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Shift Work Sleep Disorder and Night Shift Work Significantly Impair Erectile Function.

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Abstract

Objectives: Here we examine the association between shift work sleep disorder (SWSD) and erectile dysfunction (ED) in shift workers.

Methods: Men presenting to a single andrology clinic between January 2014 - July 2017 completed validated questionnaires: International Index of Erectile Function (IIEF), Patient Health Questionnair-9 (PHQ-9), and the non-validated SWSD Questionnaire. Men were also asked about shift work schedule, comorbidities, phosphodiesterase 5 (PDE5) inhibitor use, and testosterone use. Serum total testosterone values were determined for each visit. Linear regression was performed controlling for testosterone use, testosterone levels, PDE5 inhibitor use, age, and comorbidities to determine the effect of SWSD on ED as assessed using the IIEF.

Results: Of the 754 men completing questionnaires, 204 reported non-standard shift work (begins before 7 am or after 6 pm, regularly extends out of that frame, or rotates frequently) and 48 were found to have SWSD using a screening questionnaire. Non-standard shift work alone did not result in worse IIEF-EF scores ($p = 0.31$), but those who worked non-standard shifts and had SWSD demonstrated IIEF-EF scores 2.8 points lower than men without SWSD ($p<0.01$). When assessing for the type of shift work performed, men who worked night shifts had IIEF-EF scores

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7.6 points lower than men who worked during the day or evening ($p < 0.01$). Testosterone use improved IIEF-EF scores for men with SWSD by 2.9 points, ameliorating the effect of SWSD on ED. However, baseline testosterone levels were not associated with worse erectile function in this cohort.

Conclusion: Men with SWSD have worse erectile function, with men who work night shifts having even poorer erectile function. These findings suggest that circadian rhythm disturbance may significantly impact erectile function. While testosterone therapy may partly reverse the effects of SWSD, shift work is a potential risk factor for ED and should be assessed for as part of the evaluation of men with ED.

MeSH Key Words:

hypogonadism; low testosterone; sleep; shift work disorder; sexual dysfunction

INTRODUCTION

Shift work is common across the globe, involving work hours during periods normally occupied by sleep. It is estimated that >15% of the international workforce adheres to such schedules, which are common in the healthcare, hospitality, protective, and energy industries.[1, 2] Shift workers are at increased risk of developing a circadian sleep-rate rhythm disorder, Shift Work Sleep Disorder (SWSD). The International Classification of Sleep Disorders defines SWSD as a circadian disruption sleep disorder characterized by at least one month of excessive sleepiness, insomnia, and impairment of social and occupational activities attributed to a persistent shift work schedule. Non-standard shift work is defined as a work schedule that begins before 7 am or after 6 pm, regularly extends outside a 7 am - 6 pm frame, or rotates frequently in structure.[3, 4] The Bureau of Labor and Statistics reported the prevalence of such work in the United States to be >10% in 2004, a number that has likely since increased.[2]

METHODS

Study Participants

All men presenting to a single academic andrology clinic between July 2015 and June 2017 completed an IRB-approved in-office survey. The survey took approximately 45 minutes to complete and consisted of multiple validated questionnaires for conditions and co-morbidities common in the male population. Specific questionnaires applicable to this investigation integrated into the in-office survey are discussed below. Responses were collected electronically via a secure, online research platform (www.surverymonkey.com). All patients coming to the clinic were given the survey regardless of presenting complaint, age or race. Men were included if they completed the survey in its entirety.

Men were grouped as to whether they worked during standard daytime hours or performed non-standard shift work. Non-standard shifts were defined as those starting before 7 am or after 2 pm, regularly outside of the standard 7 am to 6 pm workday, or if regularly rotating in and out of standard working hour shift times.[5] Using the survey, we screened for SWSD, using a previously validated questionnaire, among men reporting non-standard shifts.[6] On

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the same survey we also assessed the details of each participants' shift work (hours per day, days per week and the amount of time performing non-standard shift work). Men were also asked to indicate their satisfaction with sleep quality as "very satisfied," "somewhat satisfied," "somewhat dissatisfied," or "very dissatisfied."

Patient surveys also screened for ED using the validated International Index of Erectile Function (IIEF) questionnaire.[7] The IIEF assesses erectile function (EF), orgasmic function (EF), sexual desire (SD), intercourse satisfaction (IS), and overall satisfaction (OS) using a series of 15 questions. Men rate each of the questions using a 0–5 Likert scale (with descriptors of points related to each question), with each domain yielding an individual score, and with the sum of the domain scores yielding the total IIEF score. EF scores are out of a possible 30 points with <14 being considered a positive screen for ED.

The Charlson Comorbidity Index (CCI) was used to account for relevant comorbidities in our population.[8] Depression was screened for using the Patient Health Questionnaire 2 (PHQ-2).[9] Physical activity levels were assessed using the Rapid Assessment of Physical Activity (RAPA), history of type two diabetes mellitus, history of PDE5 inhibitor use in the last 2 weeks, and history of testosterone use ever and in the two weeks prior to survey completion.[10]

Finally, laboratory results of survey respondents were assessed including serum testosterone (T), follicle stimulating hormone (FSH), and luteinizing hormone (LH). These were drawn as part of routine care and analyzed in the Laboratory for Male Reproductive Research and Testing at Baylor College of Medicine on a single Beckman Coulter Access2 assay system using enzyme-linked immunoassay (Beckman Coulter, Brea, CA, USA).

Statistical Analysis

Only completed questionnaires were included in analysis. If more than one entry was submitted for the same patient, only the first response was entered into analysis. Linear regression was performed to assess the impact of shift work and SWSD on ED (total IIEF, EF, OF, SD, IS and OS sub-scores) while adjusting for age, comorbidities (CCI), exercise intensity and frequency (RAPA), recent testosterone and PDE5 inhibitor use, and testosterone level. Additional regression models were created to assess factors related to circadian rhythm disruption, sleep disturbance, and associated distress (which together comprise SWD) in order to identify which factors may be most pertinent to changes in ED for men performing shiftwork. STATA 14.2IC for Mac (StataCorp, College Station, TX) was used for all statistical analyses.

RESULTS

A total of 754 men completed the in-office questionnaires. Of these, 550 (72.9%) were standard daytime workers and 204 (27.1%) reported working non-standard shifts in the past month. Of these, 46 (22.5%) fulfilled criteria for SWSD while 156 (76.5%) did not. Baseline characteristics of the three cohorts were compared (Table 1). Men who did not identify as shift workers were older and had similar rates of diabetes mellitus (DM) as the shift working group, with and without SWSD. None of the men in the SWSD group had DM.

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Comorbidities and exercise rates (RAPA scores) were similar. Non-shift workers had higher rates of PDE5 inhibitor use in the last two weeks and exogenous T use.

Linear regression compared non-standard daytime shift workers, both with and without SWSD to standard daytime shift workers. The relationship between shift work and SWSD and erectile function was assessed while controlling for age, burden of comorbidities, exercise intensity, recent testosterone use, and testosterone level, examining each IIEF domain (Table 2).

Performing non-standard shift work was not associated with worse IIEF erectile function (EF) domain scores compared to standard shifts (p=0.31). Men with SWSD however, had worse EF domain scores compared to daytime workers (2.8 point decrease, SD ± 0.88, p<0.01). Similarly, orgasmic function domain scores did not differ among standard and non-standard shift workers (p=0.97) but men who had SWSD had slightly worse OF domain scores (0.72-point decrease, SD ± 0.27, p=0.01). Sexual desire scores were lower in men with SWSD who worked non-standard shifts and but not in men who performed non-standard shift work but did not have SWSD (1.25-point decrease, SD ± 0.18, p<0.01 and p=0.06 respectively). Following the trend, both intercourse satisfaction domain and overall satisfaction scores were equivocal in men who worked non-standard shifts in the absence of SWSD (p=0.58 and p= 0.07 respectively) but were less among men with SWSD (1.29 -point decrease, SD ± 0.32, p<0.01 and 1.29-point decrease, SD ± 0.21, p<0.01 respectively).

Among all regressions of IIEF sub-score models, age was associated with lower IIEF domain and total scores, as expected (p<0.02), as was testosterone use (p<0.03), though testosterone level was not (p>0.05). Interestingly, testosterone use among men with SWSD eliminated the negative effects of SWSD on erectile function, improving EF scores by 2.90 points (SD ± 0.80, p<0.01). Increased exercise was associated with better IIEF scores in all domains among non-standard shift workers with and without SWSD in all IIEF domains except the EF domain. These results suggest that increased exercise may improve overall sexual function among men with non-traditional work hours regardless of SWSD.

Other features of SWSD including sleep disturbance and associated distress were also examined by analyzing survey questions about sleep schedule, sleep quality, and overall sense of well-being to determine what impacted EF scores. All models were again controlled for age, comorbidities, exercise, recent testosterone use, and testosterone level. Working regular shifts at night was associated with greatly worsened EF scores (7.58 point decrease, SD ± 2.94, p=0.01) as did sleeping during the day time (5.01 point decrease, SD ± 2.55, p=0.05) independent of SWSD status. Sense of well-being also impacted EF domain scores. Men who reported a very decreased sense of well-being had a large decrease in EF domain scores (10.32-point decrease, SD ± 3.03, p<0.01), while men who reported slightly or somewhat decreased sense of well-being had no decrease in reported erectile function. **(p>0.05)**. (Table 3)

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DISCUSSION

This study adds to the growing body of evidence that supports the conclusion that sleep plays a crucial role in erectile function and that this role is likely not only mediated by quantity of sleep but also by circadian rhythm. The importance of sleep for normal endocrine function is demonstrated by disease states in people with disordered sleep. These include an increased incidence of obesity, metabolic syndrome, hypogonadism and depression.[11–13] All of these conditions independently affect erectile function in healthy males.

It has been previously described that non-standard shift workers are at increased risk for insomnia, daytime sleepiness, and poor sleep quality and that this may be synergistically worsened by low serum testosterone.[14] Hypogonadal men may experience decreased libido, ED, fatigue, and loss of muscle mass.[15] It has been suggested that the low serum testosterone in non-standard shift workers is related to sleep quality because testosterone production peaks during REM sleep.[16] This would, in theory, put men suffering from SWSD at even higher risk for low testosterone and its negative effects on sexual function. Results of studies on testosterone levels in men with SWSD have been mixed but the largest study to date (766 men) observed that men with SWSD had significantly lower testosterone levels than their peers without SWSD (mean decrease 100.4 ng/dL, $p < 0.01$).[17]

In a 2017 study by Pastuszak et al, sleep quality and its relationship to ED was examined. [14] The study included 182 male non-standard shift workers, with hypogonadal symptoms and erectile function assessed using the Androgen Deficiency in the Aging Male (ADAM / quantitative (q)ADAM) and the IIEF-EF. Men with better self-reported sleep quality had a lower incidence of erectile dysfunction. Subjective sleep quality was also assessed, using “very satisfied”, “somewhat dissatisfied” and “very dissatisfied” as answer choices. The present study builds on these prior findings. In the present study, a control group of standard shift workers was included and the role of SWSD investigated. This approach is superior to a single question, subjective snapshot of sleep quality. In the present study we observe a significant contribution of SWSD to ED, permitting a focus on individuals affected by a circadian rhythm disorder, likely arising from their work schedules and sleep quality, rather than on the work schedule or sleep quality independently. These results suggest that screening for SWSD could be an effective tool when evaluating ED. [14]

Testosterone plays an important role in sexual function. It affects erectile function at multiple levels including the central nervous system (CNS), peripheral nervous system (PNS) and at the level of target tissue.[18] Testosterone has generally been associated with central release of dopamine, oxytocin and nitric oxide (NO), all of which are essential for normal erectile function.[19]

The amelioration of the effects of SWSD with testosterone therapy observed in the present study support the hypothesis that the overall decrease in erectile function seen in men with disordered sleep is at least partially attributable to hypogonadism. ED has been linked to testosterone variability and improves if testosterone levels are normalized.[21, 22] Additionally, we found that consistently working night shifts and sleeping during the day

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time predicted worse erectile function, highlighting the importance of circadian rhythm in normal male sexual function.

This study is not without limitations. The most significant limitation of the work is the large number of men already on testosterone therapy (TTh). We attribute this to the setting. All of these men presented to an academic andrology practice for a variety of reasons ranging from erectile dysfunction, low testosterone, consultation for varicocele/hydrocele, etc. This was also a cross-sectional study and not all men could be followed before and after the TTh initiation to assess improvement in their sexual symptoms with TTh. Additionally, the present investigation was a retrospective analysis of self-reported symptoms. We do not have complete data on relationship status and cannot investigate the role of partners in this complex relationship.

Another limitation is the translation of these findings to clinical practice. While something may be “statistically” different, in practice a 1-point difference in IIEF is likely negligible to a man’s life and sexual experience. The results of this study have compelled us however, to be more mindful in screening men presenting with ED. Investigations into the recovery of erectile function with improved sleep patterns is ongoing.

Further, the timing of blood draws for hormone analysis could also have impacted the results of this work, particularly in men who were not already on TTh. Importantly, the effects of circadian rhythm alterations on endogenous testosterone levels have not been published. In normal men, testosterone levels peak early in the morning and in the evenings. Testosterone peaks and variance in men who do not sleep normal hours are less clearly elucidated. Strengths of this study include the relatively large sample size and data on depressive symptoms to augment the clinical picture.

Disordered sleep affects mental, physical and social health in many ways. Erectile and sexual function is a complex interplay of physiological processes, and dysfunction is multifactorial in most patients. In the present study, men with SWSD had worse erectile function than even their peers who worked shifts but did not have SWSD. We hypothesize that this is related to androgen dysregulation, which is supported by the finding that men on TTh with SWSD did not have worse EF scores when compared to men without SWSD. There are also likely psychological contributions, as we found that men who reported poor well-being had worse erectile function. The role of sleep, mental health, and sexual function is complex but important, as there is the potential to improve erectile function and quality of life by recognizing and appropriately treating hypogonadism in these men. Furthermore, male shift workers should be evaluated for SWSD, as this can significantly impact sexual function and mental health.

CONCLUSION

Men who work non-standard shifts and have SWSD have worse erectile function. This effect is magnified in men who work mainly night shifts. This suggests that dysregulation of circadian rhythm can contribute to ED in this cohort of men. The use of TTh may ameliorate the effects of SWSD on erectile function, but the mechanisms behind this require further

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elucidation as there could be many confounding factors and this study is inconclusive. However, screening men for shift work as well as SWSD can be a useful tool in the evaluation of ED in an otherwise healthy male, and adjusting sleep schedules, wherever possible, may result in improvement of erectile and sexual function in affected men.

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Table 1:

Baseline cohort characteristics

	Non-Shift Workers	Shift workers, No Shift Work Disorder	Shift workers, + Shift Work Disorder
	n = 550	n = 156	
Age (years)	45.5 (37.1 – 58.1)	37.0 (31.9 – 45.2)	38.4 (32.7 – 45.4)
CCI			
0	459 (83%)	146 (94%)	46 (96%)
1	34 (6%)	5 (3%)	1 (2%)
2	44 (8%)	5 (3%)	0 (0%)
>2	12 (2%)	0 (0%)	1 (2%)
T2DM	26 (4%)	4 (3%)	0 (0%)
RAPA score	6 (4 – 7)	6 (5 – 7)	6 (5 – 7)
PDE5 Inhibitor use in previous 2 weeks	101 (18%)	11 (7%)	4 (8%)
Testosterone use in previous 2 weeks	290 (53%)	77 (49%)	16 (33%)
Serum Testosterone level (ng/dL)	540 (304 – 984)	589 (282 – 1101)	486 (265 – 1000)
Serum FSH * level (mIU/mL)	0.6 (0.2 – 3.5)	0.5 (0.1 – 3.0)	1.5 (0.7 – 4.4)
Serum LH * level (mIU/mL)	0.3 (0.1 – 3.0)	0.8 (0.3 – 5.0)	2 (0.2 – 3.3)
EF	23 (15 – 27)	26 (22 – 27)	23 (16 – 26)
OF	10 (7 – 10)	10 (8 – 10)	9 (6 – 10)
SD	7 (6 – 9)	8 (6 – 9)	6 (4 – 8)
IS	11 (7 – 13)	11 (9 – 13)	10 (7 – 11)
OS	7 (4 – 9)	8 (6 – 9)	6 (4 – 8)

* Only available for 414 men

SWSD: Shift work sleep disorder

RAPA Score: Rapid Assessment of Physical Activity

CCI: Charleston Comorbidity Index

IIEF: International Index of Erectile Function

EF: Erectile Function

OF: Orgasmic Function

SD: Sexual Desire

IS: Intercourse Satisfaction

OS: Overall Satisfaction

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Table 2 -

Linear Regression Assessing the Impact of Shift Work and SWSD on Sexual Function by IIEF Domain

EF	Shiftwork vs No Shiftwork			SWSD vs No SWSD		
	Coeff.	**Std Error**	**p-value**	**Coeff.**	**Std Error**	**p-value**
Shiftwork (yes/no)	0.81	0.75	0.31			
SWSD (yes/no)				−2.80	0.88	**0.00**
Age (years)	−0.17	0.03	**0.00**	−0.19	0.03	**0.00**
CCI	−1.18	0.52	**0.03**	−0.99	0.75	0.19
RAPA	0.31	0.18	0.13	0.15	0.21	0.48
Testosterone Level (ng/dL)	0.00	0.00	0.61	0.00	0.00	0.55
Testosterone Use (yes/no)	2.55	0.70	**0.00**	2.90	0.80	**0.00**
PDE5-Inhibitor Use (yes/no)	0.31	0.90	0.83	−1.57	1.08	0.15

Orgasmic Function	Shiftwork vs No Shiftwork			SWSD vs No SWSD		
	Coeff.	**Std Error**	**p-value**	**Coeff.**	**Std Error**	**p-value**
Shiftwork (yes/no)	−0.01	0.23	0.97			
SWSD (yes/no)				−0.72	0.27	**0.01**
Age (years)	−0.04	0.01	**0.00**	−0.03	0.01	**0.00**
CCI	−0.25	0.16	0.11	0.04	0.22	0.86
RAPA	0.16	0.05	**0.00**	0.12	0.06	0.05
Testosterone Level (ng/dL)	0.00	0.00	0.50	0.00	0.00	0.53
Testosterone Use (yes/no)	0.63	0.21	**0.00**	0.58	0.24	**0.02**
PDE5-Inhibitor Use (yes/no)	0.19	0.27	0.48	0.06	0.32	0.86

Sexual Desire	Shiftwork vs No Shiftwork			SWSD vs No SWSD		
	Coeff.	**Std Error**	**p-value**	**Coeff.**	**Std Error**	**p-value**
Shiftwork (yes/no)	−0.21	0.11	0.06			
SWSD (yes/no)				−1.25	0.18	**0.00**
Age (years)	−0.02	0.00	**0.00**	−0.02	0.01	**0.01**
CCI	−0.06	0.07	0.40	−0.09	0.13	0.50
RAPA	0.07	0.03	**0.01**	0.11	0.05	**0.01**
Testosterone Level (ng/dL)	0.00	0.00	**0.03**	0.00	0.00	0.35
Testosterone Use (yes/no)	0.94	0.12	**0.00**	1.01	0.18	**0.00**
PDE5-Inhibitor Use (yes/no)	0.06	0.23	0.78	0.08	0.30	0.78

Intercourse Satisfaction	Shiftwork vs No Shiftwork			SWSD vs No SWSD		
	Coeff.	**Std Error**	**p-value**	**Coeff.**	**Std Error**	**p-value**
Shiftwork (yes/no)	0.12	0.21	0.58			
SWSD (yes/no)				−1.29	0.32	**0.00**
Age (years)	−0.07	0.01	**0.00**	−0.10	0.01	**0.00**
CCI	−0.30	0.14	**0.03**	−0.48	0.24	**0.05**

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RAPA	0.20	0.05	**0.00**	0.24	0.08	**0.00**
Testosterone Level (ng/dL)	0.00	0.00	**0.03**	0.00	0.00	0.24
Testosterone Use (yes/no)	1.43	0.22	**0.00**	1.43	0.33	**0.00**
PDE5-Inhibitor Use (yes/no)	0.55	0.43	0.19	−0.09	0.54	0.86

Overall Satisfaction	**Shiftwork vs No Shiftwork**			**SWSD vs No SWSD**		
	Coeff.	**Std Error**	**p-value**	**Coeff.**	**Std Error**	**p-value**
Shiftwork (yes/no)	−0.23	0.13	0.07			
SWSD (yes/no)				−1.29	0.21	**0.00**
Age (years)	−0.03	0.00	**0.00**	−0.03	0.01	**0.00**
CCI	−0.09	0.09	0.28	−0.11	0.16	0.46
RAPA	0.11	0.03	**0.00**	0.19	0.05	**0.00**
Testosterone Level (ng/dL)	0.00	0.00	0.28	0.00	0.00	0.33
Testosterone Use (yes/no)	0.95	0.14	**0.00**	0.88	0.21	**0.00**
PDE5-Inhibitor Use (yes/no)	0.11	0.26	0.66	−0.20	0.35	0.58

SWSD: Shift work sleep disorder

RAPA Score: Rapid Assessment of Physical Activity

CCI: Charleston Comorbidity Index

IIEF: International Index of Erectile Function

EF: Erectile Function

OF: Orgasmic Function

SD: Sexual Desire

IS: Intercourse Satisfaction

OS: Overall Satisfaction

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Table 3:

Linear Regression Assessing Sleep Quality

IIEF-Erectile Function	Additional independent		
	Difference	Std Error	p-value
Duration of shifts			
Hours per day working shifts	0.04	0.09	0.68
Days per week working shifts	0.02	0.17	0.91
Duration of working shifts			
<1 month	-	-	-
1–6 months	1.69	3.26	0.60
7–12 months	2.60	3.25	0.43
1–5 years	0.34	2.80	0.90
>5 years	1.32	2.71	0.63
Type of shift			
Regular, during the day	-	-	-
Regular, during the evening	−0.17	2.03	0.93
Regular, during the nighttime	−7.58	2.94	**0.01**
Rotating	0.47	0.99	0.64
Overall sleep quantity			
Sufficient	-	-	-
Slightly insufficient	−1.19	0.91	0.19
Somewhat insufficient	−1.69	1.01	0.10
Very insufficient	−0.97	1.46	0.51
Feeling sleepy at work			
No problem	-	-	-
Minor problem	0.13	0.95	0.89
Considerable problem	−1.02	1.22	0.40
Serious problem	−1.59	1.95	0.42
Falling asleep			
No problem	-	-	-
Minor problem	0.49	0.84	0.56
Considerable problem	−0.87	1.30	0.50
Serious problem	0.68	2.31	0.77
Staying asleep			
No problem	-	-	-
Minor problem	−1.44	0.80	0.08
Considerable problem	−0.49	1.33	0.72
Serious problem	−2.41	2.02	0.23
Waking too early and being unable to fall back asleep			
No problem	-	-	-

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IIEF-Erectile Function	Additional independent		
	Difference	Std Error	p-value
Minor problem	0.17	0.83	0.84
Considerable problem	−0.40	1.26	0.75
Serious problem	−2.51	1.98	0.21
Quality of sleep			
Satisfactory	-	-	-
Slightly unsatisfactory	−1.18	0.87	0.18
Somewhat unsatisfactory	−1.20	1.08	0.27
Very unsatisfactory	−1.16	1.70	0.49
Sleep typically obtained during the…			
Night-time	-	-	-
Day-time	−5.01	2.55	**0.04**
Mix of day-time and night-time	−0.64	1.09	0.56
Sense of wellbeing			
Normal	-	-	-
Slightly decreased	−1.55	1.06	0.15
Somewhat decreased	−2.99	1.76	0.09
Very decreased	−10.32	3.03	**0.00**