A critical Appraisal of Heterogeneity in Obsessive-Compulsive Disorder Using Symptom-Based Clustering Analysis

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Abstract

Obsessive-compulsive disorder (OCD) encompasses a broad range of symptoms and is commonly considered a heterogeneous condition. Attempts were made to define discrete OCD subtypes using a range of symptom-based methods including factor and cluster analyses. The present study aims to find the most appropriate clustering model based on Yale-Brown obsessive-compulsive scale (YBOCS) checklist explaining OCD heterogeneity.

Five different clustering algorithms (FCM, K-means, Ward, Ward + K-means and Complete) applied on YBOCS symptoms of 216 patients with OCD. Data studied as four different sets including item-level raw data, item-based factor scores, category-level raw data and category-based factor scores and clustering results for 2 to 6 cluster solutions evaluated by four clustering indices (Davies-Bouldin, Calinski-Harabasz, Silhouettes and Dunn indices).

Two-cluster solution was detected as the most appropriate model for item and category-based clustering analyses of YBOCS checklist symptoms. Patients in each cluster were characterized based on their clinical and demographic properties and results showed that they had similar patterns of symptoms but in different severities.

Heterogeneity of OCD based on the YBOCS-symptoms has been challenged as OCD patients were classified based on their symptom severity not their symptom patterns. More investigations need to find appropriate measures explaining OCD heterogeneity with clinical importance.

Keyword: Clustering algorithms; OCD heterogeneity; OCD Subtypes; OCD symptoms; YBOCS

1. Introduction

Obsessive-compulsive disorder (OCD) is a neuropsychiatric heterogeneous condition that affects 1–3% of the population worldwide (Hasler et al., 2005). OCD patients may display different symptom patterns and illness courses. This phenotypic variability has led to the hypothesis that OCD is a heterogeneous disorder (Lochner and Stein, 2003; Mataix-Cols et al., 2005). Various subtypes of OCD have been reported in the literature obtained from different analytic approaches (Bloch et al., 2008). Different OCD subtypes may have different etiologic pathways and justify variability in genetic, neural, and neuropsychological correlates.(McKay et al., 2004). A better understanding of OCD clinical subtypes may lead to advances in understanding the psychobiology of the disorder, and improved treatments.

Researchers have used several different measures for identifying OCD subtypes including obsessive and compulsive symptom patterns (Calamari et al., 1999; Lochner C, 2008), age at onset of OCD (Noshirvani et al., 1991), differential treatment response, genetic backgrounds of individuals diagnosed with OCD (Katerberg et al., 2010) and the presence of comorbid conditions (Mataix-Cols et al., 2000).

The most frequently used strategy for identifying subtypes of OCD has involved the evaluation of obsessive and compulsive symptom commonalities in patients (Calamari et al., 1999). The most comprehensive and widely used inventory available and the source of data for investigation of OCD symptoms and severity is the Yale Brown Obsessive Compulsive Scale (YBOCS) (Goodman et al., 1989). YBOCS symptom checklist (YBOCS-CL) classifies the obsessions and compulsions in 13 specific categories and 2

miscellaneous groups. The item composition of each of the checklist categories was derived through clinical judgment to group the symptoms into clinically coherent categories, and to create a checklist that would facilitate data collection (Feinstein et al., 2003).

There are two common types of methods for analysis of OCD data: variable-centered factor analysis and person-centered clustering (Calamari et al., 2004; Delucchi et al., 2011; Katerberg et al., 2010). Factor analysis is used for investigating the relationships of variables for complex concepts that are not easily measured directly. This method reduces a large number of variables into a few interpretable underlying factors. Category and item based factor analyses of (YBOCS-CL) in different studies resulted into four or five factor models (Bloch et al., 2008).

Clustering strategies and latent class analysis (LCA) are person-centered methods that are used for identifying OCD symptom-specific subtypes (Calamari et al., 1999; Calamari et al., 2004; Delucchi et al., 2011; Nestadt et al., 2003; Nestadt et al., 2009). In cluster analysis, subjects are grouped into several clusters by maximizing between group differences and minimizing within group variation on the chosen set of criteria while LCA assumes an underlying latent class membership among subjects that gives rise to the subject subgroups (Vermunt and Magidson, 2004). In factor analysis, subjects may have loadings on all the identified factors so it will be hard to relate each person to a specific dimension. Cluster and latent class analyses enables researchers to form relatively homogenous subject groups within complex data set (Calamari et al., 1999).

The first reported OCD cluster analysis OCD personality data were clustered by Ward's method and were verified by K-means clustering algorithm. Four clusters that were different with each other in response to behavioral therapy were identified (Fals-Stewart and Lucente, 1993). Calamari et al. used Ward's hierarchical agglomerative cluster analysis followed by K-means clustering of YBOCS-CL scores and identified five groups that were characterized by dominant symptom patterns (Calamari et al., 1999). Further validation of results by subgroup characteristics related to treatment response or the etiology of OCD showed greater support for a seven subgroup taxonomy (Calamari et al., 2004). Another study clustered OCD patients into 3 clusters based on their comorbidity of obsessive-compulsive spectrum disorders (OSCDs) using Ward's method (Lochner et al., 2005). Cluster analysis of 45 items of YBOCS-CL reported by this sample identified six-cluster solution (Lochner C, 2008).

Attempts for classifying OCD symptoms using LCA resulted in different models based on the symptoms types. LCA analysis of neurologic signs, electroencephalographic abnormalities, attention deficit, and developmental disorder to investigate birth complications and neurologic abnormalities in individuals with OCD identified a two class model, organic and nonorganic class suggesting that OCD belongs to nonorganic class and is not the result of organic brain disease (Thomsen and Jensen, 1991). LCA analysis of OCD using patterns of comorbidity detected 4 latent classes: a minimal disorders class; a recurrent major depression and generalized anxiety class; a highly comorbid class, consisting of individuals with multiple comorbid psychiatric disorders; and a tic disorder, panic, and agoraphobia class (Nestadt et al., 2003). The subsequent study using comorbidity and clinical characteristics such as sex, age at onset, and OCD

symptom type resulted in a 2-class solution was characterized by lesser and greater comorbidity classes and a 3-class solution that consisted of an OCD-only class ($\pm$ major depression), an OCD + tics class, and an OCD + affective disorders (highly comorbid) class (Nestadt et al., 2009). Latent class analysis of the 8-item obsessive-compulsive scale of the Child Behavior Checklist suggested a 4-class model, including a “no symptoms” class, a “worries and has to be perfect” class, a “thought problems” class, and an “obsessive-compulsive scale items” class (Althoff et al., 2009). In another study analysis of YBOCS symptoms to detect latent classes yielded 3 classes differed only in frequency of symptom endorsement (Delucchi et al., 2011).

Different OCD symptom subtypes may have different psychopathological mechanisms requiring specific treatment strategies. The present study aims to shed more light on OCD symptom subtypes and suggest the best model for clustering OCD patients. We have used several clustering strategies to for categorizing OCD patients based on their YBOCS symptoms and compared the results with those of LCA.

2. Method

2.1 Participants and clinical assessment

Two hundred and sixteen patients with OCD ($n=216$, 146 female and 70 male), were included in the study (mean age at assessment, 33.7 ± 10.2) (Table 1).

Subjects were interviewed by an experienced clinician, and met the Diagnostic and Statistical Manual of Mental Disorders (DSM IV-TR) (Association, 1994) criteria for OCD on the Structured Clinical Interview for Axis I Disorders. The exclusion criteria were having a history of psychotic disorders or mental retardation, reporting severe neurological pathology and history of substance use, diagnosis with other DSM-IV-TR

Axis I disorders except depression, anxiety or tic disorder. The socio-demographic data was applied through a questionnaire. The Persian version of YBOCS severity scale and checklist (Rajezi Esfahani et al., 2012) was used to assess the severity and types of current obsession and compulsion symptoms. The study was approved by the Research Ethics Committee of Neuroscience Research Center, Shahid Beheshti University of Medical Sciences (Project No. 492.1).

2.2. Data analysis

Scores on the YBOCS –CL were analyzed in two levels: item and category levels. In item-level analyses the 5 point Likert scale data without any conversion was used as raw data. For category-level analyses each category was scored 0, 1 or 2 in the same manner as in several prior studies (Baer, 1994; Calamari et al., 1999). To increase comparability to previous studies (Calamari et al., 1999; Denys et al., 2004; Katerberg et al., 2010), the items of miscellaneous obsession and compulsion categories and 10 open-ended (i.e., ‘other’) items were excluded.

Exploratory factor analysis was conducted in both item and category levels as explained previously (Asadi et al., 2016). Briefly, exploratory factor analysis was conducted on YBOCS checklist data using the maximum likelihood estimation method, followed by varimax rotation. Results are summarized in five-factor model for item-based and four-factor model for category-based data (Table 2).

Raw item-level and category-level data as well as factor scores at each level were subjected to cluster analysis. Two common types of clustering methods are partitional and hierarchical clustering. Partitional clustering such as K-means attempts to directly decompose the data set into a set of disjoint clusters (MacQueen, 1967).

Since the result of K-means algorithm is sensitive to initial cluster centers (centroids), we used another strategy to calculate these centroids. In Ward+K-means algorithm, Ward's hierarchical agglomerative procedure was used to establish initial clusters followed by K-means clustering with the number of clusters and centroids determined based on the hierarchical solution.

Fuzzy C-means (FCM) was also used in the current study that is an extension of classical C-Means algorithm for fuzzy applications (Bezdek et al., 1984). Complete-linkage clustering was also used to analyze data. In this method, distance between clusters equals the distance between two elements (one in each cluster) that are farthest away from each other (Defays, 1977).

To evaluate different clustering algorithms, four indices (Dunn index, Davies-Bouldin index, Calinski-Harabasz index and Silhouettes validity index) were used.

Dunn index is a metric of how well a set of clusters represent compact well-separated clusters (Ilc, 2012). The higher Dunn's value indicates better clustering. Davies-Bouldin index (Davies and Bouldin, 1979) and Calinski-Harabasz (Caliński and Harabasz, 1974) are internal evaluation measures. The Davies-Bouldin index measures the average of similarity between each cluster and its most similar one. The lower Davies-Bouldin index means better cluster configuration. Calinski-Harabasz index evaluates the cluster validity based on the average between and within cluster sum of squares. The maximal Calinski-Harabasz index value indicates the best clustering of the data. Silhouettes validity index (Rousseeuw, 1987) measures the distance between each data point, the centroid of the cluster it was assigned to and the closest centroid belonging to another

cluster. The average Silhouette indicates weak clustering model if near zero, strong if near +1 and mis-clustering if near -1.

To assess cluster differences based on demographic and clinical characteristics groups of patients separated by clustering algorithms were compared by T-test (continuous variables) or Chi-square (categorical variables). All statistical analyses were conducted using Matlab version 2014a (The MathWorks Inc.).

3. Results

3.1. Sample characteristics

Demographic and clinical data were summarized in table 1. The total sample included 216 subjects 68% (n=146) of whom were female and 32% (n=70) were male. The majority of subjects were married (68%), low educated (76% school dropout or diploma) and unemployed (55%). Most of the patients reported the presence of the familial history of a psychiatric disorder (75%). The mean ages ($\pm$ SD) of assessment and of onset were 33.7 ± 10.2 and 23.7 ± 10.7 years, respectively. The mean obsession, compulsion and total severity scores ($\pm$ SD) reported by patients were 10.3 ± 4.7 , 8.9 ± 5.9 and 18.6 ± 8.8 , respectively.

3.2. Factor analyses

Exploratory factor analyses at item level resulted in five factors (Table 2): 1. aggression obsessions and related checkings; 2. contamination obsessions and cleaning compulsions; 3. hoarding obsession and compulsion, symmetry obsession, repeating, counting, ordering and arranging compulsions; 4. sexual obsessions and 5. somatic obsessions and checking compulsion tied to somatic obsessions (Asadi et al., 2016).

As presented in table 2 category-based exploratory factor analysis specified 4 factors including: 1. aggression, sexual, religious and somatic obsessions and checking and repeating compulsions; 2. symmetry obsessions and cleaning, counting and ordering compulsions; 3. contamination obsessions and cleaning compulsions and 4. hoarding obsession and compulsion.

3.3. Cluster analysis

Five different algorithms (FCM, K-means, Ward, K-means+Ward and Complete) applied on four sets of data: 1. item-level raw data; 2. item-based factor scores; 3. category-level raw data; 4. category-based factor scores. Cluster analyses were conducted for 2 to 6 cluster solutions and results were compared for 4 clustering indices (Davies-Bouldin, Calinski-Harabasz, Silhouettes and Dunn indices) to find the best clustering model for OCD patients' data.

As shown in figure 1A₁ two-cluster solutions resulted from conducting all algorithms on item-level raw data had the least Davies-Bouldin value. Less Davies-Bouldin value shows better clustering solution. Similar results obtained from applying these five algorithms on the other data sets (1A₂-1A₄) except the results of clustering item-based and category-based factor scores by Complete algorithm. In these two cases six-cluster models had the least Davies-Bouldin indices but the values were the same or even more than index values of two-cluster solutions resulted from the other algorithms.

For the other three indices (Calinski-Harabasz, Silhouettes and Dunn indices) higher index means more appropriate model. Applying almost all of the algorithms on four data sets detected 2-cluster models with the most index values (Fig 1: B₁-B₄, C₁-C₄ and D₁-

D₄). Again Complete algorithm showed different results (1B₂, 1B₄, 1C₄, 1D₃ and 1D₄), however most of two-clustering models specified by other clustering algorithms owned higher indices than models resulted from Complete algorithm. Based on these results two-cluster solutions were chosen as the best clustering models for YBOCS-CL symptoms and were assessed further for the clinical and demographic characteristics.

As presented in figure 2, two clusters obtained from applying five clustering algorithms on four sets of data were compared based on the pattern and severity of obsessive-compulsive symptoms.

The patients separated into two groups by conducting clustering algorithms on item-level raw did not show significant differences in the patterns of symptoms but they had different severity (Fig 2A₁). One group showed more severe symptoms than the other. Similar results obtained from clustering of category-level raw data (Fig 2B₁). Clustering item-based (Fig 2A₂) and category-based (Fig 2B₂) factor scores also separated subjects according to their mean severity of underlying factors.

For further clarification of clinical and demographic differences of clusters resulted from clustering of OCD data sets, different variables compared by Chi-square test (gender, marital status, educational level, occupation, familial history of psychiatric disorder, insight and avoidance levels) or T-test (age at assessment, age of onset, obsession, compulsion and depression scores) between two subgroups. Table 3 presents between subgroups differences of clustering item-level raw data and item-based factor scores. Almost no significant differences in demographic characteristics (gender, marital status, educational levels, occupation and familial history of psychiatric disorders) were detected between 2 clusters resulted from clustering item data sets by different

algorithms. However, the patients classified by most of the clustering algorithms differ significantly in age at assessment, age of onset, obsession score, compulsion score, **total score** and depression. Clusters with more obsession, compulsion, **total** and depression scores contained patients with less age at assessment and less age of onset. No significant differences were detected between the two clusters for insight and avoidance levels. Clustering category-level raw data (Table 4) by most of the studied algorithms resulted in a cluster consisting of patients with more obsession, compulsion and **total scores** as well as more depression and avoidance levels in comparison to the other cluster. FCM, K-means and Ward+K-means algorithms detected more female to male and unoccupied to occupied ratios in the more severe group in comparison to the less severe one. Results of clustering category-based factor scores specified a patient cluster with less male to female and less occupied to unoccupied ratios that mostly were low educated people with more obsession, compulsion, **total** and depression scores and less insight level (Table 4). Other variables did not show significant differences between two clusters. Moreover, Complete algorithm produced two clusters that didn't have significant differences in most of the variables (Table 4).

4. Discussion

Researchers have suggested that OCD is actually composed of distinct subtypes which play important roles in its etiology and treatment. Studies have focused primarily on obsessive and compulsive symptom presentation to detect subtypes of OCD. In the present study we aimed to investigate the best model for symptom-based clustering of OCD patients based on YBOCS-CL which can be used for further elucidation of OCD pathophysiology and treatment.

We applied five different algorithms (FCM, K-means, Ward, Ward + K-means and Complete) to detect the best fitted clustering method for grouping OCD patients. According to different scoring of YBOCS-CL we did not restrict initial data set to special type. We conducted clustering algorithms on raw Likert-scale item data and raw category data acquired based on the most common scoring strategy administered in previous studies (Baer, 1994; Calamari et al., 1999). Moreover, we conducted factor analysis for item and category level data and clustered patients based on their factor scores. To specify the best clustering model, we evaluated 2 to 6 clustering solutions to avoid missing the most appropriate model. There are no universal and effective criteria for selection of features and clustering schemes; so, we chose 4 commonly used clustering indices including Davies-Bouldin, Calinski-Harabasz, Silhouettes and Dunn indices to evaluate clustering models. Results revealed that OCD patients were not classified based on their symptoms but according to their symptoms severities.

Several clustering studies published earlier used different measures and various clustering methods and evaluated the results by employing different criteria (Calamari et al., 1999; Calamari et al., 2004; Fals-Stewart and Lucente, 1993; Lochner et al., 2005; Lochner C, 2008). Three to seven OCD subgroups were identified in these studies with different characteristics. Differences in the identified dimensions or subgroups may have resulted from methodological inconsistencies in studies: different used analytic strategies, different OCD symptom measures, different methods for the YBOCS checklist quantification, psychometric limitations of quantifying the YBOCS checklist, variability in sample sizes and different criteria to evaluate clustering results.

Results of the current study showed that almost all of the used clustering methods identified 2-cluster solution as the best fitted model and clustering raw data (item and category levels) resulted in models with better validity indices than clustering factor scores. It was interesting that none of the clustering algorithms was superior to the others. Moreover, Complete algorithm was the least appropriate method for clustering this sample. Comparing demographic and clinical characteristics of patients in two clusters revealed that they separate from each other based on their obsessive and compulsive severity. The more severe group had lower age at assessment and reported earlier age of onset. The correlation of severity and earlier age of onset was also reported previously (Kichuk et al., 2013). Moreover, category level data clustering revealed that severe group showed more female to male ratios, more unoccupied to occupied ratios, more low educated people, more depression and avoidance levels as well as less insight.

The limitation of the current study is relatively homogenous and mildly ill sample of patients (total mean severity $\pm$ SD were 18.8 ± 8.8). Moreover, YBOCS severity scores in this study are current scores rather than worst-ever scores which may be a reflection of previous treatment effects. So the patients who reported severe symptoms were limited. However, findings of the current study are consistent with the previous LCA investigation on YBOCS-CL reported by Delucchi et al (Delucchi et al., 2011). The results of both investigations described OCD patients as a single spectrum based on severity or symptom endorsement rates. According to the results of these two studies heterogeneity of OCD patients based on the YBOCS symptoms which was recommended by the previous studies (Calamari et al., 1999; Lochner C, 2008) seems

challenging and needs to be more studied. Attempts to classify OCD patients into subtypes have had limited success and were controversial. Although several studies searched for a correlation between OCD symptom subtypes and specific treatments, no precise match has been proposed yet (Starcevic and Brakoulias, 2008). However, our findings do not consistently argue against the existence of categorical subtypes of OCD. Possibly different measures must be used for different purposes in the assessment of OCD as mentioned previously by Anholt and colleagues (Anholt et al., 2009). Clustering OCD patients based on treatment course and response or comorbid characteristics rather than symptoms may produce more interpretable subgroups with clinical importance. Further investigations may clarify the most appropriate measures to assess complex heterogeneity of OCD patients for improved assessment and treatment of OCD patients.

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References

- Althoff, R.R., Rettew, D.C., Boomsma, D.I., Hudziak, J.J., 2009. Latent class analysis of the child behavior checklist obsessive-compulsive scale. *Comprehensive psychiatry* 50, 584-592.
- Anholt, G.E., van Oppen, P., Emmelkamp, P.M., Cath, D.C., Smit, J.H., van Dyck, R., van Balkom, A.J., 2009. Measuring obsessive-compulsive symptoms: Padua inventory-revised vs. Yale-Brown obsessive compulsive scale. *Journal of Anxiety Disorders* 23, 830-835.
- Asadi, S., Daraeian, A., Rahmani, B., Kargari, A., Ahmadiani, A., Shams, J., 2016. Exploring yale-brown obsessive-compulsive scale symptom structure in Iranian OCD patients using item-based factor analysis. *Psychiatry Research* 245, 416-422.
- Association, A.P., 1994. Diagnostic and statistical manual of mental disorders, 4 ed.
- Baer, L., 1994. Factor analysis of symptom subtypes of obsessive compulsive disorder and their relation to personality and tic disorders. *Journal of Clinical Psychiatry* 55, 18-23.
- Bezdek, J.C., Ehrlich, R., Full, W., 1984. FCM: The fuzzy c-means clustering algorithm. *Computers & Geosciences* 10, 191-203.
- Bloch, M.H., Angeli Landeros-Weisenberger, M., Rosario, M.C., Pittenger, C., Leckman, J.F., 2008. Meta-analysis of the symptom structure of obsessive-compulsive disorder. *The American journal of psychiatry* 165, 1532-1542.
- Calamari, J.E., Wiegartz, P.S., Janeck, A.S., 1999. Obsessive-compulsive disorder subgroups: a symptom-based clustering approach. *Behaviour Research and Therapy* 37, 113-125.
- Calamari, J.E., Wiegartz, P.S., Riemann, B.C., Cohen, R.J., Greer, A., Jacobi, D.M., Jahn, S.C., Carmin, C., 2004. Obsessive-compulsive disorder subtypes: an attempted replication and extension of a symptom-based taxonomy. *Behaviour Research and Therapy* 42, 647-670.
- Caliński, T., Harabasz, J., 1974. A dendrite method for cluster analysis. *Communications in Statistics-theory and Methods* 3, 1-27.
- Davies, D.L., Bouldin, D.W., 1979. A cluster separation measure. *Pattern Analysis and Machine Intelligence, IEEE Transactions on*, 224-227.
- Defays, D., 1977. An efficient algorithm for a complete link method. *The Computer Journal* 20, 364-366.
- Delucchi, K.L., Katerberg, H., Stewart, S.E., Denys, D.A., Lochner, C., Stack, D.E., den Boer, J.A., van Balkom, A.J., Jenike, M.A., Stein, D.J., 2011. Latent class analysis of the Yale-Brown Obsessive-Compulsive Scale symptoms in obsessive-compulsive disorder. *Comprehensive psychiatry* 52, 334-341.
- Denys, D., de Geus, F., van Megen, H.J., Westenberg, H.G., 2004. Use of factor analysis to detect potential phenotypes in obsessive-compulsive disorder. *Psychiatry research* 128, 273-280.
- Fals-Stewart, W., Lucente, S., 1993. An MCMI cluster typology of obsessive-compulsives: A measure of personality characteristics and its relationship to treatment participation, compliance and outcome in behavior therapy. *Journal of Psychiatric Research* 27, 139-154.
- Feinstein, S.B., Fallon, B.A., Petkova, E., Liebowitz, M.R., 2003. Item-by-item factor analysis of the Yale-Brown obsessive compulsive scale symptom checklist. *The Journal of neuropsychiatry and clinical neurosciences* 15, 187-193.
- Goodman, W.K., Price, L.H., Rasmussen, S.A., Mazure, C., Fleischmann, R.L., Hill, C.L., Heninger, G.R., Charney, D.S., 1989. The Yale-Brown obsessive compulsive scale: I. Development, use, and reliability. *Archives of general psychiatry* 46, 1006-1011.
- Hasler, G., LaSalle-Ricci, V.H., Ronquillo, J.G., Crawley, S.A., Cochran, L.W., Kazuba, D., Greenberg, B.D., Murphy, D.L., 2005. Obsessive-compulsive disorder symptom dimensions show specific relationships to psychiatric comorbidity. *Psychiatry research* 135, 121-132.

Ilc, N., 2012. Modified Dunn's cluster validity index based on graph theory. *Przegląd Elektrotechniczny* 88, 126-131.

Katerberg, H., Delucchi, K.L., Stewart, S.E., Lochner, C., Denys, D.A., Stack, D.E., Andresen, J.M., Grant, J., Kim, S.W., Williams, K.A., 2010. Symptom dimensions in OCD: item-level factor analysis and heritability estimates. *Behavior genetics* 40, 505-517.

Kichuk, S.A., Torres, A.R., Fontenelle, L.F., Rosário, M.C., Shavitt, R.G., Miguel, E.C., Pittenger, C., Bloch, M.H., 2013. Symptom dimensions are associated with age of onset and clinical course of obsessive-compulsive disorder. *Progress in Neuro-Psychopharmacology and Biological Psychiatry* 44, 233-239.

Lochner, C., Hemmings, S.M., Kinnear, C.J., Niehaus, D.J., Nel, D.G., Corfield, V.A., Moolman-Smook, J.C., Seedat, S., Stein, D.J., 2005. Cluster analysis of obsessive-compulsive spectrum disorders in patients with obsessive-compulsive disorder: clinical and genetic correlates. *Comprehensive psychiatry* 46, 14-19.

Lochner C, H.S., Kinnear CJ, Nel D, Hemmings SM, Seedat S, Moolman-Smook JC, Stein DJ., 2008. Cluster analysis of obsessive-compulsive symptomatology: identifying obsessive-compulsive disorder subtypes. *The Israel journal of psychiatry and related sciences* 45, 164.

Lochner, C., Stein, D.J., 2003. Heterogeneity of obsessive-compulsive disorder: a literature review. *Harvard review of psychiatry* 11, 113-132.

MacQueen, J., 1967. Some methods for classification and analysis of multivariate observations, *Proceedings of the fifth Berkeley symposium on mathematical statistics and probability*. Oakland, CA, USA., pp. 281-297.

Mataix-Cols, D., do Rosario-Campos, M.C., Leckman, J.F., 2005. A multidimensional model of obsessive-compulsive disorder. *American Journal of Psychiatry* 162, 228-238.

Mataix-Cols, D., Baer, L., Rauch, S.L., Jenike, M.A., 2000. Relation of factor-analyzed symptom dimensions of obsessive-compulsive disorder to personality disorders. *Acta Psychiatrica Scandinavica* 102, 199-202.

McKay, D., Abramowitz, J.S., Calamari, J.E., Kyrios, M., Radosky, A., Sookman, D., Taylor, S., Wilhelm, S., 2004. A critical evaluation of obsessive-compulsive disorder subtypes: symptoms versus mechanisms. *Clinical psychology review* 24, 283-313.

Nestadt, G., Addington, A., Samuels, J., Liang, K.-Y., Bienvenu, O.J., Riddle, M., Grados, M., Hoehn-Saric, R., Cullen, B., 2003. The identification of OCD-related subgroups based on comorbidity. *Biological Psychiatry* 53, 914-920.

Nestadt, G., Di, C., Riddle, M., Grados, M., Greenberg, B., Fyer, A., McCracken, J., Rauch, S., Murphy, D., Rasmussen, S., 2009. Obsessive-compulsive disorder: subclassification based on co-morbidity. *Psychological medicine* 39, 1491-1501.

Noshirvani, H.F., Kasvikis, Y., Marks, I.M., Tsakiris, F., Monteiro, W., 1991. Gender-divergent aetiological factors in obsessive-compulsive disorder. *The British Journal of Psychiatry* 158, 260-263.

Rajezi Esfahani, S., Motaghipour, Y., Kamkari, K., Zahiredin, A., Janbozorgi, M., 2012. Reliability and Validity of the Persian version of the Yale-Brown Obsessive-Compulsive scale (Y-BOCS). *Iranian Journal of Psychiatry and clinical psychology* 17, 297-303.

Rousseeuw, P.J., 1987. Silhouettes: a graphical aid to the interpretation and validation of cluster analysis. *Journal of computational and applied mathematics* 20, 53-65.

Starcevic, V., Brakoulias, V., 2008. Symptom subtypes of obsessive-compulsive disorder: are they relevant for treatment? *Australian and New Zealand Journal of Psychiatry* 42, 651-661.

Thomsen, P.H., Jensen, J., 1991. Latent class analysis of organic aspects of obsessive-compulsive disorder in children and adolescents. *Acta Psychiatrica Scandinavica* 84, 391-395.

Vermunt, J.K., Magidson, J., 2004. Latent class analysis. *The sage encyclopedia of social sciences research methods*, 549-553.

Table and Figure legends:

Table 1: Demographic and clinical characteristics of OCD patients (N=216)

Table 2: Underlying factors specified from item-based and category-based factor analysis of YBOCS-CL.

Table 3: Clinical and demographic characteristics of patients separated by clustering the YBOCS-CL item-level raw data and item-based factor scores.

Table 4: Clinical and demographic characteristics of patients separated by clustering the YBOCS-CL category-level raw data and category-based factor scores.

Figure1: Evaluation of 2 to 6 cluster solutions resulted from conducting five clustering algorithms (FCM, K-means, Ward, Ward+K-means, Complete) on different sets of data by clustering indices. **A₁- A₄**: Davies-Bouldin values of resulted models from applying clustering algorithms on item-level raw data, item-based factor scores, category-level raw data and category-based factor scores, respectively. **B₁-B₄**: Calinski-Harabasz values of resulted models from applying clustering algorithms on item-level raw data, item-based factor scores, category-level raw data and category-based factor scores, respectively. **C₁-C₄**: Silhouettes values of resulted models from applying clustering algorithms on item-level raw data, item-based factor scores, category-level raw data and category-based factor scores, respectively. **D₁-D₄**: Dunn values of resulted models from applying clustering algorithms on item-level raw data, item-based factor scores, category-level raw data and category-based factor scores, respectively.

Figure2: Mean of symptom scores in patients separated by 2-solution clustering models resulted from conducting five clustering algorithms (FCM, K-means, Ward, Ward+K-means, Complete) on different sets of data. **A1:** Mean scores on the YBOCS-CL obsession and compulsion categories for each subgroup identified from clustering item-level raw data. **A2:**

Mean YBOCS-CL item-based factor scores for each subgroup identified from clustering item-based factor scores. **B1**: Mean scores on the YBOCS-CL obsession and compulsion categories for each subgroup identified from clustering category-level raw data. **B2**: Mean YBOCS-CL category-based factor scores for each subgroup identified from clustering category-based factor scores.

Item-level raw data

Item-based factor scores

Category-level raw data

Category-based factor scores

Item-level raw data

Item-based factor scores

Category-level raw data

Category-based factor scores

Item-based

OAggression
 OContamination
 OSexual
 OHoarding
 OReligious
 OSymmetry
 OSomatic
 CCleaning
 CCChecking
 CRepeating
 CCCounting
 COrdering
 CHoarding

Item-based

Factor 1
 Factor 2
 Factor 3
 Factor 4
 Factor 5

Category-based

Factor 1
 Factor 2
 Factor 3
 Factor 4

Table 1: Demographic and clinical characteristics of OCD patients (N=216)

		Number	%
Gender	Male	70	32
	Female	146	68
Marital status	Single	70	32
	Married	145	68
Educational level	School dropout	69	33
	Diploma	93	43
	Under graduate	44	20
	Graduate	9	4
Occupation	Unemployed	118	55
	Employed	97	45
Familial history of psychiatric disorders	OCD	101	47
	Other Axis I disorders	59	27
	No history	54	26
		Mean	SD
Age at assessment		33.7	10.2
Age of onset		23.7	10.7
Obsession Severity		10.3	4.7
Compulsion Severity		8.9	5.9
Total Severity		18.6	8.8

Table 2: Underlying factors specified from item-based and category-based factor analysis of YBOCS-CL.

Factors	Item-based	Category-based
1	Aggression, Checking	Aggression, Contamination , Sexual, Religious, Somatic, Checking, Repeating
2	Contamination, Cleaning	Symmetry, Cleaning, Counting, Ordering
3	Symmetry, Ordering , Counting , Repeating, Hoarding	Contamination, Cleaning
4	Sexual	Hoarding
5	Somatic	

Table 3: Clinical and demographic characteristics of patients separated by clustering the YBOCS-CL item-level raw data and item-based factor scores.

Item-level raw data												Item-based factor scores									
	FCM			K-means		Ward		Ward+		Complete		FCM		K-means		Ward		Ward+		Complete	
	Cluster	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2
Age at assessment	Mean	34.9	31.9	32	34	29.4	34.3	32.1	34.4	29.1	34.3	31.9	34.6	30.8	35.1	35.1	32.2	35.1	30.8	32.9	34
	P-value	0.03		0.1		0.01		0.1		0.01		0.06		<0.01		0.03		<0.01		0.4	
Age of onset	Mean	25.6	21	21	25.4	20.3	24.2	20.6	25.1	20	24.2	20.6	25.4	20.3	25.4	26.3	21	25.4	20.3	22.7	24
	P-value	<0.01		<0.01		0.07		<0.01		0.06		<0.01		<0.01		0.01		<0.01		0.3	
Obsession score	Mean	9.23	12	12	9.3	12.5	10	12.3	9.5	12.5	10.1	11.9	9.5	11.9	9.6	9.6	11.2	9.6	11.9	11.1	10
	P-value	<0.01		<0.01		0.01		<0.01		0.01		<0.01		<0.01		0.01		<0.01		0.30	
Compulsion score	Mean	7.6	10.8	11	7.6	12.1	8.5	11.4	7.8	12.1	8.5	10.8	7.9	10.2	8.3	7.4	10.6	8.3	10.2	10.5	8.4
	P-value	<0.01		<0.01		<0.01		<0.01		<0.01		<0.01		0.02		<0.01		0.02		0.02	
Depression	Mean	1.42	2.07	2.08	1.4	2.2	1.6	2.2	1.4	2.33	1.6	2.1	1.4	2.1	1.4	1.5	1.8	1.4	2.1	2	1.5
	P-value	<0.01		<0.01		<0.01		<0.01		0.01		<0.01		<0.01		0.04		<0.01		0.03	
Insight	Lack	34	25	25	34	10	49	22	37	10	49	24	35	21	38	26	33	38	21	17	42
	Presence	93	63	59	97	18	138	44	112	16	140	51	105	49	107	86	70	107	49	37	119
	P-value	0.79		0.54		0.29		0.19		0.17		0.27		0.55		0.14		0.55		0.44	
Avoidance	Lack	85	49	46	88	16	118	36	98	14	120	42	92	38	96	73	61	96	38	30	104
	Presence	42	39	38	43	12	69	30	51	12	69	33	48	32	49	39	42	49	32	24	57
	P-value	0.09		0.06		0.54		0.11		0.34		0.16		0.09		0.36		0.09		0.23	
Gender	Female	86	60	57	89	19	127	45	101	18	128	50	96	42	104	74	72	104	42	32	114
	Male	41	28	27	42	9	60	21	48	8	61	25	44	28	41	38	31	41	28	22	47
	P-value	0.94		0.98		0.99		0.94		0.87		0.77		0.08		0.54		0.08		0.11	
Job	Unemployed	65	53	53	65	18	100	41	77	17	101	49	69	37	81	57	61	81	37	29	89

History	Employed	62	35	31	66	10	87	25	72	9	88	26	71	33	64	55	42	64	33	25	72
	P-value	0.18		<u>0.05</u>		0.28		0.15		0.25		0.02		0.67		0.22		0.67		0.84	
	No history	35	19	18	36	7	47	15	39	7	47	16	38	16	38	34	20	38	16	15	39
	Axis I Dis	30	29	26	33	9	50	18	41	8	51	22	37	22	37	28	31	37	22	15	44
	OCD	62	39	39	62	12	89	32	69	11	90	36	65	31	70	50	51	70	31	24	77
Education	P-value	0.27		0.5		0.82		0.88		0.86		0.66		0.61		0.18		0.61		0.85	
	Low	93	69	68	94	23	139	54	108	21	141	64	98	54	108	85	77	108	54	38	124
	High	34	19	16	37	5	48	12	41	5	48	11	42	16	37	27	26	37	16	16	37
	P-value	0.38		0.12		0.37		0.14		0.49		0.01		0.67		0.84		0.67		0.32	
Marital status	Single	34	35	32	37	11	58	26	43	10	59	29	40	29	40	34	35	40	29	19	50
	Married	93	53	52	94	17	129	40	106	16	130	46	100	41	105	78	68	105	41	35	111
	P-value	<u>0.04</u>		0.13		0.38		0.12		0.45		0.13		<u>0.04</u>		0.56		<u>0.04</u>		0.57	

Table 4: Clinical and demographic characteristics of patients separated by clustering the YBOCS-CL category-level raw data and category-based factor scores.

	Category-level raw data											Category-based factor scores									
	FCM		K-means		Ward		Ward+		Complete			FCM		K-means		Ward		Ward+		Complete	
	Cluster	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2
Age at	Mean	35.6	31.6	35.5	31.5	35.4	32.3	35.1	31.7	29.4	34.7	33	34.6	34.5	33.1	34.5	33.2	34.5	33.1	33.2	33.8
assessment	P-value	<u><0.01</u>		<u><0.01</u>		<u>0.02</u>		<u><0.01</u>		<u><0.01</u>		0.2		0.3		0.36		0.3		0.6	
Age of	Mean	26.4	20.8	26.3	20.6	26.6	21.3	26.4	20.7	20.1	24.6	22.8	25.1	25.1	22.8	25.4	22.7	25.1	22.8	22.4	24.1
onset	P-value	<u><0.01</u>		<u><0.01</u>		<u><0.01</u>		<u><0.01</u>		<u>0.01</u>		0.1		0.1		0.08		0.1		0.3	
Obsession	Mean	9.4	11.4	9.4	11.5	9	11.5	9.4	11.4	12.5	9.8	11.4	8.9	9	11.4	8.6	11.5	9	11.4	9.7	10.5
score	P-value	<u><0.01</u>		<u><0.01</u>		<u><0.01</u>		<u><0.01</u>		<u><0.01</u>		<u><0.01</u>		<u><0.01</u>		<u><0.01</u>		<u><0.01</u>		0.3	

Compulsion score	Mean	7.2	10.8	7.1	11.1	7.5	10.1	7.1	10.9	12.1	8.2	9.8	7.7	7.8	9.8	7.5	9.8	7.8	9.8	8.5	9
	P-value	<u><0.01</u>		<u><0.01</u>		<u><0.01</u>		<u><0.01</u>		<u><0.01</u>		<u>0.01</u>		<u>0.01</u>		<u><0.01</u>		<u>0.01</u>		0.5	
Depression	Mean	1.39	2	1.4	2	1.4	1.9	1.38	2	2.2	1.5	1.96	1.3	1.3	1.9	1.34	1.9	1.3	1.9	1.3	1.7
	P-value	<u><0.01</u>		<u><0.01</u>		<u>0.01</u>		<u><0.01</u>		<u><0.01</u>		<u><0.01</u>		<u><0.01</u>		<u><0.01</u>		<u><0.01</u>		0.08	
Insight	Lack	27	32	28	31	25	34	27	32	14	45	43	16	17	42	16	43	17	42	11	48
	Presence	85	71	90	66	75	81	87	69	28	128	83	73	73	83	65	91	73	83	34	122
	P-value	0.25		0.17		0.45		0.18		0.34		<u><0.01</u>		<u>0.01</u>		<u>0.04</u>		<u>0.01</u>		0.61	
Avoidance	Lack	77	57	81	53	72	62	78	56	22	112	74	60	60	74	55	79	60	74	28	106
	Presence	35	46	37	44	28	53	36	45	20	61	52	29	30	51	26	55	30	51	17	64
	P-value	<u>0.04</u>		<u>0.03</u>		<u><0.01</u>		<u>0.05</u>		0.13		0.19		0.26		0.18		0.26		0.98	
Gender	Female	68	78	72	74	64	82	70	76	30	116	97	49	50	96	46	100	50	96	23	123
	Male	44	25	46	23	36	33	44	25	12	57	29	40	40	29	35	34	40	29	22	47
	P-value	<u>0.01</u>		<u>0.01</u>		0.25		<u>0.02</u>		0.58		<u><0.01</u>		<u><0.01</u>		<u><0.01</u>		<u><0.01</u>		<u><0.01</u>	
Job	Unemployed	54	64	58	60	51	67	55	63	26	92	79	39	40	78	38	80	40	78	20	98
	Employed	58	39	60	37	49	48	59	38	16	81	47	50	50	47	43	54	50	47	25	72
	P-value	<u>0.04</u>		0.06		0.28		<u>0.03</u>		0.3		<u><0.01</u>		<u><0.01</u>		0.06		<u><0.01</u>		0.1	
History	No History	29	25	30	24	29	25	29	25	11	43	29	25	25	29	23	31	25	29	9	45
	Axis I Dis	27	32	29	30	21	38	28	31	11	48	37	22	23	36	19	40	23	36	11	48
	OCD	56	45	58	43	49	52	56	45	20	81	59	42	42	59	39	62	42	59	25	76
Education	P-value	0.48		0.59		0.12		0.61		0.97		0.62		0.72		0.51		0.72		0.43	
	Low	81	81	86	76	71	91	82	80	33	129	101	61	61	101	55	107	61	101	27	135
	High	31	22	32	21	29	24	32	21	9	44	25	28	29	24	26	27	29	24	18	35
	P-value	0.28		0.35		0.16		0.21		0.58		<u>0.05</u>		<u>0.02</u>		<u>0.04</u>		<u>0.02</u>		<u><0.01</u>	
Marital status	Single	31	38	32	37	26	43	31	38	17	52	40	29	30	39	27	42	30	39	16	53

Married	81	65	86	60	74	72	83	63	25	121	86	60	60	86	54	92	60	86	29	117
P-value	0.14		0.08		0.07		0.1		0.19		0.89		0.74		0.76		0.74		0.57	