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**Contributions from Neuroscience to the Practice of Cognitive Behaviour Therapy:** 

**Translational Psychological Science in Service of Good Practice** 

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#### Abstract

The integration of neuroscience with multiple disciplines dealing with cognition, behavior and contextual influences holds potential to create new avenues for the application of process oriented interventions and guidelines for clinical psychological practice. In this paper, the main avenues by which neuroscience may readily be used for the clinical practice of Cognitive Behavior Therapy (CBT) are outlined: (1) the selection and optimal use of CBT procedures; (2) the combination of CBT with neurocognitive and neurobiological interventions; (3) tailoring CBT to the neurocognitive characteristics of patients; and (4) the use of neuroscience in psychoeducation. This translational view may facilitate multidisciplinary collaboration in case conceptualization. Moreover, it emphasizes that CBT course programs would benefit from neuroscience training and that continued education to keep track with the latest developments in neuroscience are helpful for good CBT practice.

Keywords: Cognitive Behavior Therapy; Translational; Neuroscience; Clinical Practice; CBT training

# Contributions from Neuroscience to the Practice of Cognitive Behaviour Therapy: Translational Psychological Science in Service of Good Practice

## Introduction

Cognitive Behaviour Therapy (CBT) has a longstanding tradition in the use of interventions inspired by psychological theory and research, with the goal to improve behavioral, cognitive, and health outcomes and to decrease vulnerability for psychological disorders. Such a translational psychological science process starts from basic science, testing underlying mechanisms to develop models of change, subsequently transferring these models to interventions (Fishbein, 2006). The efficacy and effectiveness of these interventions are ideally tested thoroughly before the implementation in psychological care settings, but this does not preclude that a translation from basic science knowledge can readily provide guidelines to the practice of CBT. The basic science account supporting CBT is historically rooted in animal models of learning and more recently in experimental psychopathology. Given that therapies can only be successful at the long term if they lead to comprehensive and lasting changes in the brain, some decades ago, scholars started to integrate learning theory with neurobiology, in an attempt to provide insight into the dynamics of dysfunctional behaviour with implications for therapy (e.g. De Raedt, Schacht, Cosyns, & Ponjaert-Kristoffersen, 2002).

To date it becomes ever more clear that the integration of neuroscience with multiple disciplines dealing with cognition, behavior and contextual influences holds huge potential to create new avenues for process oriented interventions and clinical practice guidelines. Although this is an emerging field, I outline the main avenues by which neuroscience may already be instrumental to the practice of CBT. Each of these avenues is illustrated by representative examples, to clarify the relevance in a concrete way. Finally, in line with this, I suggest to enhance neuroliteracy as part of CBT course programs.

### The selection and optimal use of CBT procedures

Knowledge on neural mechanisms of action may inform CBT therapists about the selection of specific procedural aspects that should be applied in their interventions. The crucial question is which knowledge from neuroscience a CBT therapist can readily use to inform her/his daily practice. For the clinical field to use this knowledge, an accurate general level of understanding is important. For example, basic research on the cortical-subcortical circuitry of emotion processing has been applied to exposure therapy, with the proposed implication that during exposure the focus of attention should be directed towards the emotional content of the threatening situation, to facilitate prefrontal control over emotion producing systems (i.e. amygdala), and that new emotional salient contextual information must be added to create inhibitory projections from the hippocampus, which is a region involved in context associations for memory formation (De Raedt, 2006). Here, evidence from neuroscience is also discussed to propose that during the application of cognitive techniques, therapists might encourage patients to focus their attention on emotional content to facilitate inhibitory processes by the medial prefrontal cortex on the amygdala, to provoke changes in the hippocampus after successful cognitive interventions. However, these early translational efforts were still in need of specific translation to scientifically underpinned guidelines. A further elaboration on emotion focus during CBT is provided in the section on memory reconsolidation.

Recently, Craske and colleagues developed an inhibition learning model of exposure in line with knowledge from neuroscience, going beyond this basic model adding that exposure needs to target competing learning experiences (see also the implications in the section on memory consolidation) to enhance inhibitory learning and its retrieval, which led to specific

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additional steps in its application (Craske, Treanor, Conway, Zbozinek, & Vervliet, 2014). This inhibitory approach is in line with basic research on the neural mechanisms underlying fear extinction, showing that the amygdala is active during fear conditioning and can be inhibited by the medial prefrontal cortex (Milad, Wright, Orr, Pitman, Quirk & Rauch, 2007). The relationship between associative learning and the neural mechanisms of fear extinction is further illustrated by a recent study investigating the neuronal mechanisms of learned associations between sensory stimuli and fear responses. Raij, Nummenmaa Marin, Porter, Furtak, Setsompop and Milad (2018) used magnetic resonance imaging-navigated transcranial magnetic brain stimulation (TMS). Subjects were aversively conditioned to two different cues, and during extinction learning on another day, TMS on the left ventromedial prefrontal cortex (versus a control target) was paired with one of the conditioned cues but not the other. During extinction recall on the third day, only the cue paired with TMS showed significantly reduced skin conductance responses indicative of enhanced fear reduction.

Craske and colleagues provide practical guidelines on how to implement this model in clinical practice, to optimize exposure therapy in ways that go beyond the classical habituation or belief disconfirmation approach in standard CBT, by using expectancy violation, deepened extinction, occasional reinforced extinction, removal of safety signals, variability, retrieval cues, multiple contexts and affect labeling. It is important to emphasize that these strategies derived from neuroscience are not all consistent with a habituation model of extinction in which fear reduction during exposure is considered crucial for its effect. Based on this inhibitory model in line with the abovementioned neuronal correlates, Craske et al (2014) nicely illustrate how treatment that is based on this model differs from an habituation-based model of exposure, by using expectancy violation, stimulus discrimination, tying completion of exposure to behavioral goals rather than reduction of fear level, and using affect labeling which has been related to activity of the ventrolateral prefrontal cortex reducing amygdala activation (Lieberman et al., 2007).

Although one could argue that the application of these models has not yet been investigated in large RCT's comparing different procedures for exposure, they are sufficiently supported by experimental research to warrant their usefulness as guidelines for clinical practice. However, it should be emphasized that the selection of these techniques need to be delivered in the context of an individualized case formulation. For example, safety behaviors may initially be helpful for some patients to overcome their fears if this doesn't interfere with the learning that should take place at that moment in therapy.

The optimal use of existing CBT interventions can also be informed by neuroscience, to help therapists in anticipating what may be useful/harmful for their patients. Knowledge on memory consolidation is a good example. Memory consolidation is the process during which new information that has been learned transitions from a labile to a more permanent state (Dudai, 2004). Accommodation is a process by which a preexisting memory is disrupted and transformed by new information. The process of accommodation requires reconsolidation of the preexisting memory. The rich literature on the neurobiological mechanisms underlying memory reconsolidation can be readily used to infer that only discussing problems with our patients over and over again leads to reconsolidation of negative experiences and cognitions instead of relieve of mental suffering. This may be the reason why psychological interventions consisting of regular consultations to only talk about problems do not work and may even lead to a worsening of negative cognitions related to these problems. CBT, in which restructuring of maladaptive cognitions is the goal, or exposure in which new information related to safety competes with original dysfunctional memories (Bouton, 2002), may lead to positive effects that can be predicted based on neuroscientific knowledge on memory processes. In line with this, reconsolidation research has shown that an effective memory

reactivation experience must involve reorganization of memory to incorporate new learning experiences, which indicates that consolidation and reconsolidation should be understood as an integration of new and old information, leading to possible schema modification (McKenzie & Eichenbaum, 2011).

Understanding the neural mechanisms underlying therapeutic learning aimed to decrease the influence of dysfunctional past learning experiences may thus be important for therapists. In a recent review paper, Kredlow, Unger and Otto (2016) summarize evidence that specialized interventions applied under the right conditions, i.e. using post extinction retrieval, can be used to partially replace existing fear memories, to decrease relapse in various disorders, such as anxiety, traumatic stress, and substance use disorders. This is based on the theory that reconsolidation is not only a mechanism for re-solidifying a memory, but it can also be instrumental in updating the specific memory with new information, i.e. safety information (Sara, 2000). This research on extinction learning during the reconsolidation window can provide practice guidelines. Using a post-retrieval extinction procedure in which memory retrieval was followed by the administration of extinction in a rodent sample, Monfils and colleagues (Monfils, Cowansage, Klann, & LeDoux, 2009) could demonstrate that extinction following a memory retrieval cue was more effective than extinction not conducted during the reconsolidation window, reducing spontaneous recovery, renewal, reinstatement and rapid reacquisition.

In a similar vein, Lane and colleagues (Lane, Ryan, Nadel, & Greenberg, 2015) also start from the idea that therapeutic change results from updating prior emotional memories by reconsolidation, and present an integrated model supported by emerging evidence from neuroscience with three interactive components, namely autobiographical memories, semantic structures and emotional responses. They propose that the essential ingredients of therapeutic change (over different therapeutic orientations) are the reactivation of old memories, engaging

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in new emotional experiences that are incorporated into these reactivated memories via reconsolidation, and reinforcing the integrated memory structure by practicing a new way of behaving and experiencing this in different contexts. These authors provide practical guidelines how to accomplish this. For example, based on their integrated model, dysfunctional cognitions do not necessarily precede an emotional response, but they occur in parallel as part of the memory structure. The consequence of this view is that focusing only on thoughts and evaluations -by some authors this is referred to as "cold cognitions" (e.g. Roiser & Sahakian, 2013)- may not elicit change. In CBT the negative thoughts could be used to engage the memory structure, but a new positive emotional experience should take the place of the former negative responses. Based on the model of Lane et al. (2015), the experience of new contradictory episodic events may facilitate therapeutic change, but a focus on emotional experiences and emotional responses is crucial because a corrective emotional experience is part of what is reconsolidated. A very interesting part of this publication is that the journal in which this paper has been published (Behavioral and Brain Sciences) accepted open peer commentary and 28 reactions were published, with critical commentaries leading to additions, alternative explanations, therapeutic strategies to achieve change based on the framework, novel predictions, crucial omissions in the model and suggestions for further research and elaboration. Next to support for the model, also skeptical reactions regarding the limitations of the approach are included, providing useful and nuanced information about the practical implications so far. Interestingly, Liberzon and Javanbakht discuss the implications of this model in the development of more effective interventions and the identification of less effective or even harmful approaches. In this perspective, they add that, based on the model, trauma processing groups in which repeated retelling of trauma memories without corrections of cognitive distortions or reflection on authentic emotions may lead to the deeper consolidation of the fear memories.

# Combining CBT with neurocognitive and neurobiological interventions

Neuroscience has an important role in a multidisciplinary translational approach to inform not only the selection, optimal use, refinement or development of treatment strategies but also the combination of existing CBT procedures with neurocognitive or nonpharmacological neurobiological interventions.

Many techniques used in CBT require proper neurocognitive functioning, such as exposure (e.g. see the above mentioned frontal circuits involved), Socratic dialogues, guided discovery, self-monitoring, self-reflection, emotion regulation, and behavioral experiments. Patients may have difficulties to apply the demanding cognitive techniques used in CBT because deficits in executive functioning and memory processes that are characteristic of several mental disorders (e.g. for an overview of prefrontal deficits in depression, see Semkovska et al., 2019; Levin, Heller, Mohanty, Herrington & Miller, 2007). Executive functioning refers to a set of cognitive processes related to prefrontal functioning including working memory, inhibition, updating, flexibility and attention. This higher-order neurocognitive system enables individuals to organize their behavior, to engage in goal attainment, and to successfully adapt to a changing environment (Jurado & Rosselli, 2007). Moreover, research suggests that executive functioning may be a protective factor for stress (Hendrawan, Yamakawa, Kimura, Murakami & Ohira, 2012).

Neuroscience has been instrumental to develop a new generation of interventions, tackling neurocognitive mechanisms underlying dysfunctional cognitive processes that can be added to the toolbox of the CBT therapist. For example, building on the conceptualization of depression as a failure to implement prefrontal top-down cognitive control over limbic systems, De Raedt and Koster (2010) developed a framework that links decreased stress resilience to neurobiological (e.g., prefrontal and subcortical functioning), cognitive (e.g., negative self-schemas and attention control) and affective (e.g., emotion regulation and rumination) processes, which are associated with the development of recurrent episodes of depression. This framework is instrumental for the development of new avenues in the treatment of depression, to tackle underlying processes such as rumination by using interventions targeting the neurocircuitry underlying these processes. In line with this, cognitive control training to strengthen dorsolateral prefrontal cortex (DLPFC) functioning to eventually decrease rumination has been proposed (Siegle, Ghinassi, & Thase, 2007; Siegle, Price, Jones, Ghinassi, Painter, & Thase, 2014), with promising evidence showing its effectiveness in reducing cognitive vulnerability factors and residual symptoms in recovered depressed patients, underscoring the potential as a preventive tool (Hoorelbeke & Koster, 2017).

These new interventions can be implemented after a diagnostic phase during which specific neurocognitive processes are assessed, although it could be argued that such a personalized medicine approach is not yet ready to be implemented because the reliability and/or validity of neurobiological (e.g. neuroimaging such as fMRI) measures is still limited. Although there is a lot of ongoing work in this area (for an overview, see Lueken et al., 2016), it is not yet possible to use brain imaging such as fMRI in a personalized medicine approach because most brain imaging studies have relied on group based data analysis and personalized medicine involves predicting individual outcomes. Neuroscience is still struggling to achieve this, and the development of brain imaging analytics that would allow this approach is still work in progress. However, the use of validated computerized neuropsychological assessment procedures that have been developed to assess brain functioning (i.e. frontal functions such as attentional set-switching, inhibition, working memory) may overcome this barrier to implementation (for a review using the CANTAB battery in depression, see Rock, Roiser, Riedel & Blackwell, 2014). Indeed, based on a meta-analysis, Rock and coworkers (2014) could show that cognitive deficits are very frequent in depression, even beyond the depressive episode, and can be measured by a standardized computerized test battery, which could be used to provide indications for the addition of cognitive training procedures to CBT.

However, severely ill patients may not be able to use these neurocognitive training procedures or won't be able to apply cognitive restructuring techniques during CBT because of their well-documented frontal deficits. To mechanistically target these deficits, noninvasive neurostimulation techniques such as Transcranial Magnetic Stimulation (TMS) can be used. This technique induces weak electric currents to alter cortical excitability in the brain trough magnetic fields induced by a coil placed above the scalp. It has been demonstrated that repetitive TMS (rTMS) alters brain activity and functional connectivity in brain areas that are implied in the neurocircuitry underlying cognitive change processes related to cognitive techniques that are used in CBT practice, such as inhibition and switching between alternative thought patterns, attention allocation and emotion regulation (De Raedt, Vanderhasselt & Baeken, 2015). In this perspective, the effects of CBT may be increased by boosting DLPFC activity. It has been demonstrated that multiple sessions of high frequency rTMS (HF-rTMS) in depressed patients can lead to changes at the level of molecular (Baeken et al., 2011), metabolic (Baeken, De Raedt, Van Hove, Clerinx, De Mey & Bossuyt, 2009) and functional connectivity (Baeken et al., 2014), and may lead to alterations in dysfunctional processes such as difficulties to inhibit negative information (Leyman, De Raedt, Vanderhasselt, & Baeken, 2011) and reward processing (Duprat, Wu, De Raedt & Baeken, 2018). However, until now, HF-rTMS alone seems not to be able to produce long-lasting benefits in patients suffering from depression (Cohen, Boggio & Frengi, 2009). The reason may be that the patient must also acquire new learning in order to be able to use the restored brain function in an efficient way, which suggests that a combination of neurostimulation and cognitive interventions may be an interesting option (De Raedt, 2015). A neuromodulation technique that also holds

potential in this perspective is transcranial Direct Current Stimulation (tDCS), which does not induce neuronal firing by suprathreshold neuronal membrane depolarization such as rTMS, but modulates neuronal activity in an active network (Nitsche et al., 2008). It is a very costeffective and easy to apply technique able to influence cognitive functioning when applied during task performance in psychiatric patients (for an overview, see Dedoncker et al, 2016). This makes it very suitable to be combined with cognitive interventions. Given that it has been demonstrated that the prefrontal cortex is implied in the circuitries that are influenced by CBT (Goldapple et al., 2004), modulating the excitability of this brain area may boost performance during CBT, hence increasing its learning effects. Sathappan, Luber and Lisbany (2019) discuss how sequential or simultaneous application of non-invasive brain stimulation can be combined with cognitive interventions (cognitive control training, attentional bias modification, CBT), focusing on a range of neuropsychiatric disorders. They emphasize for each of the disorders the neuroanatomical circuitry that could be engaged, and review the current literature on these applications. In a recent naturalistic study (Donse, Padberg, Sack, Rush & Arns, 2018), the feasibility and clinical outcome of simultaneous rTMS over the DLPFC and CBT is tested in 196 patients with major depressive disorder. The results are promising (66% response, 56% remission and 60% remission at 6 month follow-up), but given the absence of a control group, more research is necessary to draw firm conclusions on the extra value of neurostimulation. Nevertheless, it is obvious that, in patients with severe prefrontal deficits, a restoration of these deficits is warranted to facilitate therapeutic work.

Neurofeedback, in which the patient receives real-time feedback on its own brain activity in an attempt to achieve self-regulation of brain function by operant condition, is another potential tool that could be applied to supplement CBT practice. Many studies are testing the use of functional magnetic resonance imaging neurofeedback (fMRI-NF) in the scanner, related to areas involved in emotion processing. Although this may be promising in the future, it will always remain a very expensive setup and clinical usefulness is still limited by unstandardized methodological practices, by clinical definitions that are not clearly grounded in neurobiology, and by lack of a unifying framework (but this is exciting work in progress, see e.g. Lubianiker et al., 2019). EEG neurofeedback may be a good alternative, but research findings on the effects are still mixed and a lot of issues still need to be addressed, which prevents clear conclusions on the effectiveness in several psychological problems (Marzban, Marateb & Mansourian, 2016; Thibault, Lifshitz & Raz, 2016). Nevertheless, the principle of providing feedback on physiological processes using wearables (i.e. EEG headbands; sensors for breading patterns, heart rate, smartwatches, combined with Smartphone apps) may hold great potential to be combined with CBT in clinical practice. As discussed in a review paper on the use of wearables for anxiety disorders by Hunkin, King and Zajac (2019), the literature suggests mainly potential for heart rate variability (HRV) biofeedback wearable devices. Given that HRV is associated with emotion regulation under stressful conditions (i.e. parasympathetic control), it may hold promise as a means to supplement CBT techniques. Indeed, high HRV is a marker of emotion regulation and stress adaptability, and it has been associated with increased prefrontal activity (Makovac et al., 2017). Caldwell & Steffen (2018) could demonstrate that the addition of HRV training to CBT increases HRV and improved the treatment of depression, although this training did not using neurofeedback procedures. Neurofeedback devices in combination with apps can be flexibly used outside therapy sessions, during home exercises as well as in group sessions. Nevertheless, although face validity and user friendliness are promising characteristics for tryouts in clinical practice, it is clear that we need more studies with clinical populations and with adequate control conditions. However, as stated by Hunkin et al., (2019) the use of these wearables as an add-on to therapy can anyway increase engagement. Moreover, some wearable devices (i.e. Smartwatches) come with dashboards that can be used by clinicians to

monitor consented patients, which can provide very useful information to be used during therapy sessions, as a rich alternative of the paper and pencil diaries that CBT practitioners currently use. Indeed, continuous physiological stress monitoring complemented with smartphone administered experience sampling methods can yield very important information to be discussed during therapy sessions.

Moreover, CBT heavily relies on memory for treatment elements and poor memory may hinder therapeutic success. Related to the relevance of memory processes for therapeutic benefits, Carter et al. (2018) could show that depressive patients with moderate scores on the Rey Auditory-Verbal Learning test and memory at baseline responded worse to CBT whereas patients with low baseline verbal learning and memory responded worse to schema therapy. This prediction could be used to indicate the implementation of memory training in patients who score low on this easy to administer neuropsychological test. Based on another study investigating predictors of an intensive CBT program, declarative verbal memory at baseline predicted outcome. This may tap into the ability to memorize explicit verbal instructions for practicing skills in and between sessions as it is required in CBT (Kundermann, 2015).

In this perspective a memory support intervention could be added to CBT. Harvey and colleagues (2016) developed an eight session memory support intervention to be integrated into treatment in a transdiagnostic perspective. First, high effect sizes were indicative that this intervention could indeed manipulate memory support. Moreover, although this pilot study was insufficiently powered to yield statistically significant effects, small to medium effect sizes were obtained for recall of treatment points after treatment, and several findings suggest that the addition of memory support to CBT can yield better depression outcome. Given that this pilot study is the first in his kind, caution is warranted, but it is obvious that

memory training in patients suffering from memory complaints may be relevant to CBT practice.

### Tailoring CBT to the neurocognitive characteristics of patients

As already mentioned, CBT requires a lot of intact cognitive functions. In this perspective, therapists should be able to assess whether the specific characteristics of a patient enables her/him to undergo and benefit from therapy. Given that every patient is different (i.e. age, cognitive abilities, contextual aspects, medical conditions, medication use, etc.), knowledge on neuropsychology and the use of neuropsychological testing is needed to ascertain whether a specific patient could benefit from a specific (personalized) approach, or that adaptations to existing protocols should be made to increase efficiency. Just as a medical doctor would never ask to a paralyzed patient to walk half an hour a day, a CBT therapist should not ask a severely depressed patient who's concentration is very limited to undertake elaborative reappraisal strategies as homework during daily life.

Most efficacy and effectiveness research reported includes samples of young individuals of higher socioeconomic status and without co-morbid health issues, in whom there is only limited variability in cognitive functioning. Instead of developing different protocols for all possible combinations of interindividual differences (which would never be possible), therapists should be trained in neuropsychological testing to strengthen their abilities to develop personalized adaptations, taking into account the cognitive possibilities and limitations of their patients.

The use of a personalized medicine approach by using neuropredictors for therapy response, to select the most optimal intervention for a given patient, is another promising avenue based on neuroscience. However, as demonstrated based on a recent meta-analysis focusing on depression, neuroimaging markers show promise but studies are still scarce (Cristea, Karyotaki, Hollon, Cuijpers & Gentili, 2019). Moreover, although the use of

neuroimaging methods such as fMRI (i.e. functional connectivity, Drysdale et al., 2017) to define neurophysiological subtypes of depression with implications for therapy is particularly promising, it holds many drawbacks and the implementation in clinical practice is not yet possible. In a similar vein, based a systematic review also discussing implications for clinical application in anxiety disorders, Lueken and colleagues (2016) conclude that results are very heterogeneous, showing that biomarker development for anxiety disorders is still in an early phase. However, they emphasize that cardiovascular flexibility, which is easy to apply measure that can readily be used in clinical practice (see also the section on neurofeedback), hold promise. Given that heart rate variability is an indicator of the parasympathetic nervous system that integrates autonomic, attentional, and affective systems related to adaptability to a changing environment with low variability being associated with less flexibility, patients with decreased heart rate variability might specifically benefit from CBT, which is aimed at increasing behavioral and cognitive flexibility (Lueken et al., 2016).

EEG could be another promising alternative, although reliability -which is important for individual predictions- may be an issue. Stange and colleagues (2017) started from the observation that excessive attention toward aversive information is a core mechanism underlying emotional disorders, and used EEG (Event Related Potentials) to index this process (the late positive potential: LPP), in order to predict CBT outcome in social anxious and depressive patients. Interestingly, patients with larger LPPs to aversive distractors when the targets were also aversive, indicative of increased attention toward irrelevant aversive stimuli and thus decreased top-down control, showed a better response to CBT, which is aimed at increasing control over negative valance systems. Interestingly, as mentioned by Stange and colleagues, larger LPPs to aversive versus neutral information may also be indicative of less avoidance, which may be related to the ability to engage with negative emotions, a process that is important to facilitate response to CBT (Whelton, 2004). It is important to note that indicators based on research results at mean group level are not necessary applicable as individual predictors, even when the indicator could be measured with high reliability (it is not because men are on average taller than woman, that gender of a given individual can be predicted based its length). Moreover, because these results have not yet been replicated, caution is warranted with the conclusion that patients showing top-down control deficiencies or specific attentional biases may on average be more indicated for CBT. Nevertheless, combined with the above-mentioned conclusion that a focus on emotional experiences and emotional responses may be crucial because a corrective emotional experience is part of what is reconsolidated in memory, these findings may be indicative that indicators of emotional engagement (versus emotional avoidance) may facilitate response to CBT.

#### The role of neuroscience in psychoeducation

CBT requires metacognitive abilities as it comes to understand how attentional biases, interpretation biases, reasoning and safety-seeking strategies influence problems. In this perspective, neuroscience knowledge can be readily used for psychoeducation purposes. Psychoeducation has been defined as systematic, structured, didactic information about the disorder and its treatment to the patient and/or their family and caregivers, to enable patients to cope with the illness (Rummel-Kluge & Kissling, 2008).

For many decades, the expectations patients hold regarding the effects of psychotherapy are considered to be a crucial common factor ingredient of successful psychotherapy (e.g., Goldfried, 1980). This is underscored by several studies showing that positive expectancies for treatment predict better therapy outcomes (for a meta-analysis, see Constantino, Arnkoff, Glass, Ametrano, & Smith, 2011). De Raedt and Hooley (2016) reviewed neurobiological research to explain the working mechanisms behind the effects of expectancy. The basic idea is that expectancy-related preparation is a crucial process in stress regulation and recovery. The specific dorsal neural correlates of this preparation are related to anticipation and to the proactive up- or down regulation of the neurocircuitry implicated in regulatory processes that are crucial in CBT techniques.

To increase positive expectancy, the therapist can use psychoeducation to explain the neurocognitive mechanisms behind change processes as a way to inform patients about the usefulness of their therapy work. As an example, explaining the positive consequences of physical exercise on brain and cognitive functioning (for a review, see Mandolesi et al., 2018) can be very convincing when emphasizing the importance of behavioral activation in depressed patients, who often lack motivation to engage in physical activity. In a recent article, Ekhtiari et al. (2017) provide a framework and discuss the possibilities of integrating brain-based psychoeducation into clinical practice of addiction treatment, differentiating between content (e.g. knowledge about etiology, treatment process, adverse effects of medications, coping strategies, impact of treatment on brain function) and structure (methods used to deliver psychoeducation). They discuss the function of psychoeducation to enhance motivation for compliance and destigmatizing symptoms, and to explain changes in neurocognitive processes, including salience/attention, memory, and self-awareness. Moreover, several excellent examples in the current neuroscience literature can be used to document the notion of neuroplasticity changes evidenced by changes in brain function with the use of specific CBT techniques such as reappraisal (e.g. Goldin, Jazaieri, Hahn, Heimberg, & Gross, 2013).

## Conclusions

In the current paper I outlined the most important avenues by which neuroscience knowledge can be used by CBT therapists, namely for the selection and optimal use of CBT procedures; to inform the combination of CBT with neurocognitive and neurobiological interventions; to tailor CBT to the neurocognitive characteristics of patients; and to use neuroscience in psychoeducation. This underscores that CBT programs would benefit from basic neuroscience training, and that continued education to keep track with the latest developments in neuroscience may be helpful for good practice. During this training, after an overview of basic principles of the organization of the nervous system, neuropsychology, and brain functioning including plasticity, students could be instructed about the neurobiological basis of processes that are crucially involved in CBT, such as attention, memory, emotion and thought processing. It is of particular importance to start from there, emphasizing the neurocircuitry underlying specific procedures such as extinction, mental imagery, and cognitive control training, as well as the link with emotional processing and regulation and the neuroscience of memory including consolidation and reconsolidation. Also the psychophysiology related to stress and regulatory processes should be instructed, to underpin the use of physiological processes in assessment and training. Moreover, there should be training in neuropsychological assessment, to diagnose cognitive processes relevant to CBT. It can also be instrumental to include workshops to discuss papers providing commentaries on the implication of neuroscience (e.g. the abovementioned paper in Behavioral Brain Sciences of Lane et al., 2015), to deepen critical understanding of the clinical implications. This way, students can learn to make neuroscience informed decisions about the application of CBT techniques in individual patients. Moreover this training can be a solid basis for continued education to keep track with the latest developments in neuroscience, which will certainly generate more applications in the future.

The view to use neuroscience knowledge also points to the importance of developing neuroscience informed protocols for procedures used in CBT, and not only protocols tailored for specific diagnostic categories, a standpoint which is in line with the research domain criteria (RDOC) system developed by the National Institute of Mental Health (Insel et al., 2010). As mentioned by (Spring, 2007) "...psychologists need additional skills to act as creators, synthesizers, and consumers of research evidence, who act within their scope of clinical expertise and engage patients in shared decision making (p. 626)". Moreover, this will also facilitate multidisciplinary collaboration in case conceptualization.

It is laudable that CBT conferences, such as the annual meeting of the Association of Cognitive and Behavioral Therapies (ACBT), and special interest groups related to the ABCT such as the "Neurocognitive Therapies / Translational Research" group, offer a platform for the dissemination of neuroscience research.

The questions raised by Ledoux early in 2002 whether advances in neuroscience are instrumental to learn about the biology of psychological concepts and how psychotherapy can use biological mechanisms to treat mental illnesses are, now 18 years later, perhaps not fully answered, but it is clear that major advances have been made towards an integrative account with practical guidelines.

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