferior temporal regions. These results suggest that CBT influences clinical recovery by modulating the functioning of selective areas in limbic and cortical regions.

Similar results were obtained by Mitterschiffthaler et al. (2008). They performed an fMRI study to investigate neural changes in relation to mood-biased processing in depression before and after cognitive behavioral therapy. The study included 16 middle-aged patients meeting the criteria of DSM-IV diagnosis for unipolar major depression and 16 matched healthy volunteers. Both groups underwent fMRI twice: CBT group before and after the 16 once-a-week sessions of CBT and the healthy control group in similar time intervals. In an emotional Stroop task, negative and neutral words were presented in various colors and volunteers were asked to name the color of words. Latencies were recorded to determine behavioral emotional interference effects. Before the treatment, depressive patients showed increased latency during color naming of negative words in comparison with healthy controls. After the treatment, there was no difference in the latency between these two groups. The neural basis was associated with increased activity in the amygdala, DLPFC, and VLPFC, which normalized after the treatment. CBT seems to affect behavioral biases and neural circuits involved in processing negative information.

Chronic Fatigue Syndrome

A recent longitudinal study of CBT in women with chronic fatigue syndrome found increase in the gray matter of the lateral prefrontal cortex after 16 CBT sessions (de Lange et al., 2008). Increase in the gray matter volume correlated with enhanced cognitive processing speed, suggesting that the neuroplasticity evoked by psychotherapy played a causal role in rehabilitation of cognitive performance after cerebral atrophy resulting from chronic fatigue.

Conclusion

Significant progress has been made in recent years in our understanding of neurobiological basis of mental disorders and changes that occur during psychotherapy. CBT is psychotherapeutically founded on a theory that empirical examination needs to be performed from the very beginning of the treatment. With a new generation of research methods including brain imaging, new insights have been gained into the mediators of change during CBT. The findings of these studies are consistent with the notion that CBT interventions alter brain functioning associated with problem-solving, self-referential and relational processing, and affect regulation. Research designs including pre- and post-treatment neuroimaging measurements revealed the changes in cortical and subcortical structures. It has been postulated that cognitive therapy influences top-down brain regulation; therefore, the changes are permanent and generalized to different areas of life. At the same time, it should be emphasized that neuroimaging research is still at its beginning (Peres & Nasello, 2007) and that this scientific field is still largely uninvestigated. Previous findings are important, but require caution. Research designs, as previously described, are developed with an aim to observe changes in the central nervous system induced by psychotherapy. However, the question remains if the observed changes represent neurobiological correlates of therapeutic interventions or just changes accompanying improvements in the condition. Other psychotherapeutic schools also examine neurophysiological correlates of changes in the behavior and experience. Although such studies are scarce, their results confirm that neurobiological changes occur during psychoanalytical psychotherapy (for review, see Mechelli, 2010) and interpersonal therapy (Beauregard, 2007). CBT and interpersonal therapy are structured psychotherapeutic schools with compatible results, primarily in the treatment of depressive disorders (for review, see Frewen, Dozois, & Lanius, 2008). Research of neurobiological correlates within psychoanalytical paradigm is mostly focused on the neurological organization of psychoanalytically defined phenomena and the evaluation of psychoanalytic theories based on their neurobiological evidence (Mechelli, 2010). Irrespective of the fact that psychoanalytical paradigm significantly differs from CBT; research into neurobiological correlates of basic psychoanalytic principles has produced valuable results applicable within other therapeutic schools. One of the examples is the discovery of a neural mirroring system in the premotor cortex and other areas of the brain, obviously functioning as the neurobiological correlate of action understanding, nonverbal communication, and empathy. This finding has already influenced psychotherapeutic practice, as shown by greater importance being given to the therapist-client relationship in CBT approach (Fuchs, 2004). Psychotherapy may thus be regarded as a new attachment relationship, which is able to regulate affective homeostasis and restructure attachment-related implicit memory (Gabbard, 2000).

To improve our understanding of neurobiological changes, we need comparative experimental studies aimed at specific elements of CTB and their effects on particular cognitive and neural processes involved in negative emotions. Such studies require an interdisciplinary approach, which is a prerequisite for understanding how to help people live a better life. Research into the neural substructures, without taking into account the psychosocial level of meaning and context that shapes the brain and its functions, will not provide a sufficient explanation of the symptoms and course of mental disorders.

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