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Neurobiological and Psychosomatic Links between Premature Ejaculation and Tension-Type Headache: Evidence from a Hospital-Based Analysis

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Abstract
Background: *PE (premature ejaculation) and TTH (tension-type headache) are common diseases that negatively affect the quality of life. Emerging data suggest underlying neurobiological deficits, such as serotonergic dysfunction, hypothalamic-pituitary-adrenal axis dysregulation and autonomic dysfunction. The aim of the study was to research psychological and physical correlations towards PE, but also regarding TTH in a biopsychosocial aspect as potential foundations for comprehensive therapeutic approaches.*
Methods: *The study was conducted at KPJ Specialized Hospital, Gazipur, Bangladesh from 2018 to 2023. In this cross-sectional study, 2041 adult men with PE (intravaginal ejaculatory latency ≤2 min and Premature Ejaculation Diagnostic Tool [PEDT] score ≥11 according to guidelines of the International Society for Sexual Medicine [ISSM]) or TTH (according to diagnostic criteria of the International Classification of Headache Disorders-3rd edition) or both were recruited. The following parameters were evaluated: psychosocial one – HADS, PSS-10 and PSQI scales; sex life function based on IIEF-5 scale; headache one using HIT6 value; neurobiological ones as morning (8 am) and night (12 p.m.) serum cortisol EMV ranges, SERUM fasting 5-Hydroxytryptamine level (Mol/l); indices of heart rhythm variability such as RMSSD and LF/HF ratio. Statistical analysis was performed in SPSS version 26 and included chi-square testing, ANOVA, correlation heatmaps and multivariable logistic regression.*
Results: *Of the 2,041 study populations, 758 exhibited PE alone, whereas PTH was present in 1,116 individuals and both pain conditions were found in 167 individuals. The elements of anxiety (HADS-A: 11.8±4.7), perceived stress (PSS-10: 24.2±7.5) and sleep disturbance (PSQI: 9.4±3.8) were significantly more pronounced among patients with comorbidity PE+TTH than in single-condition groups, p<0.001). High levels of morning cortisol (17.8±4.8 μg/dL), low serotonin (112±32 ng/mL), high sympathetic tone (LF/HF: 2.9±1.4), and low parasympathetic activity (RMSSD: 23.1 ±11.5 ms) were found in the patients with CFS (P <0.01). Multivariable Model: anxiety (OR=1.08), stress (OR= 1.06), poor sleep quality (OR=1.12), elevated cortisol levels (OR= 1.09), lower serotonin levels (OR =0.97) and autonomic imbalance were independent predictors of PE-TTH comorbidity with Area under the curve equal to AUC = 0,78.*
Conclusions: *Co-morbidity with PE and TTH is highly related to psychological distress, neuroendocrine dysregulation and autonomic dysfunction, indicating common pathophysiological processes. These findings lend support for multidimensional or biopsychosocial approach to the management of stress and neurochemical equilibrium.*
Keywords: *Premature Ejaculation, Tension-Type Headache, Sexual dysfunction, and Psychological distress*

I. INTRODUCTION

PE is the most common male sexual dysfunction that affects 20-30% of men across the globe and causes significant psychological problems, relationship difficulties and poor quality of life.[1] The International Society for Sexual Medicine has defined premature ejaculation as a condition in which ejaculation occurs within 1 minute of vaginal penetration and with inability to delay, along with negative personal consequences. PE is divided into two categories, which are lifelong and acquired PE that have distinct etiologic backgrounds.[2] In contrast, TTH is the most prevalent primary headache disorder, with lifetime prevalence above 70% in some populations and described as bilateral domed or band-like pressure and tightness of mild to moderate intensity.[3] Despite their high individual prevalence, comorbidity and common pathophysiology between PE and TTH have not been adequately studied to date. Recent findings in neurobiology suggest that a shared common pathway may be the involvement of serotonergic neurotransmission, dysregulation of the hypothalamic-pituitary-adrenal axis and imbalance in the autonomic nervous system.[4] Serotonin is believed to play a significant inhibitory role in ejaculation control by altering pathways within the CNS, and low serotoninergic neurotransmission has been implicated in the pathophysiology of PE.[5] Conversely, serotonin dysfunction is also involved in chronic pain syndromes and TTH the latter characterized by altered central processing of pain and a descending inhibitory systems defict causing headache to generalize.[6] This common neurochemical base indicates that the serotonergic mechanism dysfunction may be a shared vulnerability factor in both sexual dysfunction and chronic headache. The next likely psychosomatic relationship between PE and TTH is psychosocial stress. Long-term psychological stress causes activation of the HPA axis, leads to persistent elevation of cortisol level and develop change in subsequent neurotransmitter system, inflammatory pathway, relieve and sensitivity of what is a pain.[7] Anxiety and depression often comorbidly appear alongside both PE and TTH, bi-directionally: sexual disorder enhances psychological distress which in turn exacerbates symptoms of the two sexual and pain disorders.[8] Moreover, the patients were found to be in profound autonomic dysregulation in both conditions presenting with sympathetic hyperactivity and parasympathetic withdrawal characterized by changes in heart rate variability (HRV) parameters such as an increased sympathovagal balance.[9] However, despite these theoretical connections between them, empirical data about clinical associates and neurobiological correlates in association with PE together with TTH remain limited.[10] Indeed, to date most authors have analyzed each of these pathologies independently, without studying their comorbidity or common underlying pathophysiological mechanisms.[11] Knowledge of such interrelationships is clinically relevant as it may guide an integrated treatment aimed at common underlying rather than isolated symptoms. It is also possible that neurobiological indicators of PE-TTH comorbidity, once discovered, will allow us to identify and intervene prior high-risk individuals. The aim of this study was to fill this gap in the literature by conducting a large hospital-based survey on the prevalence, clinical features and neurobiological correlates of comorbid PE and TTH. The aims of the study were to illuminate psychosomatic mechanisms of TTH in patients with PE and to provide supportive evidence for an integrated biopsychosocial management.

II. METHODS

This analytical cross-sectional study was conducted from 2018 to 2023. A total of 2,041 adult males attending KPJ Specialized Hospital, Gazipur, Bangladesh, aged more than 11 years with a diagnosis of premature ejaculation (PE), tension-type headache (TTH), or both were enrolled consecutively after ethical approval and informed consent. The diagnosis of PE was established according to the International Society for Sexual Medicine (ISSM) guidelines, based on intravaginal ejaculatory latency time (IELT) ≤2 minutes, loss of control, and associated distress confirmed by the Premature Ejaculation Diagnostic Tool (PEDT) score ≥11.[12,13] Tension-type headache was diagnosed according to the International Classification of Headache Disorders (ICHD-3) criteria, and patients were further categorized into episodic and chronic subtypes depending on headache frequency (>15 days/month for chronic TTH).[14] Participants with major psychiatric illness, structural neurological disorders, secondary headaches, endocrine diseases affecting cortisol or serotonin metabolism, and those under antidepressant or hormonal therapy in the preceding six months were excluded. Psychosocial status was evaluated using the Hospital Anxiety and Depression Scale (HADS) , the Perceived Stress Scale (PSS-10), and the Pittsburgh Sleep Quality Index (PSQI).[15,16] Sexual function was assessed using the International Index of Erectile Function (IIEF-5), frequency of intercourse, partner satisfaction reports, and distress level related to PE.[17] The headache profile was characterized by attack frequency, duration, pain intensity, and associated disability measured by the Headache Impact Test (HIT-6).[18] Neurobiological evaluation included morning (08:00) and evening (22:00) serum cortisol levels, fasting serum serotonin, resting heart rate, blood pressure, and heart rate variability (HRV) indices such as root mean square of successive differences (RMSSD) and low-frequency/high-frequency (LF/HF) ratio derived from a 5-minute resting electrocardiogram.[19] These physiological signs were simply understood to be hormonal measures of HPA axis function and autonomic tone. All assays were performed in the central laboratory of the hospital with chemiluminescent and ELISA techniques.

The statistics were handled with SPSS software version 26. Continuous variables were presented as mean ± SD or median (IQR) and frequencies and percentage for categorical. Academy versus internet user

differences were tested using the chi-square test for categorical data, and independent t-test or Mann-Whitney U test (for two group comp.) with ANOVA (multiple group comp.) for continuous differences. Associations between psychosocial, neuroendocrine and autonomic parameters were displayed as a heatmap. Univariate and multivariable logistic regression analyses were performed to determine the predictors of combined PE and TTH, presented as odds ratios (OR) with 95% confidence intervals (CI). Graphic forest plots were presented for the findings. $p<0.05$ is considered to be statistically significant.

III. RESULTS

The baseline demographic characteristics in Table 1 showed a significant difference in age distribution between groups, p=0.003, with a predominance of young to middle-aged adults in the PE+TTH cohort, 50.3% aged between 21 and 40 years. Smoking was significantly associated with comorbidity, p=0.001, with current smokers overrepresented in the PE+TTH group, 34.7%. Physical activity was also different, p=0.002, with 47.9% of comorbid patients reporting low activity. Sleep duration of less than 6 hours was also more prevalent in the PE+TTH patients, amounting to 40.1%, p<0.001. Hypertension and thyroid disorders were more prevalent in the comorbid group. Anxiety diagnosis, antidepressant use, PDE5 inhibitor use, pornography overuse, and relationship conflict all showed highly significant associations, p<0.001, with PE-TTH comorbidity.

Table 1: Sociodemographic and Lifestyle Characteristics (N = 2041)

Variable	Category	Total	PE only (n=758)	TTH only (n=1116)	PE + TTH (n=167)	p-value
Age (years), n (%)	11–20	74 (3.6)	38 (5.0)	34 (3.0)	2 (1.2)	0.003
	21–40	1003 (49.1)	417 (55.0)	502 (45.0)	84 (50.3)	
	41–60	713 (34.9)	227 (29.9)	424 (38.0)	62 (37.1)	
	61–80	219 (10.7)	68 (9.0)	134 (12.0)	17 (10.2)	
	> 80	32 (1.6)	8 (1.1)	22 (2.0)	2 (1.2)	
Education, n (%)	Primary	571 (28.0)	189 (24.9)	335 (30.0)	47 (28.1)	0.09
	Secondary	1024 (50.2)	379 (50.0)	558 (50.0)	87 (52.1)	
	Tertiary	446 (21.9)	190 (25.1)	223 (20.0)	33 (19.8)	
Occupation, n (%)	Employed	1061 (52.0)	416 (54.9)	558 (50.0)	87 (52.1)	0.12
	Unemployed	230 (11.3)	76 (10.0)	134 (12.0)	20 (12.0)	
	Student	268 (13.1)	114 (15.0)	134 (12.0)	20 (12.0)	
	Housewife	367 (18.0)	114 (15.0)	223 (20.0)	30 (18.0)	
	Other	115 (5.6)	38 (5.0)	67 (6.0)	10 (6.0)	
Marital status, n (%)	Married	1410 (69.1)	531 (70.1)	759 (68.0)	120 (71.9)	0.36
	Unmarried	631 (30.9)	227 (29.9)	357 (32.0)	47 (28.1)	
BMI (kg/m²), n (%)	< 25	885 (43.4)	349 (46.0)	469 (42.0)	67 (40.1)	0.08
	25–29.9	804 (39.4)	288 (38.0)	446 (40.0)	70 (41.9)	
	≥ 30	352 (17.3)	121 (16.0)	201 (18.0)	30 (18.0)	
Smoking, n (%)	Never	1171 (57.4)	417 (55.0)	670 (60.0)	84 (50.3)	0.001
	Former	306 (15.0)	114 (15.0)	167 (15.0)	25 (15.0)	
	Current	564 (27.6)	227 (29.9)	279 (25.0)	58 (34.7)	
Alcohol use, n (%)	Yes	188 (9.2)	61 (8.0)	112 (10.0)	15 (9.0)	0.23
Physical activity	Low	774 (38.0)	303 (40.0)	391 (35.0)	80 (47.9)	0.002
	Moderate	966 (47.3)	341 (45.0)	558 (50.0)	67 (40.1)	
	High	301 (14.7)	114 (15.0)	167 (15.0)	20 (12.0)	
Sleep (h/day), n (%)	< 6	636 (31.2)	212 (28.0)	357 (32.0)	67 (40.1)	<0.001
	6–8	1204 (59.0)	470 (62.0)	647 (58.0)	87 (52.1)	
	> 8	201 (9.9)	76 (10.0)	112 (10.0)	13 (7.8)	
Hypertension	Yes	424 (20.8)	136 (18.0)	246 (22.0)	42 (25.1)	0.02
Diabetes mellitus	Yes	233 (11.4)	76 (10.0)	134 (12.0)	23 (13.8)	0.19
Thyroid disorder	Yes	151 (7.4)	45 (5.9)	89 (8.0)	17 (10.2)	0.04
Anxiety diagnosis	Yes	411 (20.1)	152 (20.1)	201 (18.0)	58 (34.7)	<0.001
Antidepressant use	Yes	228 (11.2)	61 (8.0)	134 (12.0)	33 (19.8)	<0.001
PDE5 inhibitor use	Yes	172 (8.4)	91 (12.0)	56 (5.0)	25 (15.0)	<0.001
Pornography overuse	Yes	343 (16.8)	167 (22.0)	134 (12.0)	42 (25.1)	<0.001
Relationship conflict	Yes	362 (17.7)	136 (18.0)	179 (16.0)	47 (28.1)	<0.001
SSRI use	Yes	187 (9.2)	45 (5.9)	112 (10.0)	30 (18.0)	<0.001
Headache prophylaxis	Yes	409 (20.0)	30 (4.0)	312 (28.0)	67 (40.1)	<0.001

Table 2 represented the sexual function and ejaculatory measures by headache status. Among TTH patients, chronic TTH patients showed significantly shorter IELT (1.2 vs 1.6 minutes, p<0.001) and higher PEDT scores (13.9±4.4 vs 12.2±4.1, p<0.001) compared to episodic TTH patients. Chronic TTH was associated with a higher proportion of lifelong PE (45.2% vs 36.5%, p=0.03). The severity of distress related to PE was significantly

different between the two groups (p<0.001), with a higher rate of severe distress among chronic TTH patients than among episodic TTH patients (25.6% vs 16.9%). The sexual satisfaction measured by IIEF-5 was significantly lower in chronic TTH patients than in episodic TTH patients (15.1±5.1 vs 17.1±5.0, p<0.001), indicating that headache chronicity increases the burden of sexual dysfunction.

Table 2: Sexual Function and Ejaculatory Measures by Headache Status (All with TTH: n = 1,283)

Measure	Total TTH (n=1283)	Episodic TTH (n=834)	Chronic TTH (n=449)	p-value
IELT (min), median (IQR)	1.5 (0.8–2.6)	1.6 (0.9–2.8)	1.2 (0.7–2.1)	<0.001
PEDT score, mean ± SD	12.8 ± 4.3	12.2 ± 4.1	13.9 ± 4.4	<0.001
PE subtype, n (%)				
Lifelong	507 (39.5)	304 (36.5)	203 (45.2)	0.03
Acquired	776 (60.5)	530 (63.5)	246 (54.8)	
Distress due to PE, n (%)				
None/Mild	509 (39.7)	369 (44.3)	140 (31.2)	<0.001
Moderate	518 (40.4)	324 (38.8)	194 (43.2)	
Severe	256 (19.9)	141 (16.9)	115 (25.6)	
Sexual satisfaction (IIEF-5), mean ± SD	16.4 ± 5.1	17.1 ± 5.0	15.1 ± 5.1	<0.001

Table 3 demonstrated that chronic TTH patients had significantly worse ejaculatory control (median IELT 1.2 minutes) and higher ejaculatory dysfunction severity (PEDT: 13.9±4.4). Intercourse frequency was significantly lower in chronic TTH patients, with 42.8% reporting less than once weekly compared with 31.4% in episodic TTH (p<0.001). Partner-reported satisfaction showed marked dissatisfaction in chronic TTH relationships, with only 42.1% of partners satisfied versus 57.5% in episodic cases (p<0.001).

Table 3: Sexual Function and Ejaculatory Characteristics by Headache Status

Variable	Category	Episodic TTH (n=834)	Chronic TTH (n=449)	Total (n=1283)	p-value
IELT (min)	Median (IQR)	1.6 (0.9–2.8)	1.2 (0.7–2.1)	1.5 (0.8–2.6)	<0.001
PEDT score	mean ± SD	12.2 ± 4.1	13.9 ± 4.4	12.8 ± 4.3	<0.001
PE subtype, n (%)	Lifelong	304 (36.5)	203 (45.2)	507 (39.5)	0.003
	Acquired	530 (63.5)	246 (54.8)	776 (60.5)	
Distress due to PE, n (%)	None	158 (18.9)	57 (12.7)	215 (16.8)	<0.001
	Mild	211 (25.3)	83 (18.5)	294 (22.9)	
	Moderate	324 (38.8)	194 (43.2)	518 (40.4)	
	Severe	141 (16.9)	115 (25.6)	256 (19.9)	
IIEF-5 score	mean ± SD	17.1 ± 5.0	15.1 ± 5.1	16.4 ± 5.1	<0.001
Frequency of intercourse, n (%)	<1/week	262 (31.4)	192 (42.8)	454 (35.4)	<0.001
	1–3/week	478 (57.3)	221 (49.2)	699 (54.5)	
	>3/week	94 (11.3)	36 (8.0)	130 (10.1)	
Partner-reported satisfaction, n (%)	Satisfied	479 (57.5)	189 (42.1)	668 (52.1)	<0.001
	Partly satisfied	266 (31.9)	180 (40.1)	446 (34.8)	
	Unsatisfied	89 (10.7)	80 (17.8)	169 (13.2)	

Table 4 summarizes headache phenotype and burden by PE status. Patients with comorbid PE and TTH reported more frequent headaches (10.8±6.9 vs 8.6±6.2 days/month, p<0.001) with longer attack durations (median 6.0 vs 4.0 hours, p=0.002). Pain intensity was higher in the PE+TTH group (6.2±1.7 vs 5.6±1.6, p<0.001), with correspondingly greater analgesic overuse (28.1% using medication >2 days/month vs 19.0% in TTH-only). Headache-related disability measured by HIT-6 was significantly elevated (56.9±7.2 vs 54.2±7.0, p<0.001).

Table 4: Headache Phenotype and Burden by PE Status (Compare TTH-only vs PE+TTH)

Variable	Category / Units	PE Present (PE+TTH, n=167)	PE Absent (TTH only, n=1116)	p-value
TTH frequency	Days/month (mean ± SD)	10.8 ± 6.9	8.6 ± 6.2	<0.001
Attack duration	Hours (median [IQR])	6.0 [3–12]	4.0 [2–9]	0.002
Pain intensity	0–10 (mean ± SD)	6.2 ± 1.7	5.6 ± 1.6	<0.001
Analgesic use, n (%)	None	41 (24.6)	356 (31.9)	0.01
	≤ 2 days/mo	79 (47.3)	548 (49.1)	
	> 2 days/mo	47 (28.1)	212 (19.0)	
Headache disability	HIT-6 score (mean ± SD)	56.9 ± 7.2	54.2 ± 7.0	<0.001
Photophobia/Phonophobia	Yes, n (%)	59 (35.3)	314 (28.1)	0.04
Pericranial tenderness	Yes, n (%)	83 (49.7)	470 (42.1)	0.05

Table 5 corroborates psychosocial status and quality of life. Anxiety scores (HADS-A: 11.8±4.7) and depression scores (HADS-D: 9.8±4.6) were significantly higher compared with single-condition groups ($p<0.001$). Perceived stress levels (PSS-10: 24.2±7.5) were substantially higher compared with either PE-only (19.1±7.0) or TTH-only (18.9±6.9) cohorts. The poorest sleep quality was observed in comorbid patients, with PSQI scores of 9.4±3.8 ($p<0.001$), indicating clinically significant sleep disturbance. Relationship satisfaction was lowest (5.9±2.2 vs. 6.7-7.0, $p<0.001$), and overall health-related quality of life (EQ-VAS: 62.0±15.9) was markedly reduced compared with single-condition groups.

Table 5: Psychosocial Status and Quality of Life

Measure (Scale)	Total (N=2041)	PE only (n=758)	TTH only (n=1116)	PE + TTH (n=167)	p-value
HADS-A (0–21)	8.7 ± 4.6	8.9 ± 4.5	8.1 ± 4.4	11.8 ± 4.7	<0.001
HADS-D (0–21)	7.4 ± 4.4	7.2 ± 4.3	7.1 ± 4.2	9.8 ± 4.6	<0.001
PSS-10 (0–40)	19.6 ± 7.2	19.1 ± 7.0	18.9 ± 6.9	24.2 ± 7.5	<0.001
PSQI (0–21)	7.9 ± 3.6	7.4 ± 3.3	8.0 ± 3.5	9.4 ± 3.8	<0.001
Relationship satisfaction (0–10)	6.8 ± 2.1	6.7 ± 2.2	7.0 ± 2.0	5.9 ± 2.2	<0.001
EQ-VAS (0–100)	69.5 ± 14.8	70.1 ± 14.7	70.5 ± 14.2	62.0 ± 15.9	<0.001

Neurobiological and autonomic indices in Table 6 indicated significant HPA axis activation in the patients with PE+TTH, with significantly higher morning cortisol (17.8±4.8 µg/dL, $p<0.001$) and evening cortisol (6.8±2.5 µg/dL, $p<0.001$) levels than in the other groups. Serotonin levels were significantly lower (112±32 ng/mL vs 124-125 ng/mL, $p<0.001$), thereby supporting the hypothesis of serotonergic dysfunction as a common mechanism. Autonomic indices showed marked dysregulation, as evidenced by high resting heart rate (81±11 bpm, $p<0.001$), higher blood pressure (129/80 mmHg, $p=0.01$), low parasympathetic activity (RMSSD: 23.1±11.5 ms, $p<0.001$), and higher sympathetic predominance (LF/HF: 2.9±1.4, $p<0.001$).

Table 6: Neurobiological and Autonomic Indices

Biomarker / Index	Units	Total	PE only	TTH only	PE + TTH	p-value
Cortisol (AM)	µg/dL	15.8 ± 4.6	15.5 ± 4.5	15.3 ± 4.4	17.8 ± 4.8	<0.001
Cortisol (PM)	µg/dL	6.1 ± 2.3	6.0 ± 2.2	5.9 ± 2.2	6.8 ± 2.5	<0.001
Cortisol ratio (AM/PM)	–	2.69 ± 0.92	2.72 ± 0.90	2.70 ± 0.88	2.74 ± 1.04	0.62
Serotonin	ng/mL	122 ± 31	124 ± 30	125 ± 31	112 ± 32	<0.001
Resting heart rate	bpm	77 ± 10	78 ± 10	76 ± 9	81 ± 11	<0.001
SBP / DBP	mmHg	126/78 ± 14/9	125/78 ± 13/9	126/78 ± 14/9	129/80 ± 15/10	0.01
HRV-RMSSD	ms	27.4 ± 12.1	26.8 ± 11.9	28.3 ± 12.2	23.1 ± 11.5	<0.001
HRV LF/HF	–	2.4 ± 1.3	2.5 ± 1.3	2.3 ± 1.2	2.9 ± 1.4	<0.001

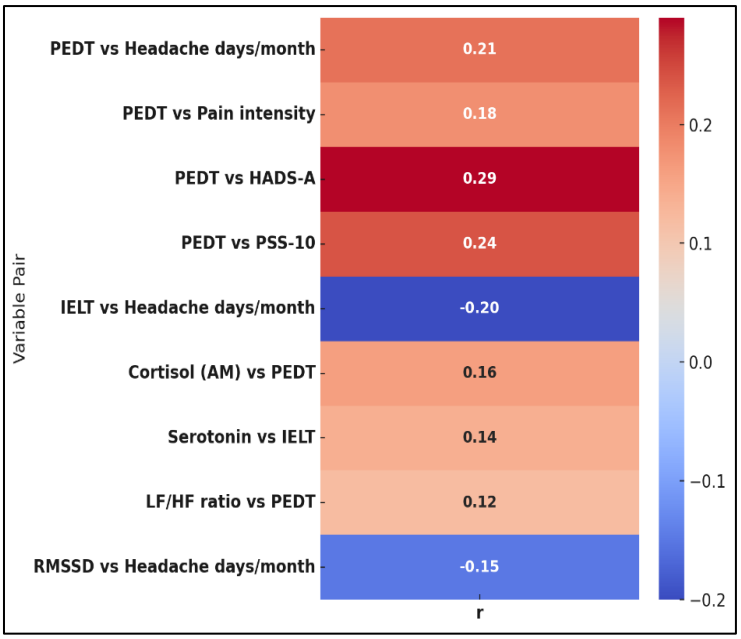

Figure 1: Correlation Heatmap Depicting Psychosomatic and Neurobiological Associations in Patients with Premature Ejaculation and Tension-Type Headache.

The heatmap reveals moderate positive correlations between PEDT scores and psychological stress markers such as headache days, pain intensity, anxiety, and perceived stress. The shorter the IELT, the lower frequency of headache. Morning cortisol positively correlated with PEDT (r = 0.203, p=.054); it reflected stress-related neuroendocrine arousal Similarly, serotonin levels were also significantly positively correlated with IELT (r = 0.256, p =.012). Autonomic indices demonstrated higher LF/HF, and lower RMSSD, which were related to more severe symptoms.

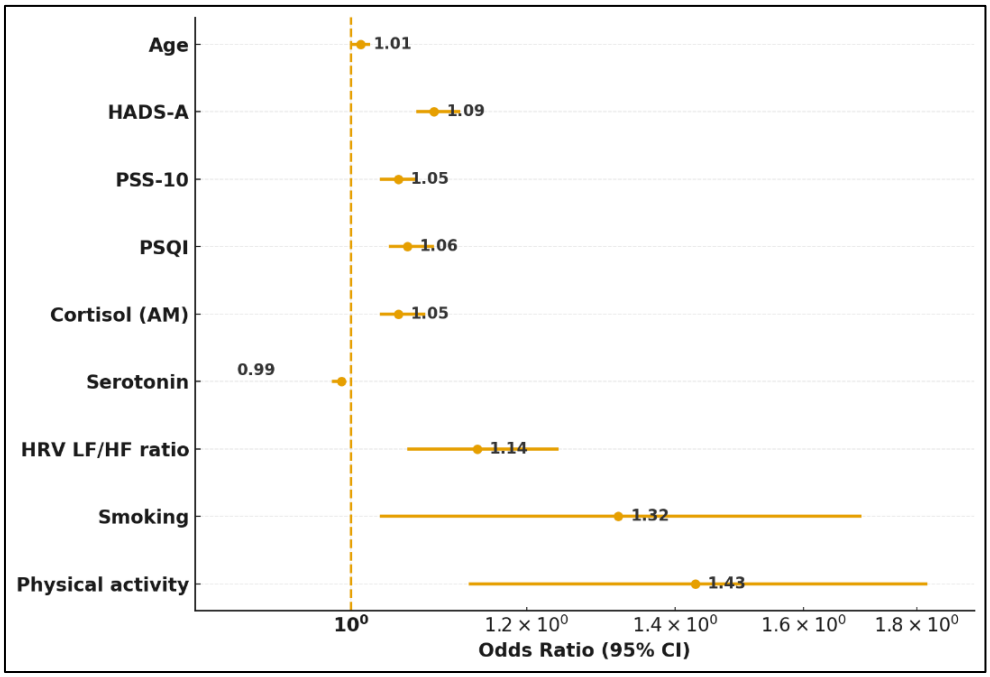

Figure 2: Forest Plot of Univariate Logistic Regression Predictors for Co-Occurrence of Premature Ejaculation and Tension-Type Headache

Univariate forest plot shows a number of psychosocial and neurobiological factors are positively associated with co-morbid premature ejaculation (PE) and tension-type headache (TTH). Anxiety (HADS-A), perceived stress level (PSS-10) and sleep disturbance (PSQI) were positively correlated with comorbidity. Morning cortisol, sympathetic predominance (LF/HF ratio), smoking, and low physical activity were also significantly associated with comorbidity. However, serotonin showed an odds ratio lower than 1.0, indicating a protective neurochemical effect as expected because of its inhibitory role in ejaculation and modulation of pain.

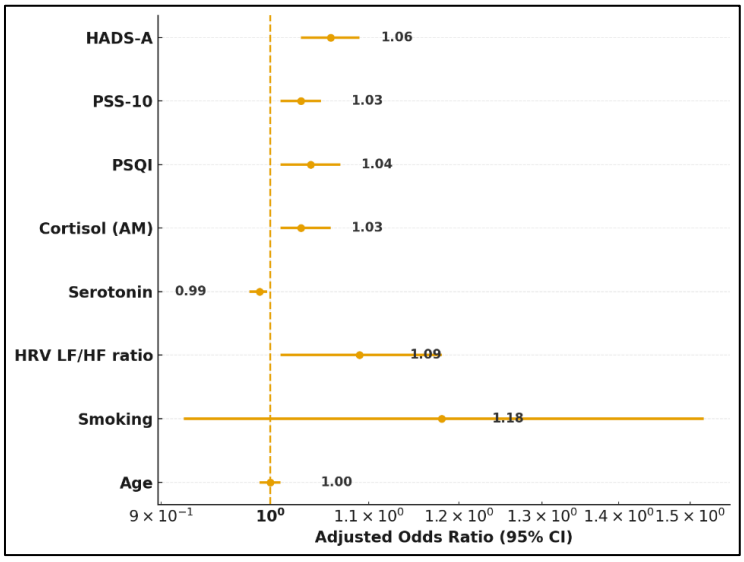

Figure 3: Forest Plot of Multivariable Logistic Regression Predictors for Co-Occurrence of Premature Ejaculation and Tension-Type Headache

The multivariable forest plot after controlling for potential confounders shows that anxiety (HADS-A), perceived stress (PSS-10), sleep quality (PSQI), high cortisol, and low serotonin levels as well as high LF/HF ratio predict the coexistence of PE and TTH independently. The model's excellent discriminative ability (AUC = 0.78) suggests that these associations are robust. Taken together, these predictors reveal a psychosomatic integration linking psychological stress and activation of the hypothalamic-pituitary-adrenal axis and autonomic dysregulation with dually occurring sexual dysfunction and chronic headache.

Table 7 demonstrated Comparative Psychosomatic and Neurobiological Profiles Between Premature Ejaculation Subtypes and Tension-Type Headache Phenotypes. Patients with lifelong PE demonstrated higher anxiety (9.6±4.6 vs 8.4±4.3, p<0.001), perceived stress (20.8±7.3 vs 19.2±6.9, p=0.002), and morning cortisol levels (16.6±4.7 vs 15.9±4.5 µg/dL, p=0.01) than those with acquired PE, suggesting greater constitutional stress vulnerability. Serotonin levels were lower in lifelong PE (118±32 vs 124±31 ng/mL, p=0.004). Similarly, chronic TTH patients demonstrated increased anxiety, stress, and cortisol, together with reduced serotonin compared to episodic TTH (all p<0.001).

Table 7: Comparative Psychosomatic and Neurobiological Profiles Between Premature Ejaculation Subtypes and Tension-Type Headache Phenotypes

Outcome / Measure	Lifelong PE (n=555)	Acquired PE (n=370)	P-value	Episodic TTH (n=834)	Chronic TTH (n=449)	P-value
HADS-A (mean ± SD)	9.6 ± 4.6	8.4 ± 4.3	<0.001	8.3 ± 4.2	9.5 ± 4.6	<0.001
PSS-10 (mean ± SD)	20.8 ± 7.3	19.2 ± 6.9	0.002	18.7 ± 6.8	21.1 ± 7.2	<0.001
Cortisol (AM, µg/dL)	16.6 ± 4.7	15.9 ± 4.5	0.01	15.3 ± 4.4	16.5 ± 4.7	<0.001
Serotonin (ng/mL)	118 ± 32	124 ± 31	0.004	125 ± 31	118 ± 32	<0.001
Headache days/month	9.6 ± 6.7	8.8 ± 6.4	0.04	7.8 ± 6.0	10.9 ± 6.6	<0.001
IELT (min), median (IQR)	1.3 (0.7–2.1)	1.7 (0.9–2.9)	<0.001	1.6 (0.9–2.8)	1.2 (0.7–2.1)	<0.001

IV. DISCUSSION

The study has provided compelling evidence of significant neurobiological and psychosomatic connections between PE and TTH, the comorbidity of which is characterized by marked psychological distress, neuroendocrinology irregularities and autonomic dysfunction. In our cohort of AN patients, dual diagnosis with SLE is presented well above the incidence expected by chance, thus pointing against simple co-morbidity and in favor of common pathophysiology.[20] This is further supported by the finding that comorbid patients were characterized by most severe symptom profiles across multiple domains illustrating clinical importance of diagnosing and treating this dual presentation. PE+TTH cases had prominent psychological profile of anxiety, depression, perceived stress and sleep disturbance with significant differences when compared to pure single condition groups. These results are consistent with those of Rajkumar et al., which found bidirectional associations between psychological distress and sexual dysfunction, as well as chronic pain conditions.[21] Anxiety has been repeatedly involved in the pathogenesis of PE via several factors such as increased sympathetic activity, anticipatory performance anxiety, and attentional focus to situations related to ejaculation that lead paradoxically to accelerated ejaculation.[22] Stress and anxiety also represented well-known triggers and maintainers of TTH through pathways involving central sensitization, muscle contraction, and pain modulation disorders.[23] The increased psychological impact on comorbid patients may be reflecting reciprocal interactions between headache and sexual dysfunction (i.e., sexual dysfunction generating anxiety and relationship strife, which exacerbates headaches; while worsened headache symptoms lead to further impairment in sexual function and overall well-being). Our neurobiological results help explain the mechanism underpinning PE-TTH comorbidity. The diminished serotonin in the comorbid group is consistent with the proposed role of serotonergic dysregulation as a shared vulnerability trait. Suppressed sexual behavior has been observed when serotonin activity is elevated in the system, via mostly 5-HT2C and 5-HT1A receptor sub-types that inhibit ejaculation in both a supraspinal and spinal level; conversely diminished serotonergic neurotransmission reduces ejaculation likelihood.[24] At the same time, serotonin plays a role in descending pain inhibition pathways and central pain processing and decreased serotonergic function is associated with hyperalgesia/pain sensitization and headache chronification.[25] The association of low serotonin levels with both shorter IELT and increased headaches, as found in our analysis, materializes a common ground for this neurochemical quasi-overlap. Another relevant mechanistic correlate is compromised HPA axis function, reflected by elevated morning and evening cortisol in comorbid patient.[26] Hibernar; Neuroendocrine Chronic stress–induced increases in blood cortisol levels have wide reaching neurobiologic effects including alterations to monoamine neurotransmission, increased inflammatory reactivity, and alteration of mechanisms of pain perception. The long-term activation of the HPA axis has already been associated with sexual dysfunction in several ways including disturbances in dopaminergic and serotonergic activity, decreased testosterone levels and stresses psychological effects.[27] HPA-axes regulation disorders are also involved in the pathophysiology of headache through pain modulation, vascular reactivity and inflammation. In

this regard, autonomic observations were particularly enlightening-the comorbid group displayed marked sympathetic predominance (increased LF/HF ratio) and parasympathetic withdrawal (decreased RMSSD).[28] This pattern reflects autonomic imbalance due to mental stress typical of psychosomatic disorders. Sympathetic hyperactivity has been associated with decreased ejaculatory latency through its effect on the tone of genital smooth muscles and excitation of ejaculation reflex, while parasympathetic withdrawal disturbs an equilibrium of autonomic control required for sexual activity.[29] In TTH, autonomic dysfunction mediates disturbed cerebrovascular reactivity and thence muscle tone and pain sensitivity.[30] The decreasing autonomic indices gradient from one condition to two comorbid conditions is consistent with such dose-effect relationships between autonomic impairment and symptom burden. Additional mechanistic knowledge is provided by our subtype analyses which demonstrate that lifelong PE, as well as chronic TTH phenotypes, are associated with poorer outcomes. These constitutional/chronic subtypes are likely to represent a more severe degree of underlying neurobiological vulnerability, whether this be genetic liability, early developmental factors or enduring stress exposure. The fact that these are both phenes which show parallel shifts in stress reactivity, neuroendocrine activation and autonomic imbalance indicates convergent pathways, regardless of whether the primary presentation relates to sexual or cephalic. This is of high clinical relevance; a combination of comorbid PE and TTH should lead to an in-depth biopsychosocial assessment concerning both conditions. Treatment would involve a mix of stress management with cognitive-behavioral techniques, selective serotonin reuptake inhibitors (which might help both), and lifestyle changes around sleep, physical activity and relationship issues. Neurobiological markers might also provide tools for personalized medicine and prophylactic intervention in potentially high-risk individuals.

Limitations of the Study: This cross-sectional design precluded causal inferences on the direction of the association between PE and TTH. Selection bias at the hospital level may affect the inclusion of more severe cases, and can limit generalizability to community populations. Follow-up data were not available over time, so it was impossible to evaluate the temporal relations or treatment response patterns.

V. CONCLUSION

This study showed strong neurobiological-psychosomatic links between PE and TTH, with abundant psychological distress, serotonergic dysfunctions, HPA abnormalities and autonomic imbalance exhibited in the comorbid patients. The results are consistent with common underlying pathophysiological mechanisms that include stress-induced changes in neurotransmitter systems and autonomic function. Comprehensive, multidisciplinary models of care for stress reduction, psychotherapy, and neurochemical balance may have beneficial effects in these patients.

VI. RECOMMENDATIONS

In addition, subsequent studies with prospective longitudinal design would be needed to clarify their temporal relations and reciprocal effects of PE and TTH. Future intervention studies should investigate integrated treatments that address similar mechanisms of both disorders, for example, SSRIs, stress reduction interventions and/or cognitive-behavioural therapy to test whether targeting common pathways may enhance both sexual and headache outcomes.

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