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Clinical characteristics of probands with obsessive-compulsive disorder from simplex and multiplex families

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Abstract

Genetic and non-genetic factors contribute to obsessive-compulsive disorder (OCD), with strong evidence of familial clustering. Genomic studies in psychiatry have used the concepts of families that are “simplex” (one affected) versus “multiplex” (multiple affected). Our study compares demographic and clinical data from OCD probands in simplex and multiplex families to uncover potential differences. We analyzed 994 OCD probands (501 multiplex,

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Monicke O Lima: Conceptualization, Methodology, Data curation, Writing – original draft, Visualization, Formal analysis, Writing – review & editing. **Leonardo C Saraiva:** Formal analysis, Writing – review & editing. **Vanessa R Ramos:** Investigation, Data curation. **Melaine C Oliveira:** Formal analysis. **Daniel L C Costa:** Writing – review & editing. **Thomas V Fernandez:** Writing – review & editing, Supervision. **James J Crowley:** Writing – review & editing. **Eric A Storch:** Writing – review & editing, Supervision. **Roseli G Shavitt:** Writing – review & editing, Supervision. **Euripedes C Miguel:** Writing – review & editing, Supervision. **Carolina Cappi:** Writing – review & editing, Supervision, Conceptualization, Methodology, Data curation, Writing – original draft, Visualization, Formal analysis.

Declaration of Competing Interest

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493 simplex) from the Brazilian Research Consortium on Obsessive-Compulsive Spectrum Disorders (C-TOC). Clinicians administered the Structured Clinical Interview for DSM-IV (SCID-IV) to diagnose, Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) to assess severity, and Dimensional Yale–Brown Obsessive-Compulsive Scale (DY-BOCS) to assess symptom dimensionality. Demographics, clinical history, and family data were collected. Compared to simplex probands, multiplex probands had earlier onset, higher sexual/religious and hoarding dimensions severity, increased comorbidity with other obsessive-compulsive-related disorders (OCRD), and higher family history of psychiatric disorders. These comparisons provide the first insights into demographic and clinical differences between Latin American simplex and multiplex families with OCD. Distinct clinical patterns may suggest diverse genetic and environmental influences. Further research is needed to clarify these differences, which have implications for symptom monitoring and management.

Keywords

Obsessive-compulsive disorder; Family history; Clinical differences; Latin America

1. Introduction

Obsessive-compulsive disorder (OCD) is a chronic neuropsychiatric condition characterized by the presence of obsessions (intrusive and recurrent thoughts, impulses, or mental images) and compulsions (repetitive and persistent behaviors or mental acts performed in response to obsessions) (American Psychiatric Association et al., 2013; Stein et al., 2019). OCD is a heterogeneous disorder (Mataix-Cols et al., 2013; Miguel et al., 2005) that affects approximately 1 to 3 % of the global population (Leckman et al., 2010) and typically emerges during childhood or adolescence (Miguel et al., 2008; Ruscio et al., 2010).

Most individuals with OCD experience at least one co-existing psychiatric disorder, such as mood, anxiety, and impulsive disorders (Mahjani et al., 2022; Ruscio et al., 2010). OCD is also associated with a high risk of developing chronic tic disorders, including Tourette Syndrome (TS) (Brander et al., 2021; Browne et al., 2015). Additionally, OCD is frequently linked to other obsessive-compulsive related disorders (OCRD), such as body dysmorphic disorder (BDD), trichotillomania (TTM), and skin-picking (American Psychiatric Association et al., 2013). Although the hallmarks of OCD are obsessions and compulsions, individual patients differ with regard to specific OCD symptom dimensions (Rosario-Campos et al., 2006), age of symptom onset, comorbidity profile, and family history of OCD (Brakoulias et al., 2017; Mattina and Steiner, 2016).

Genetic and non-genetic factors have been implicated in OCD (Fernandez et al., 2018; Hirschtritt et al., 2017; Mahjani et al., 2020; Stein et al., 2019), and more work is needed to provide a comprehensive picture of its risk factors. Twin studies first demonstrated a significant familial and genetic component to OCD, with ~40 % heritability (Browne et al., 2014; Taylor, 2011a). Recent work by Mahjani et al. with 822,843 individuals from a national Swedish epidemiological sample supports this, providing heritability estimates of 32–35 % and evidence for significant maternal effects in OCD risk (Mahjani et al.,

2020). Studies have estimated single-nucleotide polymorphism (SNP) based heritability at 25–43 %, with potentially higher estimates for childhood-onset OCD. Common and rare genetic variants are associated with risk for OCD (International Obsessive Compulsive Disorder Foundation Genetics Collaborative (IOCDF-GC) and OCD Collaborative Genetics Association Studies (OCGAS), 2018; Mahjani et al., 2020). Nevertheless, a recent genome-wide association study (GWAS) with 14, 140 OCD cases led to just a single genome-wide significant common variant finding (Strom et al., 2021), and there are only two sufficiently powered studies using whole-exome sequencing (WES) to detect rare variants in OCD (Cappi et al., 2020; Halvorsen et al., 2021), suggesting *CHD8* as a risk gene for the disorder. These studies indicate that increasing sample size will lead to the identification of additional OCD risk loci and genes, as in other psychiatric disorders (Demontis et al., 2019; Fu et al., 2022; Grove et al., 2019; Satterstrom et al., 2020; Wray et al., 2018).

In psychiatry, families with multiple affected subjects are called “multigenerational families” (Mataix-Cols et al., 2013; Mathews et al., 2007). In the psychiatric genomics field, multigenerational families are also called “multiplex,” while families with only one affected are called “simplex” (Constantino et al., 2010; Gerdts et al., 2013; Hoffmann et al., 2014; Itsara et al., 2010; Klei et al., 2012; Leppa et al., 2016; Ronemus et al., 2014; Sanders, 2013; Sebat et al., 2007; Virkud et al., 2009; Wroten et al., 2023). In OCD, Cappi et al. performed WES in simplex families and observed that rates of de novo likely protein-truncating variation (PTV) (i.e., creation or loss of a stop codon, disruption of a canonical splice site, or a frameshift indel) are significantly elevated in OCD simplex trios compared to controls (Cappi et al., 2020). Wang et al. observed an overrepresentation of de novo damaging variants in simplex, but not multiplex, families of TS (Wang et al., 2018), though the sample size was limited. Similarly, different genetic mechanisms are involved in childhood attention deficit hyperactivity disorder (ADHD) (individuals diagnosed with ADHD in childhood) and late-diagnosed ADHD (individuals diagnosed with their first ADHD diagnosis as adults). Childhood ADHD showed a greater overlap with hyperactivity and autism, as well as a higher burden of rare variants, while late-diagnosed ADHD, which exhibited overlap with depression, did not show an increased burden of rare variants (Rajagopal et al., 2022). Although these studies show that genetic risk mechanisms may differ between simplex and multiplex families, no genomic studies have examined whether demographic and clinical variables differ between probands of these families.

Up to now, there have been two published reviews and meta-analyses concerning the genetic epidemiology of OCD. The initial review from 2001 encompassed 4 family studies on OCD, yet none originated from Latin America (Hettema et al., 2001). A more recent review and meta-analysis analyzed 24 family studies on OCD and chose to focus on 14 of them (Blanco-Vieira et al., 2023). These studies were pre-dominantly conducted in the United States and Nordic countries, with no studies focused on the Latin American demographic. Furthermore, they did not estimate the prevalence of OCD symptom dimensions in probands within simplex or multiplex families, nor did they characterize the comorbidity profiles.

A greater understanding of how family history impacts the clinical presentation of OCD may shed light on the etiology of OCD, including risk factors and different heritability patterns (Berends et al., 2019). Characterizing families and investigating family history is

foundational for differentiating between diagnoses, assessing genetic risks, and guiding genetic testing, healthcare, and patient support. Beyond its informational value, the collection of family history also facilitates the examination of family dynamics, support systems, risk perceptions, and direct experiences with the disorder (Guttmacher et al., 2004; Walter and Emery, 2005; Slomp et al., 2018). This study aims to analyze the phenotypic and clinical differences between simplex and multiplex probands with OCD from a large Brazilian sample. We hypothesize that multiplex probands exhibit a distinct pattern of OCD phenotypes compared to simplex probands.

2. Methods

2.1. Ethics

This study is part of The Brazilian Research Consortium on Obsessive-Compulsive Spectrum Disorders (C-TOC) and was approved by the local ethics committee of each participating site. All participants gave written informed consent. Participants were interviewed in person by a trained psychologist or psychiatrist for 3 to 6 h. All clinicians were trained for reliability in the use of the assessment instruments. Recruitment information is in Fig. 1, and more detailed information about the Consortium and procedures regarding recruitment, instruments, and methods can be found in Miguel et al. (2008).

2.2. Participants

Nine hundred ninety-four probands with a primary OCD diagnosis were recruited between 2006 and 2015 by C-TOC, a cross-sectional study conducted by seven university sites specialized in OCD in Brazil. We consider “simplex” the families where only the proband has OCD ($n = 493$), and “multiplex” the families where the proband has OCD and at least one first-degree relative (FDR) has OCD or obsessive-compulsive symptoms (OCS) ($n = 501$). We included OCS in the multiplex group since well-controlled family studies support a shared genetic component between OCD and OCS (do Rosario-Campos et al., 2005; Hanna et al., 2005; Mathews et al., 2007; Nestadt et al., 2000; Taylor, 2011b). Additionally, Bralten et al. have demonstrated a genetic overlap between OCD and OCS using polygenic risk scores from OCD GWAS data (Bralten et al., 2020).

2.3. Clinical measures

For this study, we compared groups for the presence of current and past psychiatric diagnoses using the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (SCID-IV) – Axis I Disorders (Schizophrenia; Mood Disorders; Substances Use Disorders; Anxiety Disorders; Eating Disorders; and Impulse Control Disorders).

We aggregated the psychiatric comorbidities into a numerical variable referred to as the “number of psychiatric comorbidities”. To classify OCRD, we created a group that includes BDD, skin-picking, and TTM. Consistent with DSM-V, this classification is supported by evidence that these disorders share a common genetic basis (American Psychiatric Association et al., 2013; Mathews et al., 2008; Phillips et al., 2010).

We considered the age of onset as the age of the first OCD symptom regardless of distress, and the OCD duration was calculated by subtracting the age of onset from the age at assessment. Due to their higher negative correlation (Pearson correlation: $R = -0.31$, $p <$ 2.2e-16), and considering the bias of duration of illness variable, which can vary depending on the proband's age, we opted to use the age of onset variable in the statistical model.

The severity of OCD symptoms was measured by the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) (Goodman et al., 1989); Y-BOCS scores range from 0 to 40, with higher scores corresponding to higher severity. To assess the severity of specific OCD symptom dimensions (obsessions and compulsions related to aggression, injury, violence, and natural disasters; obsessions and compulsions related to sexual, moral, and religion; obsessions and compulsions related to symmetry/just-right and compulsions to count, order and arrange; obsessions to contamination and cleaning compulsions; obsessions and compulsions related to hoarding and miscellaneous obsessions and compulsions related to somatic concerns, superstitions and other symptoms), we used the Dimensional Yale-Brown Obsessive-Compulsive Scale (DY-BOCS) (Rosario-Campos et al., 2006). The score of each DY-BOCS dimension ranges from 0 to 15, and the global score ranges from 0 to 30.

We investigated the psychiatric diagnoses in family members using the screening session of the SCID-IV. Additionally, the rating clinicians assessed whether any first or second-degree relatives had received a diagnosis of OCD from a qualified mental health clinician.

Fig. 1. Recruitment flowchart.

2.4. Statistical analysis

Normality assumptions for the continuous variables were checked using the Shapiro–Wilk test. Logistic regression models, adjusted for age and sex, were used to compare simplex and multiplex probands in sociodemographic and clinical variables. Statistically significant variables in those models were selected as predictor variables in a multiple logistic regression model, adjusted for age and sex. In all logistic regression models, the response variable was the proband group (simplex vs. multiplex), with the reference level being the multiplex group. Odds ratios (ORs) for predictor variables were obtained by exponentiating their respective coefficients estimated in the models. 95 % confidence intervals for those ORs were estimated using the profile likelihood method.

3. Results

3.1. Sample demographics

The sample comprised 994 adults with OCD (493 simplex, 501 multiplex), with a mean age of 34.8 years (34.8 years for simplex and 34.9 years for multiplex) at the time of assessment. Most probands were female (55 % simplex, 58.9 % multiplex). There were no statistically significant differences in age and sex between the groups.

Most probands in both simplex and multiplex groups were categorized as white (80.9 % simplex, 87.8 % multiplex). However, the proportion of white and black probands was different between the groups ($p < 0.01$). The mean years of education were significantly

higher in multiplex probands compared to simplex probands, respectively 15.2 and 13.9 ($p < 0.01$) (Table 1).

3.2. Simplex versus multiplex analysis

Compared to simplex probands, multiplex probands exhibited an earlier age of onset (mean: 13.7 years for simplex, 11.4 years for multiplex; $p < 0.01$). The Y-BOCS total score and DY-BOCS global score were not significantly different between the groups. However, multiplex probands had higher severity in the DY-BOCS dimensions of Sexual/Religious (mean: 3.9 for simplex, 4.7 for multiplex; $p < 0.01$) and Hoarding (mean: 2.7 for simplex, 3.6 for multiplex; $p < 0.01$). No significant differences were observed between the two groups regarding other DY-BOCS dimensions or Y-BOCS scores (Table 1).

The variable “number of psychiatric comorbidities”, which determines the total number of psychiatric comorbidities presented by the proband at the time of the interview, was not significantly different between the groups. The most common comorbid disorders in the whole sample were MDD, with frequencies of 64.5 % for simplex and 70.1 % for multiplex probands ($p = 0.065$), followed by GAD, with frequencies of 30.7 % for simplex and 36.6 % for multiplex probands ($p = 0.055$). However, multiplex probands had a higher frequency of OCRD comorbidity compared to simplex probands, respectively 29.5 % and 22.9 %, ($p = 0.023$) (Table 1). Furthermore, a higher prevalence of family history of psychiatric disorders, other than OCD, was found in the multiplex group (90 %) compared to the simplex group (83.6 %) ($p < 0.01$) (Table 1).

Finally, we performed a multiple logistic regression model using the statistically significant variables ($p < 0.05$) in the previous model, along with age and sex, as independent predictor variables. The following characteristics remained associated with multiplex probands: higher proportion of self-reported white race (OR: 1.71, $p < 0.01$), higher years of education (OR: 1.06, $p < 0.01$), earlier age of onset (OR: 0.96, $p = 0$), higher DY-BOCS Sexual/Religious severity score (OR: 1.03, $p = 0.011$), higher DY-BOCS Hoarding severity score (OR: 1.05, $p < 0.01$), increased OCRD comorbidities (OR: 1.41, $p = 0.018$) and higher prevalence family history of psychiatric disorders (OR: 1.77, $p < 0.01$). Self-reported black race was more prevalent in simplex probands (OR: 0.59, $p < 0.01$) (Table 2).

4. Discussion

This study investigated demographic and clinical variables associated with simplex ($n = 493$) and multiplex ($n = 501$) families of 994 Brazilian probands with OCD. Our findings suggest that OCD probands from multiplex families demonstrate several distinguishing characteristics compared to simplex OCD probands. These include an earlier onset of OCD symptoms, higher severity in the sexual/religious and hoarding symptom dimensions, a higher prevalence of OCRD, and a higher occurrence of psychiatric disorders in their family history.

To our knowledge, this is the first study to explore and compare demographic and clinical characteristics of simplex and multiplex probands with OCD. In our study, the overall sample primarily comprised of women and individuals of white race with similar

educational backgrounds, primarily at the high school level. The C-TOC collected data from seven sites located in three regions of Brazil (South, Southeast, and Northeast). Additionally, the study conducted by Miguel et al., using the same sample, revealed that the Northeast region had the lowest proportion of white patients, while the South and Southeast regions had a higher concentration of white patients (Miguel et al., 2008). Nevertheless, it is noteworthy that simplex families exhibited a higher representation of black probands and displayed a statistically significant difference in educational attainment. However, the specific interplay of these characteristics in the context of OCD remains largely uninvestigated.

OCD probands from multiplex families experienced their first symptoms at an earlier age than those from simplex families. These findings are in line with previous studies that have likewise observed associations between first-degree relatives affected by OCD and earlier age of OCD onset in the proband (Geller et al., 1998; Mataix-Cols et al., 2013; Nestadt et al., 2000).

Our analysis demonstrates a similar number of comorbidities for probands from simplex and multiplex families. However, our findings indicate that OCRD, particularly BDD, TTM, and skin-picking, were more prevalent in multiplex probands. Previous studies have established that OCD often co-occurs with related disorders (Bienvenu et al., 2000; Cullen et al., 2007; Frías et al., 2015; LaSalle et al., 2004; Strom et al., 2021; Tükel et al., 2002), however, our research is pioneering in showing that this comorbidity is more common in multiplex families than in simplex families. Consistent with our results, early onset (i.e., before 10 years of age) has been associated with a specific profile regarding concurrent psychiatric conditions, including tic disorders, TMM, and BDD (Hemmings et al., 2004; de Mathis et al., 2009).

Our findings suggest that multiplex probands are more likely to have a family history of other psychiatric disorders than simplex probands. Further studies are needed to better understand the relationship between simplex and multiplex OCD families and the presence of psychiatric comorbidities.

Our analysis did not find any evidence of differences between simplex and multiplex probands concerning the severity of OCD symptoms. However, the severity of sexual/religious and hoarding symptoms was higher in subjects from multiplex families. In line with this, consistent evidence from multiple genetic methodologies indicates that symptom dimensions may have distinct genetic architectures. For instance, investigations within multiplex families have demonstrated increased concordance among family members for the aggressive/sexual/religious, symmetry/ordering, and hoarding dimensions (Brakoulias et al., 2016; Leckman et al., 2003). In addition, family and twin studies have yielded divergent findings concerning the heritability of specific dimensions of OCD symptoms (Alemany-Navarro et al., 2020; Alsobrook et al., 1999; Brakoulias et al., 2016; Hasler et al., 2007; Leckman et al., 2003). Finally, genotyping 399 individuals with OCD, Alemany-Navarro et al. identified distinct biological pathways associated with the aggressive, ordering, sexual/religious, and hoarding dimensions, implying specific genetic mechanisms for each symptom dimension, with hoarding standing out (Alemany-Navarro et al., 2020).

This study addressed a critical gap in the OCD literature by extending a well-established family study methodology to populations previously overlooked in genetic studies. Zhang et al. found that high-income countries produce 88 % of psychiatric research, with the largest shares from the US (32.68 %), UK (8.59 %), Germany (6.77 %), Australia (5.87 %), and Canada (4.9 %). Middle-income countries contribute 12 %, while less than 1 % comes from low-income countries (Zhang et al., 2017). Challenges to the generalizability of psychological research persist due to an overreliance on Western, Educated, Industrialized, Rich, and Democratic (WEIRD) samples, despite efforts to enhance inclusive collaboration and address cultural diversity, authorship diversity, and reproducibility issues (Towards a Global Psychological Science, 2022). Therefore, this manuscript represents an initial step toward broader genetic research into OCD across diverse populations. Furthermore, despite the substantial progress in psychiatric genomics through GWAS studies, there remains a significant imbalance in subject representation, with approximately 78 % of participants having European ancestry, while only 1.3 % of GWAS samples originate from Latin America (Riehm et al., 2023; Sirugo et al., 2019; Cavazos and Witte, 2021). Recent studies show that including non-European subjects increases the number of risk genomic associations and contributes to the mapping of new risk genomic regions (Riehm et al., 2023). This has raised concerns, not only from an ethical perspective in medicine but also regarding scientific implications, as GWAS study findings may not be replicable in diverse populations. Furthermore, Latin America stands out for its population diversity, characterized by variations in allelic frequencies due to historical migration patterns, with Brazil being the most populous nation in the region (Ruiz-Linares et al., 2014; Fonseca et al., 2021). Thus, increasing studies characterizing the samples from these countries is of fundamental importance.

The primary limitation of our study is the indirect method used to obtain the psychiatric family history, rather than directly interviewing the family members themselves. We recognize that direct interviews are considered the gold standard for collecting clinical data in family studies. Nonetheless, prior research has not found statistically significant differences in the clinical data collected from relatives through direct versus indirect interviews (Rougemont-Buecking et al., 2008; Vandeleur et al., 2015). Additionally, it has been noted that individuals with a disorder tend to report familial occurrences of the same disorder (Vandeleur et al., 2015), which suggests direct interviews might yield more precise data. Despite this, we are confident that our method for collecting clinical data from relatives serves as a reasonably accurate approximation of the gold standard. Another limitation is related to the variability in the expression of comorbidities during the lifetime of OCD, which can change the classification of the types of families proposed in this study. In this sense, Yaryura-Tobias et al. (2000) reported a preferential temporal sequence of comorbid conditions in OCD over a person’s lifespan. According to those authors, it may be likely for an anxiety disorder, a mood disorder, an eating disorder, or a tic disorder to manifest first in patients who later develop a comorbid diagnosis. Furthermore, the periods when these symptoms begin may influence the clinical profile and progression of each disorder (Yaryura-Tobias et al., 2000). Despite the clinical importance of this topic, few studies have adopted a developmental perspective to investigate how the onset age of comorbid disorders affects the course and severity of OCD. A study using the same database as ours reported

that OCD is a heterogeneous disorder and that the presence of specific comorbid diagnoses predating the onset of OCD may affect its clinical manifestation (de Mathis et al., 2013).

In conclusion, these results underscore the necessity for more exhaustive genetic and phenotypic investigations to elucidate the origins of this clinical diversity in OCD. Moreover, our findings suggest that the type of family pedigree, whether simplex or multiplex, plays a crucial role in the phenotypic expression of OCD, and despite its significance, this factor is often omitted in genetic studies of OCD.

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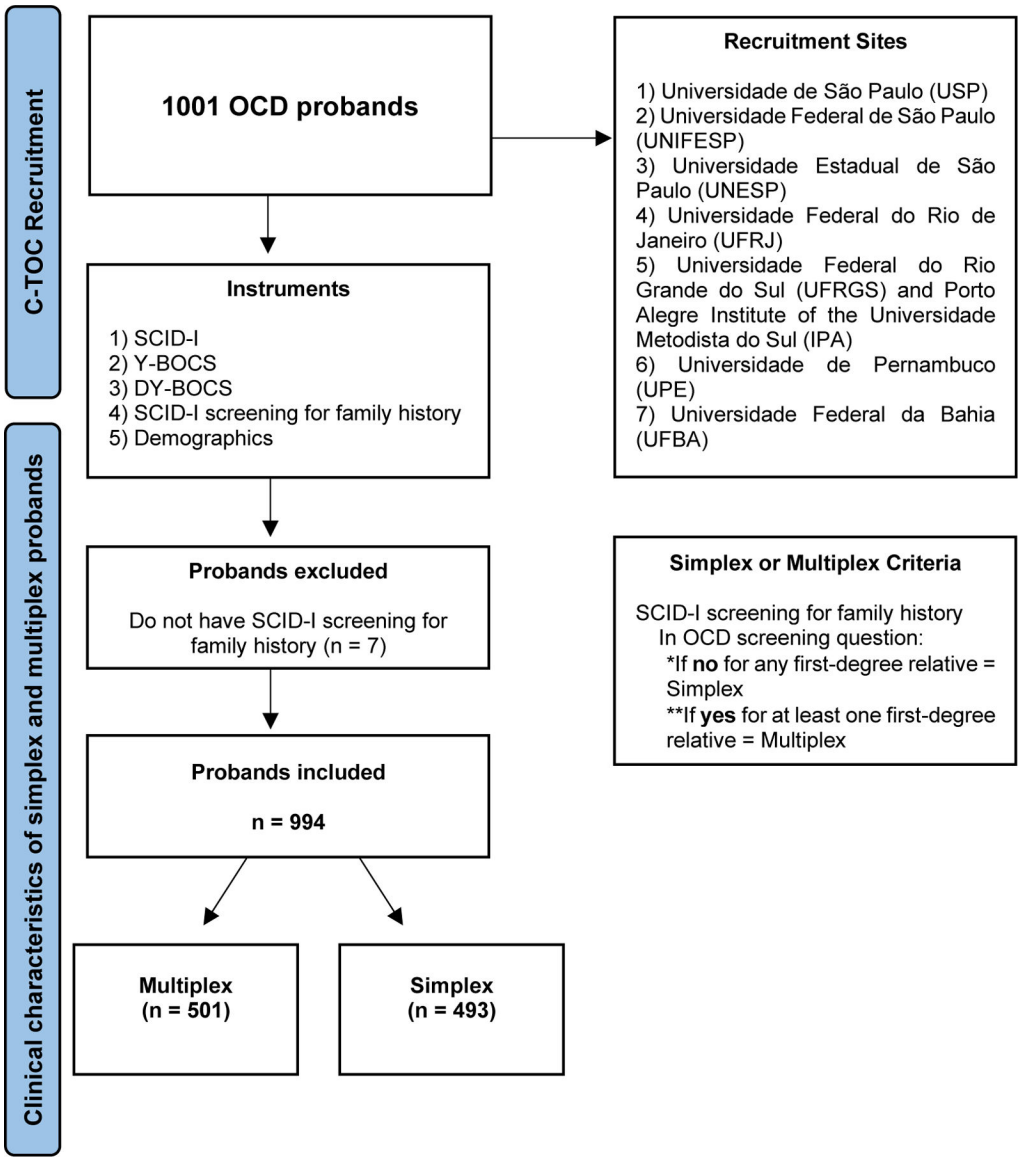

Fig. 1. Recruitment Flowchart

Illustrates the participant recruitment flow. A total of 994 probands with OCD were selected across seven recruitment sites, with inclusion criteria requiring a primary diagnosis of OCD, to be in treatment at one of the centers, and the ability to engage in the research protocol. Following the research protocol, involving interviews with five instruments (SCID-I, Y-BOCS, DY-BOCS, SCID-I screening, and Demographics), participants were categorized into simplex (n = 493) or multiplex (n = 501) families.

Table 1:

Sociodemographic characteristics and clinical features of probands

	Total (n = 994)	Simplex (n = 493)	Multiplex (n = 501)	OR	95% CI	p-value
Sociodemographic						
Age at assessment [mean years (SD)]	34.8 (13)	34.8 (13.3)	34.9 (12.7)	1.00	(0.99 – 1.01)	0.927
Sex (Women) [n (%)]	566 (56.9%)	271 (55%)	295 (58.9%)	1.18	(0.91 – 1.52)	0.214
Race (Black) [n (%)]	153 (15.4%)	93 (19.1%)	60 (12.2%)	0.59	(0.41 – 0.84)	<0.01
Years of Education [mean (SD)]	14.5 (4.9)	13.9 (4.6)	15.2 (5.2)	1.06	(1.03 – 1.09)	<0.01
Clinical Features						
Age of OCD Onset [mean years (SD)]	12.6 (7.5)	13.7 (7.8)	11.4 (6.6)	0.95	(0.93 – 0.97)	<0.01
OCD duration [mean years (SD)]	22.3 (13.6)	21 (13.6)	23.6 (12.7)	1.05	(1.03 – 1.07)	<0.01
Y-BOCS Total Score [mean (SD)]	25.5 (7.5)	25.4 (7.5)	25.7 (7.5)	1.00	(0.99 – 1.02)	0.634
DY-BOCS Global Score [mean (SD)]	21.1 (6.3)	20.9 (6.3)	21.4 (6.2)	1.01	(0.99 – 1.03)	0.327
DY-BOCS Aggressive Score [mean (SD)]	5.3 (4.9)	5.1 (5)	5.4 (4.9)	1.01	(0.99 – 1.04)	0.393
DY-BOCS Sexual/Religious Score [mean (SD)]	4.3 (4.9)	3.9 (4.8)	4.7 (5)	1.03	(1.01 – 1.06)	<0.01
DY-BOCS Symmetry Score [mean (SD)]	7.3 (4.6)	7.1 (4.7)	7.5 (4.6)	1.02	(0.99 – 1.04)	0.271
DY-BOCS Contamination Score [mean (SD)]	6.2 (5.1)	6 (5.2)	6.4 (5.1)	1.01	(0.99 – 1.04)	0.359
DY-BOCS Hoarding Score [mean (SD)]	3.1 (4.1)	2.7 (3.8)	3.6 (4.3)	1.05	(1.02 – 1.09)	<0.01
DY-BOCS Miscellaneous Score [mean (SD)]	7.5 (4.7)	7.5 (4.7)	7.6 (4.7)	1.00	(0.97 – 1.03)	0.906
Number of comorbidities [mean (SD)]	3.2 (2.6)	3.1 (2.5)	3.4 (2.6)	1.05	(1 – 1.1)	0.058
Major Depression Disorder (MDD) comorbidity [n (%)]	669 (67.3%)	318 (64.5%)	351 (70.1%)	1.29	(0.99 – 1.68)	0.065
Generalized Anxiety Disorder (GAD) comorbidity [n (%)]	333 (33.5%)	151 (30.7%)	182 (36.6%)	1.30	(0.99 – 1.69)	0.055
Social Phobia comorbidity [n (%)]	316 (31.8%)	156 (31.6%)	160 (31.9%)	1.02	(0.78 – 1.34)	0.858
Specific Phobia comorbidity [n (%)]	306 (30.8%)	158 (32.2%)	148 (29.6%)	0.87	(0.66 – 1.14)	0.320
Tics Disorder or TS comorbidity [n (%)]	186 (18.7%)	90 (18.3%)	96 (19.2%)	1.08	(0.78 – 1.49)	0.645
Post Traumatic Stress Disorder (PTSD) comorbidity [n (%)]	98 (9.8%)	55 (11.4%)	43 (8.9%)	0.74	(0.48 – 1.13)	0.161
OCRD comorbidity [n (%)]	261 (26.2%)	113 (22.9%)	148 (29.5%)	1.40	(1.05 – 1.87)	0.023
Family history of psychiatric disorders (excluding OCD) [n (%)]	863 (86.8%)	412 (83.6%)	451 (90%)	1.75	(1.20 – 2.57)	<0.01

SD: Standard deviation; OR: Odds Ratio / 95% CI: 95% Confidence Interval; p-values calculated using logistic regression

Table 2:

Multiple Logistic Regression Model

	OR	95% CI	p-value
Age	1.00	0.99 – 1.01	0.902
Sex (Women)	1.17	0.91 – 1.51	0.213
Race (White)	1.71	1.2 – 2.44	< 0.01
Years of education	1.06	1.03 – 1.08	< 0.01
Age of onset (in years)	0.96	0.94 – 0.97	0
DY-BOCS Sexual/Religious Score	1.03	1.01 – 1.06	0.011
DY-BOCS Hoarding Score	1.05	1.02 – 1.09	< 0.01
OCRD Comorbidity (Presence)	1.41	1.06 – 1.88	0.018
Family history of psychiatric disorders (excluding OCD)	1.77	1.22 – 2.6	< 0.01

OR: Odds Ratio / 95% CI: 95% Confidence Interval