


# Cardiovascular Autonomic Function Tests in Patients of Obsessive–Compulsive Disorder: A Cross-Sectional Study

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## ABSTRACT

**Background:** Patients with psychiatric disorders are at an increased risk of developing cardiovascular disease, reducing life expectancy. Autonomic dysfunction has been linked to this increased risk; many studies have found reductions in heart rate variability (HRV). Only a few studies have systematically explored the relationship between obsessive–compulsive disorder (OCD) and autonomic function, and they have found contradicting results. The present study is intended to explore comprehensive autonomic functions in OCD patients and compare them with healthy controls.

**Methods:** A total of 18 OCD patients meeting Diagnostic and Statistical Manual of Mental Disorders - 5 (DSM-5) criteria were enrolled to undergo comprehensive autonomic function testing, and the results were compared with 25 age- and sex-matched healthy controls.

**Results:** Time-domain parameters of HRV such as standard deviation of the RR intervals, coefficient of variance of RR intervals, standard deviation of differences between adjacent RR intervals, root square

of the mean of the sum of the squares of differences between adjacent RR intervals, and percentage of number of RR interval differences  $\geq 50$  ms were significantly lower in OCD patients, indicating lesser parasympathetic tone. Frequency-domain parameters such as total power and very low frequency were significantly lower in OCD patients, indicating a significant decrease in autonomic tone. Nonlinear parameters such as dispersion of points perpendicular to the line of identity and dispersion of points along the line of identity were significantly lower in OCD patients, indicating altered vagal and sympathetic tone. In autonomic reactivity tests, the fall in systolic blood pressure during the lying to standing test and change in diastolic blood pressure during the cold pressor test were significantly altered in OCD patients, indicating abnormal sympathetic reactivity. There was no significant correlation between autonomic parameters and the severity of OCD.

**Conclusion:** OCD is characterized by a decreased parasympathetic tone and abnormal sympathetic reactivity compared to normal controls.

**Keywords:** Autonomic function test, electrophysiology, heart rate variability, OCD

**Key Messages:** OCD is significantly associated with reduced parasympathetic tone and increased sympathetic reactivity, suggesting that autonomic neurocardiac integrity is substantially impaired in patients with OCD. Comprehensive autonomic function testing, including HRV and reactivity tests for parasympathetic and sympathetic systems, will provide information regarding the cardiovascular risk of these patients

Patients with severe psychiatric disorders are at an increased risk of developing cardiovascular disease,<sup>1–3</sup> and autonomic dysfunction has been implicated as a mechanism. Reduction in heart rate variability (HRV), which assesses the beat-to-beat variation in the heart rate (HR) over time, is strongly associated with an increased risk of developing cardiovascular events.<sup>4</sup> Many studies on patients with psychiatric disorders have found abnormal autonomic functions.<sup>5–8</sup> Higher

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variability in the HR protects against adverse cardiovascular events. In contrast, reduction in HRV, due to reduced parasympathetic control of SA node, or increased sympathetic activation of the heart, or both, predicts the risk of adverse cardiovascular events such as sudden cardiac death or development of cardiovascular disease.<sup>9,10</sup> HRV has been explained in the methods section.

Obsessive-compulsive disorder (OCD) may be characterized by obsessions only, compulsions only, or both obsessions and compulsions.<sup>11,12</sup> It has been proposed that hyperactivation in the frontostriatal network, dorsal anterior cingulate cortex (dACC), and the amygdala is associated with obsessions and causes nonspecific increased anxiety and thus elevated autonomic responses.<sup>13</sup>

Some studies have systematically explored the relationship between OCD and autonomic functions. Slaap et al.<sup>13</sup> reported no evidence of diminished HRV in OCD patients. Pittig et al.<sup>8</sup> reported reduced baseline high frequency (HF) among frequency-domain parameters of HRV in OCD patients compared to controls. The mixed results may be due to methodological flaws in the studies. For example, Slaap et al.<sup>13</sup> performed the HRV in the sitting position and analyzed only the frequency-domain parameters of HRV (spectral analysis). Also, Pittig et al.<sup>8</sup> analyzed only high-frequency HRV (HF-HRV) among the frequency-domain parameters. Neither analyzed the time-domain or nonlinear parameters of HRV or conducted the battery of cardiovascular autonomic reactivity tests. Hence, the findings of these studies remain inconclusive.

Comprehensive autonomic function testing that assesses autonomic tone and reactivity of parasympathetic and sympathetic systems has not been done in OCD patients. Hence, the present study was planned to investigate the relationship between OCD and autonomic functions while comparing the findings with healthy age-/sex-matched controls and to study whether the abnormal autonomic function tests have any correlation with the severity of OCD. Comprehensive autonomic function testing, including HRV and reactivity tests for parasympathetic and sympathetic systems, will provide information regarding the cardiovascular risk of these patients.

## Objectives

- **Primary objective:** To find the results of comprehensive autonomic function tests in patients with OCD and compare with healthy controls.
- **Secondary objective:** To correlate autonomic functions with the severity score of OCD.

## Material and Methods

In this cross-sectional study, patients diagnosed with OCD (DSM-5 criteria), aged 18–50 years, of either sex, who were medication-free, were included as cases. Healthy age- and sex-matched volunteers were selected as controls. Individuals with thyroid disorder; coronary artery disease; tobacco, alcohol, or other substance use disorder; neurological, medical, or surgical illness; or other Axis-I psychiatric disorders were excluded in both cases and controls. The study was undertaken, after getting institute ethical clearance (AIIMS/PHY/17/187, dated 20-05-2017) and written informed consent from the participants, in a tertiary care center between June 2017 and March 2020.

The severity of OCD was assessed by Yale Brown Obsessive Compulsive Scale (Y-BOCS). Patients with OCD and healthy controls were clinically probed for any symptoms of autonomic dysfunction.

From a previous study using values of HF (HRV) in controls vs. OCD patients, i.e., 6.03 (1.13) vs. 4.96 (1.33), we calculated the effect size to be 0.92. Assuming a similar effect size in our study, with an alpha of 0.05 and power of 80%, the sample size calculated was 17 in each group.

## Assessment of Cardiovascular Autonomic Tone

### Heart Rate Variability (HRV)

Patients and controls were instructed not to take coffee, nicotine, or alcohol for 24 hours and food two hours prior to the procedure. They were asked to avoid any over-the-counter cough or cold medications and to wear loose and comfortable clothing.

For short-term analysis of HRV, electrocardiogram (ECG) was recorded in the supine position for 5 min after 10 min of rest in the supine position.

Room temperature was maintained at 24°C. Subjects were instructed to close their eyes and to avoid talking, moving, coughing, and sleeping. The ECG was recorded to measure the HR changes; ECG signals were acquired using lead-2 at a sample rate of 1000/s and gain X 2000 from the power lab data recording system (AD Instruments, Australia). HRV analysis was based on a 5-min period of ECG signal that was artifact-free, using LabChart software AD Instruments, Australia).

The analysis of HRV was done by time-domain, frequency-domain, and nonlinear methods. The time-domain parameters included standard deviation of the RR intervals (SDRR), coefficient of variance of RR intervals (CVRR), the standard deviation of the difference between adjacent RR intervals (SDSD), the root square of the mean of the sum of the squares of the difference between adjacent RR intervals (RMSSD), number of RR interval difference  $\geq 50$  ms (RR50), and percentage of RR50 (pRR50). Most of the conventional time-domain parameters (SDRR, CVRR, SDSD, RMSSD, RR50, and pRR50) are markers of parasympathetic activity.

The frequency components of HRV were analyzed using fast Fourier transformation, and the power spectrum was subsequently divided into three frequency bands: very low frequency (VLF, 0.001–0.04 Hz), low frequency (LF, 0.040–0.15 Hz), and high frequency (HF, 0.15–0.4 Hz). The physiological explanation for VLF in the short-term recording is not well defined. HF represents parasympathetic activity, while the LF characterizes both sympathetic and parasympathetic outflows. The normalized units (nu) of the LF and HF and the LF/HF ratio, which represents the sympathovagal balance, were also calculated. An increase in the LF/HF ratio corresponds to sympathetic dominance, whereas its decrease reflects parasympathetic dominance.

The Poincare plot is a scatter plot of the current RR interval against the RR interval immediately preceding it. The RR interval Poincare plot typically appears as an elongated cloud of points oriented along the line of identity at 45° to the normal axis. The conventional parameters of nonlinear methods are: SD1, dispersion of points perpendicular to the

line of identity (vagal influence); SD2, dispersion of points along the line of identity (sympathetic influence); and the ratio of SD2 to SD1 (sympathovagal balance).

## Assessment of Cardiovascular Autonomic Reactivity

The baseline HR and blood pressure (BP) were measured before performing each reactivity test. After each test, 2 min of rest was given.

### Deep Breathing Test

The investigator gave a hand signal to maintain the rate and timing of breathing. For 6 cycles/minute, the inspiration was done for 5 s and expiration for 5 s. If cycles were not appropriately done, it was repeated after 2 min of rest, to get six complete cycles. The difference between the maximal and minimal HR during inspiration and expiration, respectively, averaged for six cycles (delta HR) and the ratio of the longest RR interval during expiration and the shortest RR interval during inspiration averaged over six cycles (E:I ratio) were calculated. This parameter assesses the vagal control of the heart, a measure of parasympathetic reactivity (normal:  $\geq 15$  beats/min, borderline: 11–14 beats/min, and abnormal:  $< 10$  beats/min; E:I ratio  $\geq 1.21$  normal).

### Valsalva Maneuver

The subjects blew into a mouthpiece attached to a sphygmomanometer. The expiratory pressure was kept at 40 mm of Hg for 15 s. A small air leak in the system was useful to prevent the closure of the glottis during the maneuver. At the end of 15 s, the pressure was released. Due care was taken to prevent deep breathing before and after the maneuver. The longest RR interval during phase IV/shortest RR interval during phase II (Valsalva ratio, VR) was calculated (normal: VR  $> 1.21$ ).

### Lying to Standing Test

The subjects were instructed to attain the standing posture from the supine position within 3 s, and recordings were taken. They were told to inform the investigator if they felt dizzy or were uncomfortable during standing. BP and HR were recorded at baseline and serially at 0.5, 1, 2, 2.5, and 5 min. The 30:15 ratio was calculated from the ECG. The fall of

systolic blood pressure (SBP) was noted, and the 30:15 ratio was calculated as the ratio between the longest RR interval at or around the 30th beat and the shortest RR interval at or around the 15th beat (normal values: fall of SBP:  $\leq 10$  mm Hg normal, 11–29 mm Hg borderline, and  $\geq 30$  mm Hg abnormal; 30:15 ratio:  $\geq 1.04$  normal, 1.01–1.03 borderline, and  $< 1.0$  abnormal).

### Isometric Grip Test

The baseline BP was recorded, and the subjects were asked to grip the hand-grip dynamometer using maximum force, with the dominant hand, for a few seconds. The value was noted down, and the procedure was repeated thrice. The maximum value of the three readings was considered as the maximal voluntary contraction. The subjects were instructed to maintain a sustained grip on the dynamometer at 30% of maximal voluntary contraction for 4 min. After the subjects started the contraction, BP was measured on the contralateral arm at 1, 2, and 4 min. One more reading was taken 2 min after the release of the grip. The change in diastolic blood pressure (DBP) was calculated as the highest DBP during the test minus baseline DBP (increase in DBP:  $\geq 16$  mm Hg normal, 11–15 mm Hg borderline, and  $\leq 10$  mm Hg abnormal).

### Cold Pressor test

Cold water of 10°C was prepared. The subjects immersed their hand in water up to the wrist for 1 min. The BP was taken at baseline and also just before the hand was taken out of the water (i.e., at the end of 1 min of immersion). The BP was taken again at 1.5 and 4 min after the hand was withdrawn from the cold water. The change in DBP was calculated as the highest DBP during the test minus baseline DBP (normal increase in DBP  $\geq 10$  mm Hg).

## Statistical Analysis

Data were entered in a Microsoft Excel sheet and checked for distribution. Data were not normally distributed; hence, parameters are described as the median and interquartile range (25–75). Nonparametric tests were done using SPSS version 23. Mann–Whitney U test was applied for testing the significance of the difference between OCD patients and controls. Correlations between parameters were measured with

Spearman's correlation coefficient. The Benjamini–Hochberg procedure, with a false discovery rate of 0.10, was used to correct for multiple testing. In total, 34 tests were conducted study-wide for the current analyses. Results were deemed significant if the obtained P-value was smaller than the Benjamini–Hochberg critical value.

## Results

### Demographic Characteristics

A total of 18 cases of OCD were clinically diagnosed and referred by the Department of Psychiatry. They were not on current medications as a few were newly diagnosed and not yet started on medication, and the rest were treated elsewhere earlier but had discontinued medication by themselves at least three months before consulting at our institute. The healthy controls ( $n = 25$ ) were selected after applying the same exclusion criteria. The cases and controls were age- and sex-matched to avoid bias.

The demographic data are presented in **Table 1**. There was no statistically significant difference between cases and controls with respect to age and sex, weight, BMI, HR, SBP, DBP. However, the controls were significantly taller than the cases. The median respiratory rate was higher in the cases.

### Autonomic Symptoms in OCD Patients, Duration, and Severity of OCD

All the 18 patients had confirmed OCD; the severity as measured by Y-BOCS were as follows: 5, mild (8–15); 6, moderate (16–23); 6, severe (24–31); and 1, extreme (32–40).

The median duration of OCD was five years (interquartile range 25–75); the median Y-BOCS score was 20 (interquartile range 14.75–20.5). The correlation of OCD duration with the severity of OCD was strongly positive ( $r = 0.56$ ,  $P = 0.02$ ), suggesting that as the duration of OCD increases, the severity of OCD as measured by Y-BOCS increases.

### Autonomic Symptoms

Nasal: Nasal disturbance (dry or runny nose) was present in four patients (22.22%), sweating disturbances in four

TABLE 1.

## Demographic Characteristics of OCD Patients vs. Controls

	OCD (n = 18)		Control (n = 25)		P-Value	BH
	Median	Interquartile Range (25-75)	Median	Interquartile Range (25-75)		
Age (years)	30.00	22.75-37.00	30.00	27.50-35.50	0.74	0.085
Height (cm)	162.50	155.75-167.00	168.00	165.50-172.00	0.003	0.021 <sup>a</sup>
Weight (kg)	62.75	49.05-68.83	60.00	58.00-62.00	0.32	0.068
BMI (kg/m <sup>2</sup> )	23.96	19.78-27.36	21.47	20.42-22.48	0.09	0.047
SBP (mm Hg)	123.50	118.00-136.50	121.00	114.00-124.00	0.09	0.050
DBP (mm Hg)	72.00	64.75-87.00	70.00	64.50-77.00	0.24	0.065
HR (BPM)	75.00	68.75-81.25	69.00	62.00-76.50	0.07	0.044
RR (BPM)	17.00	15.50-18.50	15.00	14.00-16.50	0.01	0.026 <sup>a</sup>
<b>Sex</b>	<b>Number</b>	<b>%</b>	<b>Number</b>	<b>%</b>	<b>P-Value</b>	
Male	10	55	17	68	0.40	0.074
Female	8	45	8	32		

BH, critical value for the Benjamini-Hochberg correction for multiple testing,  $(i/m)*Q$ , where  $i$  is the rank,  $m$  is the total number of tests ( $m = 34$ ), and  $Q$  is the false discovery rate ( $Q = 0.10$ ).

Note: <sup>a</sup>Result was still significant after the BH correction ( $P < BH$ ).

patients (22.22%), postural fall/dizziness in seven patients (38.88%), GIT disturbance with diarrhea and/or constipation in ten patients (55.55%), headache in 14 patients (77.77%), micturition disturbances in two patients (11.11%), bronchospasm attack in six patients (33.33%), often feeling too hot/too cold in four patients (22.22%), extremities remaining unusually warm/cold in six patients (33.33%), impotence in two patients (11.11%), stress-related physical symptoms in nine patients (50%), family history of diabetes and/or hypertension in nine patients (50%), and history of dust allergy in three patients (16.66%).

### HRV: Time-Domain Parameters

Time-domain parameters, namely SDRR, CVRR, SD Rate, SDSDD, RMSDD, and pRR50, were significantly lower in the OCD patients than the controls, indicating lesser parasympathetic tone in OCD patients as compared to healthy controls (Table 2).

### HRV: Frequency-Domain Parameters

Among the frequency-domain parameters, the values for the total power and VLF were significantly lower in the OCD patients than the healthy controls, suggesting a significant decrease in autonomic tone at rest (Table 3).

### HRV: Nonlinear Parameters

The nonlinear parameters such as SD1 and SD2 were significantly lower in OCD patients compared to healthy controls, indicating altered vagal and sympathetic tone in OCD patients. However, the SD2/SD1 ratio that denotes the sympathovagal balance was not significantly different, suggesting a normal sympathovagal balance in OCD patients at rest (Table 4).

### Autonomic Reactivity Tests

The fall in SBP during the lying to standing test and change in DBP during the cold pressor test were significantly altered in OCD patients compared to controls, indicating abnormal sympathetic reactivity in OCD patients (Table 5).

### Correlation of Autonomic Disturbances with the Severity of OCD

There was no significant correlation between autonomic disturbances as measured by time- and frequency-domain parameters, nonlinear parameters, and autonomic reactivity parameters with the severity of OCD measured by Y-BOCS.

### Discussion

In our study, the time-domain measures of HRV (SDRR, CVRR, SD Rate, SDSDD,

RMSSD, and pRR50) were significantly lower in OCD patients than controls, indicating lesser parasympathetic tone in OCD patients at rest. This is the first-ever study in the literature, to the best of our knowledge, to apply time-domain parameters of HRV in OCD patients to examine autonomic functions. The results are similar to decreased parasympathetic modulation observed in closely allied psychiatric disorders such as generalized anxiety disorders,<sup>8,14,15</sup> schizophrenia, depression, and bipolar mania.<sup>16</sup> They are presumably associated with inherent characteristics of the illness, independent of the effects of psychotropic medications.

An analysis of frequency domains of HRV showed that both "total power" and "VLF" are significantly lower in OCD patients than healthy controls. Decreased total power indicates that there is a significant decrease in the autonomic tone. Since VLF power indicates a diurnal variation of HRV and is dependent on several parameters, we cannot comment on its significance in a 5-min HRV recording.

Nonlinear parameters such as SD1 and SD2 were significantly lower in OCD patients, indicating altered vagal and sympathetic tone in them. However, the SD2/SD1 ratio that denotes the sympathovagal balance was not significantly different, suggesting a normal sympathovagal balance in OCD patients at rest.

**TABLE 2.**

**Time-Domain Parameters in OCD Patients vs. Controls**

	OCD		Control		P-Value	BH
	Median	Interquartile Range	Median	Interquartile Range		
AVG_RR (ms)	836.00	741.83–883.58	874.40	774.20–996.95	0.12	0.056
MED_RR (ms)	838.75	741.75–885.13	878.50	772.00–1002.00	0.15	0.059
SD_RR (ms)	28.18	20.99–46.16	50.42	38.16–65.22	0.001	0.009 <sup>a</sup>
SDARR (s)	0	0	0	0	>0.99	0.097
CVRR	0.04	0.03–0.05	0.05	0.05–0.07	0.002	0.018 <sup>a</sup>
AVG_R (BPM)	71.96	67.97–81.16	69.44	60.34–77.66	0.15	0.062
SD_Rate (BPM)	3.07	2.15–3.94	3.82	3.13–4.44	0.02	0.041 <sup>a</sup>
SDDSD (ms)	22.26	13.09–37.44	39.36	23.41–51.76	0.01	0.029 <sup>a</sup>
RMSSD (ms)	22.23	13.07–37.39	39.32	23.38–51.67	0.01	0.032 <sup>a</sup>
pRR50 (%)	1.78	0.47–11.23	13.78	3.72–30.52	0.02	0.038 <sup>a</sup>

BH, critical value for the Benjamini–Hochberg correction for multiple testing,  $(i/m)*Q$ , where  $i$  is the rank,  $m$  is the total number of tests ( $m = 34$ ), and  $Q$  is the false discovery rate ( $Q = 0.10$ ).

AVG\_RR, average RR interval in millisecond MED\_RR, median RR interval in millisecond SD\_RR, standard deviation of the RR intervals SDARR, standard deviation of the averages of RR intervals in all 5-min segments of the entire recording CVRR, coefficient of variance of RR intervals AVG\_R, average rate SD\_Rate, standard deviation rate SDDSD, standard deviation of differences between adjacent RR intervals RMSSD, the root square of the mean of the sum of the squares of differences between adjacent RR intervals pRR50, percentage of number RR interval differences  $\geq 50$  msOCD, obsessive compulsive disorder

Note: <sup>a</sup>Result was still significant after the BH correction ( $P < BH$ ).

**TABLE 3.**

**Frequency-Domain Parameters in OCD Patients vs. Controls**

	OCD		Control		P-Value	BH
	Median	Interquartile Range	Median	Interquartile Range		
TOTAL_P ( $ms^2$ )	696.35	429.23–1959.50	2214	1343.50–4388.00	0.002	0.015 <sup>a</sup>
VLF ( $ms^2$ )	292.05	106.96–559.43	587.4	439.30–1063.35	0.004	0.024 <sup>a</sup>
LF (nu)	50.785	36.55–68.60	55.19	40.53–66.73	0.61	0.082
HF (nu)	48.27	31.55–57.62	43.77	32.51–52.52	0.42	0.076
LF/HF (%)	1.0515	0.63–2.18	1.261	0.89–1.96	0.46	0.079

Abbreviations: BH, critical value for the Benjamini–Hochberg correction for multiple testing,  $(i/m)*Q$ , where  $i$  is the rank,  $m$  is the total number of tests ( $m = 34$ ), and  $Q$  is the false discovery rate ( $Q = 0.10$ ). TOTAL\_P, total power; VLF, very low frequency; LF, low frequency; HF, high frequency; LF/HF, ratio of LF to HF.

Note: <sup>a</sup>Result was still significant after the BH correction ( $P < BH$ ).

**TABLE 4.**

**Nonlinear Parameters in OCD Patients vs. Controls**

	OCD		Control		P-Value	BH
	Median	Interquartile Range	Median	Interquartile Range		
SD1 (ms)	15.74	9.25–26.48	27.83	16.56–36.60	0.01	0.035 <sup>a</sup>
SD2 (ms)	36.64	28.74–58.76	63.83	48.56–81.03	0.001	0.006 <sup>a</sup>
SD2/SD1	2.3465	1.96–3.13	2.64	1.90–3.13	0.81	0.088

Abbreviations: BH, critical value for the Benjamini–Hochberg correction for multiple testing,  $(i/m)*Q$ , where  $i$  is the rank,  $m$  is the total number of tests ( $m = 34$ ), and  $Q$  is the false discovery rate ( $Q = 0.10$ ).

Note: <sup>a</sup>Result was still significant after the BH correction ( $P < BH$ ).

TABLE 5.

## Autonomic Reactivity Tests of OCD Patients vs. Controls

	OCD		Control		P-Value	BH
	Median	Interquartile Range	Median	Interquartile Range		
DBT-ΔHR	27.50	16.84–31.00	21.21	17.42–28.50	0.39	0.071
E:I ratio	1.40	1.23–1.51	1.35	1.27–1.50	0.99	0.094
Valsalva ratio	1.75	1.46–2.00	1.70	1.41–2.05	0.89	0.091
LST-SBP	11.00	6.00–18.00	-4.00	-7.50 to 5.50	0.002	0.012 <sup>a</sup>
30:15 ratio	1.50	1.36–1.59	1.48	1.34–1.68	>0.99	0.100
IGT	17.00	12.00–31.25	23.00	16.00–31.50	0.09	0.053
CPT	14.00	9.00–18.00	7.00	4.00–10.50	0.001	0.003 <sup>a</sup>

BH, critical value for the Benjamini–Hochberg correction for multiple testing,  $(i/m)*Q$ , where  $i$  is the rank,  $m$  is the total number of tests ( $m = 34$ ), and  $Q$  is the false discovery rate ( $Q = 0.10$ ). DBT-ΔHR, change in heart rate during the deep breathing test; E:I ratio, ratio of heart rate during expiration and inspiration; LST-SBP, change in SBP during the lying to standing test; IGT, isometric grip test; CPT, cold pressor test.

Note: <sup>a</sup>Result was still significant after the BH correction ( $P < BH$ ).

In autonomic reactivity tests, the fall in SBP during the lying to standing test and change in DBP during the cold pressor test were significantly altered compared to controls, indicating abnormal sympathetic reactivity in OCD patients. We did not find any significant abnormality with respect to DBT, Valsalva, or 30:15 ratio, which indicate normal parasympathetic reactivity.

We did not find any significant correlation between the severity of OCD measured by Y-BOCS and autonomic parameters studied.

Our results are consistent with Pittig et al.,<sup>8</sup> who found decreased HF-HRV at baseline compared to normal controls. However, the authors analyzed only HF-HRV but not time-domain parameters or nonlinear parameters.

Our results are not in line with Slaap et al.,<sup>13</sup> who examined Autonomic Nervous System (ANS) function (measured by a spectral analysis of HRV) among 53 panic disorder patients, 54 OCD patients, and 24 age-matched normal controls. The authors analyzed frequency-domain parameters (total power, LF, HF, LF/HF) and found that OCD patients are not characterized by reduced HRV as compared to normal controls. They did not analyze time-domain and nonlinear HRV parameters. We found a significant decrease in total power and VLF, denoting a decrease in parasympathetic tone, whereas the authors did not find any difference. Our results are consistent with their findings of no difference in LF, HF, and LF/HF ratio.

It should be noted that our patients were medication-free at the time of enrolment. A previous study reported that OCD is associated with lower HRV and also that the association is mainly driven by the effects of psychotropic medications.<sup>8</sup>

Havnen et al. in 2013 studied the relationship between self-reported sleep quality, HF-HRV, and cognitive inhibition in 31 OCD patients. They found a negative correlation between HRV measured in the upright position and cognitive inhibition. The results showed that HF-HRV and cognitive inhibition were significantly correlated and that OCD was significantly related to HRV. Specifically, HRV was inversely related to the severity of OCD. However, the authors cautioned to interpret the results as they were significant only when patients were standing but not in the supine position, while we performed HRV in the supine position. Posture influences HRV: in the frequency-domain parameters, the HF component is prominent in the supine position and is decreased during upright tilt and in the standing position. The LF component is enhanced during upright tilt and in the standing position.<sup>17</sup>

Our results are consistent with the model of cardiac and emotion regulation, known as the neurovisceral model, proposed by Thayer and Lane.<sup>18,19</sup> According to this model, patients have difficulty in generating appropriate emotional responses based on the changing internal and external environmental conditions. The prefrontal cortex generates inhibitory

processes and is likely to be affected in OCD, leading to the symptoms. Hypervigilance to threat is an example of attentional bias seen in patients with OCD, and deficits in the neurovisceral network have been linked to impairment in inhibiting attentional responses. A similar role of inhibitory processes has recently been proposed for fear conditioning. Thus, low HRV might serve as an index variable of potential deficits in inhibitory processes in OCD patients.

Recent studies have shown that OCD is associated with striatal dysfunction resulting in inefficient thalamic gating that causes hyperactivity in the orbitofrontal cortex. It is proposed that this hyperactivity may cause obsessions. Several imaging studies report hyperactivation in frontostriatal networks and the dACC. Hyperactivity in dACC has been associated with obsessions and causes nonspecific elevated anxiety. Amygdala hypersensitivity has been reported in recent studies, and due to its connection to the sympathetic nervous system, it is proposed that it mediates anxiety and autonomic responses.<sup>20</sup>

Our results demonstrate that the duration of OCD in years strongly correlates with the severity of OCD as per Y-BOCS.<sup>21</sup>

The interpretation of our results should consider some limitations. Inclusion criteria with unmedicated patients reduced the sample size, because many patients attending the Outpatient Department at our tertiary care hospital had been treated before or were on

medication. Though comorbid psychiatric illnesses were ruled out by the referring physician, the cases and controls were not screened during the study. Future studies should include patients with comorbidities to address the cumulative effect or elucidate whether OCD patients with comorbid depression have distinctive neurocardiac characteristics compared to noncomorbid patients. Further studies with a larger sample are required to investigate the same. As our study involved OCD patients with a fair range of Y-BOCS scores and a wide range of disease duration, the tests for autonomic functions may be repeated in different OCD patient populations.

In conclusion, the present study indicates that OCD is significantly associated with reduced parasympathetic tone and increased sympathetic reactivity, suggesting that autonomic neurocardiac integrity is substantially impaired in patients with OCD.

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