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**Nível de *insight* em pacientes com transtorno obsessivo compulsivo: um estudo exploratório comparativo entre pacientes com “bom *insight*” e “*insight* pobre”**

Universidade Federal de Ciências da Saúde  
de Porto Alegre

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Orientador: Dr. Ygor Arzeno Ferrão

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**Nível de *insight* em pacientes com transtorno obsessivo compulsivo: um estudo exploratório comparativo entre pacientes com “bom *insight*” e “*insight* pobre”**

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## Dedicatória

Esse trabalho é dedicado a todos pacientes com transtorno obsessivo compulsivo que em algum momento do curso de sua doença suspeitaram ou afirmaram que seus pensamentos eram reais e que seus rituais eram necessários. Ou seja, esse trabalho é dedicado a todos aqueles que dão importância para seus pensamentos obsessivos. Espero que ao te compreender melhor possamos te ajudar a notar a fonte do seu sofrimento.

## **Agradecimentos**

Em uma iniciativa que já tem quase 20 anos, 1001 pacientes com transtorno obsessivo compulsivo foram avaliados em sete centros de pesquisa pelo Brasil. Existem amostras maiores pelo mundo, mas nenhum banco de dados possui tantas variáveis. Mais algumas descobertas surgem de um esforço coletivo para entender mais sobre transtorno obsessivo compulsivo (TOC). Esse trabalho é um resultado do esforço coletivo de muitos pesquisadores foram visionários quanto a investigação de fatores ligados ao TOC. Portanto, agradeço imensamente ao Consórcio Brasileiro de Pesquisa em Transtornos do Espectro Obsessivo-Compulsivo (C-TOC) e por todos seus integrantes.

De forma particular acredito que essa dissertação teve o envolvimento de muitos colegas do grupo de pesquisa, pois o incentivo e motivação transmitidas pelos meus pares me fizeram semanalmente compreender que algumas burocracias fazem parte do processo e que as dificuldades iriam passar em algum momento. Dentre esses colegas agradeço especialmente a M.e. Psic. Rafaella Landel de Moura Porto que gentilmente me aceitou como voluntário de pesquisa a muitos anos e me instigou a trabalhar com TOC.

Por fim, meu agradecimento mais sincero é destinado ao meu orientador, pois o Dr. Prof. Ygor é um orientador diferenciado, não somente pelo conhecimento em estatística e por ser um autor de renome internacional em periódicos. Mas, por ser um dos poucos que me deu algo sem pedir nada em troca, tanto na carreira acadêmica quanto na profissional. É recorrente que na sua humildade extrema o Prof. Ygor comente nas reuniões que ele é um mero trampolim para nós e que através dos contatos que ele possui nesses anos de pesquisa podemos alcançar novos voos. Contudo, duvido que alguém encontre um orientador tão bom quanto ele, por isso permanecerei sendo um dos pupilos desse indivíduo incrível.

## RESUMO

**Introdução:** *Insight* pode ser definido como a habilidade de perceber e avaliar a realidade externa e separá-la de seus aspectos subjetivos. Também se refere à capacidade de autoavaliar dificuldades e qualidades pessoais. O *insight* pode ser um preditor de sucesso no tratamento do transtorno obsessivo-compulsivo (TOC), de modo que indivíduos com *insight* insuficiente tendem a se tornar refratários ao tratamento. O objetivo deste estudo é investigar os fatores associados ao *insight* pobre em indivíduos com TOC.

**Método:** Este estudo transversal exploratório utilizou a *Brown Belief Assessment Scale* como parâmetro para a criação dos grupos de comparação: indivíduos que obtiveram pontuação nula (zero) compuseram o grupo com *insight* preservado ou bom (n = 148), e aqueles com pontuações acima do percentil 75% compuseram o grupo com *insight* ruim (n = 124); aqueles com pontuação intermediária foram excluídos. Características sociodemográficas e aspectos clínicos e psicopatológicos, intrínsecos e extrínsecos aos sintomas típicos do TOC, foram comparados em uma análise univariada. Uma regressão logística foi usada para determinar quais fatores associados ao julgamento crítico permaneceram significativos.

**Resultados:** Os indivíduos do grupo de *insight* pobre diferiram daqueles com bom *insight* em relação a: uso mais prevalente de neurolépticos (p = 0,05); maior intervalo de tempo não tratado (p <0,001); maior pontuação total na *Yale-Brown Obsessive Compulsive Scale* (YBOCS) e os fatores Obsessões e Compulsões (todos os fatores com p <0,001); maiores escores na escala dimensional de Yale-Brown Obsessive Compulsive Scale (DY-BOCS) (p de 0,04 a 0,001); maior prevalência das dimensões de sintomas de contaminação / limpeza (p = 0,006) e acúmulo (p <0,001); fenômenos sensoriais mais prevalentes (p = 0,023); níveis mais elevados de depressão (p = 0,007); e comorbidade mais prevalente com transtorno afetivo bipolar (p = 0,05) e transtorno de estresse pós-traumático (TEPT) (p = 0,04). Depois de analisar a regressão logística, concluímos que os fatores mais importantes associados ao *insight* insuficiente são: a presença de algum fenômeno sensorial (OR: 2,24), uso de neurolépticos (OR: 1,66) e sintomas de acumulação (OR: 1,15).

**Conclusão:** A variabilidade do *insight* em pacientes com TOC parece ser uma característica psicopatológica importante na diferenciação de possíveis subtipos de TOC, uma vez que o *insight* pobre está associado a fenômenos sensoriais e maior uso de neurolépticos, o que permite conjecturar o papel dos neurocircuitos dopaminérgicos na neurobiologia desta doença. Além disso, também há associação com os sintomas de acúmulo de conteúdo, reconhecidamente um dos conteúdos sintomáticos com menor resposta aos tratamentos convencionais do TOC. Estudos baseados em aspectos neurobiológicos, como neuroimagem e neuropsicologia, podem ajudar a elucidar de forma mais consistente o papel do *insight* em pacientes com TOC e as repercussões sobre os tratamentos disponíveis.

Palavras-chave: *insight*, crenças, transtorno obsessivo-compulsivo, fenômenos sensoriais, psicopatologia.



## ABSTRACT

**Introduction:** Insight may be defined as the ability to perceive and evaluate external reality and to separate it from its subjective aspects. It also refers to the ability to self-assess difficulties and personal qualities. Insight may be a predictor of success in the treatment of obsessive–compulsive disorder (OCD), so that individuals with poor insight tend to become refractory to treatment. The objective of this study is to investigate factors associated with poor insight in individuals with OCD.

**Methods:** This cross-sectional exploratory study used the Brown Belief Assessment Scale as a parameter for the creation of the comparison groups: individuals who obtained null scores (zero) composed the group with preserved or good insight ( $n = 148$ ), and those with scores above the 75% percentile composed the group with poor insight ( $n = 124$ ); those with intermediate scores were excluded. Sociodemographic characteristics and clinical and psychopathological aspects, intrinsic and extrinsic to the typical symptoms of OCD, were compared in a univariate analysis. A logistic regression was used to determine which factors associated with critical judgment remained significant.

**Results:** Individuals in the poor insight group differed from those with good insight in regard to: more prevalent use of neuroleptics ( $p = 0.05$ ); higher untreated time interval ( $p < 0.001$ ); higher total Yale–Brown obsessive–compulsive scale score and the obsessions and compulsions factors (all factors with  $p < 0.001$ ); higher dimensional Yale–Brown obsessive compulsive scale total and dimensional scores ( $p$  from 0.04 to 0.001); higher prevalence of contamination/cleaning ( $p = 0.006$ ) and hoarding ( $p < 0.001$ ) symptoms dimensions; more prevalent sensory phenomena ( $p = 0.023$ ); higher levels of depression ( $p = 0.007$ ); and more prevalent comorbidity with bipolar affective disorder ( $p = 0.05$ ) and post-traumatic stress disorder (PTSD) ( $p = 0.04$ ). After analyzing the logistic regression, we conclude that the most important factors associated with poor insight are: the presence of any sensory phenomena (OR: 2.24), use of neuroleptics (OR: 1.66), and hoarding symptoms (OR: 1.15).

**Conclusion:** The variability of insight in patients with OCD seems to be an important psychopathological characteristic in the differentiation of possible subtypes of OCD, since the poor insight is associated with sensory phenomena

and greater use of neuroleptics, which makes it possible to conjecture the role of dopaminergic neurocircuits in the neurobiology of this disorder. In addition, there is also an association with the symptoms of hoarding content, admittedly one of the symptomatic contents with less response to conventional OCD treatments. Studies based on neurobiological aspects such as neuroimaging and neuropsychology may help to elucidate more consistently the role of insight in patients with OCD and the repercussions concerning available treatments.

Keywords: insight, beliefs, obsessive–compulsive disorder, sensory phenomena, psychopathology

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Figura 1: algoritmo de tratamento para TOC;

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## LISTA DE ABREVIATURAS E SIGLAS

BABS	Escala de Avaliação de Crenças de Brown
BAI	Inventário de Ansiedade de Beck
BDI	Inventário de Depressão de Beck
BZD	Benzodiazepínicos
CTOC	Consórcio Brasileiro de Pesquisa em Transtornos do Espectro Obsessivo-Compulsivo
DSM 5	Manual de Diagnóstico e Estatístico de Transtornos Mentais 5. <sup>a</sup> edição
DYBOCS	Escala dimensional para a avaliação de presença e gravidade dos sintomas obsessivo-compulsivos
ISRS	Inibidor seletivo da recaptção da serotonina
PANAS	Escala de Afeto Positivo e Negativo
OR	Razão de chances
SCID-I DSM-IV	Entrevista Clínica Estruturada para Transtornos de Eixo I do DSM-IV
SOC	Sintomas obsessivo-compulsivos
TAB	Transtorno Afetivo Bipolar
TAG	Transtorno de Ansiedade Generalizada
TCC	Terapia Cognitivo Comportamental
TEPT	Transtorno do Estresse Pós-Traumático
THDA	Transtorno de hiperatividade e déficit de atenção
TOC	Transtorno Obsessivo Compulsivo
VIF	Fator de Inflação na Variância
Y-BOCS	Escala de Sintomas Obsessivo-Compulsivos de Yale-Brown

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## 1. INTRODUÇÃO

Como ajudar alguém que claramente precisa de auxílio, mas não consegue perceber o motivo? Pacientes com Transtorno Obsessivo Compulsivo (TOC) geralmente conseguem reconhecer que seus pensamentos são estranhos e invasivos, ou seja, reconhecem que há um problema. Contudo, uma parcela desses pacientes não consegue perceber que alguns dos seus comportamentos, privados ou não, fazem parte dos sintomas obsessivo compulsivos (SOC) (Jakubovski et al., 2011). Isso se torna um problema para o tratamento; quando o paciente não reconhece o seu sintoma como algo desadaptativo perde-se o propósito, para o paciente, de se realizar uma terapia de Exposição e Prevenção de Resposta (EPR) e/ou da adesão à medicação (Cordioli, 2014). Então, fica o questionamento: como ajudar alguém que tenha TOC, mas que tem uma percepção distorcida de seus sintomas, pois acredita que são “normais”? Logo, a caracterização de um paciente com pouca capacidade *insight* pode auxiliar no planejamento do tratamento de casos mais complexos.

Quando tentamos imaginar um paciente com *insight* ausente ou delirante que tenha TOC podemos fazer algumas suposições que nesse estudo se mostrarão corretas, ou não. A principal hipótese é de que o paciente com pouco ou nenhum *insight* tenha uma gravidade exacerbada em comparação a um paciente com boa qualidade desse especificador. Da mesma forma podemos supor que os níveis de ansiedade, depressão e suicidalidade são mais elevados nesses pacientes. Outra relação plausível é que o paciente com pouco *insight* possua mais comorbidades o que poderia predizer um prognóstico mais complicado que o de pacientes que possuam exclusivamente TOC. O fator mais interessante e que singulariza esse estudo de outros é a diferenciação das dimensões de SOC quanto a maior e menor capacidade de *insight* do paciente. Portanto, quando imaginamos que pacientes com sintomas que causam mais vergonha, das dimensões repugnantes do TOC (sexual, agressivo e religioso), teriam menos capacidade de reconhecer seus sintomas como parte do TOC e não de características pessoais, visto que muitos pacientes em consultório perguntam ativamente se podem vir a se tornarem psicopatas, agressores sexuais ou pecadores.

A literatura que relaciona TOC e *insight*, apesar de ser vasta é insuficiente quanto alguns fatores muito relevantes na prática clínica. Geralmente as amostras são pequenas ou possuem 'n' reduzido de pacientes com pouco ou nenhum *insight* além de apresentarem inadequações dos instrumentos utilizados para avaliar o especificador *insight* (Cherian et al, 2012;). Portanto, esse trabalho tem como propósito caracterizar um paciente com *insight* pobre ou ausente quanto a sua sintomatologia e fatores associados ao TOC, como qualidade de vida, histórico de tratamento, uso de medicações etc. Esse estudo só foi possível de ser elaborado graças ao esforço de muitos pesquisadores que montaram um dos maiores bancos de dados com pacientes que tenham TOC, logo, os dados coletados no passado continuam produzindo *insights* para o tratamento do TOC.

Em um estudo conduzido em um hospital da Índia Kishore, Samar, Reddy, Chandrasekhar & Thennarasu (2004) investigaram 100 pacientes com TOC com foco no uso de inibidores seletivos da recaptção da serotonina (ISRS) para o tratamento da patologia e uma melhora no *insight* dos participantes que foi medido pela 'Brown Assesmente Belief Scale (BABS)' utilizada para mensurar a capacidade de *insight* em pacientes com TOC (Eisen et al 1998). Um dos resultados desse estudo evidenciou que quanto maior o escore da BABS, ou seja, quanto menos *insight*, menor será a resposta ao tratamento. Em outro estudo (Visser et al, 2017) que buscou caracterizar os pacientes com pouco ou nenhum *insight* dentro de uma perspectiva naturalística se encontrou a evidência que a falta de *insight* está associada a uma maior gravidade, cronicidade e comorbidades, todos fatores para refratariedade nos tratamentos (Ferrão et al, 2007). Portanto, a investigação mais profunda de características associadas ao *insight* pobre, ou ausente/delirante, é fundamental para criarmos estratégias de tratamento e compreender uma parcela de indivíduos que terá suas peculiaridades no curso do TOC.

## **2. CONTEXTUALIZAÇÃO**

Classicamente, o termo "*insight*" é utilizado na psicanálise para ilustrar, no ambiente terapêutico, a compreensão súbita de alguma coisa ou situação, que envolve, de certa forma, a perspicácia ou a capacidade de aprender alguma coisa. Como foi apontado por David (1990) existem três componentes do *insight*, são *eles*: reconhecimento da própria doença, habilidade de reconhecer os



sintomas e cumprimento do tratamento. Portanto, é um conceito transdiagnóstico, aplicável a muitos transtornos psiquiátricos.

Como qualquer tema é comum pensarmos em *insight* e logo lembrarmos do extremo, ou seja, pacientes que têm uma completa ausência de crítica quanto a sua condição. Para aqueles que trabalham com psicopatologia é comum associar a pacientes psicóticos. Contudo, Konstantakopoulos, G. (2019) desmistifica em um texto breve o que alguns profissionais de saúde mental já sabem, *insight* não é um fator associado somente a delírios e alucinações, ou restrito aos transtornos psicóticos. Pois, nas últimas décadas tem se estudado em diferentes contextos, inclusive nos supracitados, a capacidade de *insight* de um indivíduo.

Dentre os autores que se debruçaram no estudo do *insight* nas psicopatologias se destaca o trabalho de Brakoulias et al, 2011 que revisou o conceito de *insight* a partir dos instrumentos de avaliação, como a OVIS e a BABS\*, utilizados nos diagnósticos complementares de TOC. Logo, os autores construíram uma escala própria para avaliação de crenças centrais/*insight* para o TOC a partir de subfatores estatisticamente relevantes de escalas mais antigas, ficando com os seguintes componentes para escala e conceitualização teórica de *insight*: convicção, rigidez, flutuação, resistência e consciência de que a crença é irracional (Brakoulias et al,2018). Essa escala ainda não é traduzida e validada para o português, mas está em fase inicial do projeto.

Apesar de não ser a única relação de psicopatologias e *insight*, há vasta literatura sobre esse fator em pacientes com transtornos psicóticos, como Esquizofrenia e Transtornos Delirantes ou Transtorno Bipolar. Em um estudo em que a principal variável estudada foi o *insight* de pacientes esquizofrênicos que foram submetidos a um tratamento com risperidona injetável de longa duração, os resultados sugerem que a capacidade de *insight* aumenta conforme a resposta ao tratamento, o que pode ser visto como consequência de melhor reconhecimento dos sintomas e da patologia (Wiffen et al., 2010). Resultados semelhantes são apresentados em outro estudo (Alenius et al., 2010) em que dois grupos de pacientes diagnosticados com esquizofrenia diferiram na capacidade de *insight*, pois o grupo com melhores condições clínicas mostrou maior capacidade de julgamento frente à própria doença ( $p < 0,001$ ) e um maior

reconhecimento do que deve ser feito frente aos sinais de alerta da doença ( $p=0,046$ ). Um resultado semelhante foi encontrado em uma pesquisa com pacientes com Esquizofrenia ou Transtorno Esquizoafetivo que haviam cometido crimes (Buckley et al., 2004), pois apresentaram uma pior capacidade *insight* frente à própria patologia ( $p<0,001$ ). Nos transtornos psicóticos, o *insight* pré-mórbido parece ter papel preditivo para o aparecimento dos primeiros sintomas psicóticos 4 anos após a avaliação do *insight* (auto-reflexão) (O'Connor et al., 2017).

Pacientes com esquizofrenia (Hill et al. 2010) que não aderiram ao tratamento depois de quatro anos apresentaram piores escores na Escala de Afeto Positivo e Negativo (PANAS), principalmente no que se refere a falta de julgamento e *insight* ( $P<0,01$ ). Da mesma forma, um outro estudo com pacientes com Transtorno Bipolar (Gonzalez-Pinto et al., 2010) mostrou associação entre capacidade preservada de *insight* e bom prognóstico ( $P<0,001$ ). Como exemplo, ao se comparar os motivos da não adesão ao tratamento de três grupos de pacientes em que dois grupos eram compostos por pacientes (dois grupos de pacientes com Transtorno Bipolar e um grupo de esquizofrênicos), descobriu-se que o grupo com pacientes com esquizofrênicos apresentou pior adesão aos medicamentos (Levin et al., 2014).

A capacidade de julgamento, ou a falta dela, não é restrita a situações relacionadas à esquizofrenia ou transtorno bipolar. Em um estudo sobre suicídio (Silva et al., 2017) os autores encontraram como resultado que o nível de *insight* é menor naqueles pacientes que tentaram suicídio previamente ( $p=0,012$ ) e que possuíam uma maior gravidade de sintomas depressivos ( $p=0,012$ ). Condições neurológicas, apesar de pouco frequentemente serem estudadas em relação ao juízo crítico, podem apresentar pior capacidade de *insight*, como o que ocorre em pacientes com Esclerose lateral Amiotrófica e/ou Demência Frontotemporal, onde os comportamentos investigados (p.ex: consciência da patologia) dos indivíduos que possuem ambas condições apresentam pior capacidade de *insight*, aumentando a possibilidade de um constituinte neurobiológico para o *insight* (Wooley et al., 2010).

O TOC, por sua vez, é caracterizado por obsessões (pensamentos, imagens ou impulsos intrusivos que causam desconforto emocional) e compulsões (comportamentos realizados para diminuir ou cessar o desconforto criado pelas obsessões) (APA, 2014; OMS, 1994). Conforme o Manual Diagnóstico e Estatístico de Transtornos Mentais 5.<sup>a</sup> edição (DSM 5) dois especificadores devem ser analisados para realizar-se o diagnóstico, sendo que um deles é a presença de tiques e o outro é a capacidade de *insight*, classificada em três variáveis categóricas (com *insight* bom ou razoável, com *insight* pobre e com *insight* ausente/crenças delirantes).

Conforme o DSM 5 para se diagnosticar TOC é necessário presença de obsessões, compulsões ou ambas; sendo que obsessões são definidas pelo mesmo manual como:

*1. Pensamentos, impulsos ou imagens recorrentes e persistentes que, em algum momento durante a perturbação, são experimentados como intrusivos e indesejados e que, na maioria dos indivíduos, causam acentuada ansiedade ou sofrimento.*

*2. O indivíduo tenta ignorar ou suprimir tais pensamentos, impulsos ou imagens ou neutralizá-los com algum outro pensamento ou ação.*

(APA, 2014)

Já as compulsões são definidas como:

*1. Comportamentos repetitivos (p. ex., lavar as mãos, organizar, verificar) ou atos mentais (p. ex., orar, contar ou repetir palavras em silêncio) que o indivíduo se sente compelido a executar em resposta a uma obsessão ou de acordo com regras que devem ser rigidamente aplicadas.*

*2. Os comportamentos ou os atos mentais visam prevenir ou reduzir a ansiedade ou o sofrimento ou evitar algum evento ou situação temida; entretanto, esses comportamentos ou atos mentais não têm uma conexão realista com o que visam neutralizar ou evitar ou são claramente excessivos.*

(APA, 2014)

Além desse primeiro critério que define os sintomas mais básicos do TOC o manual lembra que as obsessões e/ou compulsões tomam tempo, causam sofrimento ou prejuízo em áreas importantes da vida (critério B). Também é salientado que os SOC não são mais bem explicados por outra condição (critério C e D).

Para se fazer um diagnóstico completo de TOC é necessário especificar se a presença de tiques e a capacidade de *insight* do paciente. Dentro dessa dissertação *insight* pobre pode ser lido como sinônimo de *insight* ruim. Conforme o DSM 5 devemos especificar a patologia do indivíduo em:

- *Insight bom ou razoável: O indivíduo reconhece que as crenças do transtorno obsessivo compulsivo são definitivas ou provavelmente não verdadeiras ou que podem ou não ser verdadeiras.*
- *Insight pobre: O indivíduo acredita que as crenças do transtorno obsessivo-compulsivo são provavelmente verdadeiras.*
- *Insight ausente/crenças delirantes: O indivíduo está completamente convencido de que as crenças do transtorno obsessivo-compulsivo são verdadeiras.*

(APA, 2014)

O TOC é classicamente tido como a patologia em que as obsessões e compulsões compõe a sintomatologia principal. Contudo, nem sempre fatores cognitivos ou comportamentais estão associados exclusivamente ao TOC, pois alguns pacientes relatam sintomas que se aproximam menos do cognitivo e mais do sensorial. Como Stein et al (2016) propõe, elementos de outras ordens, afetiva e sensorial, deveriam compor uma nova classificação proposta pela CID-11.

Pacientes com características que preencheriam critério para Transtorno Obsessivo Compulsivo (TOC) que não tem, ou tem pouca, capacidade de perceber, ou que não conseguem interromper suas obsessões e/ou compulsões mostram pior prognóstico (Raffin et al., 2008) e podem ser classificados como resistentes aos tratamentos considerados padrão-ouro, como: Inibidores Seletivos da Recaptação da Serotonina (Katzman et al., 2014; Reddy et al., 2017; Baldwin et al., 2014; Fineberg et al., 2015) e Terapia Cognitivo Comportamental (TCC), especialmente a técnica de exposição e prevenção de resposta (Raffin et al., 2008; Reddy et al., 2017; Blakey et al., 2017). Um dos preditores para refratariedade de tratamento no TOC é o *insight* (Raffin et al., 2008), portanto, o paciente estar consciente do seu problema e dos seus sintomas é um fator a ser trabalhado em uma etapa pré-tratamento, prévio a realização da Exposição e Prevenção de Resposta (EPR), técnica consagrada para tratamento do TOC (Lindsay, Crino & Andrews, 1997; NICE, 2005; Katzman et al, 2014; Hezel & Simpson, 2019). Contudo, se o paciente não percebe seus comportamentos como parte de sua sintomatologia o prognóstico tende a ser ruim (Cordioli, 2014; Lochner & Stein, 2003).

O tratamento para TOC não é exclusivamente psicológico. Pois, alguns *guidelines* propõe que o tratamento combinado, TCC e psicofármacos, potencializa a redução de SOC. Na Figura X, logo abaixo está o algoritmo de tratamento proposto no livro Psicofármacos (Cordioli, Gallois & Isolan, 2015).

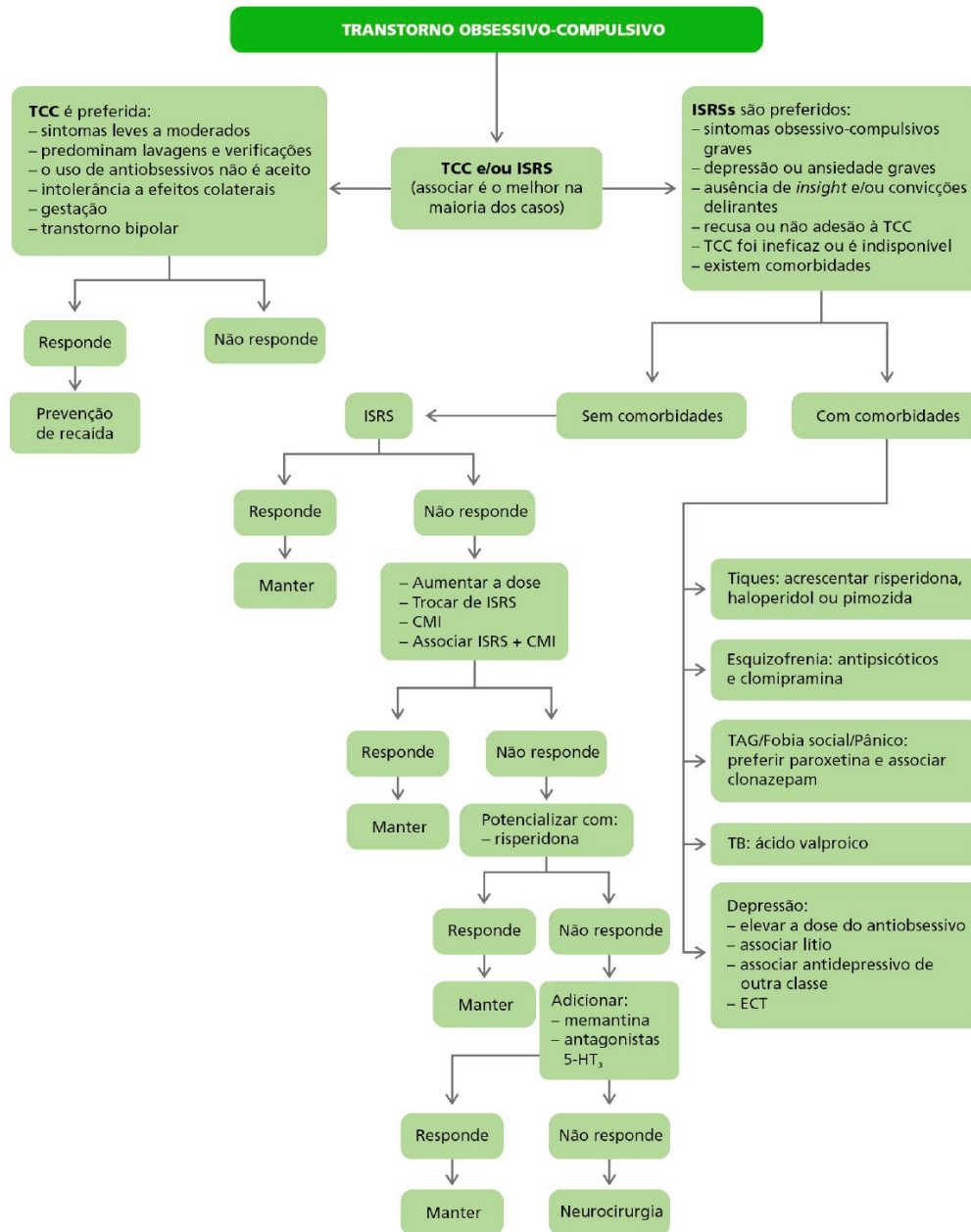


Figura 1: algoritmo de tratamento para TOC; retirado do livro *Psicofármacos: Consulta Rápida*

O paciente com TOC, classicamente, é considerado como tendo um bom nível de crítica em relação aos seus sintomas. Contudo, cerca de um quarto dos pacientes com TOC não possuem crítica alguma em relação aos seus sintomas e sua patologia. (Kashyap et al., 2015; Jakubovski et al., 2011; Catapano et al.,

2010). Esses pacientes podem se acomodar aos seus sintomas e levar mais tempo para procurar tratamento, o que associaria o *insight* pobre à maior duração da doença ou maior tempo sem tratamento, sendo que todos esses fatores são preditores negativos para o processo terapêutico do TOC (Raffin et al., 2008). O paciente com TOC, em geral, entende seus sintomas como egodistônicos, ou seja, possuem capacidade de discernir e compreender que seus pensamentos não são reais (Couto et al., 2010), mas nem todos conseguem fazer essa diferenciação.

O TOC em si é um transtorno muito heterogêneo devido a diversidade de sintomas (Bragdom & Coles, 2017; Couto, Rodrigues, Vivan & Kristensen, 2010; Hasler et al, 2005), mas, mesmo entre aqueles que possuem os mesmos sintomas a apresentação da patologia pode ser diferente graças as classificações de *insight* citadas anteriormente. Por exemplo, pacientes com sintomas de checagem podem perceber seus sintomas (será que apaguei a chama do fogão) vêm de uma vulnerabilidade do TOC e mesmo assim retornar para diminuir a ansiedade. Outro paciente com a mesma apresentação de sintomas pode achar absolutamente normal e adaptativo retornar por sete vezes seguidas alguns quilômetros do trabalho até em casa para verificar os mesmos elementos. Ou seja, a consciência sobre a falta de sentido em uma obsessão é o que podemos definir como boa capacidade de *insight*.

Uma das principais dificuldades do psicólogo clínico ou do psiquiatra no momento do diagnóstico é especificar a capacidade de *insight* do paciente, pois a entrevista estruturada diagnóstica para transtornos mentais segundo o DSM-5, ou seja, a SCID-5 versão clínica (First, Williams, Karg & Spitzer) não inclui os especificadores como critérios. Portanto, fica como responsabilidade do clínico responder qualitativamente se o paciente apresenta ou apresentou tiques e a capacidade de *insight*. Dentre os instrumentos mais utilizados para avaliar gravidade do TOC estão a questão doze da *Yale-Brown Obsessive-Compulsive Scale* (YBOCS) e *Brown Assessment of Beliefs Scale* (BABS) que medem a capacidade de insight do paciente. Ambas escalas são usadas em pesquisa com alguma amplitude para se avaliar a capacidade de insight.

Para contornar esse problema avaliativo alguns autores propuseram escalas e instrumentos que avaliassem a capacidade de *insight* do paciente com

TOC. Em um artigo de revisão bibliográfica os autores (Brakoulias & Starcevic, 2011) propuseram que a maioria desses instrumentos não avaliava *insight* propriamente dito, pois, a proporção desse especificador estaria melhor descrita como ‘crença’ que pode ser adaptativa ou desadaptativa. Esse conceito em si traz o benefício de nos libertarmos da associação por ... do termo *insight* com a psicanálise, que define na sua definição coloca esse constructo como algo espontâneo e pouco mensurável. Nessa revisão os autores comparam cinco instrumentos e suas características de conceitualização em uma tabela que pode ser vista abaixo como FIGURA 2:

Características propostas de crenças no TOC e suas conceitualizações alternativas					
Características propostas relacionadas ao TOC	Basoglu et al. [16]	Lelliot et al. [6]	Foa and Kozak [5] (Fixity of Beliefs Scale)	Eisen et al. [18] (BABS)	Neziroglu et al. [19] (OVIS)
Convicção		X; força <sup>a</sup>	Certeza <sup>a</sup>	X	Força <sup>a</sup>
Rigidez					X
Flutuação	X	Rigidez <sup>b</sup>	Flexibilidade <sup>a</sup>	X	Mudança na força <sup>a</sup>
Resistência		X		Tentativas de refutar a crença	Força da resistência <sup>a</sup>
Insight (1) Conscientização da imprecisão da crença (2) Capacidade de atribuir crença a uma doença (TOC)			Compreensão do porque eles tem a crença <sup>a</sup>	Reconhecimento de que o crença tem uma causa psiquiátrica / psicológica <sup>a</sup>	X; Razoabilidade <sup>a</sup> ; Insight sobre a doença / psicológico ser um problema <sup>a</sup>

X Os mesmos termos, como propostos neste artigo, são utilizados pelos respectivos autores  
a Termos semelhantes, sobrepostos e / ou alternativos usados por diferentes autores  
b De acordo com Lelliot et al. [6], rigidez se refere à força, explicação das visões opostas e convicção dos outros

Figura 2: adaptado de 'Brakoulias, V., & Starcevic, V. (2011).

O diagnóstico de TOC pode parecer relativamente simples quando olhamos somente para os elementos que compõe o nome do transtorno. Contudo, um erro comum é confundir um TOC com *insight* pobre ou delirante com um transtorno psicótico devido a apresentação semelhante das crenças desses pacientes (Stein et al, 2016; Brakoulias & Starcevic, 2011). Portanto, um diagnóstico errado pode conduzir a um tratamento inadequado e aumentar o fator preditor de mal prognóstico de tratamento, anos sem tratamento adequado (Raffin, Ferrão, Souza & Cordioli, 2008). Logo, compreender como o *insight*

dentro dos SOC influencia pode trazer alguma luz para o tratamento de pacientes que acabariam retornando para o tratamento de TOC depois de se tornarem refratários em outros tratamentos não específicos para seus problemas.

Alguns grupos de pesquisa se empenham para descobrir algumas relações sobre o assunto. Entre os achados há um estudo conduzido na Índia (Cherian et al, 2012) com 545 pacientes encontrou-se que a dimensão de contaminação ( $p = 0,007$ ) e a pontuação total da Y-BOCS, ou seja, a gravidade total do TOC, estariam associados a um *insight* pobre. Apesar de corroborar com os resultados esse estudo apresenta alguns problemas, pois dos 545 participantes apenas 47 tinha *insight* pobre ou ausente, sendo que a avaliação desse fator foi feita pelo item 11 da Mini Mental, ou seja, um instrumento de rastreio e não específico para *insight*. Além disso, os autores forçam a interpretação dos resultados ao afirmarem que houve diferença entre os grupos, mesmo que a análise estatística não possa comprovar isso.

Quanto a tratamentos que focam na melhora do *insight* – estudo de Eisen, 2001; estudo com sertralina que demonstrou que os pacientes conforme se tratam melhoram sua capacidade de *insight*; portanto, a YBOCS correu em paralelo com a BABS e o uso de sertralina foi igual para os grupos estudados. O estudo de Alonso (2008) 132 pacientes com TOC foram avaliados antes e depois do tratamento com sertralina em que a principal variável do estudo era *insight*. Dessa amostra um pouco menos de 30% dos participantes tinham um *insight* pobre ou delirante. Assim como no artigo desenvolvido para essa dissertação o instrumento avaliativo utilizado foi a BABS e os autores encontraram que sintomas depressivos estão associados à falta de *insight* assim como transtornos comorbidos de personalidade. Contudo, o tratamento não apresentou diferença entre os grupos estudados.

Desta forma, a investigação de fatores associados ao *insight* em pacientes com TOC pode auxiliar na compreensão da psicopatologia e em possíveis preditores de respostas aos tratamentos convencionais. A literatura científica é escassa em tentar avaliar a psicopatologia detalhada do *insight* em grandes amostras de pacientes com TOC.



### 3. OBJETIVOS

#### Objetivo Geral:

Avaliar a relação entre sintomas obsessivos compulsivos (SOC) e *insight*.

#### Objetivos específicos:

- a) Avaliar a relação entre o conteúdo dos SOC e o nível de *insight*
- b) Avaliar a gravidade dos SOC e o nível de *insight*
- c) Avaliar fatores sociodemográficos relacionados ao nível de *insight*, como: idade, anos estudados, gênero, ocupação e classificação socioeconômica
- d) Avaliar se tratamento psicológico e medicamentoso se relacionam ao nível de *insight*.
- e) Avaliar fatores intrínsecos ao TOC que influenciam ou são influenciados pelo nível de *insight*, como: tempo sem tratamento, idade de início dos sintomas, gravidade e presença dos fenômenos sensoriais\* e histórico familiar de TOC.
- f) Avaliar fatores extrínsecos ao TOC influenciando no nível de *insight*, como: sintomas depressivos, sintomas ansiosos, suicidalidade e comorbidades.

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## 5. ARTIGO

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# Level of Insight in Patients With Obsessive–Compulsive Disorder: An Exploratory Comparative Study Between Patients With “Good Insight” and “Poor Insight”

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**Introduction:** Insight may be defined as the ability to perceive and evaluate external reality and to separate it from its subjective aspects. It also refers to the ability to self-assess difficulties and personal qualities. Insight may be a predictor of success in the treatment of obsessive–compulsive disorder (OCD), so that individuals with poor insight tend to become refractory to treatment. The objective of this study is to investigate factors associated with poor insight in individuals with OCD.

**Methods:** This cross-sectional exploratory study used the Brown Belief Assessment Scale as a parameter for the creation of the comparison groups: individuals who obtained null scores (zero) composed the group with preserved or good insight ( $n = 148$ ), and those with scores above the 75% percentile composed the group with poor insight ( $n = 124$ ); those with intermediate scores were excluded. Sociodemographic characteristics and clinical and psychopathological aspects, intrinsic and extrinsic to the typical symptoms of OCD, were compared in a univariate analysis. A logistic regression was used to determine which factors associated with critical judgment remained significant.

**Results:** Individuals in the poor insight group differed from those with good insight in regard to: more prevalent use of neuroleptics ( $p = 0.05$ ); higher untreated time interval ( $p < 0.001$ ); higher total Yale–Brown obsessive–compulsive scale score and the obsessions and compulsions factors (all factors with  $p < 0.001$ ); higher dimensional Yale–Brown obsessive–compulsive scale total and dimensional scores ( $p$  from 0.04 to 0.001); higher prevalence of contamination/cleaning ( $p = 0.006$ ) and hoarding ( $p < 0.001$ ) symptoms dimensions; more prevalent sensory phenomena ( $p = 0.023$ ); higher levels of depression ( $p = 0.007$ ); and more prevalent comorbidity with bipolar affective disorder ( $p = 0.05$ ) and post-traumatic stress disorder (PTSD) ( $p = 0.04$ ). After analyzing the logistic regression, we conclude that the most

important factors associated with poor insight are: the presence of any sensory phenomena (OR: 2.24), use of neuroleptics (OR: 1.66), and hoarding symptoms (OR: 1.15).

**Conclusion:** The variability of insight in patients with OCD seems to be an important psychopathological characteristic in the differentiation of possible subtypes of OCD, since the poor insight is associated with sensory phenomena and greater use of neuroleptics, which makes it possible to conjecture the role of dopaminergic neurocircuits in the neurobiology of this disorder. In addition, there is also an association with the symptoms of hoarding content, admittedly one of the symptomatic contents with less response to conventional OCD treatments. Studies based on neurobiological aspects such as neuroimaging and neuropsychology may help to elucidate more consistently the role of insight in patients with OCD and the repercussions concerning available treatments.

**Keywords:** insight, beliefs, obsessive-compulsive disorder, sensory phenomena, psychopathology

## INTRODUCTION

“Poor insight,” or the deficit of the capacity of judgment, is usually associated with intellectual cognitive poverty, and it may decrease the capacity of evaluation of the reality despite evidence to the contrary (1). The process may be similar to that in delirium (2, 3), overvalued ideas (4), obsessions (5), or even in regular beliefs or automatic thoughts in people without a psychiatric diagnosis (6). Classically, the term “insight” is used in psychoanalysis to illustrate, in the therapeutic environment, the sudden understanding of something or some situation, which involves, in a certain way, the capacity to learn something. “Insight” can also be defined as the convergence of several judgments that lead the individual to the conclusion of a problem by non-means (7, 8), or “a form of evaluation and perception of internal power” or “a capacity for selection and prediction of consequences” (9, 10). Its function is self-evaluation, as it is able to measure difficulties and qualities (11). “Poor insight” means not understanding, perhaps even questioning, what is being done in a given situation (whether right or wrong, if appropriate or not). According to David, the concept of insight comprises three components characterized by: 1) recognition of the disease itself, 2) the ability to recognize symptoms, and 3) compliance with treatment. It is a transdiagnostic concept, applicable to many psychiatric disorders (12).

There is extensive literature on insight in patients with psychotic disorders, such as schizophrenia, delusional disorders, bipolar disorder, suicidal behavior, and neurological conditions (13–21), specially neuroimaging studies that show correlation of insight level and some brain structures as: dorsal precentral and postcentral gyri, dorsal frontal and parietal cortices (22), and ventrolateral prefrontal cortex (23), which allow us to conjecture the possibility of a neurobiological constituent for insight, especially a network of frontal, temporal, and parietal brain regions (23–25), including posterior insula as a main network node (26).

Obsessive-compulsive disorder (OCD), on the other hand, is characterized by obsessions (thoughts, images, or intrusive impulses that cause emotional discomfort) and compulsions (behaviors performed to diminish or deal with the discomfort created by obsessions) (27, 28). The OCD patient is classically considered to

have a good level of insight regarding their symptoms. The OCD patient, in general, understands their symptoms as ego-dystonic, that is, impulses, wishes, or thoughts that are unacceptable or repugnant to the ego or self (29), leading patients to realize that the obsession is totally contrary to the patients’ wishes and desires. Therefore, people with OCD are aware that their behaviors are abnormal and responding to their compulsions causes them anxiety and distress. It is very common, meanwhile, that at the exact time of the obsession/compulsion occurrence, patients present an oscillatory conviction (doubt) about the nature (true or false) of the obsession, resulting again in anxiety and distress (30). Thus, patients with OCD may present diverse psychopathological features regarding levels of insight, ego dystonicity and conviction about their own symptoms. The similarity, inconsistency, complexity, and/or overlapping of the cited conceptual constructs (and others, as “beliefs,” “overvalued ideas,” and even “delusional thoughts”) (8, 31–34) have led researchers to confound the cited concepts and to use these terms very loosely, since adequate instruments to assess them are not often used.

Therefore, the gap in the knowledge of the concept and the influence of insight on patients with OCD have been generating efforts to understand and to measure this psychopathological construct, resulting in the fact that its role in psychiatric disorders is being increasingly recognized. Recently, the *Diagnostic and Statistical Manual of Mental Disorders, 5th edition* (27) included two specifiers for OCD diagnosis: the presence of tics and, precisely, the level of insight, which may be classified in “good or fair” insight, “poor insight,” and “absent” insight/delusional beliefs. Insight in this context refers to construct regarding the reasonableness of one’s belief, not in relation to whether one believes that they have OCD, or whether they believe in receiving treatment.

To better highlight the importance of the topic (and also to illustrate the heterogeneity of how it has been approached), 4% to 36% of OCD patients have poor or no insight about their symptoms and their pathology (8, 35–38). This poor insight subset of patients can accommodate their symptoms and take more time to seek treatment, which would associate poor insight with longer duration of illness or longer time without treatment,

all of which are negative predictors for the therapeutic process of OCD, showing a worse prognosis (8, 35, 39–46).

Thus, the investigation of factors associated with poor insight in patients with OCD may help to understand some psychopathological and neurobiological aspects and to predict the response to the current conventional treatments. Therefore, the objective of this exploratory study is to verify the association of the level of insight (to a greater or lesser degree) with a great number of clinical variables in patients with OCD. Not only the presence, but also the severity of the obsessive–compulsive symptoms (OCS) content dimensions according to the dimensional Yale–Brown obsessive–compulsive scale (DY-BOCS) and sensory phenomena were evaluated. Instead of using only the Yale–Brown obsessive–compulsive scale (Y-BOCS) (45) item for insight, we assessed the presence and severity of insight with a specific instrument: the Brown assessment beliefs scale (BABS) (32). Thereby, according to the literature and to our clinical experience, we hypothesize that OCD patients with poor insight will present: earlier age of onset of obsessive–compulsive symptoms (OCS) (47, 48), longer duration of illness (8, 39, 48), higher prevalence of familial history of OCD (49), higher prevalence of neuroleptics prescription (50), higher prevalence of suicidality, more common presence and higher severity of specific OCS content [especially for contamination/washing/cleaning (51) and hoarding (36, 47, 52)], higher prevalence of any sensory phenomena (53), higher severity of depressive (54) and anxious symptoms, and higher prevalence of specific comorbid psychiatric disorders [especially major depression (47, 48), dysthymia (55), bipolar disorder (56), and delusional disorder (57)].

## MATERIALS AND METHODS

This is a cross-sectional study with the 1,001 patients database of the Brazilian Consortium for Research on Obsessive–Compulsive Spectrum Disorders (CTOC) (58), which collected data between 2003 and 2008 in seven research centers in three different Brazilian regions. The inclusion criteria for the study were: being in treatment at one of the research centers, fulfilled criteria for OCD according to the *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* (DSM-IV) and confirmed by structured clinical interview, and being able to understand and participate in the research protocol. Comorbid diagnosis of schizophrenia was excluded. The sources of recruitment of the participants were public and private psychiatric outpatient and inpatients services. Further methodological detail (as who have performed the assessment and interrater reliability) is described in Miguel et al. (58). The present study was submitted and approved by the ethics committees of the centers previously involved (USP-968/05; IPA-6600023; UFRGS-06/171; Unifesp-302/2006).

## Instruments

**A. Sociodemographic and clinical questionnaire of the Brazilian Consortium for Research on Obsessive–Compulsive Spectrum Disorders (CTOC):** This

questionnaire was created by the CTOC researchers as an initial instrument in which sociodemographic, socioeconomic data, medical history data, and a semi-structured interview on family psychiatric history were used to characterize each individual. Therefore, basic information was collected: age, weight, height, economic class, naturalness, marital status, number of children, origin, number of people living with, religion, education, others. A general medical history is also questioned in addition to the psychiatric history, which details the medications already used and the resulting effects, as well as variables related to suicidality (ideation, plan, attempt, hospitalization due to, and familial history) and other treatments, such as psychotherapy.

- B. Structured clinical interview for DSM-IV axis I disorders, research version:** DSM-IV structured interview for personality disorders. Not yet validated for DSM 5 in Brazilian Portuguese. These semi-structured interviews were used as a screening tool to assess the presence or not of OCD and psychiatric comorbidities (59).
- C. Yale–Brown obsessive–compulsive symptom scale (Y-BOCS):** This scale has 10 items, five for obsession evaluation and five for compulsion assessment. Each item can be answered by the individual on a scale of 0 (nonlinear or less pathological) to 4 (delirious or more pathological). This scale provides three scores: severity of obsessions, severity of compulsions, and total severity of OCD (45).
- D. Dimensional scale for the assessment of the presence and severity of obsessive–compulsive symptoms (DY-BOCS):** This scale is composed of six subscales according to the content of OCS (1—aggression, violence, and natural disasters; 2—sexual and religious; 3—symmetry, order, counting, and arrangement; 4—contamination, cleaning, and washing; 5—accumulation; and 6—miscellaneous content), also generating a total score of symptoms. It also has a list of symptoms (88 items), for each of the abovementioned thematic dimensions (60). The Miscellanea dimension was not evaluated in this work because it is a very heterogeneous dimension, with symptoms such as concern for diseases, magic numbers, among others, which did not add to the other factors in factorial analysis.
- E. Sensory phenomena scale of the University of São Paulo:** sensory phenomena are sensory experiences or subjective sensations, such as feelings of incompleteness, urgency, or “having to do until you feel it is right,” that precede repetitive behaviors such as tics or compulsions (61). They do not obey the logic of an obsessive thought, because they are not cognitive phenomena, but can generate anxiety and can be neutralized by behaviors, gestures, or tics. This scale was created to measure the severity of sensory phenomena occurring before or during the performance of repetitive behaviors. This scale is divided into two parts. The first is a list of the presence of current and past phenomena. The second is



a severity scale that evaluates four aspects: frequency, amount of suffering, interference in the patient's life, and a total score of the three previous ones (62).

- F. *Beck depression inventory (BDI)*: This inventory was created by Beck and colleagues in 1961 (63) and is intended to assess the severity of depressive symptoms. It is a self-report instrument composed of 21 items with four response options for each item with values ranging from 0 to 3 (64).
- G. *Beck's anxiety inventory (BAI)*: Like BDI, BAI has 21 items with four response options related to anxiety intensity within a 1-week period (65).
- H. *Brown belief assessment scale (BABS)*: This scale was constructed to rate (rather than using a dichotomous model of "with or without insight") the degree of conviction and insight that patients have concerning their beliefs. These beliefs include delusions as well as the beliefs that may underlie obsessional thinking or phobias. For patients diagnosed with OCD, it is recommended that the obsession that generated the most concerns in the previous week is considered as the "belief" and then respond to six dimensions that can be scored from 0 (absence of pathology) to 4 (delusional or more pathological). The dimensions of insight are: conviction, perception of others' view of belief, explanation of different views, rigidity of ideas, attempt to refute ideas, and ability of insight. The seventh dimension is not part of the total score: ideas/delusions of reference (32). For the purposes of this work, this instrument served to obtain the comparison groups. According to the scores of the total sample ( $n = 968$ ; 33 were missing), two groups were formed: one with the preserved "good" insight (GI group) ( $n = 148$ ; 15.3%), whose final BABS score was "zero" (that is, perfectly preserved insight) and another with the poor insight (PI group) ( $n = 124$ ; 12.8%), whose final BABS score was above the 75th percentile (score  $\geq 14$ ). Thus, 696 (71.9%) patients with BABS score between 1 and 13 were excluded. A whole sample study was already published (36), when instead of 1,001, it was possible to proceed the analysis with 842 patients. At that study, two variables were related to poor insight: hoarding and overall OCD severity. Thus, we decided for another strategy that could allow us to better explore the phenomenological aspects of poor insight in OCD patients. The selective sampling of phenotypically extreme individuals' strategy has been widely used to increase power when comparing some clinical or genetic features (66).

## Statistics

Continuous variables were described as mean (standard deviation) when they had normal distribution and as median (minimum–maximum) when there was no normal distribution. Categorical variables were described as absolute values ( $n$ ) and

relative values (%). Normal distribution was assessed by the Kolmogorov–Smirnov test. The means were compared by the Student's  $t$ -test and the medians by the Mann–Whitney  $U$ -test. Pearson's chi-square, Yates, or Fisher's exact test were used to compare categorical variables between the two groups. Variables with a  $p$ -value  $\leq 0.10$  in the univariate analysis, respecting multi-collinearity and clinical-epidemiological relevance, were included in a backward binary multiple logistic regression model of Wald to determine factors independently associated with the level of insight. The regression model included all the variables that were significant in the univariate analyses, except those with variance inflation factor  $<1$  or  $>5$ , which means high collinearity (especially for continuous variables). After the logistic regression, only variables with a  $p$ -value  $\leq 0.05$  were selected to remain in the model, since it is a conservative way to control multiple comparisons. The odds ratio, with 95% confidence intervals was also calculated for the remaining forms in the regression model. SPSS software 22.0 and WinPEPI 11.0 were used to perform the analysis.

## RESULTS

### Sociodemographic and Clinical Data

The sociodemographic and clinical aspects of the subjects of both groups are compared in Table 1. There is a tendency the good insight group to frequently have more individuals in the class A ( $p = 0.07$ ). Otherwise, the group with poor insight showed a more prevalent current use of neuroleptics ( $p = 0.05$ ).

Regarding the BABS dimensions descriptive results, the OCD patients with poor insight (total score  $\geq 14$ ) presented the following median (minimum–maximum) scores: conviction of the belief: 4 (1–4); perception of others' view of belief: 1 (0–4); explanation of the differing views: 3 (0–4); fixity of beliefs: 3 (0–4); attempt to disprove beliefs: 3 (0–4); ability of insight: 2 (0–4); and ideas/delusions of reference: 0 (0–4). Regarding the maximum score of each dimension, 81 (65.3%) of the patients are totally convinced about the reality of the "beliefs" (obsessions); 13 (10.5%) think that other people also believe completely in the "beliefs" (obsessions); 45 (36.3%) of the patients still believe in the "beliefs" (obsessions) even with the disagreement of other people about that; 44 (35.5%) completely rejected "beliefs" could be false; 78 (62.9%) makes no attempt to refute the "beliefs;" 33 (26.6%) believe that "beliefs" are not of a psychiatric nature; and 9 (7.3%) scored ideas/delusions of reference.

### Level of Insight and the Psychopathological Intrinsic Phenomena of OCD

Some clinical characteristics of OCD were different for individuals with poor insight when compared with those with good insight (Table 2): the first group started the treatment later ( $p < 0.001$ ) and remained longer untreated ( $p < 0.001$ ); showed greater overall severity of symptoms in both Y-BOCS and DY-BOCS; obtained greater severity scores in any of the symptomatologic dimensions of the DY-BOCS; higher prevalence of symptoms

**TABLE 1 |** Sociodemographic and clinical data: comparison between patients with poor and good insight.

	Poor insight ( <i>n</i> = 124); BABS ≥ 14		Good insight ( <i>n</i> = 148); BABS = 0		Statistical test	<i>p</i>
	Median	(Min-Max)	Median	(Min-Max)		
Age	35.5	(13–68)	32	(10–77)	$U_{Mann} = 8,205.0$	0.13
Studied years	14	(2–31)	14	(1–25)	$U_{Mann} = 8,412.0$	0.27
	<i>n</i>	%	<i>n</i>	%		
Male gender	52	41.9	72	48.6	$\chi^2_{Yates} = 0.97$	0.33
No spouse	76	61.3	79	53.4	$\chi^2_{Yates} = 1.56$	0.21
No occupation	27	18.2	23	18.5	$\chi^2_{Yates} < 0.01$	1.00
Ethnicity: White	94	75.8	121	81.8	$\chi^2_{Yates} = 1.11$	0.29
Socioeconomic Classification						
Class A	8	6.5	26	17.6		
Class B	54	43.5	58	39.2	$\chi^2_{Pearson} = 8.87$	0.07
Class C	48	38.7	54	36.5		
Class D	11	8.9	7	4.7		
Class E	3	2.4	3	2.0		
Current treatments						
Pharmacological						
–SSRIs	91	73.4	113	76.4	$\chi^2_{Yates} = 0.18$	0.67
–Other antidepressants	15	12.1	20	13.5	$\chi^2_{Yates} = 0.03$	0.87
–Benzodiazepines	57	46.0	61	41.2	$\chi^2_{Yates} = 0.44$	0.51
–Mood stabilizers	16	12.9	18	12.2	$\chi^2_{Yates} < 0.01$	1.00
–Lithium	8	6.5	6	4.1	$\chi^2_{Yates} = 0.38$	0.54
–Neuroleptics	35	28.2	26	17.6	$\chi^2_{Yates} = 3.81$	0.05
Any psychotherapy	73	58.9	96	64.9	$\chi^2_{Yates} = 0.79$	0.37
CBT	20	27.4	25	26.0	$\chi^2_{Yates} = 0.02$	0.90
Interment	15	12.1	8	5.4	$\chi^2_{Yates} = 0.47$	0.49

*p*, level of statistical significance; *n*, absolute value; %, relative value; Min, minimum; Max, maximum; *U*<sub>Mann</sub>, Mann–Whitney *U* test;  $\chi^2_{Yates}$ , Yates chi-square test;  $\chi^2_{Pearson}$ , Pearson chi-square test; SSRI, selective serotonin reuptake inhibitor; CBT, cognitive-behavioral therapy; BABS, Brown Belief Assessment Scale.

of symmetry, contamination/cleaning, and hoarding, according to the list of symptoms of DY-BOCS; and higher prevalence of sensory phenomena.

### Level of Insight and the Psychopathological Extrinsic Phenomena of OCD

The depression scores, measured by BDI, were higher in the group with poor insight ( $p = 0.007$ ). A statistical trend to higher anxiety levels according to the BAI was shown for the poor insight group ( $p = 0.096$ ). Among the psychiatric comorbidities that were associated with the poor insight group, major depression disorder ( $p = 0.08$ ) and attention deficit hyperactivity disorder ( $p = 0.07$ ) showed statistical tendency to the association, while bipolar disorder ( $p = 0.05$ ) and simple phobia ( $p = 0.04$ ) showed a relevant association. Neither suicidality nor other psychiatric comorbidities were significantly related to poor insight (Table 3).

### Logistic Regression Analysis

Table 4 shows the logistic regression results. The variables that were included in the model were: socioeconomic class; current use of neuroleptics; time interval without treatment; presence of symptoms of symmetry, contamination/cleaning, hoarding according to the DY-BOCS; Y-BOCS obsessions and compulsions scores; all factors related to severity as measured by the DY-BOCS; BDI and BAI

total scores; comorbidity with major depression, bipolar disorder, simple phobia, and attention deficit hyperactivity disorder. The total Y-BOCS score was excluded from the regression analysis by having variance inflation factor = 11.56 (collinearity with Y-BOCS obsessions score). “Considering that the Y-BOCS total score includes the sub score of compulsions, which is a behavioral phenomenon, and as poor insight and obsessions are both cognitive phenomena, the obsessions score was considered more clinically relevant for the purposes of this study.” Thus, the presence of sensory phenomena (OR = 2.24) remained in the model with statistical significance. Other statistical relevant variables remained in the model: current use of neuroleptics (OR = 1.66); total score of the dimensional Yale–Brown obsessive-compulsive scale (DY-BOCS) hoarding dimension (OR = 1.15); and the time interval without treatment (OR = 1.05).

### DISCUSSION

Although many variables were statistically significant in the univariate analysis, only four remained significantly associated with the presence of poor insight in patients with OCD after logistic regression analysis. However, one of them (time without treatment), despite the statistical significance, did not obtain clinical-epidemiological relevance (OR = 1.05), leading us to discuss the remaining variables in the regression model: the presence of any sensory phenomena, the use of neuroleptics, and severity of the DY-BOCS hoarding dimension.

**TABLE 2 |** Intrinsic phenomenological features of obsessive-compulsive disorder (OCD): comparison between patients with poor and good insight.

	Poor insight ( <i>n</i> = 124); BABS ≥ 14		Good insight ( <i>n</i> = 148); BABS = 0		Statistical test	<i>p</i>
	Median	(Min–Max)	Median	(Min–Max)		
OCS age of onset	10	(3–37)	11	(4–43)	$U_{MWW} = 7,680.0$	0.17
Period without treatment	17	(0–56)	11	(0–58)	$U_{MWW} = 5,281.0$	<b>&lt;0.001</b>
YBOCS						
– Total Score	29	(8–40)	23	(7–37)	$U_{MWW} = 4,670.0$	<b>&lt;0.001</b>
– Obsessions	14	(4–20)	11	(1–18)	$U_{MWW} = 4,651.0$	<b>&lt;0.001</b>
– Compulsions	15	(4–20)	12	(2–20)	$U_{MWW} = 5,286.0$	<b>&lt;0.001</b>
D-YBOCS severity						
– Total Score	24	(4–30)	21	(0–30)	$U_{MWW} = 6,476.5$	<b>&lt;0.001</b>
– Aggressiveness	7	(0–15)	3	(0–15)	$U_{MWW} = 7,220.0$	<b>0.04</b>
– Sex/Religion	6	(0–15)	0	(0–15)	$U_{MWW} = 7,599.0$	<b>0.01</b>
– Symmetry/Ordering	9	(0–15)	6	(0–15)	$U_{MWW} = 6,730.5$	<b>&lt;0.001</b>
– Contamination/Cleaning	9	(0–15)	3.5	(0–14)	$U_{MWW} = 6,676.5$	<b>&lt;0.001</b>
– Hoarding	3.5	(0–15)	0	(0–13)	$U_{MWW} = 6,051.0$	<b>&lt;0.001</b>
Severity Sensory Phenomena*	9	(1–15)	9	(1–15)	$U_{MWW} = 3,513.5$	0.24
	<b><i>n</i></b>	<b>%</b>	<b><i>n</i></b>	<b>%</b>		
Family History of OCD	60	48.4	71	48.0	$\chi^2_{Yates} < 0.001$	1.00
Family History of Tics	25	20.8	22	15.7	$\chi^2_{Yates} = 0.82$	0.37
D-YBOCS dimensions						
– Aggressiveness	87	70.2	95	64.2	$\chi^2_{Yates} = 0.83$	0.36
– Sex/Religion	77	62.1	83	56.1	$\chi^2_{Yates} = 0.78$	0.38
– Symmetry	113	91.1	121	82.3	$\chi^2_{Yates} = 3.71$	<b>0.054</b>
– Contamination/Cleaning	98	79.0	93	62.8	$\chi^2_{Yates} = 7.71$	<b>0.006</b>
– Hoarding	83	66.9	59	39.9	$\chi^2_{Yates} = 18.75$	<b>&lt;0.001</b>
Presence of any Sensory Phenomena	94	75.8	92	62.2	$\chi^2_{Yates} = 5.20$	<b>0.023</b>

\*Poor insight (*n* = 92); Good insight (*n* = 85); *p*, level of statistical significance; *n*, absolute value; %, relative value; Min, minimum; Max, maximum;  $U_{MWW}$ , Mann-Whitney *U* test;  $\chi^2_{Yates}$ , Yates chi-square test; SOC, obsessive compulsive symptoms; YBOCS, Yale-Brown Obsessive-Compulsive Symptom Scale; DYBOCS, dimensional scale for the assessment of the presence and severity of obsessive-compulsive symptoms; BABS, Brown Belief Assessment Scale.

### Sensory Phenomena and Poor Insight in Patients with OCD

Among the results, the most significant was the relation of the sensory phenomena with poor insight (OR = 2.24). The relation of the low insight capacity with sensory phenomena was previously reported by Ferrão et al., who, when comparing patients with OCD with and without sensory phenomena, found higher BABS scores for the first group (median equal to 7 and 5, respectively,  $p = 0.007$ ) (4). As suggested by some authors (67–70), the presence of sensory phenomena may predict treatment failure, which can be understood not only by its possible specific neurobiological aspects, but also by the co-occurrence of poor insight (71, 72), which can itself reduce treatment engagement and reduce the chances of an appropriate treatment response. If for psychopharmacological approaches this statement is valid, the presence of sensory phenomena and poor insight leads also to increased rates of nonresponse in psychotherapeutic therapies (39). Moritz et al. reported that the presence of sensory phenomena in patients diagnosed with OCD predicts poor insight, but it depends on the type of sensory phenomenon, with special emphasis on visual and tactile phenomena (not analyzed in our study) (71). In this study, a positive association was also found between the severity of the sensory phenomenon and the severity of the compulsions, which may be because the sensory properties may increase the subjective reality of obsession

that hinders the task of discarding thought and, thus, turning compulsions more difficult to resist (71). Consequently, sensory phenomena (and a lower insight about symptoms) would reinforce the “vicious cycle” of OCD.

Some data suggest that patients with sensory phenomena consider this trigger more important than obsessions and consequently have stronger compulsions (62, 73). About 65% of patients with OCD perform compulsions due to sensory phenomena (62). The data above corroborate a previous study, in which poor insight about the symptoms allows the individual to have a smaller capacity to interrupt or control the OCS (36), perceiving them as “correct,” “adequate,” “relevant,” or even “necessary.”

A neurobiological explanation for this precise association is not yet possible, but some conjectures may be done. It is known that in OCD patients, the anterior dorsolateral, orbitofrontal, and anterior cingulate prefrontal cortex are usually hyperactive. In general, these structures are involved in intersections with other neurocircuits to retain information, manipulate options, and assist in decision making and goal maintenance (74). When they connect with limbic circuits, for instance, they add emotional aspects (rewards) to information and decision making and provide the most diverse forms of behavior (75). The neurobiological dimensional approach recently proposed by the National Institute of Mental Health (76, 77) named Research Domain Criteria (<https://www.nimh>).

**TABLE 3 |** Extrinsic phenomenological features of OCD: comparison between patients with poor and good insight.

	Poor insight ( <i>n</i> = 124); BABS ≥ 14		Good insight ( <i>n</i> = 148); BABS = 0		Statistical test	<i>p</i>
	Median	(Min–Max)	Median	(Min–Max)		
BDI	17	(0–52)	13	(0–53)	$U_{MW} = 7,384.5$	<b>0.007</b>
BAI	15	(0–51)	12	(0–48)	$U_{MW} = 8,045.0$	<b>0.096</b>
	<i>n</i>	%	<i>n</i>	%		
Suicidality						
–Ideation	48	40.3	55	39.3	$X^2_{Yates} = 0.002$	0.96
–Plan	25	21.0	29	20.7	$X^2_{Yates} < 0.001$	1.00
–Attempt	11	9.2	15	10.7	$X^2_{Yates} = 0.03$	0.85
–Hospital Internment	4	3.2	4	2.7	$X^2_{Yates} = 0.65$	0.80
–Familial History	23	19.3	22	15.7	$X^2_{Yates} = 0.38$	0.55
Comorbidities						
–Major Depression	51	41.1	42	28.4	$X^2_{Yates} = 4.94$	<b>0.08</b>
–Dysthymia	16	12.9	21	14.2	$X^2_{Yates} = 0.02$	0.90
–BAD	6	4.8	1	0.7	Fisher	<b>0.05</b>
–Delusional Disorder	6	4.8	2	1.4	Fisher	0.15
–Anxiety Disorders						
–Panic	10	8.1	16	10.8	$X^2_{Yates} = 0.31$	0.58
–Agoraphobia	3	2.4	7	4.7	Fisher	0.35
–Social Phobia	32	25.8	35	23.6	$X^2_{Yates} = 0.08$	0.79
–Simple Phobia	30	24.2	36	24.3	$X^2_{Yates} < 0.001$	1.00
–PTSD	21	16.9	12	8.1	$X^2_{Yates} = 4.14$	<b>0.04</b>
–GAD	32	25.8	49	33.1	$X^2_{Yates} = 1.39$	0.24
–Alcohol Abuse/Dependence	5	4.0	6	4.1	$X^2_{Yates} = 1.20$	0.55
–Tics	34	27.4	41	27.7	$X^2_{Yates} < 0.001$	1.00
–Tourette Disorder	10	8.1	9	6.1	$X^2_{Yates} = 0.16$	0.69
–Separation Anxiety	7	5.6	6	4.1	$X^2_{Yates} = 0.11$	0.75
–ADHD	22	17.7	14	9.5	$X^2_{Yates} = 3.34$	<b>0.07</b>

*p*, level of statistical significance; *n*, absolute value; %, relative value; Min, minimum; Max, maximum; *UMW*, Mann–Whitney U test;  $X^2_{Yates}$ , Yates chi-square test; BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory; BAD, bipolar affective disorder; PTSD, posttraumatic stress disorder; GAD, generalized anxiety disorder; ADHD, attention deficit hyperactivity disorder; BABS, Brown Belief Assessment Scale.

**TABLE 4 |** Binary logistic regression results (WALD backwards) with predictor variables (*p* ≤ 0.10) of the univariate analysis.

	Wald $\chi^2$	<i>p</i>	OR	CI 95% of OR
Current use of Neuroleptics	8.88	0.003	1.66	1.31–1.84
Period without treatment	13.61	<0.001	1.05	1.02–1.08
Severity of Hoarding dimension	14.22	<0.001	1.15	1.07–1.24
Presence of any sensory phenomena	6.20	0.013	2.24	1.19–4.22

Variable inserted in the steps of Regression: step 1—Gravity of the accumulation dimension; step 2—Time without treatment; step 3—Current use of neuroleptics; step 4—Presence of some sensory phenomenon.

Wald  $\chi^2$ , Wald chi-square test; *p*, level of statistical significance; OR, odds ratio; CI, confidence interval.

nih.gov/research-priorities/rdoc/index.shtml) describes that the default mode network, which basically involves brain structures such as medial anterior prefrontal, posterior cingulate cortex, and angular gyrus, is hyperactive in patients with OCD (78, 79). This circuit, in healthy people, becomes more active at rest or when people are asked to reflect on their own thoughts. Thus, obsessions (intrusive thoughts) could be a consequence of the hyperactivity of this circuit (78), and this “hyperactivation” can be stimulated or facilitated by intersections with structures of other neurocircuits. One such structure is the insula, which together with the anterior cingulate cortex and the amygdala, constitute another neural circuit known as a “protrusion circuit,” which detects any “protrusion” or aspects that stand out in our perception in the environment

(both external and interoceptive aspects) (79, 80). Thus, it can be postulated that in patients with OCD, the “negative valence systems” (primarily responsible for responses to aversive situations or context, such as fear, anxiety, and loss) could, for some reason, be also hyperactive, increasing the frequency and intensity of the perception of internal (interoceptive) sensations, becoming what we call “sensory phenomena.” Once the “protrusion circuit” has been activated through insular connections (78), there would be also hyperactivation of the default network circuit and, thus, the increase or maintenance of OCD symptoms. The insula is also responsible for connecting the two circuits above with other two circuits known to be involved in OCD (81, 82): positive affects (responsible for the sensitivity to the presence of protrusions in the external

or internal environment—this circuit involves the basal ganglia) and the cognitive (which is responsible for procedural memory and selective attention—this circuit involves, for example, the dorsolateral prefrontal cortex) (79). The direction of the influences of one circuit in the other (and vice versa), however, is still a point of discussion, but it seems little evident (from clinical experience) that the motor circuits (which generate the compulsions) can generate hyperactivation of salience circuits, causing sensory phenomena; the opposite seems more likely to happen. Thus, the association of sensory phenomena with OCD with poor insight may be based on intersections of neurocircuits with distinct functions but that interact to manifest heterogeneously what we call OCD.

### Use of Neuroleptics and Poor Insight in Patients With OCD

Neuroleptics are not the first-choice treatment for OCD, but it seems to be valid as adjuvant when treating resistant or refractory OCD (83), especially atypical neuroleptics, which have augmenting synergism with selective serotonin reuptake inhibitors (SSRIs) because they also have serotonergic action (83, 84). As the CTOC sample is predominantly composed of specialized and tertiary health services, the recruitment of more severe patients, nonresponders to conventional and complex treatments (with comorbidities with tics, for example), may have biased our results, leading to a greater prevalence of the use of these specific medications in these centers (39, 42, 85). As poor insight was related to sensory phenomena, and since sensory phenomena are more prevalent in patients with OCD who also have tics (64, 86), we could speculate a “dopaminergic” modulation of “poor insight.” It could be explained by the facts that tics occur due to dopaminergic dysfunctions involving the basal nuclei, especially striatum and substantia nigra (87, 88), which may result clinically in the increased prescription of drugs with dopaminergic action, such as neuroleptics. Thus, the association of an atypical neuroleptic with SSRIs could act, in these cases, with synergism by serotonergic potentiation or with synergism by addition, adding effect in the involved dopaminergic neurocircuits. Another possibility to justify the association of poor insight and neuroleptics is the fact that, in certain patients with OCD, poor insight may, depending on its severity, remind clinical practitioners of delusion or even psychotic functioning (89, 90), leading psychiatrists to prescribe neuroleptics in association with SSRIs (35, 83, 91, 92).

### Severity of the DY-BOCS Hoarding Dimension and Poor Insight in Patients With OCD

According to the regression performed in this study, the greater severity of the DY-BOCS hoarding dimension was associated with poor insight. Similar results are pointed out in the literature when correlating a worse insight capacity with hoarding symptoms (47, 48, 51, 93–97). The reason so many papers agree to this association still needs further study. Kalogeraki and Michopoulos (97) suggest a cognitive model for hoarding disorder that includes four factors: 1) personal vulnerability, including aspects, such as heredity, stressful life events, personality traits, and interpersonal difficulties; 2) difficulties in information processing, such as attention deficit, memory and

executive functions, with difficulty to make decisions and categorize; 3) dysfunctional cognitive content, such as ownership, emotional attachment to possessions, dysfunctional beliefs about mnemonic ability, and the importance of memories; and 4) hoarding behaviors and their positive and negative reinforcement, such as pleasure in acquiring/keeping or anxiety/discomfort to discard (97). Failure to be critical in relation to hoarding acts (associated or not to the diagnosis of OCD) may be a consequence of the sum of cognitive dysfunctions of more than one of these factors. In this sense, both the neural circuits associated with the greater significance of rewards for possession/accumulation (circuits of positive valence systems, primarily responsible for responses to positive motivational situations or contexts, such as reward seeking, consummatory behavior, and reward/habit learning) and greater aversion to frustration by discard/insecurity (circuit of negative valence systems) may be hyperactive simultaneously (79). Of course, the association of the severity of the hoarding symptoms would reflect a higher intensity or complexity of interaction of these circuits, leading to a more committed insight, specifically about this symptomatology.

### CONCLUSIONS

This cross-sectional exploratory study was conducted in seven tertiary research centers in three different Brazilian regions, which may alert us to interpret the results with caution, since the generalization of the results to all sort of OCD patients is limited. Due to the methodology and recruitment strategy, it may be argued that only moderate to severe patients answered the questionnaires and, thus, results may be related only for those cases. Moreover, the sample sizes were small and not equal, which may have led to loss of statistical efficiency. Nevertheless, interesting results have been found and deserve attention.

Our results showed that patients with OCD with poor insight seem to present some specificities such as: higher presence of any sensory phenomena, higher prevalence of neuroleptic use, and greater severity of hoarding symptoms. Although the methodological nature of the study does not allow causal inferences, we can conjecture that: 1) sensorial phenomena and severity of hoarding symptoms lead to a poorer insight; and 2) a poorer insight leads psychiatrists to use neuroleptics more frequently. Neurobiological and pathophysiological aspects, as well as reactive cognitive dysfunctions, may justify the first statement, while empirical observations lead to an evidence-based clinical practice that justifies the second statement in some situations. The more detailed exploration from the psychopathological and neurobiological point of view of the sensory phenomena and their subtypes in patients with OCD could help in the better understanding of how these phenomena would make it difficult for the patient to perceive the pathological nature of the symptoms. This study did not evaluate whether the use of neuroleptics in patients with OCD with poor insight had adequate response, which could be answered only in specifically designed prospective or clinical trials. Therefore, intervention studies in this subpopulation, whether with psychotropic drugs, psychotherapeutic techniques, or neurobiological therapies, should be stimulated and conducted

properly. Because of the heterogeneity of OCD, the more detailed understanding of insight in patients with OCD should include in future studies the application of instruments that assess this phenomenon for each of the dimensions of DY-BOCS, in other words, how well the patient can judge as reasonable the contents of each of the symptoms dimensions. These results point to the need to explore patients with OCD with a poor insight, since they constitute a special and not uncommon (prevalence of 12.8% among OCD patients) subtype of patients who may require a greater effort by health professionals and services, mainly due to its greater complexity and the difficulty to respond to conventional available treatments.

## DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

## ETHICS STATEMENT

This study was carried out in accordance with the recommendations of 196/96 Resolution, from the National Commission on Research Ethics, from the National Health Council of the Brazilian Health Ministry with written informed consent from all subjects. All subjects gave written informed consent in accordance with the Declaration of Helsinki. The

protocol was approved by involved local ethics committees (USP, UNIFESP, UNESP, UFRJ, UFRGS-IPA, UFBA, UPE).

## AUTHOR CONTRIBUTIONS

RA, LN, and RP wrote the manuscript and contributed with review and the main insights in data analysis and discussion. LF, EF and YF have planned the dataset of the consortium, coordinated the data collection, and reviewed the insights in data analysis and discussion. VB proposed some change in the basic conceptual aspects of the paper and reviewed it carefully, concerning data analysis and discussion. YF performed the statistical analysis, guided the preparation, and reviewed the manuscript.

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## 6. CONCLUSÃO GERAL

Como foi citado anteriormente na conclusão do artigo, 12,5% dos pacientes com TOC apresentam *insight* pobre ou ausente e as terapia de padrão ou parecem ter menos efetividade do que para pacientes conscientes dos seus sintomas. Logo, a investigação mais profunda e detalhada nesse subtipo de TOC é fundamental para que não deixemos uma parcela de pacientes desatendidos por práticas terapêuticas que poderiam ser potencializados pela compreensão de alguns fatores associados a essa condição do transtorno.

Diferentemente do que foi hipotetizado no início dessa dissertação, os as dimensões de sintomas que mais se associaram a um TOC com *insight* pobre não são os repugnantes (sexual, agressivo e religioso), pois esses são socialmente menos aceitos e por um condicionamento social é comum os interpretarmos como *taboo* e logo percebemos a sua presença indesejada. Já os sintomas de lavagem e contaminação aparentam ser mais socialmente aceitos, principalmente nessa época de pandemia.

Apesar de não ser o foco dessa dissertação prestamos atenção para as intervenções utilizadas para gerar mais *insight* em pacientes com TOC. Inicialmente alguns artigos ligavam essas intervenções exclusivamente à psicanálise que tem como foco a eclosão de uma compreensão vinda do próprio paciente. Contudo, parece ser um método pouco reproduzível e dependente de uma motivação para o tratamento que nem sempre está presente. Já as intervenções cognitivo comportamentais estavam mais ligadas à psicoeducação para que o paciente se identificasse com os sintomas e então pudesse assumir o compromisso com a exposição e prevenção de resposta.

Enfim, ainda há muito a ser feito para poder auxiliar uma parcela de pacientes com TOC e seus familiares que ficam desiludidos pela dificuldade do tratamento que se torna mais desafiador quando o paciente possui um *insight* pobre.

## **Anexos:**

### **Anexo 1 - Relatório de produtividade**

Durante os dois anos como mestrando me dediquei a realizar as disciplinas propostas pela universidade e auxiliar alguns colegas em seus respectivos trabalhos acadêmicos ao participar de outros projetos.

Durante esse período também pude me experenciar como docente de uma disciplina eletiva que propus com auxílio do meu colega Md. André Kracker Imthon. A disciplina, apesar de curta, ousou proporcionar uma visão mais prática sobre o tema suicídio de dois profissionais que convivem com pacientes em risco diariamente. Em pouco tempo as vagas foram completadas e os feedbacks foram muito positivos.

No mesmo tema, suicídio, pude auxiliar o colega Dr. Ezequiel Teixeira Andreotti na revisão do artigo "*Instruments to assess suicide risk: a systematic review*" publicado na revista *Trends in Psychiatry and Psychotherapy* em agosto desse ano, 2020.

Além disso, em 2020 comecei a colaborar com um projeto vinculado a liga de psiquiatria da UFCSPA que visa investigar o impacto das aulas na modalidade de ensino a distância durante a pandemia de COVID-19 na saúde mental dos estudantes universitários e de graduação. A minha atuação nesse projeto inicialmente era a de um colaborador que pudesse orientar para o uso das escalas psicológicas, mas que evoluiu para redator dos futuros resultados.

Além disso, faço parte de um projeto de doutorado para tratamento de TOC em adolescentes. Portanto, durante esses dois anos estive revisando o manual da terapia com a autora M.e. Cristiane Flores Bortoncello e prospectando pacientes com idade entre 12 e 19 anos para os grupos terapêuticos que acontecerão somente em 2021, por causa da pandemia.

## Anexo 2 - Regras da revista

### 1. Summary Table

Please view the table below for a summary on currently accepted article types and general manuscript style guidelines. Article types may vary depending on journal

	Abstract (max. length)	Running title (5 words)	Figures and/or tables (combined)	Manuscript (max. length)	Peer review	Author fees	Submitted to PubMed Central or other indexing databases
Book Review	✗	✗	1	1'000 words	✓	✗	✓
Brief Research Report	250 words	✓	2	2'000 words	✓	✓	✓
Classification	250 words	✓	10	2'000 words	✓	✓	✓
Case Report	350 words	✓	4	3'000 words	✓	✓	✓
Clinical Study Protocol	350 words	✓	15	12'000 words	✓	✓	✓
Clinical Trial	350 words	✓	15	12'000 words	✓	✓	✓
Code	250 words	✓	3	3'000 words	✓	✓	✓
Community Case Study	350 words	✓	5	5'000 words	✓	✓	✓
Conceptual Analysis	350 words	✓	10	8'000 words	✓	✓	✓
CPC	250 words	✓	6	2'500 words	✓	✓	✓
Curriculum, Instruction, and Pedagogy	350 words	✓	5	5'000 words	✓	✓	✓
Data Report	✗	✓	2	3'000 words	✓	✓	✓
Editorial	✗	✗	0	1'000 words*	✓	✗	✓
Empirical Study	350 words	✓	10	8'000 words	✓	✓	✓
Evaluation	350 words	✓	5	6'000 words	✓	✓	✓
Field Grand Challenge	✗	✓	1	2'000 words	✓	✗	✓
Focused Review (1)	350 words	✓	5	5'000 words	✓	✗	✓
Frontiers Commentary (1)	✗	✗	1	1'000 words	✓	✗	✓
General Commentary	✗	✗	1	1'000 words	✓	✓	✓
Hypothesis and Theory	350 words	✓	15	12'000 words	✓	✓	✓
Methods	350 words	✓	15	12'000 words	✓	✓	✓
Mini Review	250 words	✓	2	3'000 words	✓	✓	✓
Opinion	✗	✓	1	2'000 words	✓	✓	✓
Original Research	350 words	✓	15	12'000 words	✓	✓	✓
Policy & Practice Reviews	350 words	✓	15	12'000 words	✓	✓	✓
Policy Briefs	125 words	✓	5	3'000 words	✓	✓	✓
Protocols	350 words	✓	15	12'000 words	✓	✓	✓
Perspective	250 words	✓	2	3'000 words	✓	✓	✓
Research Snapshot	50 words	✓	1	500 words	✓	✓	✓
Review	350 words	✓	15	12'000 words	✓	✓	✓
Specialty Grand Challenge	✗	✓	1	2'000 words	✓	✗	✓
Systematic Reviews	350 words	✓	15	12'000 words	✓	✓	✓
Technology Report	350 words	✓	15	12'000 words	✓	✓	✓

(1) Tier 2 article - field level article reserved to authors of selected Tier 1 articles.

\* Editorials for Research Topics with 5 to 10 published articles have a maximum of 1'000 words, for Research Topics with more than 10 published articles the following applies: 1'100 words for 11 articles, 1'200 for 12 articles, 1'300 for 13 articles etc. up to maximum 5'000 words, for 50 or more papers.

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Tahimic, C.G.T., Wang, Y., Bikle, D.D. (2013). Anabolic effects of IGF-1 signaling on the skeleton. *Front. Endocrinol.* 4:6. doi: 10.3389/fendo.2013.00006

**Article or chapter in a book:**

Sorenson, P. W., and Caprio, J. C. (1998). "Chemoreception," in *The Physiology of Fishes*, ed. D. H. Evans (Boca Raton, FL: CRC Press), 375-405.

**Book:**

Cowan, W. M., Jessell, T. M., and Zipursky, S. L. (1997). *Molecular and Cellular Approaches to Neural Development*. New York: Oxford University Press.

**Abstract:**

Hendricks, J., Applebaum, R., and Kunkel, S. (2010). A world apart? Bridging the gap between theory and applied social gerontology. *Gerontologist* 50, 284-293. Abstract retrieved from Abstracts in Social Gerontology database. (Accession No. 50360869)

**Patent:**

Marshall, S. P. (2000). Method and apparatus for eye tracking and monitoring pupil dilation to evaluate cognitive activity. U.S. Patent No 6,090,051. Washington, DC: U.S. Patent and Trademark Office.

**Data:**

Perdiguero P, Venturas M, Cervera MT, Gil L, Collada C. Data from: Massive sequencing of Ulms minor's transcriptome provides new molecular tools for a genus under the constant threat of Dutch elm disease. Dryad Digital Repository. (2015) <http://dx.doi.org/10.5061/dryad.ps837>

**Theses and Dissertations:**

Smith, J. (2008) Post-structuralist discourse relative to phenomenological pursuits in the deconstructivist arena.

[dissertation/master's thesis]. [Chicago (IL)]: University of Chicago

**Preprint:**

Smith, J. (2008). Title of the document. Preprint repository name [Preprint]. Available at: <https://persistent-url> (Accessed March 15, 2018).

For examples of citing other documents and general questions regarding reference style, please refer to the [Chicago Manual of Style](#).

[Frontiers Science Endnote Style](#)

[Frontiers Science, Engineering and Humanities Bibstyle](#)

**HEALTH, PHYSICS AND MATHEMATICS: For articles submitted in the domain of HEALTH or the journal Frontiers in Physics and Frontiers in Applied Mathematics and Statistics please apply the Vancouver system for in-text citations.**

Reference list: provide the names of the first six authors followed by et al. and [doi](#) when available.

In-text citations should be numbered consecutively in order of appearance in the text – identified by Arabic numerals in the parenthesis for Health articles, and in square brackets for Physics and Mathematics articles.

**Article in a print journal:**

Sondheimer N, Lindquist S. Rnq1: an epigenetic modifier of protein function in yeast. *Mol Cell* (2000) 5:163-72.

**Article in an online journal:**

Tahimic CGT, Wang Y, Bikle DD. Anabolic effects of IGF-1 signaling on the skeleton. *Front Endocrinol* (2013) 4:6. doi: 10.3389/fendo.2013.00006

**Article or chapter in a book:**

Sorenson PW, Caprio JC. "Chemoreception,". In: Evans DH, editor. *The Physiology of Fishes*. Boca Raton, FL: CRC Press (1998). p. 375-405.

**Book:**

Cowan WM, Jessell TM, Zipursky SL. *Molecular and Cellular Approaches to Neural Development*. New York: Oxford University Press (1997). 345 p.

**Abstract:**

Christensen S, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, editor. *Genetic Programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3–5; Kinsdale, Ireland*. Berlin: Springer (2002). p. 182–91.

**Patent:**

Pagedas AC, inventor; Ancel Surgical R&D Inc., assignee. *Flexible Endoscopic Grasping and Cutting Device and Positioning Tool Assembly*. United States patent US 20020103498 (2002).

**Data:**

Perdiguero P, Venturas M, Cervera MT, Gil L, Collada C. Data from: Massive sequencing of *Ulms minor*'s transcriptome provides new molecular tools for a genus under the constant

threat of Dutch elm disease. Dryad Digital Repository. (2015) <http://dx.doi.org/10.5061/dryad.ps837>

### **Theses and Dissertations:**

Smith, J. (2008) Post-structuralist discourse relative to phenomenological pursuits in the deconstructivist arena. [dissertation/master's thesis]. [Chicago (IL)]: University of Chicago

### **Preprint:**

Smith, J. Title of the document. Preprint repository name [Preprint] 2008). Available at: <https://persistent-url> (Accessed March 15, 2018).

For examples of citing other documents and general questions regarding reference style, please refer to [Citing Medicine](#).

[Frontiers Health Endnote Style](#)

[Frontiers Health and Physics Bibstyle](#)

### **2.3.3. Disclaimer**

Any necessary disclaimers which must be included in the published article should be clearly indicated in the manuscript.

### **2.3.4. Supplementary Material**

Frontiers journals do not support pushing important results and information into supplementary sections. However, data that are not of primary importance to the text, or which cannot be included in the article because it is too large or the current format does not permit it (such as movies, raw data traces, power point presentations, etc.) can be uploaded during the submission procedure and will be displayed along with the

published article. All supplementary files are deposited to FigShare for permanent storage, during the publication stage of the article, and receive a DOI.

The Supplementary Material can be uploaded as Data Sheet (word, excel, csv, cdx, fasta, pdf or zip files), Presentation (power point, pdf or zip files), Supplementary Image (cdx, eps, jpeg, pdf, png or tif), Supplementary Table (word, excel, csv or pdf), Audio (mp3, wav or wma) or Video (avi, divx, flv, mov, mp4, mpeg, mpg or wmv).

Supplementary material is not typeset so please ensure that all information is clearly presented, the appropriate caption is included in the file and not in the manuscript, and that the style conforms to the rest of the article. For Supplementary Material templates (LaTeX and Word) see [Supplementary Material for Frontiers](#).

### **2.3.5. File Requirements**

#### 2.3.5.1. Word Files

If working with Word please use [Frontiers Word templates](#).

#### 2.3.5.2. LaTeX Files

If you wish to submit your article as LaTeX, we recommend our [Frontiers LaTeX templates](#). These templates are meant as a guide, you are of course welcome to use any style or formatting and Frontiers journal style will be applied during typesetting.

When submitting your article please ensure to upload all relevant manuscript files including:

tex file

PDF

.bib file (if the bibliography is not already included in the .tex file)

Figures should be included in the provided pdf. In case of acceptance, our Production Office might require [high resolution files](#) of the figures included in the manuscript in eps, jpg or tif format. In order to be able to upload more than one figure at a time, save the figures (labeled in order of appearance in the manuscript) in a zip file, and upload them as 'Supplementary Material Presentation'.

To facilitate the review process, please include a Word Count at the beginning of your manuscript, one option is teXcount which also has an online interface.

During the Interactive Review, authors are encouraged to upload versions using 'Track Changes'. Editors and Reviewers can only download the PDF file of the submitted manuscript .

### **2.3.6. Additional Requirements per article types**

#### 2.3.6.1. CrossMark Policy

[CrossMark](#) is a multi-publisher initiative to provide a standard way for readers to locate the current version of a piece of content. By applying the CrossMark logo Frontiers is committing to maintaining the content it publishes and to alerting readers to changes if and when they occur. Clicking on the CrossMark logo will tell you the current status of a document and may also give you additional publication record information about the document.

#### 2.3.6.2. Commentaries on Articles

For General Commentaries, the title of your manuscript must have the following format: "Commentary: Title of the original article". At the beginning of your Commentary, please provide the citation of the article commented on. Authors commenting on a Frontiers article must submit their commentary for consideration to the same Journal and Specialty as the original article.

Rebuttals may be submitted in response to Commentaries; our limit in place is one commentary and one response. Rebuttals should be submitted as General Commentary articles and the title should have the following format: "Response : Commentary: Title of original article".

#### 2.3.6.3. Book Reviews

For book Reviews, you must provide the full book details at the beginning of the article in this format: Book Review: Full book reference"

#### 2.3.6.4. Focused Reviews

For Tier 2 invited **Focused Reviews**, to shape the paper on the importance of the research to the field, we recommend structuring the Review to discuss the paper's Introduction, Materials and Methods, Results and Discussion. In addition the authors must submit a short biography of the corresponding author(s). This short biography has a maximum of 600 characters, including spaces

A picture (5 x 5 cm, in \*.tif or \*.jpg, min 300 dpi) must be submitted along with the biography in the manuscript and separately during figure upload.

Focused Reviews highlight and explain key concepts of your work. Please highlight a minimum of four and a maximum of

ten key concepts in bold in your manuscript and provide the definitions/explanations at the end of your manuscript under “Key Concepts”. Each definition has a maximum of 400 characters, including spaces.

#### 2.3.6.5 Systematic Reviews

For Systematic Reviews, the following article structure applies.

Title: include systematic review/meta-synthesis/meta-analysis as appropriate in the title

Each of the sections should include specific sub-sections as follows

Abstract

Background

Methods

Results

Conclusions

Introduction

Rationale

Objectives

Research question

Methods

Study design

Participants, interventions, comparators

Systematic review protocol

Search strategy

Data sources, studies sections and data extraction

Data analysis

Results

Provide a flow diagram of the studies retrieved for the review

Study selection and characteristics

Synthesized findings

Risk of bias

Discussion

Summary of main findings

Limitations

Conclusions

#### 2.3.6.6. Data Reports

For Data Reports, please make sure to follow these additional specific guidelines.

1. The data sets (defined as a collection of data that contains individual data units organized in a standardized reusable format, including pre-processed or raw data) must be deposited in a public repository for long-term data preservation prior to submission of the Data Report. The data set(s) is to be fixed and made publicly available upon publication of the Data Report.

2. Our data sharing policy also requires that the dataset be made available to the Frontiers editors and reviewers during

the review process of the manuscript. Prior to submission of your Data Report manuscript, please ensure that the repository you have selected supports confidential peer-review. If it does not, we recommend that the authors deposit the datasets to figshare or Dryad Digital Repository for the peer-review process. The data set(s) can then be transferred to another relevant repository before final publication, should the article be accepted for publication at Frontiers.

Note that it is the authors' responsibility to maintain the data sets after publication of the Data Report. Any published Frontiers Data Report article will be considered for retraction should the data be removed from the final selected repository after publication or the access become restricted.

3. The submitted manuscript must include the following details:

Detailed cover letter (including a link to the data set)

Name of the data set

Name of the database/repository where the data set has been submitted

Link to the data set for confidential peer-review (which can be updated after acceptance, prior to publication once the data is made public)

Description of how the data was acquired, data collection period

Filters applied to the data

Overview of the data files and their formats

Reference to and/or description of the protocols or methods used to collect the data

Information on how readers may interpret the data set and reuse the data

All these elements will be peer-reviewed and are required for the publication of the Data Report.

Any future updates to the data set(s) should be deposited as independent versions in a repository and the relevant information may be published as General Commentaries linked on the Frontiers website to the initial Data Report.

Any detailed analyses or new scientific insights relating to the Data Report can be submitted as independent research articles which can also be linked on the Frontiers website to the Data Report article. The protocols and methodology used to collect the data can also be submitted as Methods articles.

#### 2.3.6.7. Case Reports

For Case Reports the following sections are mandatory:

##### **Introduction**

Include symptoms at presentation, physical exams and lab results.

##### **Background**

This section may be divided by subheadings. Include history and review of similar cases.

##### **Discussion**

This section may be divided by subheadings. Include diagnosis and treatment.



## **Concluding Remarks**

### 2.3.6.8. Policy & Practice Reviews

For Policy and Practice Reviews, the following article structure applies:

Abstract

Introduction

Sections on assessment of policy/guidelines options and implications

Actionable Recommendations and Conclusions

### 2.3.6.9. Policy Briefs

For Policy Briefs, the following article structure applies:

Abstract (bullet point format)

Introduction

Sections on Policy Options and Implications

Section on Actionable Recommendations

Conclusions

### 2.3.6.10. Protocols

For Protocols articles, please make sure to follow these additional specific guidelines.

The submitted manuscript must include the following sections:

An Abstract.

An Introduction outlining the protocol and summarizing its possible applications.

A Materials and Equipment section providing a list of reagents or other materials and/or equipment required to carry out the protocol. For basic-science protocols, the formulation of any solutions, e.g. buffers, should be clearly indicated in the Materials and Equipment section.

A Stepwise Procedures section listing, stepwise, the stages of the protocol. The timing of each step or related series of steps should be indicated, as should points at which it is possible to pause or halt the procedure without adversely influencing the outcome. For steps requiring repeated measurements, details of precision and accuracy should be presented. Limits of detection or quantification should also be stipulated where appropriate.

An Anticipated Results section describing, and illustrating with figures, where possible, the expected outcome of the protocol. Any analytical software or methods should be presented in detail in this section, as should possible pitfalls and artifacts of the procedure and any troubleshooting measures to counteract them. These last may also be described in an optional Notes section.

Code or training data sets referenced by the protocol and useful in its execution should be hosted in an online repository; their accession numbers or other stable identifiers should be referenced in the Anticipated Results.

The following additional information should be presented in the cover letter accompanying your manuscript:

Significance of the protocol and references to any relevant primary research manuscript(s) in which it has been previously employed.

Any advance represented by the method compared with other, similar methods.

Appropriateness of the manuscript to the Specialty Section to which it has been submitted.

Associate Editors with suitable expertise to handle the manuscript.

#### 2.3.6.11. Code

The code should be novel and presented in human-readable format, adhere to the standard conventions of the language used (variable names, indentation, style and grammar), be well documented (comments in source), be provided with an example data set to show efficacy, be compilable or executable free of errors (stating configuration of system used).

The code should only call standard (freely accessible) libraries or include required libraries, and include a detailed description of the use-scenarios, expected outcomes from the code and known limitations of the code.

Please therefore make sure to provide access to the following upon submission:

Abstract explicitly including the language of code

Keywords including the language of the code in the following format:"code:language"" e.g.: "code:matlab"

Cover Letter including the utility of the code and its language

Main Text including:

code description

application and utility of the code

link to an accessible online code repository where the most recent source code version is stored and curated (with an associated DOI for retrieval after review)

access to test data and readme files

methods used

example of use

known issues

licensing information (Open Source licenses recommended)

Compressed Archive (.zip) of the reviewed version of the code as supplementary material (.zip archives are currently available under the "Presentation" dropdown menu).

## 2.4. Figure and Table Guidelines

### 2.4.1. CC-BY Licence

All figures, tables, and images will be published under a [Creative Commons CC-BY licence](#) and permission must be obtained for use of copyrighted material from other sources (including re-published/adapted/modified/partial figures and images from the internet). It is the responsibility of the authors to acquire the licenses, to follow any citation instructions requested by third-party rights holders, and cover any supplementary charges.

### 2.4.2. General Style Guidelines for Figures

The maximum number of figures and tables for all article types are shown in the [Summary Table](#). Frontiers requires figures to be submitted individually, in the same order as they are referred to in the manuscript, the figures will then be automatically embedded at the end of the submitted manuscript. Kindly ensure that each table and figure is mentioned in the text and in numerical order.

For graphs, there must be a self-explanatory label (including units) along each axis. For figures with more than one panel, panels should be clearly indicated using labels (A), (B), (C), (D), etc. However, do not embed the part labels over any part of the image, these labels will be added during typesetting according to Frontiers journal style. Please note that figures which are not according to the guidelines will cause substantial delay during the production process.

Permission must be obtained for use of copyrighted material from other sources (including re-published/adapted/modified/partial figures and images from the internet). It is the responsibility of the authors to acquire the licenses, to follow any citation instructions requested by third-party rights holders, and cover any supplementary charges.

Frontiers takes concerns regarding image manipulation seriously. We request that no individual features within an image are modified (e.g. enhanced, obscured, moved, recycled, removed or added). Image processing methods (e.g. changes to the brightness, contrast or color balance) must be applied to every pixel in the image and the changes should not alter the information illustrated in the figure. Where cropped images of blots are shown in figures, a full scan of the entire original gel(s) must be submitted as part of the supplementary

material. Where control images are re-used for illustrative purposes, this must be clearly declared in the figure legend. Image grouping and splicing must be clearly stated in the manuscript and the figure text.

For additional information, please see our Editorial Policies: 3.5 Image Manipulation.

#### **2.4.3. General Style Guidelines for Tables**

Tables should be inserted at the end of the manuscript. If you use a word processor, build your table in word. If you use a LaTeX processor, build your table in LaTeX. An empty line should be left before and after the table.

Please note that large tables covering several pages cannot be included in the final PDF for formatting reasons. These tables will be published as supplementary material on the online article abstract page at the time of acceptance. The author will notified during the typesetting of the final article if this is the case. A link in the final PDF will direct to the online material.

For additional information, please see our Editorial Policies: 3.5 Image Manipulation.

#### **2.4.4. Figure and Table Requirements**

##### Legends

Figure and table legends are required to have the same font as the main text (12 point normal Times New Roman, single spaced). Legends should be preceded by the appropriate label, for example "Figure 1" or "Table 4". Figure legends should be placed at the end of the manuscript (for supplementary images you must include the caption with the

figure, uploaded as a separate file). Table legends must be placed immediately before the table. Please use only a single paragraph for the legend. Figure panels are referred to by bold capital letters in brackets: (A), (B), (C), (D), etc.

#### Image Size

Figure images should be prepared with the PDF layout in mind, individual figures should not be longer than one page and with a width that corresponds to 1 column or 2 columns.

**All articles are prepared using the 2 column layout:** 2 column articles can contain images 85 mm or 180 mm wide.

#### 2.4.5. Format

The following formats are accepted:

TIFF (.tif) TIFF files should be saved using LZW compression or any other non-lossy compression method. JPEG (.jpg)

EPS (.eps) EPS files can be uploaded upon acceptance

#### Color Image Mode

Images must be submitted in the color mode RGB.

#### Resolution Requirements

All images must be uploaded separately in the submission procedure and have a resolution of **300 dpi at final size**. Check the resolution of your figure by enlarging it to 150%. If the resolution is too low, the image will appear blurry, jagged or have a stair-stepped effect.

Please note saving a figure directly as an image file (JPEG, TIF) can greatly affect the resolution of your image. To avoid this, one option is to export the file as PDF, then convert into

TIFF or EPS using a graphics software. EPS files can be uploaded upon acceptance.

#### Chemical Structures

Chemical structures should be prepared using ChemDraw or a similar program. If working with ChemDraw please use [Frontiers ChemDraw Template](#), if working with another program please follow the guidelines given below:

Drawing settings: chain angle, 120° bond spacing, 18% of width; fixed length, 14.4 pt; bold width, 2.0 pt; line width, 0.6 pt; margin width 1.6 pt; hash spacing 2.5 pt. Scale 100% Atom Label settings: font, Arial; size, 8 pt.

Assign all chemical compounds a bold, Arabic numeral in the order in which the compounds are presented in the manuscript text. Figures containing chemical structures should be submitted in a size appropriate for incorporation into the manuscript.

#### Legibility

Figures must be legible. Check the following:

The smallest visible text is no less than 8 points in height, when viewed at actual size.

Solid lines are not broken up.

Image areas are not pixilated or stair stepped.

Text is legible and of high quality.

Any lines in the graphic are no smaller than 2 points width.

#### 2.5. Funding disclosure

Details of all funding sources must be provided in the funding section of the manuscript including grant numbers, if applicable. All Frontiers articles are published with open access under the CC-BY Creative Commons attribution license. Articles published with Frontiers automatically fulfil or exceed the requirements for open access mandated by many institutions and funding bodies, including the National Institutes of Health, the Medical Research Council, Research Councils UK, and the Wellcome Trust. Frontiers submits funding data to the Open Funder Registry which is a funder identification service from CrossRef resulting from collaboration between scholarly publishers and funding agencies.

## **2.6. Materials and Data Policies**

Frontiers is committed to open science and open data, and we strongly encourage authors to maximize the availability of data included in their articles by making generated data publicly available where possible, and ensuring that published data sets are cited in accordance with our [data citation guidelines](#). We aim to achieve the best community standards regarding data availability, ensuring increased levels of transparency and reproducibility in our published articles.

Our policies on data availability are informed by community-driven standards, which Frontiers endorses, such as the [Transparency and Openness](#) (TOP) guidelines, and the joint declaration of data citation principles produced by [FORCE 11](#).

### **2.6.1. Availability of Materials**

Authors are strongly encouraged to make all materials used to conduct their research available to other researchers.

Research materials necessary to enable the reproduction of an experiment should be clearly indicated in the Materials and Methods section. Relevant materials such as protocols, analytic methods, and study material should preferably be uploaded to an online repository providing a global persistent link/identifier. If this is not possible, authors are strongly encouraged to make this material available upon request to interested researchers, and this should be stated in the manuscript.

### **Resource Identification Initiative**

Authors wishing to participate in the [Resource Identification Initiative](#) should cite antibodies, genetically modified organisms, software tools, data, databases, and services using the corresponding catalog number and RRID in your current manuscript. For more information about the project and for steps on how to search for an RRID, please click [here](#).

### **2.6.2. Availability of Data**

Frontiers requires that authors make all data relevant to the conclusions of the manuscript available to editors and reviewers during peer-review to enable complete and objective evaluation of the work described.

We strongly encourage authors to make the raw data supporting the conclusions of the manuscript available in publicly accessible repositories. To comply with best practice in their field of research, authors are required to make certain types of data available to readers at time of publication in specific stable, community-supported repositories such as those listed below. Authors are encouraged to contact our data availability office at [datapolicy@frontiersin.org](mailto:datapolicy@frontiersin.org) prior to submission with any queries concerning data reporting.

### 2.6.3. Data Citation Guidelines

Authors are encouraged to cite all datasets generated or analyzed in the study. Where datasets are cited, they should be included in the [references list](#) to maximize future usability. The following format should be used:

[Dataset] Author names. (year) Data Title. Repository name. Version. Persistent identifier

### 2.6.4. Data Availability Statements

Data availability statements are required for all manuscripts published with Frontiers. During the submission process, authors will be asked to detail the location of the raw data underlying the conclusions made in the manuscript, and whether it will be made available to other researchers following publication. Authors will also be asked for the details of any existing datasets that have been analysed in the manuscript. These datasets should be cited in accordance with our data citation guidelines.

A statement will be automatically generated using the information provided in the submission form; however, manuscripts containing incomplete or incorrect statements will be prevented from entering the review process.

#### Examples of acceptable statements

##### **Datasets are in a publicly accessible repository:**

The datasets [GENERATED/ANALYZED] for this study can be found in the [NAME OF REPOSITORY] [LINK]

##### **Datasets are available on request:**

The raw data supporting the conclusions of this manuscript will be made available by the authors, without undue reservation, to any qualified researcher.

##### **All relevant data is contained within the manuscript:**

All datasets [GENERATED/ANALYZED] for this study are included in the manuscript and the supplementary files.

##### **Restrictions apply to the datasets:**

The datasets for this manuscript are not publicly available because: [VALID REASON]. Requests to access the datasets should be directed to [NAME, EMAIL].

##### **Data has been obtained from a third party:**

The data analyzed in this study was obtained from [SOURCE], the following licenses/restrictions apply [RESTRICTIONS]. Requests to access these datasets should be directed to [NAME, EMAIL].

##### **No datasets were generated for this study**

### 2.6.5. Recommended and Required Repositories

**Authors are required to deposit the following data-types in public, community-supported repositories, such as those listed below, prior to publication of an associated Frontiers manuscript:**

Data-type	Recommended Repositories	Metadata Standard
Genetic and genomic sequence (DNA/ RNA) <sup>^</sup>	GenBank DNA Data Bank of Japan (DDJ) European Nucleotide Archive (ENA)	MIxS
Metagenomic sequence	EBI Metagenomics	MIxS
DNA and RNA trace or short-read sequencing data	NCBI Trace Archive NCBI Sequence Read Archive	MIxS
Genetic polymorphism data, including SNP and CNV data	dbSNP dbVar European Variation Archive DGVa	MIxS
Gene expression data; chromatin immunoprecipitation data (deep-sequencing or microarray)	ArrayExpress Gene Expression Omnibus (GEO)	MIAME / MINSEQE
Data linking genotype to phenotype	dbGaP	
Protein sequence data	UniProt	
Proteome profiling data	PRIDE PeptideAtlas ProteomeXchange	MIAPe
Small molecule, protein, protein complex data structural data	Crystallography Open Database Cambridge Structural Database wwPDB (Protein DataBank) Electron Microscopy Databank	CIF
Taxonomy data	Zoobank	

<sup>^</sup> Genetic sequence variants should be annotated according to the guidelines established by the [Human Variome Project](#).

**Authors are encouraged to consider deposition in public, community-supported repositories of the data-types listed below:**

Data-type	Recommended Repositories	Metadata Standard
Protein-protein interaction data	Database of Interacting Proteins (DIP)	MIMix
Metabolite and metabolome profiling data	MetaboLights Human Metabolome Database	MSI
Small-molecule screening data, chemical compound data	PubChem	CIF
Flow cytometry data	Flow Repository	
Brain imaging data / Neuroimaging data	OpenNeuro INDI NITRC NeuroVault (Statistical maps)	BIDS
Trait data	TRY database	
Phenology data	National Phenology Network	
Any data	FigShare Dryad Digital Repository	None

## 2.6.6. Inclusion of Zoological Nomenclature

The International Code of Zoological Nomenclature, in a recent 2012 amendment to the [1999 Zoological Code](#), allows all electronic-only papers, such as those published by the Frontiers journals, to have valid new taxon names and

nomenclatural acts. However, these new names or nomenclatural acts must be registered in [ZOOBANK](#) and have associated Life Science Identifiers (LSIDs). Registration must be done by the authors before publication. Should your manuscript include any zoological new taxon names and/or nomenclatural acts, please ensure that they are registered prior to final publication.

## 2.6.7. Inclusion of RNAseq Data

Studies employing RNASeq for comparative transcriptomic analyses must contain at least 3 biological replicates (unless otherwise justified). Each biological replicate should be represented in an independent library, each with a unique barcode if libraries are multiplexed for sequencing. Validation on a number of key transcripts highlighted in the study is also highly recommended.

Full data accompanying these experiments must be made available to reviewers at the time of submission in a freely accessible resource e.g the [sequence read archive \(SRA\)](#) or [European Nucleotide Archive \(ENA\)](#). Depending on the question addressed in a manuscript, de novo assemblies of transcriptomes may also require multiple replicates and assembled sequences together with sequence annotation must be made freely available e.g [figshare](#) or [dryad](#).

## 2.6.8 Inclusion of Proteomics Data

Authors should provide relevant information relating to how peptide/protein matches were undertaken, including methods used to process and analyse data, false discovery rates (FDR) for large-scale studies and threshold or cut-off rates for peptide and protein matches. Further information should include software used, mass spectrometer type, sequence

database and version, number of sequences in database, processing methods, mass tolerances used for matching, variable/fixed modifications, allowable missed cleavages, etc.

Authors should provide as supplementary material information used to identify proteins and/or peptides. This should include information such as accession numbers, observed mass (m/z), charge, delta mass, matched mass, peptide/protein scores, peptide modification, miscleavages, peptide sequence, match rank, matched species (for cross-species matching), number of peptide matches, etc. Ambiguous protein/peptide matches should be indicated.

For quantitative proteomics analyses, authors should provide information to justify the statistical significance, including biological replicates, statistical methods, estimates of uncertainty, and the methods used for calculating error.

For peptide matches with biologically relevant post-translational modifications (PTMs) and for any protein match that has occurred using a single mass spectrum, authors should include this information as raw data or annotated spectra, or submit data to an online repository (recommended option; see table below).

Raw or matched data and 2-DE images should be submitted to public proteomics repositories such as those participating in ProteomeXchange. Submission codes and/or links to data should be provided within the manuscript.

## 2.7. Statistics

Frontiers requires that all statements concerning quantitative differences should be based on quantitative data and statistical testing. For example, if a quantitative statement is

made regarding the abundance of a certain protein based on a western blot, we request that the blot be scanned and the abundance assessed quantitatively using the correct analytic software (e.g. ImageJ) and statistics in order to support that statement.

Statistics should/must be applied for independent experiments. The number of independent samples and the deviation parameters (e.g. Standard Error of the Mean, Standard Deviation, Confidence Intervals) should be clearly stated in the Methods or the Figure legends. In general, technical replicates within a single experiment are not considered to be independent samples. Where multiple comparisons are employed (e.g. microarray data or Genome-wide association studies), any analysis should correct for false positive results. Descriptions of statistical procedures should include the software and analysis used, and must be sufficiently detailed to be reproduced.

## 3. Editorial Policies and Publication Ethics

Frontiers' ethical policies are a fundamental element of our commitment to the scholarly community. These policies apply to all the Frontiers in journal series. Frontiers has been a member of the Committee of Publication Ethics since January 2015 and follows COPE guidelines where applicable.

### 3.1. Authorship and Author Responsibilities

Frontiers follows the [International Committee of Medical Journal Editors](#) guidelines which state that, in order to qualify for authorship of a manuscript, the following criteria should be observed:



Substantial contributions to the conception or design of the work; or the acquisition, analysis or interpretation of data for the work;

Drafting the work or revising it critically for important intellectual content;

Provide approval for publication of the content;

Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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AB, CDE and FG contributed conception and design of the study; AB organized the database; CDE performed the statistical analysis; FG wrote the first draft of the manuscript; HIJ, KL, AB, CDE and FG wrote sections of the manuscript. All authors contributed to manuscript revision, read and approved the submitted version.

The corresponding author takes primary responsibility for communication with the journal and editorial office during the submission process, throughout peer review and during publication. The corresponding author is also responsible for ensuring that the submission adheres to all journal requirements including, but not exclusive to, details of authorship, study ethics and ethics approval, clinical trial registration documents and conflict of interest declaration. The corresponding author should also be available post-publication to respond to any queries or critiques.

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*This study was carried out in accordance with the recommendations of [name of guidelines], [name of committee]. The protocol was approved by the [name of*

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Should the study be exempt from ethics approval, authors need to clearly state the reasons in the cover letter and manuscript. In order to protect subject anonymity, identifying information should not be included in the manuscript unless such information is absolutely necessary for scientific purposes AND explicit approval has been granted by the subjects.

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The reporting of unethical research, the publication of an article that did not have the required ethics committee approval

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### **Anexo 3 – Artigo em formato editável**

Level of insight in patients with OCD: an exploratory comparative study between patients with “good insight” and “poor insight”

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Running title: good versus poor insight OCD

Word count: 4,614 excluding tables and 102 references.

Tables:4



## **Abstract**

**Introduction:** Insight may be defined as the ability to perceive and evaluate external reality and to separate it from its subjective aspects. It also refers to the ability to self-assess difficulties and personal qualities. Insight may be a predictor of success in the treatment of Obsessive Compulsive Disorder (OCD), so that individuals with poor insight tend to become refractory to treatment. The objective of this study is to investigate factors associated with poor insight in individuals with OCD.

**Methods:** This cross-sectional exploratory study used the Brown Belief Assessment Scale (BABS) as a parameter for the creation of the comparison groups: individuals who obtained null scores (zero) composed the group with preserved or good insight (n = 148) and those with scores above the 75% percentile comprised the group with poor insight (n = 124); those with intermediate scores were excluded. Socio-demographic characteristics and clinical and psychopathological aspects, intrinsic and extrinsic to the typical symptoms of OCD were compared in a univariate analysis. A logistic regression was used to determine which factors associated with critical judgment remained significant.

**Results:** Individuals in the poor insight group differed from those with good insight in regards to: more prevalent use of neuroleptics (p=0.05); higher untreated time interval (p<0.001); higher total Y-BOCS score and the obsessions and compulsions factors (all factors with p <0.001); higher DY-BOCS total and dimensional scores (p from 0.04 to 0.001); higher prevalence of contamination/cleaning(p=0.006) and hoarding (p<0.001) symptoms dimensions; more prevalent sensory phenomena (p=0.023); higher levels of depression (p=0,007); more prevalent comorbidity with Bipolar Affective Disorder (p=0.05) and Post-traumatic stress disorder (PTSD) (p=0.04). After analyzing the logistic regression, we conclude that the most important factors associated with poor insight are: the presence of any sensory phenomena (OR: 2.24), use of neuroleptics (OR: 1.66), hoarding symptoms (OR: 1.15).

**Conclusion:** The variability of insight in patients with OCD seems to be an important psychopathological characteristic in the differentiation of possible

subtypes of OCD, since the poor insight is associated with sensory phenomena and greater use of neuroleptics, which makes it possible to conjecture the role of dopaminergic neurocircuits in the neurobiology of this disorder. In addition, there is also an association with the symptoms of hoarding content, admittedly one of the symptomatic contents with less response to conventional OCD treatments. Studies based on neurobiological aspects such as neuroimaging and neuropsychology may help to elucidate more consistently the role of insight in patients with OCD and the repercussions concerning available treatments.

**Keywords:** Insight; Beliefs, Obsessive compulsive disorder; Sensory Phenomena; Psychopathology.

## 1. Introduction

“Poor Insight”, or the deficit of the capacity of judgement, is usually associated with intellectual cognitive poverty and it may decrease the capacity of evaluation of the reality despite evidence to the contrary (1). The process may be similar to that in delirium (2,3), overvalued ideas (4), obsessions (5), or even in regular beliefs or automatic thoughts in people without a psychiatric diagnosis (6). Classically, the term "insight" is used in psychoanalysis to illustrate, in the therapeutic environment, the sudden understanding of something or some situation, which involves, in a certain way, the capacity to learn something. “Insight” can also be defined as the convergence of several judgments that lead the individual to the conclusion of a problem by non-means (7,8), or "a form of evaluation and perception of internal power" or "a capacity for selection and prediction of consequences" (9,10). Its function is self-evaluation, as it is able to measure difficulties and qualities (11). “Poor insight” means not understanding, perhaps even questioning, what is being done in a given situation (whether right or wrong, if appropriate or not). According to David (1990), the concept of insight comprises three components characterized by: 1) recognition of the disease itself, 2) the ability to recognize symptoms, and 3) compliance with treatment. It is a transdiagnostic concept, applicable to many psychiatric disorders (12).

There is extensive literature on insight in patients with psychotic disorders, such as Schizophrenia, Delusional Disorders, Bipolar Disorder, suicidal behavior and Neurological conditions (13-21), specially neuroimaging studies which show correlation of insight level and some brain structures as: dorsal pre-central and post-central gyri, dorsal frontal and parietal cortices (22), ventrolateral prefrontal cortex (23), which allow us to conjecture the possibility of a neurobiological constituent for insight, especially a network of frontal, temporal and parietal brain regions (23-25), including posterior insula as a main network node (26).

Obsessive-Compulsive Disorder (OCD), on the other hand, is characterized by obsessions (thoughts, images or intrusive impulses that cause emotional discomfort) and compulsions (behaviors performed to diminish or deal with the discomfort created by obsessions) (27, 28). The OCD patient is classically considered to have a good level of insight regarding their symptoms. The OCD patient, in general, understands their symptoms as ego-dystonic, that

is, impulses, wishes, or thoughts that are unacceptable or repugnant to the ego or self (29), leading patients to realize that the obsession is totally contrary to the patients' wishes and desires. Therefore, people with OCD are aware that their behaviors are abnormal and responding to their compulsions causes them anxiety and distress. It is very common, meanwhile, that at the exact time of the obsession/compulsion occurrence, patients present an oscillatory conviction (doubt) about the nature (true or false) of the obsession, resulting again in anxiety and distress (30). *Thus, patients with OCD may present diverse psychopathological features regarding levels of insight, ego dystonicity and conviction about their own symptoms. The similarity, inconsistency, complexity and/or overlapping of the cited conceptual constructs (and others, as "beliefs", "overvalued ideas", and even "delusional thoughts") (8, 31-34), have led researchers to confound the cited concepts and to use these terms very loosely, since adequate instruments to assess them are not often used.*

Therefore, the gap in the knowledge of the concept and the influence of insight on patients with OCD have been generating efforts to understand and to measure this psychopathological construct, resulting in the fact that its role in psychiatric disorders is being increasingly recognized. Recently, the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (27) included two specifiers for OCD diagnosis: the presence of tics, and, precisely, the level of insight which may be classified in "good or fair" insight, "poor insight" and "absent" insight/delusional beliefs. Insight in this context refers to construct regarding the reasonableness of one's belief, not in relation to whether one believes that they have OCD, or whether they believe in receiving treatment.

To better highlight the importance of the topic (but also to illustrate the heterogeneity of how it has been approached), from 4 to 36% of OCD patients have poor or no insight about their symptoms and their pathology (8,35-38). This poor insight subset of patients can accommodate their symptoms and take more time to seek treatment, which would associate poor insight with longer duration of illness or longer time without treatment, all of which are negative predictors for the therapeutic process of OCD, showing a worse prognosis (8,39-47).

Thus, the investigation of factors associated with poor insight in patients with OCD may help to understand some psychopathological and neurobiological

aspects and to predict the response to the current conventional treatments. Therefore, the objective of this exploratory study is to verify the association of the level of insight (to a greater or lesser degree) with a great number of clinical variables in patients with OCD. Not only the presence, but also the severity of the obsessive-compulsive symptoms (OCS) content dimensions according to the Dimensional Yale-Brown Obsessive-Compulsive Scale (DY-BOCS) and sensory phenomena were evaluated. Instead of using only the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) (45) item for insight, we assessed the presence and severity of insight with a specific instrument: The Brown Assessment Beliefs Scale (BABS) (32). Thereby, according to the literature and to our clinical experience we hypothesize that OCD patients with poor insight will present: earlier age of onset of obsessive-compulsive symptoms (OCS) (48,49), longer duration of illness (8,39,49), higher prevalence of familial history of OCD (50), higher prevalence of neuroleptics prescription (51), higher prevalence of suicidality, more common presence and higher severity of specific OCS content (especially for contamination/washing/cleaning (52) and hoarding (48,53,54)), higher prevalence of any sensory phenomena (55), higher severity of depressive (56) and anxious symptoms, and higher prevalence of specific comorbid psychiatric disorders (especially major depression (48,49), dysthymia (57), bipolar disorder (58) and delusional disorder (59)).

## **2. Materials and methods**

This cross-sectional study with the 1,001 patients database of the Brazilian Consortium for Research on Obsessive-Compulsive Spectrum Disorders (60), which collected data between 2003 and 2008 in seven research centers in three different Brazilian regions. The inclusion criteria for the study were: being in treatment at one of the research centers; fulfilled criteria for OCD according to the DSM-IV and confirmed by structured clinical interview; and being able to understand and participate in the research protocol. Comorbid diagnosis of schizophrenia was excluded. The sources of recruitment of the participants were public and private psychiatric outpatient and inpatients services. Further methodological detail (as who performed the assessment and interrater reliability) is described in Miguel et al (2008) (60). The present study was submitted and

approved by the ethics committees of the centers previously involved (USP-968/05; IPA-6600023; UFRGS-06/171; Unifesp-302/2006).

### **2.1. Instruments:**

- A. Sociodemographic and clinical questionnaire of the Brazilian Consortium for Research on Obsessive-Compulsive Spectrum Disorders (CTOC). This questionnaire was created by the CTOC researchers as an initial instrument in which socio-demographic, socioeconomic data, medical history data and a semi-structured interview on family psychiatric history were used to characterize each individual. Therefore, basic information was collected: age, weight, height, economic class, naturalness, marital status, number of children, naturalness, origin, number of people living with, religion, education, others. A general medical history is also questioned in addition to the psychiatric history that details the medications already used and the resulting effects, as well as variables related to suicidality (ideation, plan, attempt, hospitalization due to, familial history) and other treatments, such as psychotherapy.
- B. Structured Clinical Interview for DSM-IV Axis I Disorders, Research Version (SCID-I). DSM-IV Structured Interview for Personality Disorders (SIPD-IV). Not yet validated for DSM 5 in Brazilian Portuguese. These semi-structured interviews were used as a screening tool to assess the presence or not of OCD and psychiatric comorbidities (61).
- C. Yale-Brown Obsessive-Compulsive Symptom Scale (Y-BOCS). This scale has 10 items, five for obsession evaluation and five for compulsion assessment. Each item can be answered by the individual on a scale of 0 (non-linear or less pathological) to 4 (delirious or more pathological). This scale provides three scores: severity of obsessions, severity of compulsions, and total severity of OCD (45).
- D. Dimensional scale for the assessment of the presence and severity of obsessive-compulsive symptoms (DYBOCS). This scale is composed of 6 subscales according to the content of SOC (1-aggression, violence, natural disasters, 2-sexual and religious, 3-symmetry, order, counting and arrangement, 4-contamination, cleaning and washing; 5-accumulation, and 6-miscellaneous content), also generating a total score of symptoms.

It also has a list of symptoms (88 items), for each of the above-mentioned thematic dimensions (62). The Miscellanea dimension was not evaluated in this work because it is a very heterogeneous dimension, with symptoms such as concern for diseases, magic numbers, among others, that did not add to the other factors in factorial analysis.

- E. Sensory Phenomena Scale of the University of São Paulo (USP-SPS): sensorial phenomena are sensory experiences or subjective sensations, such as feelings of incompleteness, urgency or "having to do until you feel it is right") that precede repetitive behaviors such as tics or compulsions (63). They do not obey the logic of an obsessive thought, because they are not cognitive phenomena, but can generate anxiety and can be neutralized by behaviors, gestures or tics. This scale was created to measure the severity of sensory phenomena occurring before or during the performance of repetitive behaviors. This scale is divided into two parts. The first is a list of the presence of current and past phenomena. The second is a severity scale that evaluates four aspects: frequency, amount of suffering, interference in the patient's life and a total score of the three previous ones (64).
- F. Beck Depression Inventory (BDI): This inventory was created by Beck and colleagues in 1961(65) and is intended to assess the severity of depressive symptoms. It is a self-report instrument composed of 21 items with four response options for each item with values ranging from 0 to 3 (66).
- G. Beck's Anxiety Inventory (BAI): Like BDI, BAI has 21 items with 4 response options related to anxiety intensity within a one-week period (67).
- H. Brown Belief Assessment Scale (BABS). This scale was constructed to rate (rather than using a dichotomous model of "with or without insight") the degree of conviction and insight patients have concerning their beliefs. These beliefs include delusions as well as the beliefs that may underlie obsessional thinking or phobias. For patients diagnosed with OCD it is recommended that the obsession that generated the most concerns in the previous week is considered as the "belief" and then respond to 6 dimensions that can be scored from 0 (absence of pathology) to 4 (delusional or more pathological). The dimensions of insight are:

conviction; perception of others' view of belief; explanation of different views; rigidity of ideas; attempt to refute ideas; ability of insight. The seventh dimension is not part of the total score: ideas/delusions of reference (32). For the purposes of this work, this instrument served to obtain the comparison groups. According to the scores of the total sample (n=968; 33 were missing), two groups were formed: one with the preserved "good" insight (GI group) (n = 148; 15,3%), whose final BABS score was "zero" (that is, perfectly preserved insight) and another with the poor insight (PI group) (n = 124; 12,8%), whose final BABS score was above the 75% percentile (score  $\geq 14$ ). Thus, 696 (71,9%) patients with BABS score between 1 and 13 were excluded. A whole sample study was already published (53), when instead of 1,001, it was possible to proceed the analysis with 842 patients. At that study two variables were related to poor insight: hoarding and overall OCD severity. Thus, we decided for another strategy which could allow us to better explore the phenomenological aspects of poor insight in OCD patients. The selective sampling of phenotypically extreme individuals' strategy has been widely used to increase power when comparing some clinical or genetic features (68).

## **2.2. Statistics**

Continuous variables were described as mean (standard deviation) when they had normal distribution and as median (minimum-maximum) when there was no normal distribution. Categorical variables were described as absolute values (n) and relative values (%). Normal distribution was assessed by the Kolmogorov-Smirnov test. The means were compared by the Student's t-test and the medians by the Mann-Whitney U-test. Pearson's chi-square, Yates or Fisher's Exact Test were used to compare categorical variables between the two groups. Variables with a p-value  $\leq 0.10$  in the univariate analysis, respecting multi-collinearity and clinical-epidemiological relevance were included in a backward binary multiple logistic regression model of Wald to determine factors independently associated with the level of insight. The regression model included all the variables that were significant in the univariate analyzes, except those with Variance Inflation Factor (VIF)  $< 1$  or  $> 5$ , which means high collinearity (especially for continuous



variables). After the logistic regression, only variables with a p-value  $\leq 0.05$  were selected to remain in the model, since it is a conservative way to control multiple comparisons. The odds ratio, with 95% confidence intervals were also calculated for the remaining forms in the regression model. SPSS software 22.0 and WinPEPI 11.0 were used to perform the analysis.

### **3. Results**

#### **3.1. Sociodemographic and clinical data**

The sociodemographic and clinical aspects of the subjects of both groups are compared in Table 1. There is a tendency to the Good Insight group to have more frequently individuals in the Class A ( $p=0.07$ ). Otherwise, the group with Poor Insight showed a more prevalent current use of neuroleptics ( $p = 0.05$ ).

INSERT TABLE 1 HERE

Regarding the BABS dimensions descriptive results, the OCD patients with Poor Insight (total score  $\geq 14$ ) presented the following median (minimum-maximum) scores: conviction of the belief: 4 (1-4); perception of others' view of belief: 1 (0-4); explanation of the differing views: 3 (0-4); fixity of beliefs: 3 (0-4); attempt to disprove beliefs: 3 (0-4); ability of insight: 2 (0-4); and ideas/delusions of reference: 0 (0-4). Regarding the maximum score of each dimension, 81 (65.3%) of the patients are totally convinced about the reality of the "beliefs" (obsessions); 13 (10.5%) think that other people also believe completely in the "beliefs" (obsessions); 45 (36.3%) of the patients still believe in the "beliefs" (obsessions) even with the disagreement of other people about that; 44 (35.5%) completely rejected "beliefs" could be false; 78 (62.9%) makes no attempt to refute the "beliefs"; 33 (26.6%) believe that "beliefs" are not of a psychiatric nature; and 9 (7.3%) scored ideas/delusions of reference.

#### **3.2. Level of Insight and the Psychopathological intrinsic phenomena of OCD**

Some clinical characteristics of OCD were different for individuals with Poor Insight when compared to those with Good Insight (Table 2): the first group started the treatment later ( $p<0.001$ ) and remained longer untreated ( $p<0.001$ ); showed greater overall severity of symptoms in both Y-BOCS and DY-BOCS;

obtained greater severity scores in any of the symptomatologic dimensions of the DY-BOCS; higher prevalence of symptoms of symmetry, contamination/cleaning and hoarding, according to the list of symptoms of DY-BOCS; and higher prevalence of sensory phenomena.

INSERT TABLE 2 HERE

### **3.3. Level of Insight and the Psychopathological extrinsic phenomena of OCD**

The depression scores, measured by BDI, were higher in the group with Poor Insight ( $p=0.007$ ). A statistical trend to higher anxiety levels according to the BAI was shown for the Poor Insight group ( $p=0.096$ ). Among the psychiatric comorbidities that were associated with the poor insight group, major depression disorder ( $p=0.08$ ) and Attention Deficit Hyperactivity Disorder (ADHD) ( $p=0.07$ ) showed statistical tendency to the association, while bipolar disorder ( $p=0.05$ ) and simple phobia ( $p=0.04$ ) showed a relevant association. Neither suicidality nor other psychiatric comorbidities were significantly related to poor insight (Table 3).

INSERT TABLE 3 HERE

### **3.4. Logistic regression analysis.**

Table 4 shows the logistic regression results. The variables that were included in the model were: socioeconomic class; current use of neuroleptics; time interval without treatment; presence of symptoms of symmetry, contamination/cleaning, hoarding according to the D-YBOCS; YBOCS obsessions and compulsions scores; all factors related to severity as measured by the D-YBOCS; BDI and BAI total scores; comorbidity with major depression, bipolar disorder, simple phobia and ADHD. The total Y-BOCS score was excluded from the regression analysis by having VIF = 11.56 (collinearity with Y-BOCS obsessions score). "Considering that the Y-BOCS total score includes the sub score of compulsions, which is a behavioral phenomenon, and as poor insight and obsessions are both cognitive phenomena, the obsessions score was considered more clinically relevant for the purposes of this study." Thus, the presence of sensory phenomena (OR = 2.24) remained in the model with statistical significance. Other statistical relevant variables remained in the model:

current use of neuroleptics (OR = 1.66); total score of the DY-BOCS hoarding dimension (OR = 1.15); and the time interval without treatment (OR = 1.05).

INSERT TABLE 4 HERE

#### **4. Discussion**

Although many variables were statistically significant in the univariate analysis, only 4 remained significantly associated with the presence of poor insight in patients with OCD after logistic regression analysis. However, one of them (time without treatment), despite the statistical significance, did not obtain clinical-epidemiological relevance (OR = 1.05), leading us to discuss the remaining variables in the regression model: the presence of any sensory phenomena, the use of neuroleptics and severity of the DY-BOCS hoarding dimension.

##### **4.1. Sensory phenomena and poor insight in patients with OCD:**

Among the results, the most significant was the relation of the sensory phenomena with poor insight (OR=2.24). The relation of the low insight capacity with sensory phenomena was previously reported by Ferrão et al (2012), who, when comparing patients with OCD with and without sensory phenomena, found higher BABS scores for the first group (median equal to 7 and 5 respectively,  $p = 0.007$ ) (4). As suggested by some authors (69-72), the presence of sensory phenomena may predict treatment failure, which can be understood not only by its possible specific neurobiological aspects, but also by the co-occurrence of poor insight (73,74), which can itself reduce treatment engagement and reduce the chances of an appropriate treatment response. If for psychopharmacological approaches this statement is valid, the presence of sensory phenomena and poor insight leads also to increased rates of non-response in psychotherapeutic therapies (39). Moritz et al. (2018) reported that the presence of sensory phenomena in patients diagnosed with OCD predicts poor insight, but it depends on the type of sensory phenomenon, with special emphasis on visual and tactile phenomena (not analyzed in our study) (73). In this study, a positive association was also found between the severity of the sensory phenomenon and the severity of the compulsions, which may be because the sensory properties may increase the subjective reality of obsession which hinders the task of discarding thought

and, thus, turning compulsions more difficult to resist (73). Consequently, sensory phenomena (and a lower insight about symptoms) would reinforce the “vicious cycle” of OCD.

Some data suggest that patients with sensory phenomena consider this trigger more important than obsessions, and consequently have stronger compulsions (64,75). About 65% of patients with OCD perform compulsions due to sensory phenomena (64). The data above corroborate a previous study, in which poor insight about the symptoms allows the individual to have a smaller capacity to interrupt or control the OCS (36), perceiving them as "correct", "adequate", "relevant" or even "necessary".

A neurobiological explanation for this precise association is not yet possible, but some conjectures may be done. It is known that in OCD patients, the anterior dorsolateral, orbitofrontal and anterior cingulate prefrontal cortex are usually hyperactive. In general, these structures are involved in intersections with other neurocircuits to retain information, manipulate options, assist in decision making and goal maintenance (76). When they connect with limbic circuits, for instance, they add emotional aspects (rewards) to information and decision making and provide the most diverse forms of behavior (77). The neurobiological dimensional approach recently proposed by the National Institute of Mental Health (78-79) named Research Domain Criteria (<https://www.nimh.nih.gov/research-priorities/rdoc/index.shtml>) describes that the default mode network, which basically involves brain structures such as medial anterior prefrontal, posterior cingulate cortex and angular gyrus, is hyperactive in patients with OCD (80-81). This circuit, in healthy people, becomes more active at rest or when people are asked to reflect on their own thoughts. Thus, obsessions (intrusive thoughts) could be a consequence of the hyperactivity of this circuit (80), and this "hyperactivation" can be stimulated or facilitated by intersections with structures of other neurocircuits. One such structure is the insula, which together with the anterior cingulate cortex and the amygdala constitute another neural circuit known as a "protrusion circuit", which detects any "protrusion" or aspects that stand out in our perception in the environment (both external and interoceptive aspects) (81,82). Thus, it can be postulated that in patients with OCD, the “negative valence systems” (primarily

responsible for responses to aversive situations or context, such as fear, anxiety, and loss) could, for some reason, be also hyperactive, increasing the frequency and intensity of the perception of internal (interoceptive) sensations, becoming what we call “sensory phenomena”. Once the “protrusion circuit” has been activated through insular connections (80), there would be also hyperactivation of the default network circuit and, thus, the increase or maintenance of OCD symptoms. The insula is also responsible for connecting the two circuits above with other two circuits known to be involved in OCD (83,84): positive affects (responsible for the sensitivity to the presence of protrusions in the external or internal environment - this circuit involves the basal ganglia) and the cognitive (which is responsible for procedural memory and selective attention - this circuit involves, for example, the dorsolateral prefrontal cortex) (81). The direction of the influences of one circuit in the other (and vice versa), however, is still a point of discussion, but it seems little evident (from clinical experience) that the motor circuits (which generate the compulsions) can generate hyperactivation of salience circuits, causing sensory phenomena; the opposite seems more likely to happen. Thus, the association of sensory phenomena with OCD with poor insight may be based on intersections of neurocircuits with distinct functions, but that interact to manifest heterogeneously what we call OCD.

#### **4.2. Use of neuroleptics and poor insight in patients with OCD:**

Neuroleptics are not the first-choice treatment for OCD, but it seems to be valid as adjuvant when treating resistant or refractory OCD (85), especially atypical neuroleptics, which have augmenting synergism with SSRIs because they also have serotonergic action (85,86). As the CTOC sample is predominantly comprised of specialized and tertiary health services, the recruitment of more severe patients, non-responders to conventional and complex treatments (with comorbidities with tics, for example), may have biased our results, leading to a greater prevalence of the use of these specific medications in these centers (39,42,87). As poor insight was related to sensory phenomena, and since sensory phenomena are more prevalent in patients with OCD whom also have tics (64,88), we could speculate a “dopaminergic” modulation of “poor insight”. It could be explained by the facts that tics occur due to dopaminergic dysfunctions involving the basal nuclei, especially striatum and substantia nigra (89,90), which

may result clinically in the increased prescription of drugs with dopaminergic action, such as neuroleptics. Thus, the association of an atypical neuroleptic with SSRIs could act, in these cases, with synergism by serotonergic potentiation or with synergism by addition, adding effect in the involved dopaminergic neurocircuits. Another possibility to justify the association of poor insight and neuroleptics is the fact that, in certain patients with OCD, poor insight may, depending on its severity, remind clinical practitioners of delusion or even psychotic functioning (91,92), leading psychiatrists to prescribe neuroleptics in association with SSRIs (35,85,93,94).

#### **4.3. Severity of the DY-BOCS hoarding dimension and poor insight in patients with OCD:**

According to the regression performed in this study, the greater severity of the DY-BOCS hoarding dimension was associated with poor insight. Similar results are pointed out in the literature when correlating a worse insight capacity with hoarding symptoms (95-102). The reason so many papers agree to this association still needs further study. Kalogeraki and Michopoulos (2017) suggest a cognitive model for hoarding disorder that includes 4 factors: 1) personal vulnerability, including aspects such as heredity, stressful life events, personality traits and interpersonal difficulties; 2) difficulties in information processing, such as attention deficit, memory and executive functions, with difficulty to make decisions and categorize; 3) dysfunctional cognitive content, such as ownership, emotional attachment to possessions, dysfunctional beliefs about mnemonic ability and the importance of memories; and 4) hoarding behaviors and their positive and negative reinforcement, such as pleasure in acquiring/keeping or anxiety/discomfort to discard (102). Failure to be critical in relation to hoarding acts (associated or not to the diagnosis of OCD) may be a consequence of the sum of cognitive dysfunctions of more than one of these factors. In this sense, both the neural circuits associated with the greater significance of rewards for possession/accumulation (circuits of positive valence systems, primarily responsible for responses to positive motivational situations or contexts, such as reward seeking, consummatory behavior, and reward/habit learning) and greater aversion to frustration by discard/insecurity (circuit of negative valence systems) may be hyperactive simultaneously (81). Of course, the association of the

severity of the hoarding symptoms would reflect a higher intensity or complexity of interaction of these circuits, leading to a more committed insight, specifically about this symptomatology.

#### **4.4. Conclusions**

This cross-sectional exploratory study was conducted in seven tertiary research centers in three different Brazilian regions, which may alert us to interpret the results with caution, since the generalization of the results to all sort of OCD patients is limited. Due to the methodology and recruitment strategy, it may be argued that only moderate to severe patients answered the questionnaires and, thus, results may be related only for those cases. Moreover, the sample sizes were small and not equal, which may have led to loss of statistical efficiency. Nevertheless, interesting results have been found and deserve attention.

Our results showed that patients with OCD with poor insight seem to present some specificities such as: higher presence of any sensory phenomena, higher prevalence of neuroleptic use, and greater severity of hoarding symptoms. Although the methodological nature of the study does not allow causal inferences, we can conjecture that: 1) sensorial phenomena and severity of hoarding symptoms lead to a poorer insight; and 2) a poorer insight leads psychiatrists to use neuroleptics more frequently. Neurobiological and pathophysiological aspects, as well as reactive cognitive dysfunctions, may justify the first statement, while empirical observations lead to an evidence-based clinical practice that justifies the second statement in some situations. The more detailed exploration from the psychopathological and neurobiological point of view of the sensory phenomena and their subtypes in patients with OCD could help in the better understanding of how these phenomena would make it difficult for the patient to perceive the pathological nature of the symptoms. This study did not evaluate whether the use of neuroleptics in patients with OCD with poor insight had adequate response, which could be answered only in specifically designed prospective or clinical trials. Therefore, intervention studies in this subpopulation, whether with psychotropic drugs, psychotherapeutic techniques or neurobiological therapies, should be stimulated and conducted properly. Because of the heterogeneity of OCD, the more detailed understanding of insight

in patients with OCD should include in future studies the application of instruments that assess this phenomenon for each of the dimensions of DY-BOCS, in other words, how well the patient can judge as reasonable the contents of each of the symptoms dimensions. These results point to the need to explore patients with OCD with a poor insight, since they constitute a special and not uncommon (prevalence of 12.8% among OCD patients) subtype of patients that may require a greater effort by health professionals and services, mainly due to its greater complexity and the difficulty to respond to conventional available treatments.

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### **Author and contributions**

RC, LN, RP wrote the manuscript and contributed with review and the main insights in data analysis and discussion. LF, EM and YAF have planned the dataset of the consortium, coordinated the data collection, reviewed the insights in data analysis and discussion. VB proposed some change in the basic conceptual aspects of the paper and reviewed it carefully, concerning data analysis and discussion. YAF performed the statistical analysis, guided the preparation and reviewed the manuscript.

### **Conflict of interest statement**

The authors declare no conflict of interest for the purpose of this study. The present work was carried out with the support of the Coordination of Improvement of Higher Education Personnel - Brazil (CAPES) - Financing Code 001 [Ygor Arzeno Ferrão, Leonardo Franklin Fontenelle and Eurípedes Constantino Miguel Filho are stockholders of the National Research Council (CNPq), Richard Chuquel and Laura G Nascimento are CNPQ scientific initiation fellows].



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#### Anexo 4 - Tabelas

Table 1 - Socio-demographic and clinical data: comparison between patients with poor and good insight.

	Poor Insight (n=124); BABS $\geq$ 14		Good Insight (n=148); BABS=0		Statistical test	p
	Median	(Min- Max)	Median	(Min- Max)		
Age	35,5	(13-68)	32	(10-77)	UMW=8205,0	0,13
Studied years	14	(2-31)	14	(1-25)	UMW=8412,0	0,27
	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>		
Male gender	52	41,9	72	48,6	X <sup>2</sup> <sub>Yates</sub> =0,97	0,33
No spouse	76	61,3	79	53,4	X <sup>2</sup> <sub>Yates</sub> =1,56	0,21
No occupation	27	18,2	23	18,5	X <sup>2</sup> <sub>Yates</sub> <0,01	1,00
Ethnicity: White	94	75,8	121	81,8	X <sup>2</sup> <sub>Yates</sub> =1,11	0,29
Socioeconomic Classification						
Class A	8	6,5	26	17,6	X <sup>2</sup> <sub>Pearson</sub> =8,87	<b>0,07</b>
Class B	54	43,5	58	39,2		
Class C	48	38,7	54	36,5		
Class D	11	8,9	7	4,7		
Class E	3	2,4	3	2,0		
Current Treatments						
Pharmacological						
- SSRIs	91	73,4	113	76,4	X <sup>2</sup> <sub>Yates</sub> =0,18	0,67
- Other antidepressants	15	12,1	20	13,5	X <sup>2</sup> <sub>Yates</sub> =0,03	0,87
- Benzodiazepines	57	46,0	61	41,2	X <sup>2</sup> <sub>Yates</sub> =0,44	0,51
- Mood stabilizers	16	12,9	18	12,2	X <sup>2</sup> <sub>Yates</sub> <0,01	1,00
- Lithium	8	6,5	6	4,1	X <sup>2</sup> <sub>Yates</sub> =0,38	0,54
- Neuroleptics	35	28,2	26	17,6	X <sup>2</sup> <sub>Yates</sub> =3,81	<b>0,05</b>
Any psychotherapy	73	58,9	96	64,9	X <sup>2</sup> <sub>Yates</sub> =0,79	0,37
- CBT	20	27,4	25	26,0	X <sup>2</sup> <sub>Yates</sub> =0,02	0,90
Internment	15	12,1	8	5,4	X <sup>2</sup> <sub>Yates</sub> =0,47	0,49

Legend: p = level of statistical significance; UMW = Mann-Whitney U test;  $\chi^2$ <sub>Yates</sub> = Yates chi-square test; SSRI = selective serotonin reuptake inhibitor; CBT = cognitive-behavioral therapy; BABS = Brown Belief Assessment Scale.

Table 2 – Intrinsic Phenomenological Features of OCD: comparison between patients with poor and good insight.

	Poor Insight (n=124); BABS≥ 14		Good Insight (n=148); BABS=0		Statistical test	p
	Medi an	(Min- Max)	Med ian	(Min- Max)		
OCS age of onset	10	(3-37)	11	(4-43)	U <sub>MW</sub> =7680,0	0,17
Period without treatment	17	(0-56)	11	(0-58)	U <sub>MW</sub> =5281,0	<b>&lt;0,001</b>
YBOCS						
- Total Score	29	(8-40)	23	(7-37)	U <sub>MW</sub> =4670,0	<b>&lt;0,001</b>
- Obsessions	14	(4-20)	11	(1-18)	U <sub>MW</sub> =4651,0	<b>&lt;0,001</b>
- Compulsions	15	(4-20)	12	(2-20)	U <sub>MW</sub> =5286,0	<b>&lt;0,001</b>
D-YBOCS severity						
- Total Score	24	(4-30)	21	(0-30)	U <sub>MW</sub> =6476,5	<b>&lt;0,001</b>
- Aggressiveness	7	(0-15)	3	(0-15)	U <sub>MW</sub> =7220,0	<b>0,04</b>
- Sex / Religion	6	(0-15)	0	(0-15)	U <sub>MW</sub> =7599,0	<b>0,01</b>
- Symmetry / Ordering	9	(0-15)	6	(0-15)	U <sub>MW</sub> =6730,5	<b>&lt;0,001</b>
- Contamination/Cleaning	9	(0-15)	3,5	(0-14)	U <sub>MW</sub> =6676,5	<b>&lt;0,001</b>
- Hoarding	3,5	(0-15)	0	(0-13)	U <sub>MW</sub> =6051,0	<b>&lt;0,001</b>
Severity Sensory Phenomena *	9	(1-15)	9	(1-15)	U <sub>MW</sub> =3513,5	0,24
	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>		
Family History of OCD	60	48,4	71	48,0	X <sup>2</sup> <sub>Yates</sub> <0,001	1,00
Family History of Tics	25	20,8	22	15,7	X <sup>2</sup> <sub>Yates</sub> =0,82	0,37
D-YBOCS dimensions						
- Aggressiveness	87	70,2	95	64,2	X <sup>2</sup> <sub>Yates</sub> =0,83	0,36
- Sex / Religion	77	62,1	83	56,1	X <sup>2</sup> <sub>Yates</sub> =0,78	0,38
- Symmetry	113	91,1	121	82,3	X <sup>2</sup> <sub>Yates</sub> =3,71	<b>0,054</b>
- Contamination/Cleaning	98	79,0	93	62,8	X <sup>2</sup> <sub>Yates</sub> =7,71	<b>0,006</b>
- Hoarding	83	66,9	59	39,9	X <sup>2</sup> <sub>Yates</sub> =18,75	<b>&lt;0,001</b>
Presence of any Sensory Phenomena	94	75,8	92	62,2	X <sup>2</sup> <sub>Yates</sub> =5,20	<b>0,023</b>

Legend: \* Poor insight (n = 92); Good insight (n = 85); p = level of statistical significance; U<sub>MW</sub> = Mann-Whitney U test;  $\chi^2$ <sub>Yates</sub> = Yates chi-square test; SOC = obsessive compulsive symptoms; YBOCS = Yale-Brown Obsessive-Compulsive Symptom Scale; DYBOCS = Dimensional scale for the assessment of the presence and severity of obsessive-compulsive symptoms; BABS = Brown Belief Assessment Scale.

Table 3: Extrinsic Phenomenological Features of OCD: comparison between patients with poor and good insight.

	Poor Insight (n=124); BABS ≥ 14		Good Insight (n=148); BABS=0		Statistical test	p
	Median	(Min-Max)	Median	(Min-Max)		
<b>BDI</b>	17	(0-52)	13	(0-53)	U <sub>MW</sub> =7384,5	<b>0,007</b>
<b>BAI</b>	15	(0-51)	12	(0-48)	U <sub>MW</sub> =8045,0	<b>0,096</b>
	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>		
<b>Suicidality</b>						
- Ideation	48	40,3	55	39,3	X <sup>2</sup> <sub>Yates</sub> =0,002	0,96
- Plan	25	21,0	29	20,7	X <sup>2</sup> <sub>Yates</sub> <0,001	1,00
- Attempt	11	9,2	15	10,7	X <sup>2</sup> <sub>Yates</sub> =0,03	0,85
-Hospital internment	4	3,2	4	2,7	X <sup>2</sup> <sub>Yates</sub> =0,65	0,80
-Familial History	23	19,3	22	15,7	X <sup>2</sup> <sub>Yates</sub> =0,36	0,55
<b>Comorbidities</b>						
- Major Depression	51	41,1	42	28,4	X <sup>2</sup> <sub>Yates</sub> =4,94	<b>0,08</b>
- Dysthymia	16	12,9	21	14,2	X <sup>2</sup> <sub>Yates</sub> =0,02	0,90
- BAD	6	4,8	1	0,7	Fisher	<b>0,05</b>
- Delusional Disorder	6	4,8	2	1,4	Fisher	0,15
- Anxiety Disorders						
- Panic	10	8,1	16	10,8	X <sup>2</sup> <sub>Yates</sub> =0,31	0,58
- Agoraphobia	3	2,4	7	4,7	Fisher	0,35
- Social phobia	32	25,8	35	23,6	X <sup>2</sup> <sub>Yates</sub> =0,08	0,79
- Simple Phobia	30	24,2	36	24,3	X <sup>2</sup> <sub>Yates</sub> <0,001	1,00
- PTSD	21	16,9	12	8,1	X <sup>2</sup> <sub>Yates</sub> =4,14	<b>0,04</b>
- GAD	32	25,8	49	33,1	X <sup>2</sup> <sub>Yates</sub> =1,39	0,24
-Alcohol Abuse/Dependence	5	4,0	6	4,1	X <sup>2</sup> <sub>Yates</sub> =1,20	0,55
-Tics	34	27,4	41	27,7	X <sup>2</sup> <sub>Yates</sub> <0,001	1,00
-Tourette Disorder	10	8,1	9	6,1	X <sup>2</sup> <sub>Yates</sub> =0,16	0,69
-Separation Anxiety	7	5,6	6	4,1	X <sup>2</sup> <sub>Yates</sub> =0,11	0,75
-ADHD	22	17,7	14	9,5	X <sup>2</sup> <sub>Yates</sub> =3,34	<b>0,07</b>

Legend: p = level of statistical significance; U<sub>MW</sub> = Mann-Whitney U test;  $\chi^2_{Yates}$  = Yates chi-square test; BDI = Beck Depression Inventory; BAI = Beck Anxiety Inventory; BAD = Bipolar Affective Disorder; PTSD = Post Traumatic Stress Disorder; GAD = Generalized Anxiety Disorder; ADHD = Attention Deficit Hyperactivity Disorder; BABS = Brown Belief Assessment Scale.

Table 4 - Binary logistic regression results (WALD backwards) with predictor variables ( $p \leq 0.10$ ) of the univariate analysis.

	<b>Wald <math>\chi^2</math></b>	<b>p</b>	<b>OR</b>	<b>CI 95% of OR</b>
Current use of Neuroleptics	8,88	0,003	1,66	1,31 - 1,84
Period without treatment	13,61	<0,001	1,05	1,02 – 1,08
Severity of Hoarding dimension	14,22	<0,001	1,15	1,07 – 1,24
Presence of any sensory phenomena	6,20	0,013	2,24	1,19 – 4,22
Variable inserted in the steps of Regression: step 1 - Gravity of the accumulation dimension; step 2- Time without treatment; step 3- Current use of Neuroleptics; step 4 - Presence of some sensory phenomenon.				

Legend: Wald  $\chi^2$  = Wald chi-square test; p = level of statistical significance. OR = odds ratio; CI = confidence interval.

## **Anexo 5 – Carta ao editor**

**Dear Editor,**

We have read with the utmost attention the comments and suggestions of the reviewer. With them we believe the paper now is very much improved. The answers to each of the queries are bellow. To better answer them we had to add some references.

We would like to thanks the effor of both to make the paper improved.

Thanks in advance for your kind attentio, hoping it will now be considered for publication.

Ygor Arzeno Ferrão and Richard de Ávila.

<b>Answers to Reviewer 1</b>
------------------------------

**1.Introduction - It is very lengthy and provides many details on insight in various psychiatric disorders. Insight in OCD is a well researched subject and one should directly come to the point.**

We thanks for the suggestion and suppressed some parts of the introduction. Instead of 1,325 words it now has 895. We suppressed the sentences about insight in other psychiatric disorders and the statements about treatment response, trying to “come more straightly to the point”.

**2.There is a huge section on insight and treatment response. Is this a very clear relationship? Studies have not always found a relationship. This section needs to be tidied up.**

We agree with the reviewer and have suppressed it from the introduction.

**3.Line 127 - "For the first time not only the presence, but also the severity, of the obsessive-compulsive symptoms (OCS) content and sensory**

**phenomena were evaluated." Severity of OCD and insight has been examined earlier; hence this statement is not entirely correct.**

We thanks the reviewer for the comment and agree that the sentence was not clear. Now it is written as follows:

"Not only the presence, but also the severity of the obsessive-compulsive symptoms (OCS) content dimensions according to the Dimensional Yale-Brown Obsessive-Compulsive Scale (DY-BOCS) and sensory phenomena were evaluated."

**4.Line 132 - "Thereby, we hypothesize that OCD patients with poor insight will present: earlier age of onset of obsessive-compulsive symptoms (OCS), longer duration of illness, higher prevalence of familial history of OCD, higher prevalence of neuroleptics prescription, higher prevalence of suicidality, more common presence and higher severity of specific OCS content (especially for contamination/washing/cleaning and hoarding), higher prevalence of any sensory phenomena, higher severity of depressive and anxious symptoms, and higher prevalence of specific comorbid psychiatric disorders (especially major depression, dysthymia, bipolar disorder and delusional disorder)." - If these are derived from previous literature, then they need to be quoted!**

We agree with the reviewer and now the paragraph was rewritten as follows. New references needed to be added.

" Thereby, according to the literature and to our clinical experience we hypothesize that OCD patients with poor insight will present: earlier age of onset of obsessive-compulsive symptoms (OCS) (48,49), longer duration of illness (8,39,49), higher prevalence of familial history of OCD (50), higher prevalence of neuroleptics prescription (51), higher prevalence of suicidality, more common presence and higher severity of specific OCS content (especially for contamination/washing/cleaning (52) and hoarding (48,53,54)), higher prevalence of any sensory phenomena (55), higher severity of depressive (56) and anxious symptoms, and higher prevalence of specific comorbid psychiatric

disorders (especially major depression (48,49), dysthymia (57), bipolar disorder (58) and delusional disorder (59))."

**5. Who performed the assessments, and under whose supervision. Who confirmed the diagnosis? Was there interrater reliability exercises performed?**

As it was written at line 149, "Further methodological detail is described in Miguel et al (2008) (45)." But to make it more complete, the sentence was rewritten to:

"Further methodological detail (as who performed the assessment and interrater reliability) is described in Miguel et al (2008) (60).

**6. Extremes of group were taken for analysis. But what are the results of an analysis using continuous scores? This also needs to be shown. The sample size will then become large (1000) and generalized results are possible.**

Another study with the same dataset was conducted with all sample analysis by Jakubovski E, Pittenger C, Torres AR, et al. (2011) [Dimensional correlates of poor insight in obsessive-compulsive disorder. *Prog Neuropsychopharmacol Biol Psychiatry*. 2011;35(7):1677–1681. doi:10.1016/j.pnpbp.2011.05.012, when instead of 1,001 patients, it was possible to proceed the analysis with only 842. At that study only two variables were related to poor insight: hoarding and overall OCD severity. Thus, we decided for another strategy which could allow us to better explore the phenomenological aspects of poor insight in OCD patients, as written at line 218 "The selective sampling of phenotypically extreme individuals' strategy has been widely used to increase power when comparing some clinical or genetic features (53)." To let it more clear, we added the following sentence after the above mentioned:

"A whole sample study was already published (53), when instead of 1,001, it was possible to proceed the analysis with 842 patients. At that study two variables were related to poor insight: hoarding and overall OCD severity. Thus,

we decided for another strategy which could allow us to better explore the phenomenological aspects of poor insight in OCD patients. The selective sampling of phenotypically extreme individuals' strategy has been widely used to increase power when comparing some clinical or genetic features (68).”

#### **7. Line 283 - why was obsession score considered more importante**

We thanks the reviewer for the observation. The sentence now is written as follows:

“Considering that the Y-BOCS total score includes the subscore of compulsions, which is a behavioural phenomena, and as poor insight and obsessions are both cognitive phenomena, the obsessions score was considered more clinically relevant for the purposes of this study.”

#### **8. Results - only statistically significant results to be put in results text. Overall results are available in table.**

We thanks for the observation. The paragraphs with significant results were suggested to be located above each table exactly to “link” the text with the tables. Only one paragraph has no tabled results: the one which describes BABS itens results.

#### **9. Age, age of onset and gender and clinically relevant variables for insight and need to be used for regression analysis as covariates.**

We thanks for the observation, but when proceeding the multiple regression analysis, to be more conservative as possible, authors decided to include only those variables with  $p < 0.10$  at the univariate analysis, as described at line 228. Thus, age, age of onset and gender reached no level of statistical relevance to be included at the Regression Model. The regression model included all the variables that were significant in the univariate analyzes, except those with Variance Inflation Factor (VIF)  $< 1$  or  $> 5$ , which means high collinearity.



**10. What is the relationship with family history of OCD/other diagnoses like psychoses?**

As it was not a significant result at the Regression Analysis, it was not discussed.

**11. Line 326 onwards - There is a lot of speculation about neurobiology here. This needs to be crisp and focus on what is known about neurobiology of poor insight and then try to build in the relationship with sensory phenomena.**

Thanks again for the suggestion, but since almost nothing is known about the neurobiology of Poor Insight and as the paper will be published in the Research Topic **“Advances in Biological Approaches to Treating Resistant/Refractory Obsessive-Compulsive and Related Disorders”** the authors tried to speculate important aspects of the subject, which may, in the future, guide other authors to investigate insight and its neurobiology. When searching for papers at Pubmed, using “poor insight” and “neurobiology”, for instance, we found 12 papers, but no one about OCD. Thus, it seemed appropriate to maintain what was conjectured about that in this paper.

**12. Line 364 - Use of neuroleptics may be related to poor treatment outcome itself? People use augmentation when pure SSRI treatment fails, as an augmentation strategy. Again, there is speculation on tics and sensory phenomena; Is such a relationship found in the current sample.**

We thanks for the observation. We rewrote some parts of the paragraph to make it clear that may be a “dopaminergic” modulation of poor insight in OCD patients. We speculate that “poor insight”, sensory phenomena and tics may be due to some neurocircuits which comprise dopamine as the main neurotransmissor. The sentence was rewritten as follows:

“As poor insight was related to sensory phenomena, and since sensory phenomena are more prevalent in patients with OCD whom also have tics (64,88), we could speculate a “dopaminergic” modulation of “poor insight”.”

**13. As current treatment has been taken into analysis, maybe current YBOCS improvement may also need to be taken (or treatment outcome). If not, both should not be used. There is too much focus on neuroleptics in discussion**

As described at line 142, this was a cross-sectional study and, thus, we, unfortunately do not have a follow-up to proceed to a “YBOCS improvement” analysis. But, as our clinical experience points to the fact that many poor insight OCD patients are treated with neuroleptics, it seemed interesting to keep this variable in the analysis and, as at the regression analysis it remained significant, our “clinical impression” was confirmed. There is only one paragraph discussing neuroleptics (from line 363 to 381) and it was one important aspect of our results, which may reinforce some knowledge for this “**Advances in Biological Approaches to Treating Resistant/Refractory Obsessive-Compulsive and Related Disorders**” to be published in **Frontiers in Psychiatry** - section **Psychopharmacology**. We had already stated that limitation at line 397 (“This study did not evaluate whether or not the use of neuroleptics in patients with OCD with poor insight had adequate response, which could be answered only in specifically designed prospective or clinical trials.”).

**14. Table 4 - what is gravity of accumulation dimension? Hoarding**

We apologize for the bad English. It was corrected to “Hoarding Dimension Severity”.

**15. Period without treatment is an important finding in regression and needs to be discussed.**

Thanks for the opportunity to discuss that point. We agree that “p-value” was significant, but as stated at line 295, the OR value of “1.05” did not reach a

clinical-epidemiological relevance, since it means only a 5% probability of “period without treatment” to be related to poor insight in the sample.

## **16. Study limitations are not stated.**

Some study limitations were already described in the Conclusion section: at line 410 (“Although the methodological nature of the study does not allow causal inferences...”); at line 419 (“This study did not evaluate whether or not the use of neuroleptics in patients with OCD with poor insight had adequate response...”). But we added the following sentence at the beginning of the Conclusion section:

This cross-sectional exploratory study was conducted in seven tertiary research centers in three different Brazilian regions, which may alert us to interpret the results with caution, since the generalization of the results to all sort of OCD patients is limited. Due to the methodology and recruitment strategy, it may be argued that only moderate to severe patients answered the questionnaires and, thus, results may be related only for those cases. Moreover, the sample sizes were small and not equal, which may had led to loss of statistical efficiency. Nevertheless, interesting results have been found and deserve attention.

**Reviewer 2**

**I really liked the manuscript**

Thanks for that!

**Nonetheless I would like to point out the following:**

**1) the hypothesis of the existence of a neurobiological constituent of insight based on a single ALS / FTD study; seems scarce. After extensive contextualization in schizophrenia and bipolar disorder, this jump seems somewhat forced. This component of the manuscript can be improved. It**

**pales in comparison to the rest of the manuscript. P.e. the question of insight in the OCD is best brought in a more elegant way.**

We thanks the reviewer for the observation and included some more neurobiological aspects/references to the paragraph, though not too much, since it is located in the Introduction section. It was rewritten like follows:

“There is extensive literature on insight in patients with psychotic disorders, such as Schizophrenia, Delusional Disorders, Bipolar Disorder, suicidal behavior and Neurological conditions (13-21), specially neuroimaging studies which show correlation of insight level and some brain structures as: dorsal pre-central and post-central gyri, dorsal frontal and parietal cortices (22), ventrolateral prefrontal cortex (23), which allow us to conjecture the possibility of a neurobiological constituent for insight, especially a network of frontal, temporal and parietal brain regions (23-25), including posterior insula as a main network node (26).”

**2) Comorbid schizophrenia was an exclusion factor. However Bipolar disorder wasn't. This appears even more relevant since a relevant association (between Bipolar Disorder and OCD)**

Thanks for the opportunity to discuss this point, since apparent comorbidity between bipolar disorder (BD) and obsessive-compulsive disorder (OCD) is a common condition in psychiatry, but treatment of BD-OCD remains a clinical challenge. As the OCD symptoms that occur in individuals with BD often occur during the depressive episodes or during the intervals between episodes of depressive or manic symptoms (real comorbidity) we decided to include this comorbidity in our dataset. Otherwise, the OCD symptoms that occur in individuals with schizophrenia often occur throughout the disease period, leading us to interpret it as part of schizophrenia psychopathology manifestation and not as OCD. However the authors didn't find important to include this statement at the paper.

**Excellent article.  
I would like to suggest:**

- 1) the correction of some typos such as (but not limited to):
  - a) Line 90 "to have to respond to their"
  - b) Lines 100-101; 121-122: are partially highlighted in pale blue
  - c) "Kolmogorov-Smirnof" should be "Kolmogorov-Smirnov"

We apologize for the inconvenience. The typos were all reviewed all along the paper and correct when needed.