




# Sensory Hypersensitivity Severity and Association with Obsessive-Compulsive Symptoms in Adults with Tic Disorder

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**Background:** Sensory hypersensitivity, defined as heightened awareness of and reactivity to external stimuli, is a bothersome symptom that affects up to 80% of adults with Tourette syndrome (TS). Such widespread prevalence suggests sensory hypersensitivity is a core feature of the disorder, but its severity and association with other clinical features of TS remain largely unexplored. Complicating matters, sensory hypersensitivity has been observed in two neurodevelopmental disorders commonly comorbid with TS: obsessive-compulsive disorder (OCD) and attention deficit hyperactivity disorder (ADHD).

**Objective:** We sought to measure sensory hypersensitivity in TS patients relative to healthy controls and to investigate the relationship of sensory hypersensitivity with OCD and ADHD symptoms in the context of TS.

**Methods:** We recruited 34 adults with TS or chronic tic disorder to undergo evaluation with the Yale Global Tic Severity Scale (YGTSS) and a battery of validated self-report instruments assessing sensory hypersensitivity (Sensory Gating Inventory, SGI; Sensory Perception Quotient, SPQ), premonitory urge (Premonitory Urge to Tic Scale, PUTS), OCD (Dimensional Obsessive-Compulsive Scale, DOCS), and ADHD (Adult ADHD Self-Report Screening Scale for DSM-5, ASRS-V). Age- and sex-matched healthy controls were recruited to complete SGI and psychiatric measures.

**Results:** SGI and SPQ scores strongly correlated ( $r_s = -0.73$ ,  $p < 0.0001$ ) within patients. SGI total score was significantly higher in patients versus controls (119.0 vs 67.6,  $U = -5.3$ ,  $p < 0.0001$ ), indicating greater sensory hypersensitivity in the tic disorder group. SGI score correlated modestly with PUTS, DOCS, and ASRS-V scores but not with YGTSS total tic score. Hierarchical linear regression analysis revealed that, of the tested variables, only DOCS score contributed significantly to mean SGI score, with  $\beta$  ranging from 1.03 ( $p = 0.044$ ) to 1.41 ( $p = 0.001$ ). A simple linear regression model with DOCS as the independent variable accounted for 31.9% of SGI score variance.

**Conclusion:** Sensory hypersensitivity is prominent in adults with tic disorder and is independently associated with obsessive-compulsive symptom severity.

**Keywords:** Tourette syndrome, tic disorder, sensory hypersensitivity, sensory sensitivity, obsessive-compulsive symptoms

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## Introduction

Bothersome sensory symptoms are common in Tourette syndrome (TS).<sup>1-3</sup> The most widely recognized sensory symptom is premonitory urge, an unpleasant bodily sensation that waxes in the moments preceding a tic and typically wanes with execution of the tic.<sup>3</sup> Premonitory urges are reported by 90% of adults and

older children with TS,<sup>3,4</sup> and many patients find these more disturbing than the tics themselves.<sup>1</sup>

In addition to premonitory urges, as many as 80% of individuals with TS experience sensory hypersensitivity, defined as heightened awareness of and reactivity to external stimuli.<sup>1,5</sup> Patients with sensory hypersensitivity describe, for example, enhanced perception of clothing rubbing against their skin; noise from electrical appliances; and intensity of ambient light.<sup>1,5</sup> This heightened exteroceptive awareness is typically associated with avoidant behavior of provocative stimuli. Faint, repetitive sensations seem to be particularly grating.<sup>1,5</sup> Although sensory hypersensitivity is endorsed by the vast majority with TS, patients actually exhibit normal detection thresholds for tactile,<sup>5,6</sup> olfactory,<sup>5</sup> and auditory stimuli.<sup>5</sup> Higher-order sensory processing anomalies, however, have been identified in this population.<sup>7-9</sup> For example, children with TS habituate abnormally to repetitive tactile stimuli,<sup>7</sup> and they process visual information differently than their typically developing peers.<sup>8</sup> It remains unclear whether such higher-order sensory processing aberrations give rise, in full or in part, to the clinical phenomenon of sensory hypersensitivity. Studies exploring sensory processing in TS at the psychophysical or neurophysiologic level have yet to quantitatively evaluate for patient-reported sensory hypersensitivity, resulting in a translational knowledge gap.

Research into sensory hypersensitivity in TS patients has been predominantly confined to qualitative description.<sup>1,5</sup> A single study has examined the severity of the clinical phenomenon in adults with TS, finding significantly increased extent of sensory hypersensitivity in patients relative to healthy controls.<sup>10</sup> However, the study was limited by a small patient sample size (9 adults and 9 children). Thus, sparse quantitative, patient-reported data exists regarding sensory hypersensitivity in adults with TS. Sensory hypersensitivity is likely present in children with TS, but varied terminology and operational definitions in adult and pediatric studies pose major challenges for comparisons across age groups.<sup>9,11-13</sup> Despite these ambiguities, the current body of evidence suggests that sensory hypersensitivity is an integral clinical feature of TS that is associated with diminished quality of life.<sup>9</sup>

Sensory hypersensitivity is not unique to TS. It has been reported in several other neurodevelopmental disorders, including obsessive-compulsive disorder (OCD)<sup>14-16</sup> and attention deficit hyperactivity disorder (ADHD).<sup>17</sup> Both OCD and ADHD are highly prevalent in TS, with respective lifetime rates of 50.0% and 54.3%.<sup>18</sup> Even TS patients

not meeting formal diagnostic criteria for OCD or ADHD frequently exhibit symptoms of these disorders.<sup>19</sup>

The complexity of the TS phenotype makes it difficult to disentangle the relationship between sensory and psychiatric dimensions of the disorder.<sup>18</sup> Conflicting results have emerged regarding associations between obsessive-compulsive symptoms and perceptual dysfunction in TS, with the sole study in adults failing to detect a relationship,<sup>10</sup> but studies in children repeatedly demonstrating such a relationship.<sup>12,13</sup> A single study in a pediatric TS sample found that children with dual diagnoses of ADHD and TS experienced more sensory processing dysfunction than children with TS alone,<sup>20</sup> a similar study has yet to be conducted in adults with TS. Understanding the relationship of sensory hypersensitivity with OCD and ADHD symptomatology may sharpen definitions of clinically relevant TS subtypes and may facilitate transdiagnostic research into the neural basis of this shared phenomenon.

Thus, existing evidence suggests sensory hypersensitivity is a core clinical manifestation of TS and is possibly linked with comorbid OCD and/or ADHD. Here we sought to replicate, in a larger sample, previous findings showing increased sensory hypersensitivity in adults with TS relative to healthy controls. We also sought to examine the relationship of sensory hypersensitivity with OCD and ADHD symptoms in adults with TS. We recruited adult patients with TS or chronic tic disorder, as well as age- and sex-matched healthy controls, to complete a battery of validated, self-report rating scales assessing sensory hypersensitivity and common TS psychiatric comorbidities. Patients were also administered the Yale Global Tic Severity Scale (YGTSS) and the Premonitory Urge to Tic Scale (PUTS). We hypothesized that patients would endorse significantly more sensory hypersensitivity compared to controls. Given the known link between sensory hypersensitivity and obsessive-compulsive symptoms in other populations, we further hypothesized that severity of sensory hypersensitivity among patients would positively correlate with obsessive-compulsive symptoms.

## Methods

### Participants

Between April 2019 and May 2020, we prospectively recruited 34 adults (>18 years of age) with TS ( $n = 32$ ) or chronic (motor or vocal) tic disorder ( $n = 2$ ) from Vanderbilt University Medical Center (VUMC) Tourette

Syndrome Clinic and from VUMC research registries. Tic disorders were diagnosed according to *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5) criteria. Notably, evidence indicates chronic motor tic disorder (defined as one or more motor tics but no vocal tics, persistent for more than one year with tic onset before 18) and chronic vocal tic disorder (defined as one or more vocal tics but no motor tics, persistent for more than one year with tic onset before 18) exist on a common clinical continuum with TS (defined as at least two motor tics and one vocal tic, persistent for more than one year with tic onset before 18), with chronic motor tic disorder and chronic vocal tic disorder being less severe forms of TS.<sup>21</sup> In this article, the term “tic disorder” encompasses chronic motor tic disorder, chronic vocal tic disorder, and TS.

A non-clinical sample of healthy adult controls was recruited through ResearchMatch. ResearchMatch is a web-based recruitment registry designed to link investigators with volunteers interested in clinical research; volunteers are notified of new research studies for which they may qualify based on self-reported demographic and medical information.<sup>22</sup> For this study, individuals with no reported history of neurologic or psychiatric diagnoses were recruited through this platform. Once enrolled, controls completed assessments online and were not interviewed or examined in person. Patients and healthy controls were one-to-one matched on sex and age ( $\pm 3$  years).

All participants were required to have capacity for providing informed consent and to speak English (given the validated scales employed). All participants gave informed consent electronically prior to engaging in any study-related activity. This study was approved by the VUMC Institutional Review Board and was conducted in accordance with the Declaration of Helsinki.

## Measures

Table 1 summarizes the rating scales used in this study. The YGTSS was administered to all patients by a neurologist experienced with the scale (D.I.). Patients were then invited to complete a battery of self-report rating scales in Research Electronic Data Capture (REDCap), a secure online, HIPPA-compliant research database.<sup>23,24</sup> Median time between YGTSS and completion of self-report scales was 8.5 days (range 0–100 days). Controls completed an identical battery, except they were not asked to complete TS-specific scales or the Sensory

**Table 1** Clinical Rating Scales

Scale Name	# of Scale Items	Scale Range	Score Interpretation
Sensory Gating Inventory (SGI) <sup>25</sup>	36	0–216	Higher scores indicate more abnormal sensory gating experiences
Sensory Perception Quotient (SPQ) <sup>26*</sup>	35	0–105	Lower scores indicate greater sensory hypersensitivity
Dimensional Obsessive-Compulsive Scale (DOCS) <sup>28</sup>	20	0–80	Higher scores indicate more obsessive-compulsive symptoms
Adult ADHD Self-Report Screening Scale for DSM-5 (ASRS-V) <sup>54</sup>	6	0–24	Higher scores indicate more ADHD symptoms
Generalized Anxiety Disorder 7 (GAD-7) <sup>55</sup>	7	0–21	Higher scores indicate more anxiety
Patient Health Questionnaire 9 (PHQ-9) <sup>56</sup>	9	0–27	Higher scores indicate more depression
Premonitory Urge to Tic Scale (PUTS) <sup>27*</sup>	10	9–36	Higher scores indicate more severe premonitory urge
YGTSS Total Tic Score <sup>57*</sup>	10	0–50	Higher scores indicate more severe tics; the total score is comprised of two subscales: motor tic score (0–25) and phonic tic score (0–25)

**Note:** \*Administered to patients only.

Perception Quotient (SPQ). All participants were asked to start and finish the battery of self-report scales in a single sitting.

The primary outcome of interest was the Sensory Gating Inventory (SGI), a self-report measure of “sensory gating-like subjective experiences” developed and validated in healthy controls.<sup>25</sup> For this instrument, respondents rate 36 statements about sensory perception on a six-point Likert scale from “never true” to “always true.” Higher total score signifies more abnormal sensory gating experience. No established scale cutoffs delineate normal from abnormal sensory perception. The SGI is

comprised of four domains, identified by confirmatory factor analysis: Perceptual Modulation, Distractibility, Over-Inclusion and Hyperawareness, and Fatigue and Stress Vulnerability.<sup>25</sup> Domain scores were calculated for this study. As no accepted gold standard scale exists for quantifying sensory hypersensitivity, the SGI was selected as the primary outcome because it was rigorously developed ( $n > 1000$  participants) and validated ( $n > 800$  participants) in large sample populations, with systematic assessment for scale test–retest reliability, factor structure, convergent and discriminant validity, and sex differences.<sup>25</sup> Notably, the scale showed good convergent validity with the Highly Sensitive Person Scale ( $r = 0.65$ ,  $p < 0.001$ ,  $n = 219$ ),<sup>25</sup> another measure of sensory sensitivity. Furthermore, the scale has previously been administered in a TS sample.<sup>10</sup>

Because no accepted gold standard measure of sensory hypersensitivity exists, a second sensory hypersensitivity scale, the SPQ, was also administered to patients in order to test convergent validity of the SGI in a population with chronic tic disorders. The SPQ is a self-report questionnaire validated in healthy adults and in adults with autism spectrum disorder.<sup>26</sup> Respondents use a four-point Likert scale to rate level of agreement on 35 statements about basic sensory perception, with 29 items devoted to hypersensitivity and six devoted to hyposensitivity. The hyposensitivity items are reverse-scored. Lower total SPQ score indicates greater sensory hypersensitivity. As with the SGI, no established score thresholds distinguish normal from abnormal sensory perception. The SPQ has also undergone careful development and validation, with assessment for scale factor structure, convergent validity, and sex differences.<sup>26</sup>

Tic disorder patients were also administered the PUTS, a widely used 10-item self-report survey quantifying severity of premonitory urge.<sup>27</sup> Item 10 asks patients to rate tic suppressibility and, in accord with prior studies, is not included in the total score given its lack of correlation with the remainder of the scale items and its intended measurement of a distinct construct (tic suppressibility as opposed to premonitory urge).<sup>27</sup> Higher total PUTS score indicates more severe premonitory urge(s).

To ascertain the impact of psychiatric comorbidities on sensory phenomena, validated self-report scales for OCD, ADHD, depression, and anxiety were included in the assessment battery. Dimensional Obsessive-Compulsive Scale (DOCS) score cutoff of  $\geq 21$  provides 70% sensitivity and 70% specificity in discriminating OCD from other anxiety disorders.<sup>28</sup> Adult ADHD Self-Report Screening Scale for DSM-5 (ASRS-V) score cutoff of

$\geq 14$  provides 81% sensitivity and 70% specificity in identifying ADHD in clinical populations.<sup>29</sup>

## Statistics

To evaluate scale internal consistency, Cronbach's  $\alpha$  was computed for all self-report measures. A threshold of 0.70 was deemed the minimum acceptable reliability.<sup>30</sup> Spearman's rank correlation ( $r_s$ ) was used to assess convergent validity of SGI and SPQ measures, as well as to quantify the association between other clinical rating scales. Between-group comparisons of variables were conducted with Wilcoxon-rank sum test statistic ( $U$ ). Effect size of between-group differences was also quantified with the Wilcoxon-rank sum statistic.<sup>31</sup>

To determine the potential modifying influence of OCD and ADHD symptoms on sensory hypersensitivity, two approaches were taken. First, the subset of tic disorder patients ( $n = 11$ ) who screened negative for OCD (DOCS score  $< 21$ ) and ADHD (ASRS score  $< 14$ ) were compared to age- and sex-matched healthy controls. Second, hierarchical linear regression analysis, with backwards elimination, was conducted with patient data to identify variables independently associated with SGI score. Independent variables included in the first model included age, sex, YGTSS total tic score, DOCS score, and ASRS-V score. Initial regression diagnostics included assessment for outliers, defined as observations with Cook's  $D$  value  $> 4/n$ . Three outliers were identified and removed from the first model and from all subsequent nested models in the hierarchical regression analysis. Additional regression diagnostics included assessments for normality of residuals (using Shapiro–Wilk test of residuals), heteroscedasticity (by application of Breusch–Pagan test), and multicollinearity (defined as variance inflation factor (VIF)  $> 10$ ). These procedures were repeated iteratively for each model in the hierarchical regression analysis. Because OCD<sup>14,15</sup> and ADHD<sup>17</sup> have been associated with altered sensory perception, DOCS and ASRS-V were pre-specified to be the last two independent variables in the nested models. Interactions between independent variables were not included in the regression analysis due to the study sample size. Model goodness-of-fit was indicated by  $R^2$ , and model quality was further measured by Akaike information criteria (AIC). For a given model of a dependent variable, lower AIC values signify less information loss, ie superior model quality.<sup>32</sup>

Data were complete for each participant on all scales except GAD-7. For this scale, two controls failed to answer one item, and one patient failed to answer two items. Predictive mean matching was used to impute these missing values. For all calculations, the Type 1 error rate threshold

was set at 0.05. Given the exploratory nature of the study, error rate thresholds were not corrected for multiple comparisons. Statistical analyses were performed in STATA.

## Results

Demographic and clinical characteristics of patients and controls are shown in Table 2.

## Reliability and Convergent Validity of SGI and SPQ

SGI exhibited excellent internal reliability in controls and patients, with Cronbach's  $\alpha$  of 0.92 and 0.97, respectively. Within tic disorder patients, Cronbach's  $\alpha$  was 0.92 for SPQ. SGI and SPQ total scores strongly correlated

( $r_s = -0.73, p < 0.0001$ ) in patients, supporting convergent validity of these scales in tic disorder populations (see Figure 1). Cronbach's  $\alpha$  for all other self-report measures is provided in the Supplemental Material. Of the four SGI domains, SPQ most strongly correlated with Over-Inclusion and Hyperawareness ( $r_s = -0.78, p < 0.0001$ ), followed by Distractibility ( $r_s = -0.68, p < 0.0001$ ), Perceptual Modulation ( $r_s = -0.62, p = 0.0001$ ), and Fatigue and Stress Vulnerability ( $r_s = -0.62, p = 0.0001$ ).

## Contrasts Between Tic Disorder Patients and Controls

SGI score significantly differed between patients and controls (see Table 3). Of patients, 67.6% had SGI total scores two standard deviations higher than the control mean. Based on the Wilcoxon-rank sum statistic, patients were 87.4% (95% CI: 78.7–96.2%) more likely to have a higher SGI score than controls. Patients had significantly higher scores than controls on each of the four SGI subscales. When comparing the subset of tic disorder patients who screened negative for OCD and ADHD ( $n = 11$ ) to their age- and sex-matched controls, SGI scores still significantly diverged: 100.1 (36.3) versus 63.6 (11.0),  $U = -2.7, p < 0.01$ . Notably, matched patients and controls in this subanalysis did not differ by DOCS total (10.6 (5.3) and 8.4 (4.3),  $U = -1.3, p = 0.21$ ) but did differ by ASRS-V score (9.64 (1.86) and 5.18 (2.48),  $U = -3.4, p < 0.001$ ).

## Within Tic Disorder Patient Analysis

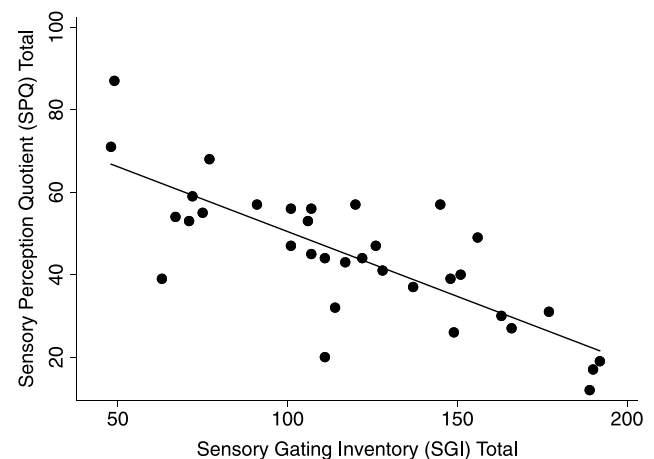
Correlations between scales for tic disorder patients are displayed in Table 4. SGI and SPQ correlations with psychiatric scales were similar so only SGI correlations are presented. SGI scores correlated modestly with PUTS,

**Table 2** Population Characteristics

	Tic Disorder Patients	Healthy Controls
Sex (M:F)	24:10	24:10
Age (years)	33.5 (22–49) <sup>^</sup>	33 (23–48)
Ethnicity		
Hispanic or Latino	0	2
Not Hispanic or Latino	34	30
Unknown/not reported	0	2
Race		
Asian	1	2
Black or African American	0	2
White	32	28
More than one race	1	2
Self-reported history of:		
OCD	18	0
ADHD	9	0
Anxiety	24	0
Depression	24	0
Autism spectrum disorder	0	0
Impulse control disorder	3	0
Self-reported current use of psychotropic medications:		
None	5	32
SSRI and/or SNRI	20	0
Benzodiazepine	9	0
Antipsychotic	9	0
Mood stabilizer <sup>+</sup>	6	0
$\alpha$ -Agonist	3	0
Stimulant	3	0
Not reported	0	2

**Notes:** <sup>^</sup>Median (interquartile range). <sup>+</sup>In this sample, mood stabilizers used included lamotrigine, oxcarbazepine, and/or lithium.

**Abbreviations:** SSRI, selective serotonin reuptake inhibitor; SNRI, serotonin-norepinephrine reuptake inhibitor.



**Figure 1** Scatterplot of SGI scores versus SPQ scores.

**Table 3** Scale Scores for Tic Disorder Patients and Healthy Controls

Scale Name	Tic Disorder Patients	HC	Wilcoxon Rank Sum Statistic (U)	p-value
SGI Total	119.0 (40.5) 115.5 (91–149)*	67.6 (19.0) 64.5 (54–78)	–5.3	<0.0001
SGI Subscale for Perceptual Modulation	43.6 (17.7) 43.5 (30–56)	22.1 (6.4) 20 (18–27)	–5.3	<0.0001
SGI Subscale for Distractibility	31.9 (10.2) 33 (24–41)	19.5 (8.9) 18.5 (12–25)	–4.5	<0.0001
SGI Subscale for Over-Inclusion and Hyperawareness	24.5 (9.6) 25.5 (18–32)	14.8 (6.0) 13 (11–19)	–4.0	0.0001
SGI Subscale for Fatigue and Stress Vulnerability	19.0 (6.9) 18.5 (14–25)	11.3 (4.4) 10 (8–15)	–4.5	<0.0001
SPQ	44.5 (16.3) 44.5 (32–56)	–	–	–
PUTS	24.9 (4.9) 25 (22–29)	–	–	–
YGTSS Total Tic Score	24.9 (10.7) 24.5 (15–32)	–	–	–
DOCS	23.9 (16.3) 20.5 (12–34)	8.9 (4.9) 9 (5–12)	–4.5	<0.0001
ASRS-V	13.7 (4.5) 19.5 (17–22)	6.1 (2.7) 12 (10–14)	–6.3	<0.0001
GAD-7	10.5 (5.8) 10 (5–15)	2.9 (3.1) 3 (0–5)	–5.6	<0.0001
PHQ-9	10.9 (6.0) 10.5 (5–15)	3.0 (2.6) 3 (1–4)	–5.8	<0.0001

**Note:** \*In each cell, mean (standard deviation) are listed above and median (interquartile range) below.

DOCS, and ASRS-V scores. SGI scores did not correlate with age or YGTSS total tic score.

Results of the hierarchical linear regression analysis, with SGI score as the dependent variable, are shown in Table 5. Only DOCS score significantly predicted mean SGI score in any model, with  $\beta$  ranging from 1.03 ( $p = 0.044$ ) in Model 2 to 1.41 in Model 5 ( $p = 0.001$ ). The model inclusive of all five independent variables (Model 1) accounted for 37.9% of SGI score variance, and the simple linear regression model with DOCS as the independent variable (Model 5) accounted for 31.9% of SGI score variance. By AIC, Models 4 and 5 were superior to Models 1, 2, and 3.

## Discussion

Here we demonstrate two important findings in adults with tic disorder. First, sensory hypersensitivity is common in

adult tic disorder patients. Second, the extent of sensory hypersensitivity parallels obsessive-compulsive symptom burden, even after accounting for ADHD symptoms, tic severity, and sex. These findings will be discussed sequentially.

Findings from the current study show that sensory hypersensitivity is both prevalent and prominent in adults with tic disorders, replicating in a larger sample results observed by Sutherland-Owens et al.<sup>10</sup> No established SGI score thresholds exist for delineating normal from abnormal sensory perception, but patients were 87.4% more likely to score higher on SGI than age- and sex-matched controls. Even patients who screened negative for both OCD and ADHD had significantly higher SGI scores relative to controls. As a caveat to this last

**Table 4** Correlation Matrix for Scales Within Patient Data Set

	TTS <sup>+</sup>	PUTS	SGI	SPQ	DOCS	ASRS-V	PHQ-9
PUTS	0.27						
SGI	0.28	0.34*					
SPQ	-0.23	-0.42*	-0.73***				
DOCS	0.44**	0.35*	0.34*	-0.35*			
ASRS-V	0.44**	0.20	0.37*	-0.39*	0.43*		
PHQ-9	0.21	0.15	0.24	-0.27	0.57***	0.58***	
GAD-7	0.49**	0.22	0.30	-0.40*	0.71***	0.32	0.48**

Notes: \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ . <sup>+</sup>YGTSS Total Tic Score.

**Table 5** Hierarchical Regression Model Analysis

Model	Independent Variables (IVs)	VIF for Model IVs	Shapiro-Wilk Test for Normality of Model Residuals <sup>+</sup>	Breusch-Pagan Test for Heteroscedasticity, $p$ -values	Model F-Value	Model R <sup>2</sup>	$\Delta R^2$	AIC	IVs That Predict Mean SGI Score
1 <sup>^</sup>	Age Sex DOCS ASRS-V TTS	1.13 1.06 1.68 1.51 1.66	0.97 $p = 0.51$	$p = 0.23$	$F(5,25) = 3.05$ $p = 0.028$	0.379	–	308	None
2	Sex DOCS ASRS-V TTS	1.06 1.58 1.45 1.59	0.97 $p = 0.63$	$p = 0.21$	$F(4,26) = 3.85$ $p = 0.014$	0.372	$\Delta R^2 = 0.07$ $F(1,25) = 0.279$ $p = 0.60$	306	DOCS, $\beta = 1.03$ $p = 0.044$
3	DOCS ASRS-V TTS	1.58 1.45 1.50	0.98 $p = 0.92$	$p = 0.32$	$F(3,27) = 5.03$ $p = 0.007$	0.358	$\Delta R^2 = 0.014$ $F(1,26) = 0.566$ $p = 0.458$	305	DOCS, $\beta = 1.05$ $p = 0.039$
4	DOCS ASRS-V	1.34 1.34	0.98 $p = 0.73$	$p = 0.23$	$F(2,28) = 7.59$ $p = 0.002$	0.352	$\Delta R^2 = 0.007$ $F(1,27) = 0.291$ $p = 0.594$	303	DOCS, $\beta = 1.15$ $p = 0.015$
5	DOCS	–	0.97 $p = 0.64$	$p = 0.41$	$F(1,29) = 13.6$ $p < 0.001$	0.319	$\Delta R^2 = 0.032$ $F(1,28) = 1.39$ $p = 0.248$	303	DOCS, $\beta = 1.41$ $p = 0.001$

Notes: <sup>^</sup>Same three outliers excluded from all models given Cook's  $D > 4/n$  in Model 1. <sup>+</sup> $p$ -value  $> 0.05$  signifies inability to reject null hypothesis of normality of model residuals.

statement, subthreshold ADHD symptoms remain a potential confound because ASRS-V scores differed between this patient subset and their matched controls. Notably, the SGI displayed excellent internal reliability and good convergence with the SPQ in this sample. Of the four SGI domains, the Over-Inclusion and Hyperawareness domain corresponded most strongly with SPQ total, suggesting this domain best aligns with sensory hypersensitivity as captured by the SPQ. A larger patient sample is needed to more robustly investigate the

psychometric properties of the SGI and SPQ measures in adults with tic disorders.

Using hierarchical linear regression analysis, we identified a significant relationship between sensory hypersensitivity and obsessive-compulsive symptoms, even after accounting for ADHD symptoms, tic severity, and sex. The only other study that administered the SGI to a TS sample did not observe any correlation between SGI score and obsessive-compulsive symptoms.<sup>10</sup> This result, discrepant from our own, may be due to the other study's smaller

sample size ( $n = 18$  patients), heterogeneous cohort of both adults and children (as SGI has not been validated in minors), and/or use of a different OCD measure.<sup>10</sup> In accord with our study, an investigation in 92 pediatric TS patients found those with sensory processing abnormalities had more obsessive-compulsive symptoms.<sup>12</sup> A moderate correlation between sensory hypersensitivity and obsessive-compulsive symptoms ( $r = 0.39, p < 0.001$ ) has also been observed in a large ( $n = 274$ ) sample of neurotypical adults, suggesting the interrelationship between these two domains is not confined to pathologic conditions.<sup>15</sup>

In the correlation analysis, severity of ADHD symptoms and extent of sensory hypersensitivity significantly correlated. However, no significant relationship between these variables emerged from the regression analysis. It has previously been shown that children with dual diagnoses of TS and ADHD manifest greater sensory perceptual dysfunction than those with TS alone.<sup>20</sup> Additional study, likely involving a larger sample size, is needed to further examine the relationship between sensory hypersensitivity and ADHD symptoms in adults with tic disorders.

Sensory hypersensitivity and premonitory urge severity correlated modestly in our cohort. Two prior studies did not identify a relationship between premonitory urge and abnormal sensory perception in TS.<sup>10,12</sup> However, in the first study, the young age of some of the participants (sample population ages ranged from 7 to 14 years) calls into question the reliability of their PUTS scores,<sup>12</sup> since this scale has been shown to bear inconsistent results in populations younger than 10 years of age.<sup>27</sup> In the second study, the sample size, smaller than that of the current investigation, may have been underpowered to identify a significant association between sensory hypersensitivity and premonitory urge.<sup>10</sup> A separate study of 14 adult TS patients did not find any relationship between premonitory urge severity and (predominantly static) tactile detection thresholds,<sup>6</sup> but this is not necessarily inconsistent with our findings showing a correlation between the clinical phenomena of premonitory urge and sensory hypersensitivity, given that both of these phenomena likely arise from higher-order sensory processing abnormalities.<sup>4,9</sup> Notably, YGTSS total tic score did not correlate with either sensory hypersensitivity measure in our sample, suggesting that sensory hypersensitivity may be more tightly associated with premonitory urge than with tics. Identifying clinical associations of and potential contributors to premonitory

urge is of great relevance because this symptom is more distressing than tics in many patients.<sup>1</sup>

The neurobiological basis of sensory hypersensitivity in TS is uncertain, but impaired sensory gating is strongly implicated.<sup>33–39</sup> Sensory gating is the pre-conscious process by which irrelevant sensory input is filtered out, thereby facilitating attention to the most pertinent aspects of the sensory environment.<sup>25,40</sup> Sensory gating is disrupted in TS, as demonstrated by multiple psychophysical and neurophysiologic studies.<sup>33–39,41</sup> Tactile sensory gating impairment has been associated with deficient gamma-aminobutyric acid levels in the sensorimotor cortex of TS patients.<sup>7</sup> While such findings are deepening insights into TS pathophysiology, the actual phenotypic manifestations and clinical relevance of impaired sensory gating in TS remain ambiguous. More specifically, it is uncertain whether sensory gating impairment gives rise to the subjective experience of sensory hypersensitivity. Thus, clarifying the nature and extent of sensory symptoms in TS is imperative to facilitate translation between clinical and physiologic research.

A growing body of evidence on sensory hypersensitivity and its neural substrates in OCD may offer important clues for TS research.<sup>16</sup> As with TS, impaired sensory gating has been repeatedly observed in OCD,<sup>42–44</sup> raising the possibility sensory gating dysfunction underlies sensory hypersensitivity in both disorders. Obsessive-compulsive symptoms are also associated with impaired sensory gating in neurotypical adults, implying a fundamental connection between these two phenomena.<sup>15,45</sup> A precise understanding of the mechanisms responsible for altered sensory gating in TS and OCD is lacking. Sensory hypersensitivity in OCD has also been associated with increased volume of the sensorimotor cortex<sup>14</sup> and with hyperactivation of the insula, a structure involved in integration of bodily sensations.<sup>46</sup> Notably, the insula is key to urge formation in healthy individuals<sup>47,48</sup> and to emergence of premonitory urge in TS.<sup>4</sup> Thus, while significant knowledge gaps exist, current evidence suggests shared neural mechanisms underpin sensory hypersensitivity in both OCD and TS.

Future research should elucidate the extent to which sensory hypersensitivity is related to disorders of sensory modulation and sensory regulation already identified in pediatric TS populations.<sup>12,13,20</sup> Longitudinal studies are needed to explore the potential role of sensory dysfunction in emergence of the broader TS phenotype during development and to quantify its impact on quality of life. And, clinical trials should be conducted to assess whether



interventions targeting sensory dysfunction in other neurodevelopmental disorders<sup>49–51</sup> can be effectively translated to tic disorder populations.<sup>52</sup>

Our study has several limitations. First, we did not screen for autism spectrum disorder, schizophrenia, or other less-common psychiatric comorbidities of TS. Prevalence of autism is estimated at 8.7% in adults with TS and lifetime prevalence of primary psychotic disorders at 0.8%.<sup>18,53</sup> The impact of these conditions on study findings is likely low, but they do represent potential unmeasured confounders. Second, we employed self-report measures for OCD and ADHD symptoms rather than gold-standard, clinician-rated scales. That said, the DOCS and ASRS-V have both undergone rigorous validation and demonstrated good sensitivity in clinical populations.<sup>28,29</sup> Third, the study sample size precluded development of more complex regression models for examining medication effect and interactions between variables. Lastly, the patient sample, consisting of adults with tic disorder referred to a tertiary care center, represented a more severe phenotype, potentially limiting the generalizability of our findings to the wider disorder spectrum. Furthermore, the study cohort was predominantly non-Hispanic white, and thus is not representative across racial and ethnic groups.

In conclusion, study results confirm sensory hypersensitivity is prevalent and pronounced in adults with tic disorders, providing additional evidence this is a core feature of these disorders, one deserving of further research. Future studies investigating sensory hypersensitivity in TS should account for and explore the influence of obsessive-compulsive symptoms.

## Abbreviations

TS, Tourette syndrome; SGI, Sensory Gating Inventory; SPQ, Sensory Perception Quotient; PUTS, Premonitory Urge to Tic Scale; DOCS, Dimensional Obsessive-Compulsive Scale; ASRS-V, Adult ADHD Self-Report Screening Scale for DSM-5; GAD-7, Generalized Anxiety Disorder 7; PHQ-9, Patient Health Questionnaire 9; YGTSS, Yale Global Tic Severity Scale.

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## Author Contributions

All others made substantial contributions to conception and design, acquisition of data, or analysis and

interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed on the journal to which the article will be submitted; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

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