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**COGNITIVE DEFICITS AND SYMPTOM PATTERNS IN
OBSESSIVE-COMPULSIVE DISORDER**

PhD Thesis Summery

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Budapest, 2012.

Introduction

Obsessive-Compulsive Disorder (OCD) is one of the most common mental health conditions based on major international epidemiological surveys. Obsessions are intrusive, unwanted thoughts, images, urges, ideas or worries that produce strong anxiety. Obsessions are not related to problems of everyday life, and frequently recur to the patients mind despite the effort to ignore or block them. OCD patients are aware that their thoughts, urges or worries are unrealistic products of their own mind unlike psychotic patients who lack this insight. Compulsions are perseverative behaviors (e.g. tapping, touching or hand washing) or mind rituals (e.g. counting, silently repeating words or backwards spelling) performed according to rigid rules. Acting out these perseverative behaviors or mental rituals can help the patients to prevent or reduce distress, anxiety or prevent a feared event from occurring; while these rituals are either not related to the feared events or obviously exaggerated. OCD is a chronic illness that in many cases, despite therapeutic efforts, could lead to debilitating symptoms, and eventually progress to therapy-resistant state. Over the last 20-30 years the disorder has become the focus of intensive research.

Clinical presentation of the OCD is heterogeneous. Despite the phenomenologic heterogeneity of the disorder, the most frequently used disease classification systems (DSM-IV-TR, ICD-10) describe OCD as a unified illness. The internationally used gold standard test for the assessment of OCD symptom severity is the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS symptom checklist), which contains of 71 different OCD symptoms. Obsessions and compulsions are grouped into 13 major categories: 1. Aggressive obsessions; 2. Contamination obsessions; 3. Sexual obsessions; 4. Hoarding/Saving obsessions; 5. Religious obsessions; 6. Obsession With Need for Symmetry or Exactness; 7. Somatic obsessions; 8. Cleaning/Washing compulsions; 9. Checking compulsions; 10. Repeating compulsions; 11. Counting compulsions; 12. Ordering/Arranging Compulsions; 13. Hoarding/Collecting Compulsions. Over the last decade many research studies have attempted to divide the heterogeneous OCD symptoms into clinically relevant subgroups. The classification can be based on “hard” or “soft” (permissive) categorization. OCD subgroups based on “hard” categorization include the followings: obsessions or compulsions; early or late onset disease; with or without encephalitis at the onset of the disease. The permissive or “soft” categorization is based on the probabilities of the symptoms, and statistical approaches are used for the formation of dimensions or categories. This categorization allows overlapping

categories, and describes the co-occurrence or associations of certain symptoms. This categorization includes the modern, up-to-date dimensional (or factorial) classification of OCD symptoms. The dimensional approach tries to identify the underlying endophenotypes by creating phenotype-based subgroups from OCD symptoms. The method of this approach based on the quantitative measurement of the phenotypes and mathematical (statistical) methods are used for the formation of subgroups. The data of not one but several hundred or – in case of international collaboration – even several thousand of patients are processed during the statistical analysis. Such methods are, for example, the Principal Component Analysis (PCA) or Cluster Analysis (CA). Leckman, Matrix-Cols, Rauch and their colleagues, who are acknowledged researchers in the field of factor analysis of OCD symptoms, summarized their results in an international consensus statement on OCD for the work group of the forthcoming issue of DSM (DSM-5). The Y-BOCS scores of several thousand patients were used for statistical analysis. The following 5 major dimensions (or phenotype subgroups) were created from the heterogeneous symptoms of OCD: (I) Aggressive (or harmful) obsessions with Checking compulsions; (II) Sexual and Religious obsessions; (III) Obsession With Need for Symmetry or Exactness with Repeating, Counting and Ordering/Arranging compulsions; (IV) Contamination and Somatic obsessions with Cleaning/Washing compulsions; (V) Hoarding/Collecting compulsions and obsessions. In 2006, Leckman and Rosario-Campos revised the Y-BOCS based on the dimensional approach of OCD symptoms and developed a new scale called the Dimensional Yale-Brown Obsessive-Compulsive Scale (DY-BOCS). This new scale classify (and score) the OCD symptoms on the basis of the 5 major dimensions described in the international consensus statement.

Over the last decade several genetic and environmental (psychological) factors have been identified in the etiology of OCD. Additionally, functional imaging techniques were extensively used in several studies founding the involvement of the prefrontal cortex (orbitofrontal cortex: OFC; dorsolateral prefrontal cortex: DLPFC and anterior cingulate cortex: ACC) and the basal ganglia (striatum, amygdala) in the pathophysiology of OCD. The involvement of prefrontal cortex in the disease was also supported by several psychological studies using cognitive tests. The dysfunction of the prefrontal cortex was first described in brain injured patients (for example by stroke, trauma or tumor). Damage to the prefrontal cortex areas affects the executive functions causing dysexecutive syndrome. The classic symptoms of the dysexecutive syndrome after Luria: rigidity of the behaviour; distractibility; perseverations; problems in the flexibility of planning and implementation. Prior research has

revealed that dysexecutive symptoms can be identified not only in patients with brain injury, but also in those with psychiatric diseases like schizophrenia, depression and bipolar affective disorder. Over the last decades several studies have found prefrontal cortex dysfunctions, executive dysfunctions and dysexecutive symptoms in OCD patients. According to Norman, Shallice and Burgess's approach executive functions are required in the following situations: those that involve planning or decision making; those that involve error correction or troubleshooting; situations where responses are not well-learned or contain novel sequences of actions; dangerous or technically difficult situations; and situations which require the overcoming of a strong habitual response or resisting temptation. The significance of failure of inhibitory functions in dysexecutive syndrome was proposed by several research groups. Shimura suggested that failure of inhibitory functions may account for the dysexecutive symptoms seen in patients with frontal lobe injury, and this is why these patients are unable to block irrelevant information and search strategies that earlier proved to be wrong. Therefore, the brain might be unable to eliminate the interfering and disturbing effects of irrelevant details, resulting in that the irrelevant information may intrude into the mind causing executive dysfunctions. Behavioral symptoms of psychiatric disorders – like obsessions and compulsions in the case of OCD - are the consequence of executive dysfunctions. In Miyake's view inhibitory functions are required to deliberately suppress dominant, automatic, or prepotent responses. Deficits in inhibitory control may lead to the appearance of perseverative tendencies. For intact executive functioning it is necessary that the brain not only handle relevant information but also eliminate or block irrelevant information.

Several validated cognitive tests and questionnaires are available recently to assess dysexecutive symptoms. One of them is the BADS (Behavioral Assessment of the Dysexecutive Syndrome) which is a cognitive test battery that includes the DEX questionnaire (Dysexecutive Questionnaire) which was developed by Bursess and his colleagues in 1998. The BADS includes several cognitive tests measuring various cognitive functions (e.g. memory, set-shifting, sustained attention, inhibitory functions, etc.) and also includes two versions of the DEX (self-reported and informant-reported versions). The DEX was developed for measuring dysexecutive symptoms at the behavioral level and is particularly designed to assess errors in goal-directed behaviors that occur during everyday life. Burgess et al. used factor analysis to identify different dimensions (factors) of the DEX and described a model with five dimensions (I. factor: inhibition, II. factor: intentionality, III. factor: executive memory, IV. factor: positive affect, V. factor: negative affect). Several

research groups have found executive dysfunctions with the help of the DEX in numerous psychiatric diseases (such as schizophrenia, schizotypal personality disorder, bipolar affective disorder) but has not yet been used to study the dysexecutive symptoms in OCD.

The failure of inhibitory functions in dysexecutive syndrome has a particular significance in OCD. However, the term 'inhibition' has been used to signify various different features of distinct aspects of OCD. In the present thesis we followed the 2005 theoretical approach of Chamberlain et al. who identified two different failures of inhibitory processes in OCD, namely, a failure of cognitive inhibition that primarily relates to obsessive symptoms and a failure in behavior inhibition that is linked to compulsions. These two failures in inhibitory processes are associated with distinct neural pathways and different cognitive dysfunctions. This hypothesis is in accordance with the 1994 model of Wegner et al. who studied chronic thought suppression. Wegner described chronic thought suppression as a coping mechanism against unwanted intrusive thoughts in several psychiatric diseases like depression, post-traumatic stress disorder and obsessive-compulsive disorder. He hypothesized two underlying concurrent systems: one of these systems is a conscious operating process and the other is an implicit monitoring process. The operation of two systems has paradoxical effects because it may cause the unwanted thought being immediately enhanced and returns after suppression. In 1994, Wegener and his colleagues constructed and validated a questionnaire called the White Bear Suppression Inventory (WBSI). The test measures the unwanted intrusive thoughts and thought suppression tendencies. The WBSI was originally published as a unidimensional construct, however, later several research groups decomposed the test into two or three dimensions by using factor analysis. In 2000, Blumberg et al. published their study which involved the largest number of patients yet, and identified 3 WBSI factors: I. unwanted intrusive thought; II. thought suppression; III. self-distraction.

Specific Aims

One of the aims of the present thesis was to investigate Chamberlain's theory of the two different failures of inhibitory processes in OCD on a clinical sample. In the first and second thesis point I divided OCD symptoms into obsessive and compulsive subgroups based on Y-BOCS subscales. By using these groups, in the first thesis point I analyzed the correlation between

symptom severity and the scores of the Dysexecutive Questionnaire (DEX), which measures the executive symptoms at the behavioral level, and a test battery measuring executive functioning. In the second thesis point I analyzed the correlation between the obsessive and compulsive symptoms severity and the scores of the White Bear Suppression Inventory (WBSI), which measures the unwanted intrusive thoughts and thought suppression tendencies, and a test battery measuring cognitive functioning.

In the second part of the PhD thesis I studied the division of OCD symptoms into dimensional subgroups. In third thesis point I analyzed the dimensional subgroups by using principle component analysis on the Y-BOCS scores of a Hungarian population. In the fourth thesis point I validated the Hungarian version of the Dimensional Yale-Brown Obsessive-Compulsive Scale (DY-BOCS) in a Hungarian population by testing the inner consistency, the convergent and divergent validity of the scale.

New scientific results

Thesis point I: The severity of the OCD symptoms is correlated with the dysexecutive symptoms. We found that the severity of dysexecutive symptoms, as assessed by the DEX, was significantly correlated with the executive functions, measured by cognitive tests.

The severity of OCD symptoms of the total of 51 OCD patients was assessed with the Y-BOCS. OCD patients participated in the study were analyzed as a unified group. However, first we defined two subgroups – according to our best knowledge - within the OCD group based on the Y-BOCS subscale scores (i.e., Y-BOCS obsessive score and Y-BOCS compulsive score). The dysexecutive symptoms of the patients were estimated by close family members using the informant-reported version of the DEX. Following Burgess's dimensional approach 5 individual factors of the DEX were created. Executive functions were tested using a neurocognitive test battery composed specifically for this study. This

neurocognitive test battery includes the followings: Verbal Fluency Test, Category Fluency Test, Trail Making Test Part A and B, Stoop Test, Wisconsin Card Sorting Test. Comorbid depressive symptoms were assessed with the Hamilton Rating Scale for Depression (HDRS).

Based on the normative scales of the DEX questionnaire the participated OCD patients showed a severe executive impairment comparing to the normal control. In our view this result implies that OCD patients have impaired frontal lobe functioning. The severity of OCD symptoms positively correlated with dysexecutive symptoms. The total DEX score, which indicates the level of dysexecutive (prefrontal) symptoms, was significantly correlated with the Y-BOCS. Therefore, the more serious the symptoms of an OCD patient were, the more likely it was for the patient's family members to report dysexecutive symptoms. However, the Y-BOCS obsessive and compulsive subscores were differently associated with the dysexecutive symptoms. The dysexecutive symptoms were found not to be correlated with the obsessive subgroup, whereas significant correlation was found with the compulsive subgroup. Neither the total DEX score, nor the DEX factor scores were correlated with the Y-BOCS obsessive score. Nevertheless, both the total DEX score and the three DEX factor scores (i.e., 'inhibition', 'positive' and 'affect' factors) were significantly correlated with the Y-BOCS compulsive score. We found that the inhibition factor score of the DEX was correlated with the compulsive severity score, but not with the obsessive score. The Burgess's 'inhibition' factor item of the DEX is not correlated with a failure of cognitive inhibition (i.e., obsessions) but is instead correlated with inhibitory dysfunction at the behavioral level (i.e., compulsions). These results suggest that executive impairments, as measured by the DEX seem to be associated with compulsions rather than obsessions, which is in accordance with the theory of Chamberlain et al., namely that obsessive and compulsive subgroups are associated with distinct type of failure in inhibitory processes.

Severe and broad executive dysfunction was detected by several cognitive tests in the compulsive subgroup. Set-shifting disturbance (impaired cognitive flexibility) and impaired motor inhibition in the compulsive subgroup of OCD patients was detected by cognitive assessments, such as Verbal and Category Fluency Test, Trail Making Test, Wisconsin Card Sorting Test. These results support the hypothesis of Chamberlain et al., namely that compulsions are more associated with different cognitive dysfunctions than obsessions. That is, compulsions are correlated with impaired executive functions leading to ineffectiveness of behavior inhibition.

Thesis point II.: The severity of the OCD symptoms is correlated with the number of intrusive thoughts and thought suppression tendencies, as measured by the WBSI. This is connected to obsessive symptoms but not to compulsive symptoms. We found that the number of intrusive thoughts and thought suppression tendencies, as indicated by the total score the WBSI, was not correlated with the executive functions, measured by cognitive tests.

A total of 51 OCD patients were participated in the study (the same patients as in the I. thesis point). Besides the aforementioned tests and questionnaires patients also filled out the White Bear Suppression Inventory (WBSI).

The severity of the OCD symptoms, as indicated by the total Y-BOCS score, was significantly correlated with the number of intrusive thoughts and thought suppression tendencies, as measured by the total WBSI score. Impairment of cognitive inhibition was detected in the obsessive group with the help of the White Bear Suppression Inventory (WBSI), which is a sensitive indicator of both intrusive thoughts and chronic thought suppression. These findings are in accordance with the hypothesis of Chamberlain et al. However, the compulsive Y-BOCS subscore was not correlated with intrusive thoughts and thought suppression tendencies, as measured by the WBSI. Following Blumberg's 3 factor model of the White Bear Suppression Inventory, we found that the Y-BOCS obsessive subscores were correlated with each of the three WBSI factors, whereas the Y-BOCS compulsive subscores were not correlated with any of the WBSI factor scores.

Furthermore, the total WBSI score was not correlated with the cognitive test results, indicating that thought suppression tendencies are not associated with executive dysfunctions. These results support Wegner's theory that monitoring processes do not require relevant cognitive capacity. However, in the compulsive subgroup – where no correlation was found with the thought suppression tendencies - significant executive dysfunction was detected (see I. thesis point). This result also supports Wegner's theory that compulsions are associated with operating process dysfunction, which requires greater cognitive capacity. This is why both the DEX and the cognitive tests showed relevant executive dysfunctions in the compulsive OCD subgroup. Our results are especially intriguing considering Purdon et al.'s results. They supposed that a first line of defense is a kind of suppression against an obsession

and if the first line is ineffective then in a higher or second stage of defense is to perform a ritualistic behavior. She theorized that rituals are performed, when the obsessive-intrusive thoughts are negated, because of the extreme level of distress they causes. This is in accordance with the two types of defense mechanism described by Freud in psychoanalytic theory nearly 100 years ago. In obsession mature defense mechanisms, like repression, thought suppression, can be seen, whereas in compulsion denial as an infantile defense process is present. Denial is in the same defense mechanism group as projections and projective identifications. This implies to the schizo-obsessive OCD subgroup and to the everyday clinical experience that OCD patient, without efficient therapy, become disabled in a very high rate. Supposedly, the denial is responsible for the high rate of treatment resistance (40-60%) in OCD.

Thesis point III.: In accordance with the international consensus statement on OCD we found 5 factors of OCD symptoms in a Hungarian population using principal component analysis on the DY-BOCS scores.

We were interested whether the 5 OCD symptom dimensions found in international studies can also be found in our Hungarian OCD sample. We separated 5 symptom dimensions (associations) using principal component analysis of the Y-BOCS scores of 118 Hungarian OCD patients. These dimensions are well in line with those described in the international consensus statement on OCD. We found the following 5 dimensions: 1. factor: Hoarding/Collecting compulsions and obsessions (26%); 2. factor: Contamination obsessions with Cleaning/Washing compulsions and Somatic obsessions (14.49 %); 3. factor: Aggressive obsessions with Checking compulsions and Repeating compulsions (12.94 %); 4. factor: Obsession With Need for Symmetry or Exactness with Ordering/Arranging compulsions (8.38 %); 5.factor: Sexual and Religious obsessions (8.08%). (The “explained variance” can be found in parentheses). This dimensional classification will be found in the forthcoming 2013 issue of DSM (DSM-5) as recommended classification of OCD symptoms.

Thesis point IV: The Hungarian version of the Dimensional Yale-Brown Obsessive-Compulsive Scale (DY-BOCS) proved to be valid in Hungarian OCD population.

The thesis point IV of my thesis is closely related to the point III. I validated the Hungarian version of the Dimensional Yale-Brown Obsessive-Compulsive Scale (DY-BOCS), which measures the dimensionality of OCD symptoms, based on the results of 30 Hungarian OCD patients. The DY-BOCS was originally published in English by Leckman and his colleagues. The Hungarian version of the Dimensional Yale-Brown Obsessive-Compulsive Scale showed similar inner consistency as the original English version, and both the convergent and divergent validity of the scale was high. Thus, the Hungarian version of the DY-BOCS is proved to be a valid test for the assessment of symptom dimensions of OCD.

Possible utilization of the results of our research work

The significance of our results is two-folded. First, the identified two different failures of inhibitory processes in OCD are of significant importance for the research of cognitive dysfunctions in OCD patients. Our present study is the first research about Chamberlain's 2005 proposed theory which is based on scientific data. Based on our results, from now on two questionnaires are available for the clinicians for the separation of the two different kinds of failures of inhibitory processes: the WBSI questionnaire and the DEX. According to our best knowledge the later test was first used by our research team in OCD. The WBSI is correlated with obsessive symptoms, whereas the DEX is correlated with compulsive symptoms, which makes these tests useful for the separation of OCD's obsessive and compulsive symptoms. Consequently, the two scales could be used as screening tests for the assessment of the presence and severity of OCD symptoms. Second, our scientific results draw the attention of the Hungarian scientific community to the dimensional approach of OCD symptoms. The translation and validation of the Hungarian version of the DY-BOCS will be particularly relevant after the issue of DSM-5 because the new version of DSM supposedly contains the 5 symptom dimensions of OCD. A scale will be required for the diagnosis of OCD which identifies the different symptom dimensions, and in our hope the DY-BOCS will be this scale.

Publications related to the thesis:

I.-II./ Harsányi A., Csigó K., Rajkai Cs., Demeter Gy., Németh A., Racsmány M. 2012. Two types of impairments in OCD: obsessions, as problems of thought suppression; compulsions,

as behavioral-executive impairment. *Psychiatric Research* (is accepted for publication / 7th of Sept. 2012.)

III. / Harsányi András, Csigó Katalin, Demeter Gyula: Kényszerbetegség. Elmélet, kutatás, terápia. Lélekben otthon könyvek, Budapest, 2010. 9/3. fejezet (Szerző: Harsányi András).

IV. / Harsányi A., Csigó K., Demeter Gy., Rajkai Cs., Németh A., Racsmány M. 2012. The validation of the Hungarian version of the Dimenzional Yale-Brown Obsessive-Compulsive Scale (DY-BOCS). *Ideggyógyászati Szemle / Clinical Neuroscience* 65 (1-2), 25-33.

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