Understanding Treatment Response and Resistance in Obsessive Compulsive Disorder in the Context of Cognitive Neuropsychological Model

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SUMMARY

Cognitive-behavioral therapies, antidepressants and neuromodulation techniques are current treatment options used in various stages of the treatment procedure for obsessive-compulsive disorder (OCD). The factors that disparate treatment options—from psychological approaches to invasive surgical techniques—in a psychiatric disorder have in common have scarcely been described in the relevant literature. The cognitive neuropsychological model (CNM) is a novel approach that offers a common framework in which psychological and neurobiological models of different psychopathologies are reconciled by means of impaired emotional processing. In this paper, an integrated approach of disrupted top-down and bottom-up emotional processing is described to understand the efficacy of the different treatment modalities for OCD. In this model, cognitive therapy is proposed to contribute to the gradual breakdown of schemata through the effect on top-down emotional processing instead of acting on information processing biases directly. Antidepressant drugs and behavioral therapy are proposed to alter the brain's emotion processing in a bottom-up process. Resistance to pharmacotherapy and CBT is a common problem in patients with OCD, and many factors have been described as negative predictors of these treatment options. The severity of symptoms, presence of specific symptoms, poorer insight, high level of dissociation and family accommodation are the factors associated with resistance to both pharmacotherapy and CBT. The underlying reasons establishing an association between the presence of these diverse factors and treatment resistance are discussed in the context of CNM.

Keywords: Obsessive-compulsive disorder, antidepressants, cognitive-behavioral therapy

INTRODUCTION

Serotonin reuptake inhibitors (SRI) and cognitive-behavioral therapies (CBT) are two primary treatment options for depression as well as obsessive-compulsive disorder (OCD) (Pittenger and Bloch 2014, McKay et al. 2015). According to evidence on hand, even when both methods are used together, the treatment efficacy can be limited (Romanelli et al. 2014). Although somatic treatments like Deep Brain Stimulation (DBS) and Transcranial Magnetic Stimulation (TMS) are used in resistant cases, the efficacy of these applications is limited (Bais et al. 2014).

The ability to use a wide-ranging spectrum of options to treat a psychiatric disorder ranging from psychological therapies to invasive techniques is rather surprising. By obtaining empirical evidence through a treatment, a reasonable model that clarifies the etiopathogenesis of an illness can be easily designed only when considered within the boundaries of the related application. However, the limited efficacy of each method prevents the theoretical model based on this treatment from being inclusive and clear enough. At this point, there arise some questions to be answered. Is each treatment option effective on only one side of OCD, which in fact has diverse sides? Are the causes of resistance to one treatment the same as the underlying reasons of resistance to another

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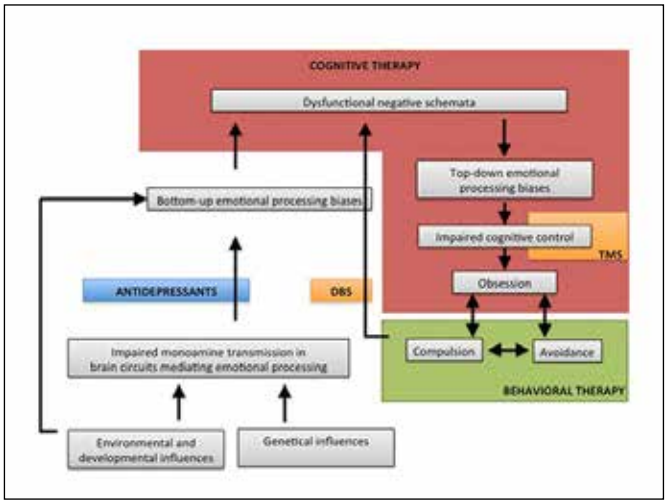

Figure 1. A cognitive neuropsychological model for obsessive-compulsive disorder. DBS: Deep Brain Stimulation; TMS: Transcranial Magnetic Stimulation. [Figure modified from Cognitive Neuropsychological Model for depression with permission of J.P. Roiser (Roiser et al. 2012)].

treatment option? How can it be possible to have a model that integrates different models and also enables cross interaction among them? For example, antidepressants influence mood, but how can the change created in the serotonin level lead to a change in faulty beliefs and appraisals without a cognitive therapeutic application? On the other hand, how does a psychotherapeutical use affect neurobiological processes that lead to mood changes? Or, how does a change appearing in a person's behavior alter his appraisal and belief styles? This paper has been written to find answers to these questions and is an output of trying to understand OCD as a whole. The mechanisms of antidepressant treatment and CBT in OCD and underlying possible causes of resistance to these treatments have been discussed in the context of the Cognitive Neuropsychological Model (CNM) suggested for depression. It is expected that curiosity about new research interests over the discussion of what and how treatment method will result.

Cognitive Neuropsychological Model (CNM)

The CNM, which has been suggested for depression, can be found interesting as a model that emphasises the interaction between cognition, emotion and behavior during information processing, and which clarifies how antidepressant treatment and CBT regulate this interaction (Roiser et al. 2012, Roiser and Sahakian 2013). According to this model, while the processing systems from dysfunctional beliefs or cognitions to experience or behavior are defined as top-down conceptually-driven processes, systems from perception and experience to sense and cognition are defined as bottom-up data-driven processes. In both top-down and bottom-up processes, while internal or external sourced data can be processed through an emotion-laden process (hot process), an emotion-independent process (cold process) is also possible (Roiser and Sahakian 2013). In this model, there is an emphasis on the existence of a meeting point for diverse models composed through emotional bias to interact in every manner. As in the classical cognitive model, negative schemata are not considered as direct results of developmental experiences, but as biased reasoning forms created through top-down emotional processing. On the other hand, emotional dysregulation, developed because of a neurobiological problem (e.g. monoamine dysregulation) based on genetic or developmental reasons, causes the person to produce faulty or biased reasoning through bottom-up emotional processing with data from his outer world. Thus, a model that centers a negatively biased pattern of information processing based upon emotional dysregulation offers an opportunity to consider psychological and biological models as integrated. As for this model, an antecedent emotional dysregulation based on genetic inheritance may not only cause biased information processing to work problematically at the beginning, but may also be a problem caused by developmental or environmental factors (Figure 1). CNM, without feeling the necessity to emphasize causal relationships between cognition and behavior, identifies the intermediary role of emotional systems in these relationships during treatment.

The efficacy of CBT can be defined through CNM as explained below. As for CNM, cognitive therapy regulates the relationship between dysfunctional schemata and emotional systems through a top-down manner instead of affecting biased cognitions directly during information processing (Roiser et al. 2012). It shows its effect by re-regulating emotional valence of a stimulus or an internal representation and through a learning process that provides the development of functional interpretations and beliefs. Behavioral techniques, on the other hand, create a new interaction form by changing dysfunctional old behavior templates through bottom-up processes between emotion and behavior.

CNM provides the opportunity to reconsider the effect of antidepressant drugs. The conventional theories of antidepressants on the effect mechanism are built on their efficacy of improving mood, while how this change is transferred to cognitive and behavioral systems has not been considered well enough. As for CNM, antidepressants regulate the bias that negative emotions create on cognition through bottom-up processes of the information gathered from the inner and outer world (Roiser et al. 2012). Occuring of antidepressant effect on mood necessitates a length of time to pass. This period includes changes on the receptors and postsynaptic activities. When examined from the CNM point of view, because reinforcing re-interpreting and re-learning processes purified from negative emotional valence by experiencing them over and over again necessitates a certain length of time, the drug effect also takes time to develop (Harmer et al. 2009).

Cognitive Model in OCD

According to the cognitive model, normal intrusive thoughts may be experienced by the majority of the population (Rachman and De Silva 1978). On the other hand, normal intrusions and clinical obsessions differ in several respects. Compared to clinical obsessions, normal intrusions are less intense, less frequent, shorter lasting and less discomforting thoughts, images or urges (Rachman 1998). Intrusions initially turn into clinical obsessions by means of misinterpretations, faulty appraisals, and coping styles, and later repetitive behaviors and avoidance develop (Salkovskis 1985). Although there are many cognitive formulations describing this case that interrupts the continuous stream of human conscious thought, researchers have reached agreement on only a few. Cognitive models such as overestimation of threat, inflated responsibility, intolerance of uncertainty, perfectionism, over-importance of thoughts, control of thoughts and intolerance of anxiety have been proposed as the critical processes of faulty appraisals for the development and maintenance of obsessive-compulsive phenomena (Obsessive Compulsive Cognitions Working Group 1997). Models such as inferential confusion, metacognitive and thought-action fusion are also other cognitive models developed for OCD (Shafran and Rachman 2004, Pelissier and O'Connor 2002, Wells and Papageorgiou 1998). Even though there are differences between these formulations, it is clearly seen that they are built on a conventional perspective (top-down) based on faulty appraisals and reasoning biases. However, there are also approaches that synthesize bottom-up mental processes such as attentional and memory bias and difficulty in inhibiting the processing of irrelevant information with the conventional perspective (Foa et al. 1993, Lavy et al. 1994, Radomsky and Rachman 1999).

While each model mentioned above appears to be more related to a specific phenomenological dimension of the disorder, they are still not sufficient enough to explain OCD in all aspects (Clark 2005). Although it is not the purpose of this paper to discuss all the evidence questioning the validity of each model, it is necessary to lay emphasis on an important limitation of the cognitive model since it suits the aim of the paper well. It is apparent that in cognitive-behavioral models, the role of emotions and emotion-related processes in the relationship between obsession and compulsion is partly identified while its effect on the development of an obsession as a clinical phenomenon is ignored. Therefore, it is necessary to mention briefly the role of emotional factors on the development of obsessions.

The basic mechanism starts with the intentional suppression of unwanted thoughts in the process of normal intrusive thoughts that are becoming an obsession (Salkovskis and Campbell 1994). Suppression has to be considered different from repression - an ego defense mechanism - in a psychodynamic aspect. A person's effort to suppress unwanted ego dystonic thoughts or images in fact paradoxically strengthens those thoughts even more (Wegner and Zanakos 1994). The critical role of emotions in the process from nonclinical thoughts to obsession has been identified in a simple way in a few studies. When unwanted thoughts are related with greater emotional discomfort or there is the presence of antecedent negative mood states, the paradoxical effect of suppression that results in obsession is more likely to be clear (Wenzlaff et al. 1988, Purdon and Clark 2001). One's mental control abilities and strategies on emotions may be genetically and permanently impaired (e.g. increased anxiety sensitivity) or they may be affected by situational states such as life events (e.g., pregnancy, stressful life events).

Sensorimotor gating is a basic physiological mechanism that helps to filter out unnecessary stimuli so that the brain functions can work healthily. In some studies, it was found that this mechanism is impaired in OCD just like in many other psychiatric diseases (de Leeuw et al. 2010, Hashimoto et al. 2008, Rossi et al. 2005). Gating functions are affected negatively not only in the presence of psychopathology but also with emotional valence of stimuli without psychopathology. When a stimulus causes a negative emotional arousal, habituation expected with the repetition of the stimulus does not take place (Farb et al. 2013, Yamashita et al. 2005). In other words, the brain processes even data that has not yet reached the awareness level in terms of emotional relationship, and, when negative emotional valence exists, physiological habituation does not occur. The role of mood states on information processing has not sufficiently been included into the mechanism in the conventional cognitive models designed for OCD. However, a person's habituation of a nonclinical intrusive thought may not occur because of the negative emotions that interfere with the thought. While an intrusive thought without negative emotional valence simply dies out, a natural decline or habituation process of thoughts does not occur when it is associated with negative emotions. In addition, on a second stage, in each conditioning experience where negative emotions are neutralized by compulsions, the person reinforces a process that makes him feel oversensitive against the negative thought.

Understanding Treatment Response in OCD

The Latin term '*ex juvantibus*' is used in a medical context for the process of the whole etiopathogenesis based on the effect of a drug that is symptomatically useful for treatment. Nevertheless, there are limitations in forming an etiopathonetic model based on merely empirical evidence. The problem with such reasoning has been clearly explained by Abramowitz and Deacon (2005) in the following example:

'When I take an aspirin my headache goes away. Therefore, the reason I get headaches is that my acetylsalicylic acid level is too low'. Even though the effects of antidepressants on a synaptic level have been well identified, how neurotransmitter changes help OC symptoms improve is not clearly known. At this point, studying models like CNM to explain the interaction of cognitive processes with the mood changes that antidepressants cause will make the treatment effect clearer. With this idea, Besiroglu et al. (2011a) found that antidepressants have a positive effect on dysfunctional cognitions in addition to their expected effect on the severity of the illness. These results led the researchers to ask the following: How does antidepressant treatment affect faulty beliefs and appraisals that are supposed to be the target of cognitive therapy? Researchers suggested that in the presence of factors with negative emotional valence, antidepressants are more likely to change faulty beliefs and appraisals (Besiroglu et al. 2011a).

Although a length of time has to pass before the antidepressant and anxiolytic effects of antidepressants occur, the emotional processing effect starts with the first dose (Harmer 2008, Capitao et al. 2015). Studies carried out on the startle response, emotional memory and attention bias support this hypothesis (Browning et al. 2007, Harmer et al. 2004, Pringle et al. 2011). It is possible to consider that in the context of OCD, antidepressants cause a new interaction form via their emotional processing effect between obsessive thoughts, emotions and behaviors (avoidance, compulsions). A patient left alone under the plain effect of a psychopharmacological agent does the processing in his own way without any guidance, whereas changing the drug effect in a favorable way can possibly be done through regulating it with a therapeutic relationship. This can partly be considered the same as a wound healing with the help of a surgeon. Within this new interaction formed between thoughts, emotions and behavior, the change in emotional processing stays unrefined without psychotherapeutic intervention and does not lead to a healthy and permanent change. A different level of beneficial effects can be noticed as far as the patient's own psychosocial opportunities intervene with this change. On the other hand, an emotion regulation problem based on potent neurobiological factors determined by genetical predisposition can be the fundamental promoter of interaction between cognition, emotion and behavior. This situation, which develops on a neurobiological basis, may be the basic reason of resistance being difficult to overcome with psychotherapy alone. In this case, both cognitive and behavioral systems purified from negative emotional valence with antidepressant effect (bottom-up) are more open to CBT effect (Pringle et al. 2011, Roiser et al. 2012). Cognitive therapy shows its effect by changing the relationship between emotional system and faulty beliefs and appraisals (top-down effect), while behavioral techniques, such as exposure and response inhibition, regulate the role of bottom-up emotional processing on learning during the re-experiencing process caused by new behavior styles. In earlier CBT models, it was predicted that when cognitive biases changed, behavior style would change as well, but also a change created in behavior style would result in a negative schemata. CNM highlights the intermediary role of emotional processing in this change. Thus, re-experiencing an unwanted emotion which interfered with a cognition or behavior before, through behavioral therapy and processing the same emotion under the guidance of a therapist through re-interpreting with cognitive therapy, is ensured. Carrying out both methods at the same time makes the therapy more effective.

CNM also explains the effect mechanism of neuromodulation techniques in depression (Roiser and Sahakian 2012). TMS, whose usage in OCD as in depression is more widespread, reduces the cortical excitability effect on corticostriatal circuits in top-down processes, while DBS affects bottom-up processes through limbic connections. Although it is suggested that TMS effect is independent from emotional processing (cold processes), the recovery effect of both applications is in fact related to antecedent mood remissions (Bais et al. 2014). The possible effect mechanism of treatment options in OCD in Figure 1 has been illustrated with the aid of CNM.

Understanding Treatment Resistance in OCD

Resistance to psychotherapy or pharmacotherapy among patients with OCD is common (40-60%) (Hollander et al. 2002). Despite having identified many factors related to resistance to pharmachological treatment and CBT separately, the underlying reasons relating these factors to resistance have not been given enough consideration. In this case, considering the intersection of diverse models over CNM will help us better understand resistance. For the purposes of this paper, only factors found to be related to resistance to both treatments will be reviewed. Features such as severity of illness, presence of religious-sexual obsessions, poor insight, dissociation and family factors (reaction or accommodation of family) that are related to showing negative response to both antidepressant treatment and CBT are distinguished in various studies. Below, there is a need to consider possible reasons that make these clinical features related to resistance in more detail.

Symptom Severity

In OCD, the more severe the illness becomes, the more likely the treatment response will be negative (Besiroglu et al. 2008, Denys et al. 2003, Prasko et al. 2009). If the OCD is more severe, it means that, in the interaction between the person's psychological integrity and the environment, there is a new equilibrium that is difficult to interfere with. In this new

equilibrium condition, the severity, function and reasoning of the symptoms may also change (Bhar and Kyrios 2005). For example, in advanced stages of the illness, the severity of compulsions is more obvious (Starcevic et al. 2011). Recurrent behaviors of a patient who tries to neutralize an emotional distress caused by obsessions may have a restorative value even if they are maladaptive (Starcevic et al. 2011). An increase in depressive symptoms in some patients when their compulsions are prevented indicates this role of compulsions (Foa et al. 1984). That is why an applied treatment model may not show the expected result when the symptom dimensions and their function for the patient were not taken into consideration. When considered in terms of CNM, whose rationale has been presented above, as a case which reinforces bottom-up emotional processing bias, if compulsions or avoidance dominate the clinical picture, there is a possibility for them to stay outside the target of a cognitive (top-down) therapy because the interaction between cognition and behavior evolves into interaction between emotion and behavior. Thus, compulsions are encountered as habit formations that regulate negative emotions, instead of goal-directed behaviors that test the possibilities of cognitive schemata. For this reason, most cognitive approaches have to make use of diverse variations of behavioral techniques in application (Clark 2005). When negative emotions, through exposure techniques, are included in the interaction to be re-processed, grounds for the effect of antidepressants and cognitive therapy will be prepared. In this way, the interaction between negative emotions and the other systems are re-regulated.

Symptom Dimensions

Although the available data distinguish some symptom groups, there is no consistent evidence about a particular symptom group that responds to a treatment option better (Besiroglu 2014). OCD is a phenomenologically highly heterogenous disorder where cognitive, emotional and behavioral factors related to the same symptom dimension may change. For example, some authors stated that contamination obsessions are related to disgust sensitivity in one group of patients, while in another group they are related to fear of getting harmed by the contaminant (Olatunji et al. 2010). Different CBT applications are proposed according to accompanying cognitive emotional features (McKay 2006). In this sense, phenomenological distinctions made by considering the symptoms together with the cognitive-emotional-behavioral features should be useful in both understanding the treatment effect and to develop more research questions.

Lee and Kwon (2002) suggested that in the context of cognitive theory, symptoms can be divided into two different groups: autogenous and reactive obsessions. Symptoms in both groups have been found to be related to different cognitive processes (Lee and Kwon 2002), emotional and behavioral reactions (Moulding et al. 2007), clinical factors (Besiroglu et al. 2006), neurobiological processes (Alveranga et al. 2012, Besiroglu et al. 2011b, Subira et al. 2013), and treatment response (Belloch et al. 2010, Besiroglu et al. 2007). Autogenous obsessions are thoughts, images or urges which tend to come abruptly into consciousness without identifiable evoking stimuli and which are perceived as ego-dystonic and absurd, more repetitive and disturbing. Agression, religious and sexual obsessions are included in this group. Reactive obsessions, on the other hand, are obsessions the person does not need to hide so much, and they tend to be evoked by identifiable external stimuli and are perceived as relatively realistic and rational as a response to the stimuli. This group also includes thoughts or doubts about contamination, symmetry, ordering-arranging, somatic, and hoarding obsessions (Besiroglu et al. 2006, Moulding et al. 2007).

When the nature of factors that differantiate the two groups is examined, it is obvious that autogenous group symptoms, as being more upsetting and anxiety provoking obsessions, have a more direct relationship with emotional factors (Diniz et al. 2012, Purdon 2004, Rowa et al. 2005). In addition, through several neurobiological studies, they were found to be more related to emotion-related limbic brain changes (Besiroglu et al. 2011b, Harrison et al. 2012, Subira et al. 2013). Therefore, the presence of autogenous group symptoms creates a more noticeable case in terms of valence, controllability and arousal as quality and quantity of emotional factors. In terms of CBT, while for autogenous obsessions—defined also as pure obsessions, taboos or repugnant obsessions by different researchers—cognitive therapy is claimed to be more effective, reactive obsessions respond better to behavioral techniques like exposure and response inhibition (Lee and Kwon 2002, Moulding et al. 2007). In terms of response to antidepressant treatment, Besiroglu et al. (2007) found that in the presence of autogenous symptoms, compared to other symptoms, it is more likely to have positive changes in cognitive appraisals with treatment. It was found that in patients with autogenous obsessions, antidepressants cause more positive neurobiological changes in the limbic system in a different research (Besiroglu et al. 2011b). These results have been interpreted in the way that, depending on the related neurobiological and clinical factors, these symptoms cause emotional overload, and for this reason they are more open to the drug influence.

Insight

In patients with OCD, poor insight has been found to be related to resistance to both drug treatment and CBT separately (Catapano et al. 2010, Erzegovesi et al. 2001, Santana et al. 2013). To make the relationship between poor insight and resistance to treatment more understandable, it is necessary to examine initially the nature of the relationship between insight in OCD and symptom severity. In terms of

descriptive approach, poor insight is defined as the person partly believing in his thoughts about the symptoms being or becoming true, whereas, if he is completely convinced about his beliefs, it is called absence of insight (American Psychiatric Association 2013). Through several studies, poor insight has been found to be related to severity of illness (Jacob et al. 2014, Jakubovski et al. 2011, Türksoy et al. 1997). As a result of these studies, it would make sense that stronger severity of illness with poor insight, which is always supposed to be associated with the severity, may also be a predicting factor of negative response to treatment. On the other hand, there are also studies that show that there is not always a linear relationship between poor insight and severity of illness and functionality level (Besiroglu et al. 2004, Storch et al. 2004). OCD sufferers who have never sought health care are more likely to have lower severity of illness, a poorer insight and a better quality of life compared to those who already have sought health care (Besiroglu et al. 2004). These diverse findings propose that there may be different relationships between severity of illness and insight level: 'more severe-poorer insight', 'less severe-poorer insight', 'less severe-better insight', 'more severe-better insight'. Hence, insight is supposed to be a feature that predicts the treatment response related to different characteristics, and not because it simply is a severity or functionality specifier.

Insight degree in OCD can be diversely affected by factors related or non-related with the illness (Besiroglu and Ağargün 2006). Poor insight may either be related to an inherent cognitive incapacity that prevents awareness of the effects of the illness (Kashyap et al. 2012) or to the non-illness related characteristics like mental health literacy (Besiroglu and Ağargün 2006). When poor insight is related with a top-down antecedent neurocognitive impairment, which inhibits awareness of the symptoms, it may not be easy to observe positive effects of antidepressants or behavioral techniques which affect bottom-up processes. In this respect, there are researchers who propose use of cognitive enhancers like D-cycloserine in order to increase the benefits gained from antidepressants or behavioral techniques (Sulkowski et al. 2014).

Insight degree can also be defined as a feature such as awareness, with diverse components for cognitive, emotional and behavioral problems related with the disorder (Leckman et al. 2010, Veale 2002). Alexithymia, known as difficulty in identifying and describing one's own emotions, has been found to be related with poor insight and resistance to treatment in OCD (De Berardis et al. 2005). If the negative effect of the disorder on emotions cannot be distinguished by the patient, possibly the change in the positive emotional processing that the treatment causes will not be noticed either. That is why, having a person with difficulty in identifying and describing his own emotions, letting them experience this negative emotion with exposure techniques initially, and then preparing them for cognitive processing by making them acquainted with this feeling will be the most important element of the treatment. By the moment the emotion is included in the equation through exposure techniques, it is more likely for antidepressants to influence in a bottom-up manner.

Dissociative Tendency

Dissociative tendency is a factor that predicts resistance to both CBT and drug treatments (Rufer et al. 2006, Semiz et al. 2014). Dissociation is defined as impaired association between the person's thought, emotion and behavior and the disintegration of one of these functions from the others in relation to negative effects of traumatic events (American Psychiatric Association 2013). However, the presence of dissociative experiences does not mean there is a psychopathology. Researchers classify dissociation into two groups, pathological and nonpathological (Waller et al. 1996). Çelikel and Beşiroğlu (2008), in a non-clinical sampling, found that dissociative tendency related with OC symptoms does not result from traumatic effects. In a similar way, Selvi et al. (2012), in a clinical sample, noted that dissiociative experiences are more related with metacognitions and thought suppression than childhood traumatic events, and that it can be immanent as a cognitive feature result of a deficit in the illness. In this context, dissociative tendency in OCD may be the result of a person processing routinely information by isolating emotional valence. Also, when considered from a psychodynamic point of view, dissociation is defined as a defense mechanism to isolate a negative emotion caused by a disturbing internal or external stimulus. Dissociation tendency, which isolates emotional valence of symptoms, may disable the antidepressant treatment that works through emotional processing. Likewise, the necessity of a synchronized processing between cognition, emotion and behavior can be foreseen for the CBT effect to come true. Reprocessing the negative emotions the patients experienced is provided under the control of a therapist through exposure techniques. However, patients with dissociative tendency fail to bring together the necessary components for a healthy integrity of thought-emotion-behavior as they are frequently dissociated during exposure techniques (Rufer et al. 2006). This way, treatment methods working over both top-down and bottom-up emotional processes cannot show their efficacy in the presence of emotional isolation with dissociation tendency.

Family Reactions And Accommodation

The negative effect of OCD on patients' family lives is at least as severe as schizophrenia (Magliano et al. 1996). Family members of patients with OCD are often involved in the patients' symptoms, either attempting to stop the patient from performing the repetitive behaviors, or aiding the patient by performing the rituals. Negative effects of the illness on family

life and social functionality prevent the patients from seeking medical help, affect adjustment and response to treatment negatively, and worsen the prognosis (Gomes et al. 2014, Yanagisawa et al. 2015). While treating a patient, it is necessary to consider the burden of the disorder within his/her close environment. For example, as long as the behavior of an authoritarian father associating religious obsessions with devil or sin, or a spouse accusing the partner for not having a real illness, or an overprotective mother involved in compulsions of the child, continues being influential, the treatment will never be successful. So, a balance where external factors keep forcing internal factors is the only obstacle in front of the change. Since OCD sufferers cannot dare to face emotional discomfort caused by impaired balance within close circle, they may be more likely to give up distant rational targets of the treatment. In this case, it does not matter which treatment is applied during experience and learning processes because the external barriers will not allow the patient to experience the emotion that has to be processed together with cognitive and behavioral factors, and there will never be a chance to re-regulate these emotions through treatment.

Conclusion

Looking into theories emphasizing causal relationships about human mind functioning in general, the common tendency alternates between reasoning-centered theories and experience or perception priority approaches (Bolton and Hill 2003). In terms of OCD, cognitive model builds one that proceeds from reasoning and interpretation to behavior (Clark 2005), while it emphasises that it has a top-down psychopathological mechanism that starts with an obsession and continues with a compulsion: e.g., 'I fear doing harm to my baby and therefore I feel compelled to check whether I did or not; to use a metaphor, itching is the cause of scratching'. On the other hand, according to some recent opinions, it is claimed that there is a behavioral change from ordinary habits to unstoppable acts (compulsions), and that there is a bottom-up model into which reasoning and interpreting were included later on (Gillan and Robbins, 2014). According to this model, compulsive behaviors evoked by peripheral hints are behavioral patterns the person unavoidably finds himself in and obsessions are cognitive factors that join in this behavior: e.g., 'I feel compelled to check excessively, and therefore I must be afraid of harming my baby; to complete the metaphor, scratching is the cause of itching'.

In the story The Little Prince, the part of 'the tippler' is a very good example that enlightens the rationale of both approaches identified above (Saint-Exupery 1943). In the story, the Little Prince meets a drunkard on the planet and asks him a chain of questions starting with 'Why do you drink?' The man gives answers that identify a vicious circle that goes on forever by explaining that he drinks to forget his shame, and that he is ashamed because he drinks. The Little Prince says 'Grown-ups are certainly very, very odd' and leaves the planet. In mental processes, each model that unidirectionally designs causal relationships can get its own evidence from the dilemma of the tippler. Yet, the tippler might have antecedent cognitive biases that enable him to feel remorse, or might even have a strong antedecent urge to seek reward arising from neurobiological predispositions. In this respect, interaction between cognitive, emotional and behavioral components is much more complicated than it seems, and existence of relational evidence supporting diverse models at the same time is also possible. The author brilliantly describes the nature of indeterminateness that exists in the cycles between cognitive processes and repetitive behaviors. CNM, on the other hand, clarifies the intermediary role of emotional systems without emphasizing which one comes first in relationships between cognition and behavior in a design that enables a bidirectional interaction.

The brain never leaves input plain without putting it through implicit or explicit emotional processing, but transfers information into another system by matching it with an emotional load (Farb et al. 2013). In the presence of a psychopathology, the emotional load added to the information might increase or decrease, whereas resistance to treatment might be a factor arising from not noticing well enough the effect of this emotional load. While some clinical features may possess a nature that increases the load of emotional factors, some others may intervene through a process that isolates emotions. As a result, our treatment approach will be closer to success as long as we can keep emotional factors in balance at the right time and measures.

Modern life, which makes it difficult to avoid pace, performance and consumption habits, affects the quality of doctor-patient relationship. Nowadays, many psychiatrists can spare limited time for their patients because of routine conditions. Within this limited relationship, managing a patient with a simple diagnostic evaluation without considering diverse components will result in limited treatment efficacy. When a psychiatrist is faced with failure to respond to the drug treatment he prescribed, he might find the patient's liver microsomal drug-metabolizing enzyme activity problematic. Yet, focusing on this problem as if the drug he has given is providing absolute effect might inhibit the thought of the presence of other resistance factors. On the other hand, an omniopotent therapeutic appoach without considering strong neurobiological predispositions might not provide a satisfactory outcome. This is why, in heterogeneous disorders like OCD, main symptoms, which are the most apparent aspect of the clinical as well as cognitive, emotional and behavioral factors related implicitly or explicitly, have to be investigated adequately. For a more effective result, considering internal and external factors related with resistance should be the

psychiatrist's or the therapist's priority. In all cases, as the need arises, treatment options aimed at top-down and bottom-up processes should be applied within an integrated interaction after estimating resistance.

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