Symptom Profiles and Executive Function in Childhood Obsessive-Compulsive Disorder.

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Abstract

Obsessive-compulsive disorder (OCD) often becomes manifest in childhood. It has been suggested that the symptom heterogeneity of the disorder could mask subgroups associated with executive function (EF) impairment. Though supported in adult studies, this is scarcely investigated in children. The aims of the present study were to: (i) investigate OCD symptom subgroups using an empirically supported and age-appropriate definition of symptom dimensions (SD) as well as latent profile analysis (LPA); (ii) compare the identified subgroups with respect to EFs, demographic, and clinical descriptives; and (iii) explore the associations between SDs and EFs. The study included 50 pediatric OCD patients and 50 matched controls. Patients were assessed with the Children's Yale-Brown Obsessive-Compulsive Scale from which three SD factor scores were generated. Participants were assessed with EF tasks from which latent variables measuring working memory, set shifting and response inhibition were derived. Parents rated executive function behaviors in their children. Three subgroups were identified, each predominantly characterized by one of the SDs. Subgroups differed with respect to parent-rated working memory and several demographic and basic clinical characteristics. The findings suggest the presence of clinically relevant child and adolescent OCD SD subgroups, but do not support the relevance of EFs in distinguishing SDs.

Highlights

- Three obsessive-compulsive subgroups were identified, each mapping onto one of the symptom dimensions of symmetry/hoarding, harm/sexual, or contamination/cleaning.
- The subgroups differed with respect to parent-reported working memory, and several basic clinical characteristics, but not performance-based executive functions.
- Symptom dimensions were not associated with executive functions in children and adolescents with OCD.

Keywords

Obsessive-compulsive disorder; symptom dimension subgroups; executive function; latent profile analysis; children.

1. Introduction

1.1. Pediatric Obsessive-Compulsive Disorder and Symptom Dimensions

Obsessive-Compulsive Disorder (OCD) is a serious mental disorder characterized by intrusive thoughts and/or compulsive acts (American Psychiatric Association, 2013). The disorder often becomes manifest in childhood with prevalence estimates in children and adolescents ranging from 0.5 % to 3 % (Heyman, Fombonne, Simmons, Ford, Meltzer, & Goodman, 2003). Obsessive-Compulsive Disorder is highly heterogeneous with several suggested distinct, albeit overlapping, symptom dimensions (SD; Bloch, Landeros-Weisenberger, Rosario, Pittenger, & Leckman, 2008; Leckman et al., 2010; Mataix-Cols, Rosario-Campos, & Leckman, 2005). Studies of adults have typically identified four to five SDs in OCD including cleaning, symmetry, forbidden thoughts, harm, and hoarding based on factor analysis of the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS; Bloch et al., 2008; Goodman et al., 1989). Symptom presentation in children and adolescents with OCD is less investigated (Mataix-Cols, Nakatani, Micali, & Heyman, 2008; McKay, Piacentini, Greisberg, Graae, Jaffer, & Miller, 2006; Stewart et al., 2007). However, in a recent item level factor analysis of the Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS; (Scahill et al., 1997) three SDs: harm/sexual, symmetry/hoarding, and contamination/cleaning were identified in a large group of children and adolescents with OCD (Højgaard et al., 2016). The slightly varying results from adult and child samples most likely reflect the fact that OCD symptoms are measured at different stages of development (American Psychiatric Association, 2013; Geller et al., 2001; Kalra & Swedo, 2009) and the use of different methods to define symptom categories (e.g., by predefined higher level symptom categories versus lower level symptom items).

1.2. Defining OCD Symptom Subgroups

Due to the heterogeneous nature of OCD it has been suggested that symptom subgroups could constitute more homogeneous entities with distinct patterns of comorbidity, neural correlates, heritability, etc. (Hasler et al., 2005; Taberner et al., 2009; van den Heuvel et al., 2009), and that symptom subgroups have predictive value related to treatment response (Mataix-Cols, Marks, Greist, Kobak, & Baer, 2002; Rufer, Fricke, Moritz, Kloss, & Hand, 2006). Previously applied subgroup categorization methods using the Y-BOCS/CY-BOCS have been limited in their ability to account for and include SDs which are overlapping, that is, present in individual patients at the same time and in varying magnitude (McKay et al., 2004). This problem can be addressed by application of Latent Profile Analysis (LPA) with inclusion of SD factor scores. This statistical method identifies probability-based clusters (e.g., patient subgroups) based on shared characteristics (e.g., symptoms) by forming a number of category latent variables representing each cluster (DiStefano & Kamphaus, 2006; Vermunt & Magidson, 2002). The method has been used to identify homogeneous subgroups in several areas of clinical research (e.g., Flensborg Damholdt, Shevlin, Borghammer, Larsen, & Ostergaard, 2012; Gomez, Gomez, Winther, & Vance, 2014; Rajendran, O'Neill, Marks, & Halperin, 2015; Van Hulst, De Zeeuw, & Durston, 2015; Ulbricht, Rothschild, & Lapane, 2015; Dhingra, Boduszek, & Klonsky, 2016), but has not previously been applied to examine OCD SDs.

1.3. Executive Functions in OCD

The prevailing neurobiological model of OCD focuses on abnormalities in frontal-striatal circuits, implying associated neuropsychological dysfunction (Menzies,Chamberlain, Laird, Thelen, Sahakian, & Bullmore, 2008; Saxena & Rauch, 2000). Following this line of reasoning, aspects of executive function (EF) have been suggested to constitute possible intermediate endophenotypes in

OCD (Chamberlain, Blackwell, Fineberg, Robbins, & Sahakian, 2005; Olley, Malhi, & Sachdev, 2007; Taylor, 2012). Executive functions can be defined as a set of general-purpose control processes that regulate thought and behavior (Miyake & Friedman, 2012). They reflect a general underlying ability, often referred to as common EF, as well as specific functions, including the EF subdomains of working memory, set shifting, and response inhibition (Miyake, Friedman, Emerson, Witzki, Howerter, & Wager, 2000). Executive functions can be measured through performance-based tasks or through ratings of daily life behavior. Though EF questionnaires were initially developed to provide ecologically valid ratings of EF aspects corresponding to those reflected by performance tests (e.g., aspects such as set shifting, inhibition, and working memory; Gioia, Kenworthy, & Isquith, 2010), several studies have documented that the two types of measures are poorly correlated (Barkley & Fischer, 2011; Davidson, Cherry, & Corkum, 2016; McAuley, Chen, Goos, Schachar, & Crosbie, 2010; Toplak, West, & Stanovich, 2013). Consequently, the two measurement approaches have been hypothesized to capture different underlying aspects of EF (Toplak et al., 2013). According to this suggestion, EF task performance reflects "processing efficiency" measured in a structured situation, whereas EF behavior ratings reflect "success in goal pursuit" measured in a daily life context (Toplak et al., 2013).

Performance-based EF underperformance in OCD has been supported in meta-analyses based on adult samples with small to medium effect sizes (ES; Abramovitch, Abramowitz, & Mittelman, 2013; Shin, Lee, Kim, & Kwon, 2014; Snyder, Kaiser, Warren, & Heller, 2014), but, performance-based EF underperformance in children and adolescents is generally not supported (Abramovitch et al., 2015a; Geller et al., 2017; Hybel, Mortensen, Lambek, Thastum, & Thomsen, 2016). Contrary to studies of performance-based EFs, the literature on rating-based EFs in OCD is rather limited and solely based on child and adolescent samples. In a small case-control study, Zandt, Prior, & Kyrios (2009) found children and adolescents with OCD to have significantly

elevated levels of parent rated EF difficulties compared to typically developing counterparts. In another study investigating the relationship between EF, OCD severity, and treatment outcome, McNamara et al. (2014) found parent-rated EFs to predict symptom severity, indicating that EF behavior was more impaired in OCD patients with higher symptom levels. In sum, the limited literature suggests that, as a group, pediatric OCD patients are significantly impaired in daily life EF behavior, whereas studies of performance-based EF indicate that EF task performance deficits are not present in children and adolescents with OCD relative to typically developing children and adolescents.

1.4. Executive Functions in OCD Symptom Subgroups

It is generally acknowledged that neuropsychological OCD research is characterized by mixed findings, and several methodological explanations for this have been put forward (Abramovitch, Mittelman, Tankersley, Abramowitz, & Schweiger, 2015). One such explanation concerns the heterogeneous symptom presentation in OCD and implies that different SDs or subtypes could be associated with different neuropsychological profiles (Abramovitch et al., 2015b). This has received some empirical support in adults and, to a limited extent, in child and adolescent OCD. For instance, a meta-analysis by Leopold and Backenstrass (2015) investigated differences in (performance-based) neuropsychological functioning between patients exhibiting washing symptoms (the contamination/cleaning dimension) and patients exhibiting checking symptoms (also referred to as the harm dimension). Results indicated that “checkers” performed inferior to “washers” on the EF subdomains response inhibition, planning, and set shifting. Lawrence and et al. (2006) investigated the association between the EF subdomain of set shifting and multiple SDs, and found the symmetry/ordering dimension to be associated with lower levels of set shifting ability.

Executive function impairments associated with the symmetry/ordering dimension was further supported in a more recent study by Hashimoto et al. (2011).

As already noted, the association between OCD SDs and EFs is under-investigated in children and adolescents, and, as we documented in a previous study (Hybel et al., 2016), EF task performance (contrary to daily life EF behavior) is generally unimpaired in pediatric OCD. This, however, does not exclude the possibility of SD subgroups with EF task underperformance as well as between subgroup differences. One previous study investigated the association between SDs and performance-based neuropsychological functioning in children and adolescents with OCD, and found patients who experienced symptoms of symmetry/ordering and hoarding to have greater neuropsychological impairment across different neuropsychological domains, including memory, fluency, verbal learning, processing speed, response inhibition, and set shifting (McGuire et al., 2014). Further, the symmetry/ordering dimension (albeit, not the hoarding dimension) was specifically associated with deficits in response inhibition and set shifting. In this study a five-factor SD solution based on adult OCD symptom presentation was applied. A more recent pediatric study investigated rating-based EFs in patients characterized by hoarding symptoms (Park et al., 2016). Patients were dichotomized into groups with and without hoarding symptoms, and the two groups were found to differ significantly with respect to daily life EF behavior with higher levels of impairment in the group exhibiting hoarding symptoms (Park et al., 2016).

In sum, only one previous study has investigated EF task performance and SDs in a pediatric sample, and this study applied predefined SDs derived from studies on adults, thereby disregarding possible differences in symptom presentation between children and adults, and one study has investigated daily life EF behavior and CY-BOCS category hoarding symptoms in children and adolescents, but this study did not examine further CY-BOCS category symptoms or SDs.

1.5. Aims and Hypotheses

No previous study has applied LPA to investigate SD subgroups in OCD, or examined OCD SDs' association with performance-based EFs using a latent variable approach based on several basic EF tasks, and no studies have investigated rating-based EFs in this context. In line with this, the presents study had three overall aims. The first aim was to investigate symptom profiles in children and adolescents with OCD by conducting an LPA with empirically derived SDs within this age group. The second aim was to investigate performance- and rating-based EFs in the identified subgroups and typically developing children and adolescents, and to characterize the subgroups with respect to demographic and basic clinical descriptives. The final aim was to explore the relationship between the three empirically derived OCD SDs and EFs independently of the identified symptom profile subgroups. This was considered an important complementary aim as the subgrouping of patients possibly could mask significant effects related to the three SDs.

As this was the first time LPA was applied in this field, no hypotheses were formulated regarding the composition of SDs, demographic, or basic clinical characteristics of potential subgroups. Based on prior work, it was hypothesized that if subgroups with higher scores on the symmetry/hoarding and/or the harm/sexual SDs were found, these would exhibit greater impairment on performance-based set shifting and response inhibition. In a similar vein, we expected that groups characterized by symmetry/hoarding would exhibit greater impairment on rating-based EFs. Finally, concerning the complementary analyses, it was expected that the symmetry/hoarding and the harm/sexual SDs would be associated with the performance-based EF subdomains of set shifting and response inhibition, and that the symmetry/hoarding SD would be associated with rating-based EFs.

2. Methods

2.1. Participants

The present study was an add-on to the Nordic long-term OCD treatment study (Thomsen et al., 2013) and included 100 participants: 50 patients aged 7-17 years referred to a specialized OCD clinic and a control group consisting of 50 typically developing children and adolescents recruited from local schools.

Inclusion criteria for the OCD group were an OCD diagnosis according to DSM-IV (American Psychiatric Association Task Force on DSM-IV, 2009) and a CY-BOCS total score ≥ 16 (CY-BOCS total M = 25.34, 95% CI [23.84, 26.84]). Co-morbid conditions with a lower Clinical Global Impression – Severity Scale rating (CGI-S; (Guy, 1976) than the CGI-S rating for OCD were included. Co-occurring conditions in the sample were: separation anxiety disorder (n = 1), specific phobia (n = 4), social phobia (n = 1), generalized anxiety disorder (n = 3), oppositional defiant disorder (n = 1). Patients fulfilling criteria for neurodevelopmental disorders (e.g., attention-deficit/hyperactivity disorder, autism spectrum disorders, tic disorders) and/or depressive disorders (e.g., major depressive disorder, dysthymia), patients in treatment with psychotropic medication, and patients with an IQ < 85 were excluded. Appendix A, figure A.1, presents frequencies of CY-BOCS symptom categories in the sample.

Typically developing children and adolescents were matched with individual children and adolescents in the OCD group according to age and gender. Exclusion criteria were a psychiatric diagnosis, a family history of OCD, referral to community mental health services within one year of participation in the study, and inadequate Danish language proficiency. Demographic and clinical descriptives of the two groups in the sample are presented in Table 1.

Table 1. Sample Demographic and Clinical Descriptives[*]

	Children and adolescents with OCD *n* (%) or *mean* (SD)	Typically developing children and adolescents *n (%) or mean (SD)*
Gender (girls)	35 (70)	35 (70)
Age	13.08 (2.35)	13.12 (2.38)
Parental education[**]	13.28 (2.53) [a]	15.04 (1.97) [a]
RIST full IQ estimate	100.40 (6.36) [a]	104.40 (6.43) [a]
CBCL Total Problems Scale	21.26 (14.13) [a]	4.74 (4.72) [a]
CBCL Internalizing Problems Scale	13.50 (8.49) [a]	3.36 (3.22) [a]
CBCL Externalizing Problems Scale	7.76 (7.23) [a]	1.38 (2.15) [a]
CBCL OCD Scale	7.88 (4.20) [a]	.80 (.99) [a]

RIST = *Reynolds Intellectual Screening Test,* CY-BOCS = *Children's Yale-Brown Obsessive-Compulsive Scale,* CBCL = *Child Behavior Checklist.*

[*] *OCD vs. typically developing group difference analyses performed using two sample t-tests.*

[**] *Parental education in years (scale range 5-17,5) calculated as an average for both parents.*

[a] *p=<.05 OCD versus typically developing children and adolescents.*

2.2. Procedures

Procedures have been detailed elsewhere (Hybel et al., 2016; Torp et al., 2015), but will be described briefly below. Participants with OCD were consecutively referred to the clinic from June 2010 to July 2013. Controls were recruited during the same period. Children and adolescents with OCD were diagnosed according to the Schedule for Affective Disorders and Schizophrenia for School-Age Children – Present and Lifetime version for DSM-IV (Kaufman et al., 1997), and assessed with the CY-BOCS including the CGI-S before entering into the study. Diagnostic assessments were conducted by experienced and trained clinicians. Before inclusion, controls were screened according to the exclusion criteria via telephone. After inclusion, parents completed the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001; Andersen & Bilenberg, 2012) and a brief background questionnaire.

Neuropsychological assessments were conducted in a 2½-3-hour in-hospital session with a fixed test sequence. Parent questionnaires were administered on-line and completed during the test session at the clinic. Parents were unaware of the results from the neuropsychological assessment when they completed the questionnaires.

2.3. Measures

2.3.1. Psychopathology Interviews and Questionnaires

The Children's Yale-Brown Obsessive-Compulsive Scale is a semi-structured interview which measures past and current OCD symptom presentation as well as present OCD severity in patients aged 6-17 years. The instrument is the most frequently used to assess OCD in children and adolescents, and it has been found reliable and valid for this age group (Storch et al., 2004). In the present study three SDs were used: (1) harm/sexual, (2) symmetry/hoarding, and (3)

contamination/cleaning. Factor scores were derived from a recently conducted CY-BOCS item level factor analysis, pooling several pediatric OCD samples which also included the children and adolescents from the present study (Højgaard et al., 2016).

The Child Behavior Checklist is a parent questionnaire assessing a broad range of behavioral and emotional problems in children and adolescents aged 6-18 (Achenbach & Rescorla, 2001). It has acceptable to good validity and reliability (Deighton, Croudace, Fonagy, Brown, Patalay, & Wolpert, 2014). The scale has a total problem scale and several subscales, including the internalizing problems, the externalizing problems, and the OCD subscales which were used in the present study.

3.3.2. Background Questionnaire and IQ Measure

The background questionnaire queried about the education of the parents. Length of parental education in years was calculated as an average for both parents and converted to a scale ranging from 5-17.5. Reynolds Intellectual Screening Test (Reynolds, Kamphaus, & Raines, 2012) was applied to measure general cognitive ability.

3.3.3. EF Questionnaire.

The Behavior Rating Inventory of Executive Function (BRIEF; Gioia, Isquith, Guy, & Kenworthy, 2000) is a parent questionnaire developed to capture daily life EF behavior in children. The questionnaire was developed to reflect ecologically valid ratings of EFs (Gioia et al., 2010). It is validated for children and adolescents aged five to eighteen years and widely used in clinical research within this age group (e.g., Mahone et al., 2002; McCandless & O'Laughlin, 2007; Zandt et al., 2009). The BRIEF contains a number of subscales. BRIEF subscales corresponding to the

performance-based EF subdomain measures: working memory, shift, (corresponding to set shifting), and inhibit (corresponding to response inhibition) were included in the present study.

2.3.4. EF Tasks

Participants completed a battery of six widely used, well-described, and generally recognized EF tasks with two tasks for each of the basic EF subdomains: working memory, set shifting, and response inhibition. The EF battery included the following tasks of which four are from the Cambridge Automated Neuropsychological Battery (CANTABeclipse, 2006) as indicated by an asterisk [(*)] below (for a more detailed presentation of tasks, see Hybel et al., 2016):

Working Memory Tasks:

- *Spatial Working Memory*[*]; the outcome measure was number of errors.
- *Spatial Span*[*] (SSP); the outcome measure was span length (i.e., the maximum sequence successfully recalled).

Set Shifting Tasks:

- *Intra/Extra Dimensional Set Shift*[*]; the outcome measure was total errors adjusted for number of completed stages.
- *Trail Making Test – part B* (Reitan, 1971); the outcome measure was time to complete the task.

Response Inhibition Tasks:

- *Stop Signal Task*[*] (Logan & Cowan, 1984; Verbruggen & Logan, 2008); the outcome measure was stop signal reaction time (i.e., the length of time between the go and the stop stimulus at which the subject is able to successfully inhibit response on 50% of trials).
- *Flanker Task* (Eriksen & Eriksen, 1974; Huyser, Veltman, Wolters, de Haan, & Boer, 2011); the outcome measure was accuracy (i.e., percent correct on incongruent trials).

In order to reduce the number of comparisons in the statistical analyses and improve performance-based EF measure quality, latent variables reflecting the basic EF subdomains of working memory, set shifting, and response inhibition, were used in the present study. Latent EF variables have been recommended as they may be less influenced by lower level cognitive functions and consequently constitute "purer" measures than observed level EF variables (Miyake, Emerson, & Friedman, 2000). Factor scores were derived from a previous confirmatory factor analysis (CFA) conducted with the above-mentioned tasks (Hybel et al., 2016). Appendix B, figure B.1, illustrates the CFA model.

2.4. Data Analysis

Prior to analyses, the data were inspected and tested for normality. Only the performance-based EF measures met assumptions of normality. Therefore, CY-BOCS SDs and BRIEF scales raw data were transformed through ranking and subsequently z-transformation in all analyses requiring normally distributed data. Missing data were minimal (0.1 % for the rating-based EF measures).

First, latent profile analysis (LPA) was applied to identify mutually exclusive subgroups of children and adolescents who displayed similar OCD SD profiles. Untransformed CY-BOCS SD factor scores were entered into the model as class indicators. The resulting models were

evaluated based on theoretical considerations and traditional fit statistics including Akaike's information criterion (AIC) and Bayesian information criterion (BIC), where lower values indicate better fit. Further, entropy criterion values which reflect classification accuracy (with values above 0.90 indicating good classification accuracy) and Likelihood Ratio Tests, which indicate whether models are significantly different from each other, were considered (Vermunt & Magidson, 2002). The LPA was performed using Mplus version 7 (Muthén & Muthén, 2015).

Second, subgroups identified in the LPA and the control group were compared with respect to demographic and clinical variables using the non-parametric Wilcoxon Rank-Sum Test. These analyses were conducted with Stata version 14 (StataCorp, 2015).

Third, LPA subgroups and the control group were compared with respect to performance-based EFs and rating-based EFs using ANCOVAs with adjustment for age, gender, and parental education. Secondary analyses included adjustment for IQ, and in the OCD subgroup comparisons, OCD severity (i.e., CY-BOCS total score) was also included. The results of the secondary analyses will be described to the extent that the adjustments influenced the group comparisons significantly. Significance level was adjusted according to the Bonferroni procedure by dividing the alpha level of .05 by the number of tasks within each family of tests, that is the performance-based EF measures and the rating-based measures (performance-based EF: $p < 0.05 / 3 = p < 0.017$; rating-based EF: $p < 0.05 / 3 = p < 0.017$). Effect sizes are reported as standardized (z-score) adjusted mean group differences. Analyses were conducted with Stata version 14 (StataCorp, 2015).

Finally, the three SD measures, the three performance-based EF measures, and the three rating-based EF measures were subjected to second-order partial correlation analysis with age and gender as covariates.

3. Results

3.1. Latent Profile Analysis of Symptom Dimensions

Fit statistics for the six LPA models are presented in Table 2.

Table 2. Fit Indices for the Latent Profile Analysis Models.

Model	AIC	BIC	Entropy	Likelihood ratio test[a]
1	147	159	-	
2	126	146	0.91	$p = 0.01$
3	**125**	**152**	**0.93**	$\mathbf{p = 0.31}$
4	120	155	0.91	$p = 0.60$
5	120	162	0.92	$p = 0.20$
6	119	169	0.93	$p = 0.25$

AIC = *Akaike information criterion*; BIC = *Bayesian information criterion*.

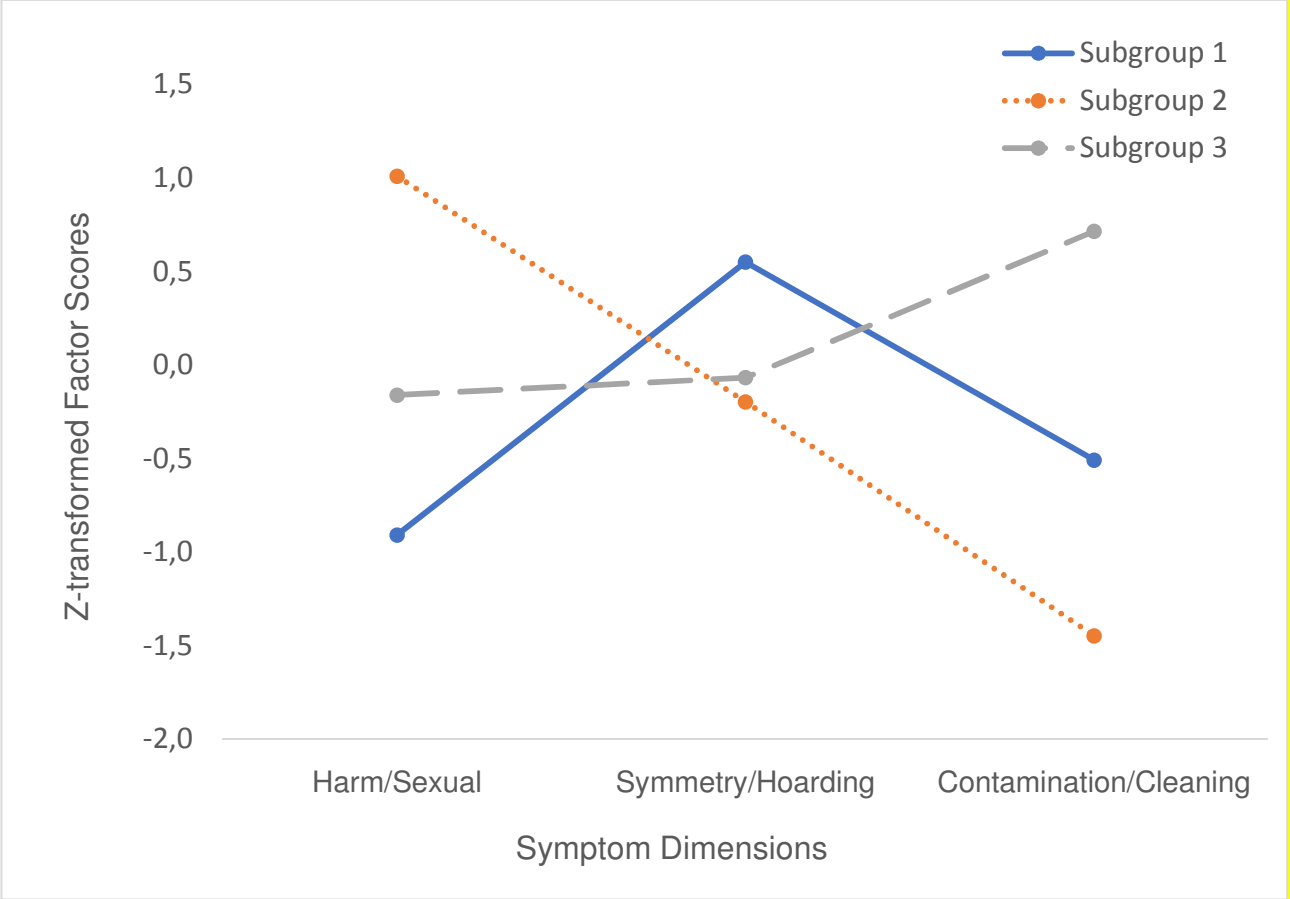
[a]*Vuong-Lo-Mendell-Rubin Likelihood ratio test for 2 vs. 1, 3 vs. 2, 4 vs. 3, 5 vs. 4, and 6 vs. 5 subgroups.*

Preferred model in bold.

Initial evaluation of the fit indices indicated that the two-subgroup and the three-subgroup models fitted the data best. The two-subgroup model displayed the lowest BIC value, had a high entropy value (> .90) indicating high degree of certainty in classification, and a Likelihood Ratio Test indicating a significant difference relative to the one-subgroup model. In the three-subgroup model there was a slight decrease in AIC and an increase in BIC and entropy values compared to the two-subgroup model. However, as the likelihood ratio test did not indicate a significant difference to the two-subgroup model, and the three-subgroup model fitted theoretical assumptions of separate patient subgroups primarily characterized by one of the three symptom factors: (1) harm/sexual, (2)

symmetry/hoarding, or (3) contamination/cleaning, it was decided to proceed with this model. The symptom profiles for the three-subgroup model are presented in Figure 1.

Figure 1. The Latent Profile Analysis Three-Subgroup Model Symptom Dimension Profiles.



As can be seen in Figure 1, patients belonging to subgroup 1 (n = 8 [16 %]) were primarily characterized by symmetry/hoarding dimension symptoms, secondarily by contamination/cleaning dimension symptoms and relatively lower levels of harm/sexual dimension symptoms. Patients in subgroup 2 (n = 12 [24 %]) were predominantly characterized by harm/sexual dimension symptoms, lower levels of symmetry/hoarding dimension symptoms, and a low level of contamination/cleaning dimension symptoms. Patients in subgroup 3 (n = 30 [60 %]) were

predominately characterized by contamination/cleaning dimension symptoms with relatively lower levels of symmetry/hoarding and harm/sexual dimension symptoms.

The three LPA subgroups differed significantly on the harm/sexual dimension (Wilcoxon Rank-Sum Test: subgroup 1 vs. 2: $p < .001$; subgroup 1 vs. 3: $p = .02$; subgroup 2 vs. 3: $p < .001$) and the contamination/cleaning dimension (Wilcoxon Rank-Sum Test: subgroup 1 vs. 2: $p < .001$; subgroup 1 vs. 3: $p < .001$; subgroup 2 vs. 3: $p < .001$). However, the subgroups did not differ significantly on the symmetry/hoarding dimension (Wilcoxon Rank-Sum Test: subgroup 1 vs. 2: $p = .11$; subgroup 1 vs. 3: $p = .10$, subgroup 2 vs. 3: $p = .78$).

3.2. Demographic and Clinical Characteristics of LPA Subgroups

Demographic and clinical characteristics of the LPA subgroups and the control group are presented in Table 3.

Table 3. Demographic and Clinical Descriptive Statistics for the LPA Subgroups and the Control Group[*].

	Subgroup 1 (*n* = 8)	Subgroup 2 (*n* = 12)	Subgroup 3 (*n* = 30)	Control (*n* =50)
	Mean (SD) or *n* (%)	*Mean* (SD) or *n* (%)	*Mean* (SD) or *n* (%)	*Mean* (SD) or *n* (%)
Gender (girls)	4 (50%)	7 (58.33%)	24 (80%)	35 (70%)
Age	13.87 (1.86)	14.03 (1.70)	13.32 (2.69)	13.59 (2.34)
Parental education[**]	11.72 (1.48)[bd]	13.46 (2.30)[e]	13.63 (2.73)[bf]	15.04 (1.97)[def]
OCD symptom onset	9.88 (2.70)	10.45 (3.11)	9.00 (2.98)	-
RIST full IQ estimate	94.63 (3.70)[abd]	100.92 (6.24)[a]	101.73 (6.26)[bf]	104.40 (6.43)[df]
CY-BOCS Total Scale	22.75 (5.63)	23.08 (4.60)[c]	26.93 (4.95)[c]	-
CY-BOCS Obsessions Scale	11.38 (3.02)	11.75 (2.22)[c]	13.57 (2.49)[c]	-
CY-BOCS Compulsions Scale	11.38 (3.02)	11.33 (2.57)[c]	13.37 (2.77)[c]	-
CBCL Total Problems Scale	10.75 (9.15)[b]	21.92 (13.75)[e]	23.8 (14.43)[bf]	4.74 (4.72)[ef]
CBCL Internalizing Problems Scale	6.5 (5.58)[ab]	14.75 (9.02)[ae]	14.87 (8.71)[bf]	3.36 (3.22)[ef]
CBCL Externalizing Problems Scale	4.25 (4.89)	7.17 (5.29)[e]	8.93 (8.19)[f]	1.38 (2.15)[ef]
CBCL OCD Scale	4.63 (3.02)[bd]	8.17 (3.69)[e]	8.63 (4.35)[bf]	0.80 (0.99)[def]

LPA = Latent Profile Analysis, RIST = Reynolds Intellectual Screening Test, CY-BOCS = Children's Yale-Brown Obsessive-Compulsive Scale, CBCL = Child Behavior Checklist.

[*] *Analyses performed using Wilcoxon Rank-Sum Test. Raw data means presented.*

[**] *Parental education in years (scale range 5-17.5) calculated as an average for both parents.*

[a] *Subgroup 1 vs. Subgroup 2: p = < .05,* [b] *Subgroup 1 vs. Subgroup 3: p = < .05,* [c] *Subgroup 2 vs. Subgroup 3: p = < .05,* [d] *Subgroup 1 vs. control group: p = < .05,* [e] *Subgroup 2 vs. control group: p = < .05,* [f] *Subgroup 3 vs. control group: p = < .05.*

Subgroup 1 had significantly lower IQ scores and lower scores on the CBCL internalizing problems subscale than subgroup 2. Also, compared to subgroup 3, subgroup 1 had lower parental education level, lower IQ scores, lower scores on the CBCL total scale, lower scores on the CBCL internalizing problems subscale, and lower scores on the CBCL OCD subscale. Subgroup 2 differed significantly from subgroup 3 on all CY-BOCS scales with higher scores in subgroup 3.

All LPA subgroups had significantly higher levels of parent-reported OCD on the CBCL and shorter parental education than the control group. Further, subgroups 1 and 3 had significantly lower IQ scores than controls, and subgroups 2 and 3 displayed significantly higher scores on the CBCL total score, the CBCL internalizing problems, and externalizing problems subscales relative to the control group.

3.3. Latent Profile Analysis Subgroups and Executive Functions

Tables 4A and 4B present EF performance and EF ratings in the three LPA subgroups and the control group.

Table 4A. Performance- and Rating-Based Executive Function Differences in the Three Latent Profile Analysis Subgroups.[*]

	Subgroup 1 vs. Subgroup 2				Subgroup 1 vs. Subgroup 3				Subgroup 2 vs. Subgroup 3			
EF measure	Subgroup 1 *Adj. mean*	Subgroup 2 *Adj. mean*	*p*	*ES*[^]	Subgroup 1 *Adj. mean*	Subgroup 3 *Adj. mean*	*p*	*ES*[^]	Subgroup 2 *Adj. mean*	Subgroup 3 *Adj. mean*	*p*	*ES*[^]
Performance-based measures												
Working memory (↑)	.01	.03	.91	-.05	-.04	-.08	.81	.09	.06	-.05	.39	.24
Set shifting (↓)	-.01	.00	.93	-.05	.03	.06	.85	-.07	-.02	.04	.49	-.19
Response inhibition (↓)	.18	-.01	.35	.40	.21	.03	.31	.38	-.01	.01	.86	-.05
Rating-based measures												
Working memory (↓)	.23	.90	.09	-.75	.06	.48	.20[*]	-.47	.75	.44	.27	.34
Shift (↓)	.15	.70	.15	-.62	.21	.77	.10	-.63	.55	.76	.40	-.23
Inhibit (↓)	.35	.52	.74	-.20	.50	.57	.85	-.08	.41	.55	.61	-.16

[*]*Analyses performed using ANCOVA's with adjustment for age, gender and socioeconomic status.*

Upwards and downwards arrows designate that higher scores indicate better performance (↑) or that lower scores indicate better performance (↓) for each measure.

[^]*Effect sizes corresponding to Cohen's d.*

**p = < .017 after IQ adjustment indicating significance according to the Bonferroni adjusted alpha level.*

EF measure	Subgroup 1 vs. Control Group				Subgroup 2 vs. Control Group				Subgroup 3 vs. Control Group			
	Subgroup 1 *Adj. mean*	Controls *Adj. mean*	*p*	*ES*^	Subgroup 2 *Adj. mean*	Controls *Adj. mean*	*p*	*ES*^	Subgroup 3 *Adj. mean*	Controls *Adj. mean*	*p*	*ES*^
Performance-based measures												
Working memory (↑)	.03	.14	.53	-.24	.16	.15	.92	.03	-.00	.13	.15	-.29
Set shifting (↓)	.01	-.10	.34*	.36	-.08	-.10	.76	.08	.02	-.09	.06	.36
Response inhibition (↓)	.20	-.13	.07	.72	-.06	-.14	.54	.17	-.01	-.12	.23	.24
Rating-based measures												
Working memory (↓)	.12	-.40	.08	.58	.74	-.42	.00**	1.29	.36	-.41	.00**	.86
Shift (↓)	.16	-.56	.01*	.80	.50	-.56	.00**	1.18	.73	-.57	.00**	1.45
Inhibit (↓)	.25	-.40	.05*	.73	.28	-.41	.00**	.79	.50	-.41	.00**	1.04

Table 4B. Performance- and Rating-Based Executive Function in the Three Latent Profile Analysis Subgroups versus the Control Group.*

**Analyses performed using ANCOVA's with adjustment for age, gender and socioeconomic status.*

Upwards and downwards arrows designate that higher scores indicate better performance (↑) or that lower scores indicate better performance (↓) for each measure.

^*Effect sizes corresponding to Cohen's d.*

**p = < .05 after IQ adjustment.*

***p = < .017 after IQ adjustment indicating significance according to the Bonferroni adjusted alpha level.*

No significant differences emerged between any of the LPA subgroups on any EF measure. However, differences in rating-based working memory between subgroup 1 and 3 became significant when adjusted for IQ, with higher levels of EF impairment in subgroup 3. Effect sizes for the performance-based measures were generally small, whereas ESs for the rating-based measures varied (ranging from small to moderate).

Comparisons between the three LPA subgroups and the control group revealed no significant differences with respect to performance-based EF, and ESs were generally small except for response inhibition which was moderate in the subgroup 1 versus control group comparison. On the rating-based measures several differences emerged. In the comparison between subgroup 2 and the controls, and between subgroup 3 and the controls there were significant differences with large ESs in all three EF subdomains indicating higher levels of impairment in LPA subgroups. In the comparison between subgroup 1 and controls there was a significant difference in the subdomain shift. However, when adjusted for IQ this difference was no longer significant.

3.4. Symptom Dimensions and Executive Functions

Table 5 presents the associations between and within the OCD SDs, the performance-based EF measures, and the rating-based EF measures adjusted for the effects of age and gender.

Table 5. Partial Correlations Between Symptom Dimension Measures, Performance-Based EF Measures, and Rating-Based Executive Function Measures with Adjustment for Age and Gender.

		Symptom dimensions			Performance-based EFs			Rating-based EFs		
		Harm/ sexual	Symmetry/ hoarding	Contamination/ cleaning	Working memory	Set shifting	Response Inhibition	Working memory	Shift	Inhibit
Symptom dimensions	Harm/sexual	-								
	Symmetry/ hoarding	-.41*	-							
	Contamination/ cleaning	-.42*	.09	-						
Performance-based EFs	Working memory	.16	-.00	-.21	-					
	Set shifting	-.14	.04	.14	-.96*	-				
	Response inhibition	-.21	.08	.13	-.82*	.83*	-			
Rating-based EFs	Working memory	.06	-.16	.03	-.12	.06	.12	-		
	Shift	-.02	.05	.17	.04	-.09	-.07	.65*	-	
	Inhibit	-.23	.16	.07	.13*	-.18	-.06	.45*	.73*	-

*$p = < 0.01$

No significant correlations emerged between SDs and EFs. Correlations within SDs were moderate and significant, except the association between the symmetry/ordering dimension and the contamination/cleaning dimension which was found to be non-significant. Correlations between performance-based and rating-based measures were generally small and non-significant, whereas correlations between EF subdomains within each EF measurement type were moderately to strongly correlated.

4. Discussion

The aims of this study were to investigate symptom subgroups in children and adolescents with OCD and to investigate EFs in the identified subgroups. Further, the aims were to characterize these subgroups with respect to demographic and clinical variables, and to explore the associations between SDs and EFs.

When factor scores for the harm/sexual, the symmetry/hoarding, and the contamination/cleaning SDs were entered into LPA, three separate subgroups emerged. Each subgroup was primarily characterized by specific OCD symptoms related to one of the SDs, albeit (as expected) considerable overlap was also present. The identified subgroups differed with respect to several clinical variables. Most notably, group 1 (symmetry/hoarding) was characterized by lower IQ and less internalizing problems and group 3 (contamination/cleaning) was characterized by higher OCD severity than the other subgroups. As this study was the first to apply LPA with CY-BOCS factor scores, results must be considered preliminary and are in need of replication in larger samples. Results, however, do suggest that symptom subgroups in childhood OCD could constitute more homogeneous and clinically relevant entities.

Contrary to the hypotheses, the only EF subdomain which differentiated the subgroups was rating-based working memory, where subgroup 3 (contamination/cleaning) was significantly

more impaired than subgroup 1 (symmetry/hoarding) when adjusted for group differences in IQ. Regarding subgroup comparisons with the control group, subgroup 2 (harm/sexual) and 3 (contamination/cleaning) were clearly impaired on all rating-based EFs relative to typically developing children and adolescents. Effect sizes in the moderate to large range in the subgroup 1 versus control group comparison suggested that the lack of significant group differences in this comparison could be due to the small number of patients in this subgroup (n = 8) resulting in loss of statistical power. Therefore, and in line with previous findings (see Zandt et al., 2009; McNamara, 2014), it is possible that children and adolescents with OCD, irrespectively of symptom profile, are generally more impaired with respect to daily life ratings of EF behavior than are typically developing children and adolescents. This could imply that children and adolescents with OCD may be able to recruit resources to perform on EF lab tasks, but experience more difficulty in real life settings that may be loaded with emotional and disorder-specific stimuli. Consequently, and in line with what has previously been suggested within ADHD research (Barkley & Fischer, 2011), it is possible that EF behavior ratings may have greater clinical utility, as they seem to reflect general daily life impairment to a higher extent than EF task performance. Future studies should determine the clinical utility of the two types of measures, for instance by investigation of the predictive values in relation to treatment effects.

The proposed association between the symmetry/hoarding dimension and daily life EF behavior problems was not supported by the findings of the present study. This to some degree contradicts previous research where the EF subdomains shift and working memory were found to be associated with hoarding symptoms (cf., Park et al., 2016). These contradictory results could be due to methodological differences between the Park et al. study and the present study, most prominently, the use of symptoms versus SDs and different sample sizes. Notably, neither the Park et al. study nor the present study found an association between hoarding and the inhibit subdomain.

Initial hypotheses regarding the harm/sexual and the symmetry/hoarding dimension's associations with performance-based set shifting and response inhibition underperformance were not confirmed in the subgroup comparisons nor in the complementary analyses. The correlational analyses did not indicate an association between the three SDs and EFs. Such an association was hypothesized based on studies conducted with adult rather than child OCD samples, due to the scarcity of such studies. Therefore, it is possible that the different findings in the present study reflect actual differences between pediatric and adult OCD with regard to SDs (i.e., symptoms might group in fewer dimensions or SDs may be differently composed in children and adolescents; Højgaard et al., 2016) as well as EFs (i.e., EF task underperformance does not seem to be a characteristic of pediatric OCD; Abramovitch et al., 2015a; Geller et al., 2017; Hybel et al., 2016). Findings, however, also diverge from the only previous pediatric study in the field which found patients with symmetry/ordering dimension symptoms (i.e. not including hoarding symptoms) to be more impaired on performance-based inhibition/switching tasks relative to patients without these symptoms (McGuire et al., 2014). There are several possible explanations for this discrepancy. First, in the McGuire et al. (2014) study a five-factor SD solution based on adult OCD symptoms was applied, and it is possible that this clustering approach (for instance, the division of symmetry/ordering and hoarding symptoms) is less characteristic of child samples. Second, in the McGuire et al (2014) study patients were grouped according to SDs by symptom count (i.e., dichotomously exhibiting vs not exhibiting one or more of the symptoms included in a dimension), whereas factor scores for each dimension (i.e., weighted scores for each specific symptom included in a dimension) were used in the present study. Finally, in the McGuire et al (2014) study the scope was to investigate impairment across several neuropsychological domains, not EF specifically, and only performance-based measures and observed variables (as opposed to latent variables) were applied.

Regarding the possible difference between pediatric and adult SDs, the relatively few previous studies that invested the factor structure of pediatric OCD symptoms have supported a four-factor solution (i.a., most often segregating symmetry and hoarding as in the McGuire et al. (2014) study; Delorme et al., 2006; Mataix-Cols et al., 2008; McKay et al., 2006; Stewart et al., 2007), but these studies were all conducted at the level of predefined CY-BOCS symptom categories, and this poses a significant methodological limitation. The only previous pediatric item level factor analytical study supported a three-factor solution (Højgaard et al., 2016) as applied in the present study. Although the most frequently applied adult SD factor solutions include four SDs and often segregate symmetry and hoarding (e.g., Bloch et al., 2008; Leckman et al., 1997), three factor SD solutions and/or factor solutions integrating symmetry and hoarding in one factor are also supported in several studies conducted with adults (Baer, 1994; Denys, de Geus, van Megen, & Westenberg, 2004; Girishchandra & Khanna, 2001; Hantouche & Lancrenon, 1996; Kim, Lee, & Kim, 2005; Stein, Andersen, & Overo, 2007; Stein, Carey, Lochner, Seedat, Fineberg, & Andersen, 2008). This suggests that many additional factors other than age and maturation may have influenced previous OCD SD factor structure findings. It is possible that distinct factors, such as the reliance on parent ratings in assessment, parent intervention in daily life OCD behavior (e.g. hoarding behavior) play a significant role in the SD factor structure of children and such factors might be different from factors influencing SDs in adults. More research is definitely needed to determine the best SD solution in children (and adults), as well as the possible difference or similarity of SDs between age groups.

In order to determine whether differences in the OCD symptom categorization method between the present and previous studies could be causing the contradictory results, additional explorative analyses were performed. When patients were dichotomized into groups based on whether they exhibited predefined CY-BOCS hoarding category symptoms or not, and whether they

exhibited predefined CY-BOCS symmetry/ordering category symptoms or not, no differences emerged on any EFs[1]. The idea that symptom categorization method caused the divergence from findings of the McGuire et al (2014) and the Park et al (2016) studies was therefore not supported.

This study has a number of strengths, including being the first to investigate performance-based as well as rating-based EFs in SD subgroups of childhood OCD. The study introduced a method, LPA, not previously applied in this field, which enabled a clinically relevant categorization of patients. The categorization was based on OCD SDs empirically derived from a large age-relevant OCD sample. The use of factor-scores, as opposed to categorization by symptom counting, enabled that variation in magnitude of SDs in individual patients and SD overlap were included in the analyses. The present study was the first to apply latent EF variables, which have been suggested to reflect 'purer' aspects of EF (Snyder, Miyake, & Hankin, 2015), and rating-based EF measures, which have been suggested to reflect more ecological EF behaviors (Gioia et al., 2010), in the context of OCD SD investigation. Further, the study design was well-controlled, with the inclusion of assessment of background variables (gender, age, parental education, and IQ), clearly specified exclusion criteria (e.g., IQ, medication status, co-occurring depressive and neuropsychiatric disorders), and an age- and gender-matched control group. There are also some limitations. As several symptom subgroups were identified in the LPA and some subgroups included relatively few children, power was low in some of the comparisons. For comparisons including the subgroup with a small number of patients (i.e., $n = 8$) only large ESs could be detected (power = 0.80 if Cohen's $d = 1.35$ if group $n = 8$). Therefore, it is possible that significant differences could have been detected if subgroups were larger. However, in the LPA subgroup comparisons of EF performance the ESs were generally in the small to moderate range, suggesting

[1] Predefined CY-BOCS hoarding category symptoms present: $n = 38$. Predefined CY-BOCS hoarding category symptoms not present: $n = 12$. Predefined CY-BOCS symmetry/ordering category symptoms present: $n = 30$. Predefined CY-BOCS symmetry/ordering category symptoms not present: $n = 20$. Analyses conducted using two tailed t-tests [significance level range: $p = .21 – .89$] as well as ANCOVAS with adjustment for age, gender and parental education [significance level range: $p = .22 – .80$]

modest clinical relevance of any significant subgroup differences. Further, as the symptom measure used (i.e., the CY-BOCS) did not include clinical impact ratings of SDs, we were not able to include such ratings in the analyses. Future research could advantageously develop and apply child-based instruments incorporating dimensional impact ratings in the same way as it has been undertaken in studies with adults (Pertusa, Fernández de la Cruz, Alonso, Menchón, & Mataix-Cols, 2012).

In conclusion, three latent symptom profile subgroups were identified in pediatric OCD, each predominantly characterized by the symmetry/hoarding, harm/sexual, or contamination/cleaning SDs. Groups had similar levels of EF performance, but differed with respect to parent-rated EF behavior and several demographic and clinical characteristics. This suggests that while symptom subgroups may have clinical value, they are not associated with different EF performance. Overall, the findings do not support that EFs are associated with SDs. As the present study was the first to focus specifically on the relationship between SDs and EFs and to apply a SD factor solution which was empirically founded in children and adolescents, the conclusions would be strengthened by replication.

5. Compliance with ethical standards

5.1. Ethical approval

The study was approved by the Danish regional ethics committee and informed consent was obtained from all the individual participants included in the study. All youths were offered a minor gift voucher for study participation.

5.2. Role of funding sources

The study was funded by The Danish Council for independent Research, Medical Sciences, The Research Fund for Psychiatric Research, Central Denmark Region, The Fru C. Hermansen's Memorial Foundation, The A.P. Møller Foundation for the Advancement of Medical Science and The G.J.'s Foundation. The funding sources had no involvement in study design, collection, analysis, or interpretation of data, writing of the report or decision to submit the article for publication.

5.3. Conflict of interest

The fifth author has received a speaker's fee from Shire and Medice, and royalties from different publishers for textbooks on child and adolescent psychiatry. The remaining authors declare that they have no conflicting interests.

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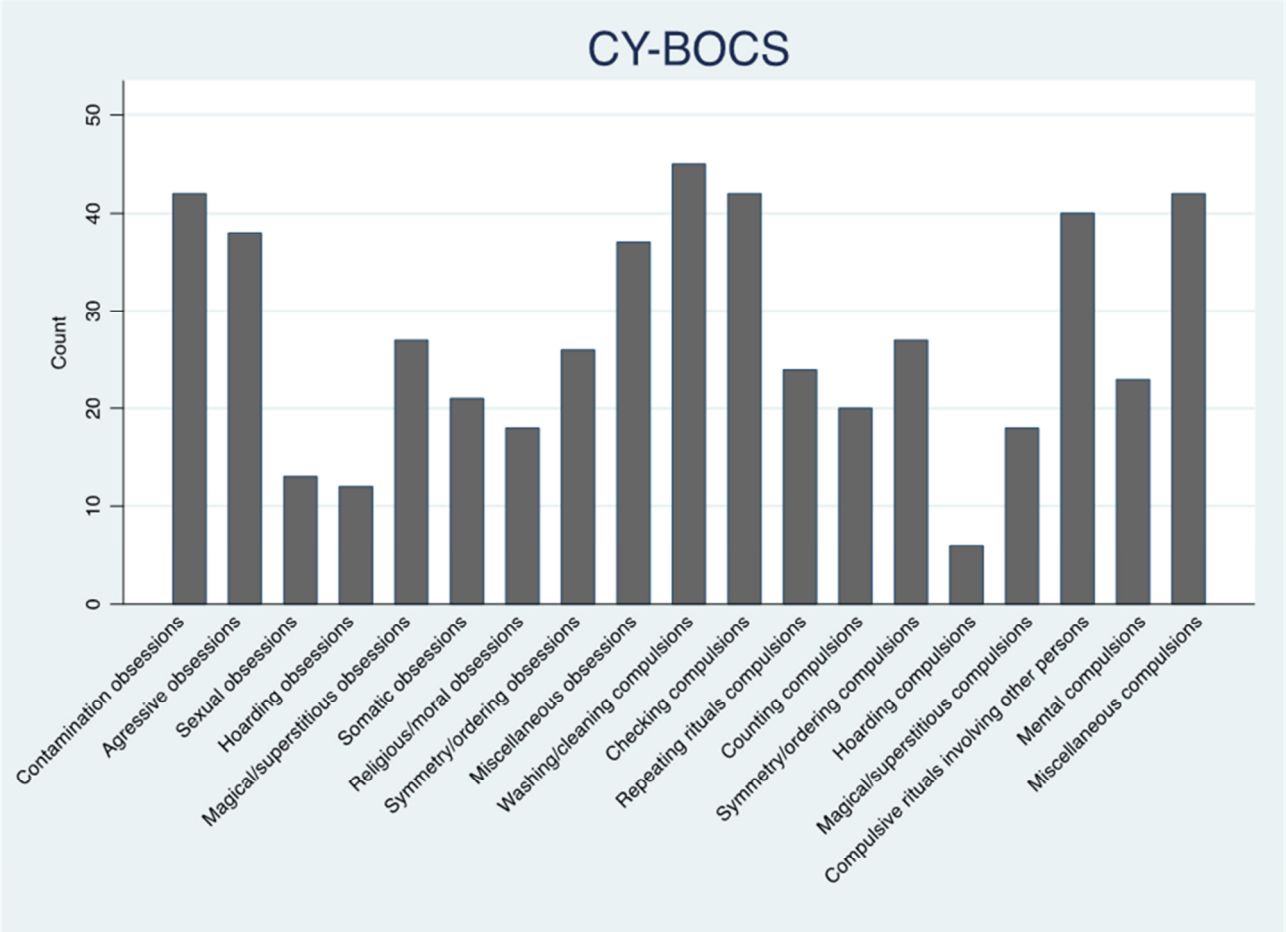
Appendix A.

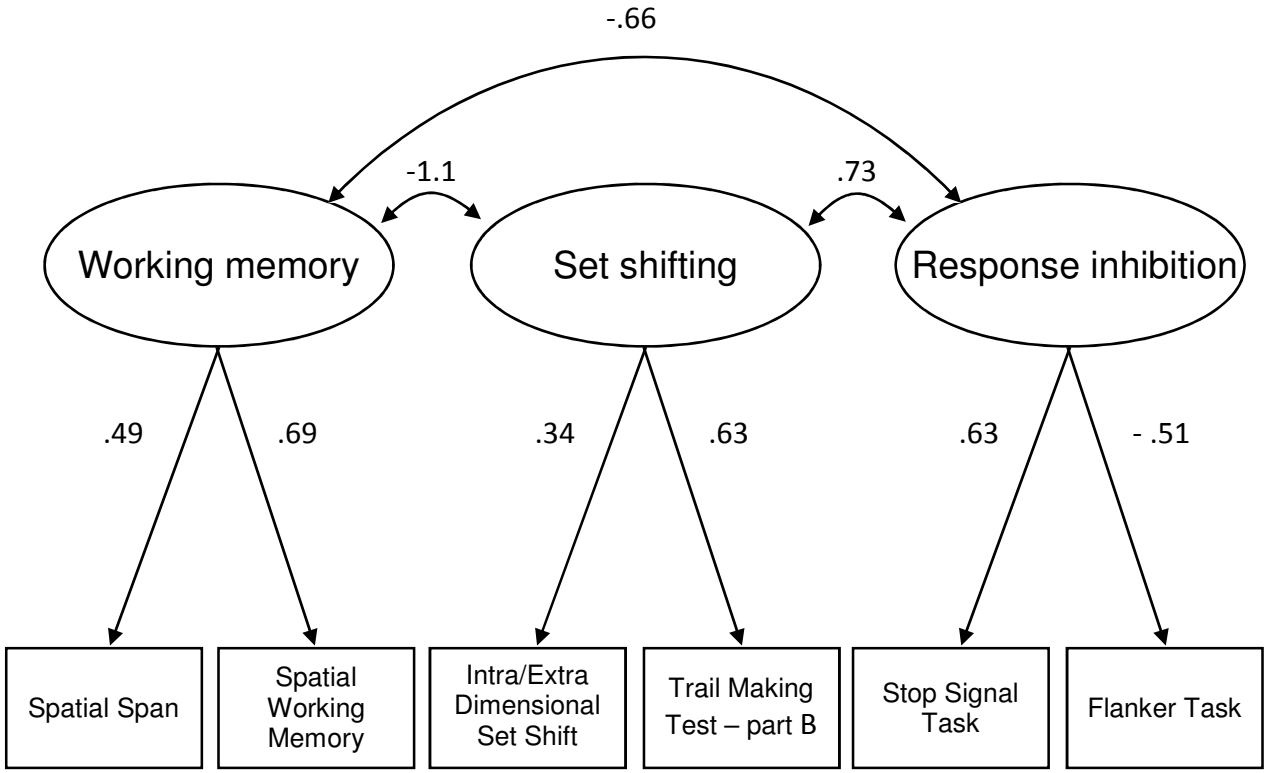
Figure A.1.
Children's Yale-Brown Obsessive-Compulsive Scale Symptom Category Frequencies in the Sample.



Appendix B.

Figure B.1.

The Confirmatory Factor Analytical Three-Factor Model of Basic Executive Functions[2].



Notes: Numbers besides arrows indicate standardized factor loadings.

[2] Hybel, K. A., Mortensen, E. L., Lambek, R., Thastum, M., & Thomsen, P. H. (2016). Cool and hot aspects of executive function in childhood obsessive-compulsive disorder. *Journal of Abnormal Child Psychology,* doi:10.1007/s10802-016-0229-6