ORIGINAL RESEARCH

# Sexual function and distress in postmenopausal women with chronic insomnia: exploring the role of stress dysregulation

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<sup>1</sup>Division of Sleep Medicine, Thomas Roth Sleep Disorders & Research Center, Henry Ford Health System, Detroit, MI, USA; <sup>2</sup>Departments of Reproductive Biology and Psychiatry, Case Western Reserve University, Cleveland, OH, USA **Objective:** Menopause triggers changes in sexual function and many women develop sexual problems. Insomnia is common in postmenopausal women, and disturbed sleep has been linked to poor sexual health. Thus, postmenopausal women with insomnia may be especially vulnerable to developing sexual difficulties. This study estimated rates of sexual distress in postmenopausal women with chronic insomnia and explored associations between various facets of sexual health, insomnia symptoms, and insomnia-related stress dysregulation. **Design:** Cross-sectional.

Setting: Large multi-site health system in the US.

**Participants:** 150 postmenopausal women diagnosed with DSM-5 chronic insomnia disorder (56.44±5.64 years) completed measures of sexual distress, sexual function, hot flashes, insomnia symptoms, depression, and stress dysregulation in the forms of cognitive-emotional arousal (worry, rumination), sleep reactivity, and somatic hyperarousal.

**Results:** Nearly half of the sample endorsed clinically significant sexual distress (46.9%). Insomnia symptoms were largely associated with poor sexual arousal, orgasmic dysfunction, sexual distress, and sexual dissatisfaction. Insomnia-related stress dysregulation was similarly associated with these facets of sexual health but was also linked to problems with low desire and greater vaginal pain during sex. Hot flashes and depression were negatively associated with sexual health.

**Conclusion:** Postmenopausal women with chronic insomnia endorse high rates of sexual distress. Although compromised sexual function appears directly related to poor sleep itself, our data suggest that stress dysregulation may play vital role in sexual problems endorsed by postmenopausal insomniacs, particularly regarding low desire and vaginal pain. Prospective research is needed to characterize the evolution of these co-occurring symptoms.

Keywords: menopause, sexual function, sexual distress, sleep, worry, rumination

#### Introduction

The menopause transition is associated with changes in sexual function, and some women with menopausal symptoms have increased sexual problems and dysfunction.<sup>1–6</sup> Insomnia is among the most common complaints during and after the menopause transition.<sup>7–11</sup> Critically, poor sleep impairs female sexual health and satisfaction,<sup>10,12</sup> particularly in the domains of sexual desire and arousal.<sup>13–15</sup> Moreover, the menopause transition is a period of heightened vulnerability to depression, and women with menopausal insomnia have elevated depression levels.<sup>16–19</sup> Therefore, postmenopausal women with insomnia may be especially

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vulnerable to the effects of depression/low positive affect on female sexual problems.<sup>20–23</sup> That is, not only is the menopause transition a window of vulnerability for sexual distress and dysfunction, but women with menopauserelated insomnia are likely at even greater risk for sexual problems due to the added burden of insomnia and commonly comorbid depressive symptoms. It is therefore imperative to investigate the relationship between menopause-related insomnia disorder and sexual problems. A better understanding of the connection between sleep and sexual function in postmenopausal women can also guide treatment development to improve both sleep and sexual health in those with menopausal insomnia.

Menopause is marked by myriad hormonal and psychobiological changes that produce several clinical symptoms and can exacerbate medical conditions.<sup>24</sup> For some women, the areas of sexual health and sleep become compromised. Menopause is associated with changes in sexual function, particularly concerning low sexual desire and difficulties with sexual arousal.<sup>4-6,25,26</sup> Higher rates of sexual distress and complaints have been reported by women transitioning through menopause naturally and surgically.<sup>27,28</sup> Although etiological processes in sexual dysfunction share somatic, psychosocial, and neurobiological influences, menopause has long been assumed to result in decreased desire due to a decline in ovarian testosterone production and estrogen loss. Estrogen loss leads to vulvovaginal atrophy and dryness, in addition to changes in genital function via reduced clitoral blood flow and decreased sensory perception.<sup>4</sup> These bodily changes are associated with decreases in sexual arousal and increased vaginal pain during sex. And, though not all women develop sexual distress or dysfunction during menopause, a large but distinct subgroup of midlife women may be especially vulnerable to sexual problems: those struggling to sleep.

Nearly half of women complain of difficulty sleeping after menopause,<sup>7</sup> and 50% of those who report this difficulty obtain <6 hrs of nightly sleep.<sup>29</sup> Menopause itself via hormonal changes and related symptoms—disrupts sleep and increases the risk for insomnia,<sup>8</sup> which is among the top complaints during and after the transition.<sup>7–9,11</sup> An emerging body of research shows that poor sleep is negatively associated with female sexual function,<sup>14,15</sup> and recent evidence from a daily diary study showed that insufficient sleep leads to reductions in desire and more difficulties with arousal during sex.<sup>13</sup> Indeed, recent epidemiological data from the Women's Health Initiative Observational Study showed that 31% of postmenopausal women screened positive for insomnia and that these women reported less sexual activity, lower sexual satisfaction, and greater worry about sexual activity affecting their health as compared to good-sleeping postmenopausal women.<sup>10</sup> Indeed, 36% of postmenopausal insomniacs were unsatisfied with their sex lives relative to 30% of postmenopausal good sleepers. This study highlights that insomnia itself may exacerbate the menopause-related deterioration of sexual health for some women.

Although poor sleep may produce sexual distress or other problems in women with menopausal insomnia, a critical aspect of insomnia cannot be ignored: stress dysregulation. Insomniacs-menopausal or otherwise-have serious difficulty regulating stress. Indeed, the foundation of insomnia etiological models tends to focus on: 1) stressinduced cognitive-emotional hyperarousal<sup>30-34</sup> often in the forms of rumination and worry, especially during the presleep period, to promote nocturnal wakefulness; 2) sleep reactivity,<sup>34,35</sup> which is the degree to which stress disrupts sleep regulation thereby resulting in trouble falling/staying asleep; and 3) somatic or physiological hyperarousal, which is incompatible with sleep.<sup>34,36–39</sup> Along these lines, insomnia-related stress dysregulation is tied to depression-risk and depression itself,<sup>32,40,41</sup> which is the most common comorbidity associated with Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5)<sup>42</sup> insomnia disorder. Thus, in addition to poor sleep, women with menopausal insomnia suffer severe stress dysregulation and elevated depression that may also impair sexual health. Importantly, stress dysregulation and depression are elevated in those with poor sexual health,<sup>20–23,43–47</sup> but these associations have rarely been explored in the context of women with insomnia.

The primary goal of this cross-sectional study was to characterize the associations among insomnia symptoms, stress dysregulation, and sexual health in 150 postmenopausal women with DSM-5 chronic insomnia disorder that either onset or exacerbated during the menopause transition. Specifically, we explored how sexual distress and multiple facets of sexual function were related to trouble falling/staying asleep, daytime insomnia sequelae, worry, rumination, stress-related sleep reactivity, depressive symptoms, somatic hyperarousal, and hot flashes. Broadly, we predicted that greater severity of insomnia symptoms and stress dysregulation would be associated with greater sexual distress and poorer sexual function, particularly regarding low sexual desire and arousal difficulties.

# **Participants and methods** Participants and procedure

This present study was conducted across a large multihospital health system in Metro Detroit. All study procedures were approved by the Henry Ford Health System institutional review board and are compliant with the Declaration of Helsinki. Subjects were recruited from primary care and sleep clinics within the health system, from the community through newspaper advertisements, and from a research database of previous sleep studies from our lab. All subjects provided written informed consent prior to participation. Inclusionary criteria included:  $\geq 12$ consecutive months without menses, self-reported mean wake after sleep onset (WASO) of  $\geq 1$  hr on  $\geq 3$  nights per week, polysomnography (PSG) defined mean WASO of  $\geq$ 45 mins across 2 nights (neither of which could have WASO <30 mins), and DSM-5 chronic insomnia disorder with onset or exacerbation during or after the menopause transition per clinical interview with a sleep medicinetrained registered nurse. Exclusionary criteria included: prior/current DSM-5 major depression, sleep or circadian disorders (other than insomnia) as determined by patient report and PSG on the adaptation night (obstructive sleep apnea defined as apnea-hypopnea index  $\geq 15$ , periodic limb movements defined as arousal frequency  $\geq 15$ ), and medications affecting sleep (prescription sleep aids, over-the-counter sleep aids, herbal supplements, and antidepressants taken at night). However, women prescribed hormone therapy were eligible to participate. The present study was part of a randomized controlled trial comparing cognitive-behavioral therapy for insomnia (CBTI), sleep restriction therapy, and sleep education on menopausal insomnia; the results of which have been published elsewhere.<sup>19,48</sup> As no posttreatment data were collected on sexual health, treatment effects could not be tested.

We screened 317 postmenopausal women for eligibility. Of these, 107 women were identified as ineligible. Reasons for ineligibility included subclinical insomnia, insomnia unrelated to menopause, comorbid sleep apnea, comorbid restless legs syndrome, low WASO on PSG, comorbid bipolar disorder, and prior exposure to CBTI treatment. Another 56 women did not participate due to scheduling conflicts or declined due to disinterest in

#### Measures

#### Sexual health

Sexual distress was measured using the Female Sexual Distress Scale – revised (FSDS-R).<sup>49</sup> FSDS-R scores ≥11 reflect clinical levels of sexual distress that may indicate female sexual dysfunction. Thus, in the present study, women in the clinical range are referred to as "sexually distressed," whereas women who scored below the cutoff were referred to as "sexually healthy." Sexual function was measured using the Female Sexual Function Index (FSFI),<sup>50</sup> which assesses sexual desire, sexual arousal, vaginal lubrication during sexual activity, orgasmic function, sexual satisfaction, and vaginal pain during sexual activity over the prior 4 weeks. Higher scores on the FSFI reflect better sexual function. In order to not over-pathologize sexual inactivity,<sup>51,52</sup> when subjects responded to items on the FSFI arousal, lubrication, orgasmic function, and pain scales that they had not engaged in sexual activity over the past 4 weeks, these data were treated as missing. By extension, the original FSFI cutoffs cannot be applied to our data. Thus, we scored the FSFI such that each scale score represents the item-average within the scale. Therefore, scores range from 1 to 5 with 1 representing the poorest sexual function and 5 representing the healthiest sexual function on that scale. For descriptive purposes, we described FSFI mean scale values of 2 or below as problematic, scores of 3 to be in the moderate range, and of 4 or above as good.

#### Insomnia, sleep, and daytime sequelae

Insomnia symptoms were measured using the Insomnia Severity Index (ISI).<sup>53</sup> Total scores on the ISI represent overall global insomnia symptom severity with higher scores indicating greater severity. ISI scores  $\geq$ 15 indicate clinically significant insomnia. At the symptom level, the ISI measures 1) difficulty falling asleep, 2) difficulty staying asleep, 3) problems waking up too early, i.e., terminal insomnia, 4) dissatisfaction with sleep, 5) reduced quality of life, 6) worry and distress about sleep problems, and 7) the extent to which insomnia interferes with daytime functioning (e.g., concentration, memory, mood, fatigue, etc.). Stress-related sleep reactivity was measured using the Ford Insomnia Response to Stress Test (FIRST).<sup>54</sup> Higher FIRST scores indicate greater sleep reactivity with scores  $\geq 18$  reflecting high reactivity of the sleep system. Daytime fatigue was measured using the Fatigue Severity Scale (FSS),<sup>55</sup> which is a 9-item self-report survey of daytime fatigue. Scores range from 9 to 63, with higher scores indicating greater fatigue.

#### Depression, maladaptive thinking, and hyperarousal

Depressive symptoms were measured using the Beck Depression Inventory, 2nd edition (BDI-II),<sup>56</sup> a 21-item self-report measure of depressive symptoms. Higher scores on the BDI-II indicate greater depressive symptoms. The 16-item Dysfunctional Beliefs and Attitudes about Sleep scale (DBAS)<sup>57</sup> was used to assess dysfunctional beliefs about sleep (e.g., "I am worried that I may lose control over my abilities to sleep"). Mean item scores >4 indicate dysfunctional or irrational attitudes toward sleep. The Penn State Worry Questionnaire (PSWQ)<sup>58</sup> assesses trait-like tendency to worry. Higher PSWQ scores indicate greater trait worry with scores  $\geq 40$  representing moderate worry or worse. The 8-item Presleep Arousal Scale Cognitive scale (PSAS Cognitive)<sup>59</sup> was administered to assess nocturnal cognitive arousal/rumination when trying to fall asleep. Scores range from 8 to 40 and higher scores indicate higher levels of presleep cognitive arousal. The 8-item Presleep Arousal Scale Somatic factor (PSAS Somatic)<sup>59</sup> was used to measure somatic hyperarousal when trying to fall asleep (e.g., "heart racing, pounding, or beating irregularly"). Scores range from 8 to 40 and higher scores indicate greater presleep somatic hyperarousal.

In addition, subjects reported their age and race (White, Black, Hispanic or Latinx, Asian, Native American, Multiracial, Other) while completing surveys on sleep, mood, and sexual function. We collected menopauserelated information via interview with a registered nurse. Subjects were asked whether they were using hormone replacement therapy, whether they had undergone medical or surgical menopause, and were asked to estimate the time since their last menstruation. Daytime and nighttime hot flashes were reported in diaries across 14 days and are represented in this study by daily means.

### Analyses

We first explored descriptives for the full sample including sociodemographics, menopause-related information, sleep parameters, and sexual health indices by providing summary statistics on these variables. Next, we split the sample into two groups: postmenopausal women with vs without sexual distress, per the FSDS-R. These two groups were then compared on all variables using independent samples t-tests to test for significance, and we calculated Cohen's d to describe effect sizes for statistically significant group differences. We then conducted a series of zero-order correlations to identify which aspects of insomnia and related symptoms and maladaptive thinking were associated with sexual distress and the various measured facets of female sexual function.

### Results

#### Full sample characteristics

Our sample was largely comprised of non-Hispanic White (52.0%) and non-Hispanic Black women (39.3%). Reflecting the sample's clinical nature, insomnia symptom severity was in the clinical range (ISI:  $15.17\pm3.98$ ) and sleep reactivity was high (FIRST:  $21.86\pm6.05$ ). Mean sexual distress scores were in the elevated range (FSDS-R:  $11.29\pm9.96$ ) and nearly half of the sample was classified as having significant sexual distress (n=68/145; 46.9%). Desire scores were low, whereas levels of arousal, lubrication, orgasmic function, and satisfaction were in the moderate range. Vaginal pain during sex was low in the sample. See Table 1 for full sample characteristics.

# Comparing subjects with vs without sexual distress on sleep and stress dysregulation

We first established that women with sexual distress did not differ from sexually healthy women regarding the prevalence of hormone replacement therapy or medical or surgical menopause (Table 1). Further, the two groups did not differ on years since last menses. We then compared subjects with vs without sexual distress on indices of sexual and sleep health (see Table 1 for full results). Verifying that the FSDS-R's clinical cutoff accurately identifies those with sexual problems among postmenopausal insomniacs, sexually distressed women, relative to sexually healthy women, reported poorer arousal, vaginal lubrication, orgasmic function, and sexual satisfaction, as well as more vaginal pain during intercourse; these group differences were large. However, desire levels did not differ between the two groups (P=0.09), which were low in both groups (both group means below the scale midpoint). Groups did not differ on daytime or nighttime hot flashes.

#### Table I Sample characteristics for full sample and comparisons between sexually healthy vs sexually dysfunctional women

	All subjects	Sexual distressed	Sexually healthy	
Sample size	150	68	77	
Age	56.44±5.64 years	56.07±4.90	56.79±6.24	t(143)=0.76, P=0.45
Race				
White	78; 52.0%	44; 64.7%	34; 44.2%	Black vs White risk for FSD
Black	59; 39.3%	20; 29.4%	39; 50.6%	χ <sup>2</sup> (1)=6.84, <i>P</i> <0.01
Hispanic or Latinx	1; 0.7%	1; 1.5%	_	White:Black isk Ratio for
Multiracial	1; 0.7%	_	1; 1.3%	FSD=1.67
Other	2; 1.3%	_	1; 1.3%	
Did not answer	9; 6.0%	3; 4.4%	2; 2.6%	
Hormone replacement therapy	4; 2.7%	3; 4.4%	1; 1.3%	$\chi^2 = 1.31, P = 0.25$
Medical or Surgical Menopause	35; 23.3%	18; 26.5%	16; 20.8%	$\chi^2 = 0.65, P = 0.42$
Years since last menstruation	7.12±7.04	6.61±6.34	7.53±7.74	t(135) = -0.75, P = 0.45
FSDS-R	11.29±9.96	20.04±7.31	3.56±3.39	t(143)=17.74, P<0.001, d=2.89
FSFI				
Desire	2.22±1.06	2.06±0.92	2.36±1.16	t(143)=-1.70, P=0.09
Arousal	3.35±1.21	2.94±1.06	3.84±1.20	t(85)=-3.71, P<0.001, d=0.79
Lubrication	3.39±1.28	2.79±1.16	4.07±1.06	t(77)=-5.08, P<0.001, d=1.15
Orgasmic Function	3.55±1.21	3.09±1.03	4.10±1.18	t(83)=-4.21, P<0.001, d=0.91
Satisfaction	3.11±1.26	2.54±1.33	3.61±1.16	t(143)=5.56, P<0.001, d=0.86
Pain	4.00±1.27	3.54±1.44	4.49±0.83	t(72)=-3.43, P<0.01, d=0.81
ISI	15.17±3.98	16.44±4.24	13.77±3.23	t(143)=4.30, P<0.001, d=0.71
Fall asleep	1.51±1.05	1.81±1.03	1.21±0.96	t(143)=3.64, P<0.001, d=0.60
Stay asleep	2.67±0.88	2.78±0.93	2.52±0.82	t(143)=1.79, P=0.08
Early morning awakening	2.13±1.09	2.21±1.91	2.04±1.09	t(143)=0.91, P=0.37
Dissatisfaction	3.19±0.78	3.25±0.84	3.12±0.74	t(143)=1.02, P=0.31
Noticeable	2.02±0.99	2.31±0.89	1.71±1.00	t(143)=-3.77, P<0.001, d=0.63
Worried	1.29±0.97	1.44±0.95	1.13±0.95	t(143)=1.97, P=0.05
Daytime interference	2.35±1.02	2.65±1.00	2.04±0.95	t(143)=3.74, P<0.001, d=0.63
FSS	30.86±12.16	34.30±11.38	27.36±12.06	t(142)=3.53, P<0.01, d=0.59
Hot flashes, daytime	2.08±1.63	2.16±1.64	2.01±1.64	t(143)=0.53, P=0.60
Hot flashes, nighttime	1.67±1.23	1.75±1.24	1.60±1.22	t(143)=0.73, P=0.47
BDI-II	8.93±6.35	10.29±6.72	7.68±5.85	t(143)=2.50, P=0.01, d=0.41
FIRST	21.86±6.05	23.73±5.77	20.21±5.85	t(143)=3.65, P<0.001, d=0.61
DBAS	4.43±1.50	4.89±1.48	3.99±1.40	t(143)=3.74, P<0.001, d=0.62
PSWQ	46.13	48.99±13.04	43.26±13.25	t(142)=2.61, P=0.01, d=0.44
PSAS – cognitive	12.43±3.80	13.56±4.17	11.44±3.14	t(143)=3.48, P<0.01, d=0.57
PSAS – somatic	20.01±7.41	22.51±7.17	17.81±6.94	t(143)=4.01, P<0.001, d=0.67

**Abbreviations:** FSD, female sexual distress; FSDS-R, Female Sexual Distress Scale – revised; FSFI, Female Sexual Function Index; ISI, Insomnia Severity Index; FSS, Fatigue Severity Scale; Daytime and Nighttime Hot Flashes measured using daily diaries across 14 days with values reflecting daily means; BDI-II, Beck Depression Inventory, 2nd edition; FIRST, Ford Insomnia Response to Stress Test; DBAS, Dysfunctional Beliefs and Attitudes about Sleep scale; PSWQ, Penn State Worry Questionnaire; PSAS Cognitive, Presleep Arousal Scale, Cognitive factor; PSAS Somatic, Presleep Arousal Scale, Somatic factor; t, t-statistic;  $\chi^2$  chi-square; *p*, significance value; d, Cohen's d.

Regarding sleep, sexually distressed women, relative to sexually healthy women, reported greater severity of insomnia, particularly concerning difficulty falling asleep; these effects were medium-large (Table 1). Regarding insomnia-related daytime sequelae, sexually distressed women endorsed higher levels of daytime impairment, diminished quality of life, and fatigue. Sexually distressed women with insomnia also endorsed elevated levels of stress dysregulation (Table 1). Compared to sexually healthy women, those with sexual distress reported greater stress-related sleep reactivity, worry, presleep rumination, presleep somatic hyperarousal, and more dysfunctional beliefs about sleep. In accordance, sexually distressed women endorsed moderately greater depressive symptoms than their sexually healthy counterparts. After establishing that sexually distressed women endorsed elevated levels of sleep problems and stress dysregulation, we investigated for the specificity of associations.

# Symptom-level analyses reveal the specificity of associations among various facets of sleep and sexual health

Next, we explored associations among sleep problems, hot flashes, and various indices of sexual health (see Table 2 for full results). Daytime and nighttime hot flashes were associated with greater sexual pain and lower arousal, vaginal lubrication, orgasmic function, and sexual satisfaction. Women with greater insomnia severity endorsed higher sexual distress, sexual dissatisfaction, and orgasmic dysfunction.

Regarding nocturnal symptoms (Table 2): Difficulty falling asleep was linked to greater sexual distress and sexual dissatisfaction, as well as poorer vaginal lubrication during sexual activity. Having trouble staying asleep corresponded to difficulty achieving orgasm during sexual activity. Early morning awakenings, quite surprisingly, were associated with *better* sexual function. Specifically, terminal insomnia was associated with better sexual desire, arousal, vaginal lubrication, and sexual satisfaction.

Daytime insomnia sequelae were also associated with poor sexual function (Table 2). Insomnia-related daytime impairment was linked to greater sexual distress and poorer sexual arousal, vaginal lubrication, orgasmic function, and sexual satisfaction. Similarly, diminished quality of life was associated with greater sexual distress and sexual dissatisfaction, as well as lower desire and orgasmic function. Greater fatigue was associated with greater sexual distress and lower arousal, vaginal lubrication, orgasmic function, and sexual satisfaction.

# Symptom-level analyses reveal the specificity of associations among various facets of stress dysregulation and sexual health

Higher levels of stress dysregulation and depression were associated with poorer sexual health (see Table 3 for full results). Higher depression was associated with greater sexual distress and sexual dissatisfaction, as well as poorer desire, arousal, and orgasmic function. Women with highly

stress-reactive sleep systems reported greater sexual distress and sexual dissatisfaction, as well as lower sexual desire, arousal, and orgasmic function. Regarding maladaptive thinking, greater tendency to worry was linked to impairments in all measured indices of sexual health. Presleep rumination was also tied to several indices of sexual health such that nocturnal ruminators endorsed greater sexual distress, sexual dissatisfaction, and vaginal pain, and poorer subjective and genital arousal. The corbetween rumination and relation sexual desire approached significance (P=0.056). Greater presleep somatic hyperarousal was associated with greater sexual distress and sexual dissatisfaction as well as poorer subjective and genital arousal. Dysfunctional beliefs about sleep were associated with greater sexual distress and sexual dissatisfaction.

### Discussion

In a sample of 150 postmenopausal women with DSM-5 chronic insomnia disorder, we explored associations of sexual health with insomnia, depression, and stress dysregulation. Nearly half of the women in our study endorsed clinically significant sexual distress, indicating that impaired sexual health may be endemic to women with menopausal insomnia. Both nocturnal and daytime insomnia symptoms largely corresponded to problems with sexual arousal and orgasmic function, whereas high levels of stress dysregulation-in the forms of cognitive-emotional arousal, sleep reactivity, and somatic hyperarousal-were associated with low sexual desire and greater vaginal pain during sex, in addition to arousal and orgasmic difficulties. More frequent hot flashes were associated with poorer sexual function, although daytime and nighttime hot flashes were related to different facets of sexual response. These data offer preliminary evidence that both poor sleep itself and related stress dysregulation are directly linked to impaired sexual health and high rates of sexual distress associated with menopausal insomnia.

# Insomnia and sexual health in postmenopause

In 2018, data from the Women's Health Initiative highlighted that postmenopausal women with insomnia symptoms report reduced sexual activity and satisfaction and heightened sexual health-related worry.<sup>10</sup> Our study builds on current knowledge by characterizing sexual distress and function in postmenopausal women diagnosed

	ISI	ISI -	- ISI -	ISI – early morning		- ISI -	ISI – worried	ISI – daytime	FSS	Hot flashes –	Hot flashes –
		talling asleep	stayıng asleep	awakenings	dissatisfaction	QOL	about sleep	impairment		daytime	nighttime
Sexual	0.25**	0.26**	60.0	-0.05	0.10	0.22**	0.14	0.27**	0.29**	0.12	0.15
distress											
Desire	-0.04	-0.08	0.02	0.24**	0.02	-0.20*	-0.08	-0.09	-0.15	-0.10	-0.06
Arousal	-0.17	-0.15	-0.18	0.21**	-0.07	-0.18	-0.16	-0.22*	-0.23**	-0.27*	-0.15
Lubrication	-0.08	-0.25*	-0.01	0.31**	-0.09	-0.05	-0.08	-0.22*	-0.24**	-0.20	-0.39**
Orgasm	-0.29**	-0.13	-0.37***	0.14	-0.24*	-0.22*	-0.15	-0.29**	-0.32**	-0.29**	-0.32
Satisfaction	-0.19*	-0.22**	0.01	0.18*	-0.10	-0.27**	-0.14	-0.24**	-0.39***	-0.30***	-0.24**
Pain	0.02	-0.13	0.09	0.15	0.06	0.07	-0.04	-0.08	-0.12	-0.22	-0.29**
Note: Sexual d	istress assess	ed by the Female	Sexual Distress Sc	Note: Sexual distress assessed by the Female Sexual Distress Scale - revised. Desire, arousal, lubrication, orgasm, satisfaction, and pain measured using the Female Sexual Function Index. *P<0.01. ***P<0.01	Iubrication, orgasm,	satisfaction, a	and pain measured usin	g the Female Sexual Fund	ction Index. *	P<0.05. **P<0.01. ***	P<0.001.

Note: Sexual distress assessed by the remaie Sexual Listress cale – revised. Lesire, arousa Abbreviations: ISI, Insomnia Severity Index; QOL, quality of life; FSS, Fatigue Severity Scale.

Table 3 Correlations among sexual problems, stress dysregulation, and hot flashes	sexual problems, stress d	ysregulation, and hot flas	shes			
	BDI-II	FIRST	DBAS	PSWQ	PSAS – cognitive	PSAS – so
	******	14** 0				*** L C

	BDI-II	FIRST	DBAS	PSWQ	PSAS – cognitive	PSAS – somatic
Sexual distress	0.32***	0.27**	0.28**	0.28**	0.29***	0.35***
Desire	-0.25**	-0.30***	-0.04	-0.23**	-0.16	-0.12
Arousal	-0.38***	-0.33**	-0.19	-0.27*	-0.22*	-0.25*
Lubrication	-0.13	-0.14	-0.18	-0.23*	-0.23*	-0.27*
Orgasm	-0.34**	-0.21*	-0.15	-0.29**	-0.20	-0.23
Satisfaction	-0.40***	-0.23**	-0.21*	-0.21*	-0.29***	-0.22**
Pain	-0.06	-0.17	-0.01	-0.25*	-0.29*	-0.20

Note: Daytime and nighttime hot flashes measured using daily diaries across 14 days with values reflecting daily means. Sexual distress assessed by the Female Sexual Distress Scale – revised. Desire, arousal, lubrication, orgasm, satisfaction, and pain measured using the Female Sexual Function Index. \*P<0.01. \*\*P<0.001. \*\*P<0.00

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with DSM-5 insomnia disorder with confirmed objective sleep disturbance via PSG. An alarmingly high 46.9% of postmenopausal insomniacs endorsed significant sexual distress. These rates are higher than those reported in other US studies of similarly aged naturally postmenopausal women (19–33%), but similar to rates reported by similarly aged surgically postmenopausal women (44%).<sup>27,28</sup>

Rates of sexual distress in the present sample are similar to, or perhaps even slightly higher than, rates of sexual problems in postmenopausal women with metabolic syndrome (37.9%).<sup>28</sup> In the present study, trouble falling asleep and staying asleep were key nocturnal symptoms linked to sexual distress and difficulties with vaginal lubrication and orgasmic achievement. Insomnia-related day-time sequelae—namely fatigue, daytime impairments, and diminished quality of life—were also tied to a wide range of sexual problems but largely centered on problems with sexual arousal and orgasmic function. The only measured facet of sexual health *unrelated* to insomnia was vaginal pain during sexual activity.

A robust yet unexpected finding was that early morning awakenings (i.e., problems waking earlier than intended) were associated with better sexual function. That is, women with terminal insomnia reported higher sexual desire and better subjective and genital arousal during sex. Given that several sexual indices were associated with this insomnia phenotype, we do not believe these results to be type III errors. And quite interestingly, terminal insomnia is the one insomnia phenotype that is unrelated to depression.<sup>60</sup> One possible explanation for the association between early morning awakenings and better sexual function is that we are detecting, in part or even largely, a circadian effect; that early chronotype is associated with better sexual function. Notably, insomniacs with terminal insomnia exhibit early chronotype; i.e., they are early birds/morning larks.<sup>61</sup> And human sex hormones have a circadian rhythm such that androgen levels are highest in the morning in women.<sup>25</sup> It is possible that individuals with the early chronotype may be more likely to engage in solo and/or partnered sexual activity in the morning when bioavailability of sexual hormones is highest. This interpretation is of course largely speculative, and research is needed to better understand the relationship between circadian rhythmicity and sexual health and behavior.

#### Stress dysregulation and sexual health

underlies Severe stress dysregulation insomnia disorder,35,36,39 and stress dysregulation is elevated in those with sexual complaints and dissatisfaction.43-47 Thus, we investigated whether insomniogenic stress dysregulation was linked to sexual health in postmenopausal women. Sexual problems were closely tied to insomniarelated cognitive-emotional arousal and somatic hyperarousal. Prior studies examining relationships between cognitive-emotional arousal and sexual dysfunction have largely focused on worry. These studies have produced mixed results.<sup>47,62–64</sup> Yet, among stress dysregulation factors in the present study, worry and presleep rumination were most robustly associated with impairments in sexual health, indicating that over-active cognitive-emotional processing-central hallmarks of both insomnia<sup>30,34,65</sup> and depression<sup>66–68</sup>—may contribute to compromised sexual health for women with menopausal insomnia. Important to emphasize here is that cognitive-emotional dysregulation was associated with low sexual desire and increased vaginal pain, whereas insomnia itself was not related to either of these facets of sexual health.

Regarding somatic dysregulation, women who reported greater physiological hyperarousal when trying to fall asleep (e.g., heart racing, muscle tension, shortness of breath) also reported greater difficulty with subjective arousal and vaginal lubrication during sexual activity. This is consistent with prior studies linking physiological stress dysregulation, such as alterations in cortisol response and heart rate variability, to impaired sexual arousal.<sup>69,70</sup>

Providing evidence for a basal connection between sleep and sexual function, results showed that stress-related sleep reactivity-i.e., the degree to which the sleep system is corruptible in response to stress exposure—was robustly associated with most aspects of sexual health. Highly reactive sleepers reported elevated sexual distress and problems largely pertaining to desire, arousal, and orgasmic function. Although sleep reactivity has been linked to other non-sleep phenomena, such as depression and anxiety,<sup>34,35</sup> this is the first study to connect sleep system-specific stress dysregulation to impairments in sexual health. In a prior investigation, we showed that poor sleep itself impairs sexual response.<sup>13</sup> The present study builds upon these findings by suggesting that perturbations of psychobiological systems regulating sleep and stress-response may manifest as co-occurring insomnia and sexual dysfunction.

# Tying together insomnia, stress dysregulation, and sexual health

Taken together, insomnia is closely tied to sexual distress and myriad sexual problems in postmenopausal women with chronic insomnia. Due in part to hormonal changes, the menopause transition is associated with deteriorations in sexual health for many women.<sup>25</sup> Evidence from our study suggests that the added burden of insomnia is associated with even greater sexual distress and reduced functioning in this already vulnerable population. Although we found that poor quality sleep and fatigue directly correspond to sexual distress and difficulties, our data also suggest that psychobiological perturbations to systems regulating sleep, mood, and stress response may also connect insomnia to poor sexual health. Indeed, cognitiveemotional dysregulation, somatic hyperarousal, and stress-related sleep reactivity were moderately strong correlates of sexual distress and problems. Thus, not only does poor sleep impair sexual health as previously shown.<sup>13</sup> but co-occurring impairments in sexual health and sleep could potentially represent manifestations of overlapping stress-related disease processes.

Interestingly, insomnia symptoms were largely associated with the sexual arousal and orgasmic function aspects of sexual function. And while stress dysregulation was also associated with these aspects of sexual function, we want to highlight that low sexual desire and vaginal pain were largely only related to stress dysregulation rather than to insomnia itself. Declines in sexual desire are associated with the menopause transition and low sexual desire is a common sexual complaint among postmenopausal women.<sup>4,26,27</sup> Similarly, vaginal dryness, which is associated with pain during sex, increases throughout the transition and is most severe in postmenopause.<sup>71</sup> In our sample of postmenopausal insomniacs, desire and vaginal pain were not associated with insomnia symptoms. Rather, low sexual desire was associated with high worry, rumination, and sleep reactivity, whereas vaginal pain was associated with high levels of worry and rumination only. Thus, while insomnia itself may not impair sexual desire or pain in this population, insomniogenic, depressogenic, and anxiogenic maladaptive regulation of stress may produce co-occurring insomnia and hypoactive desire and sexual pain. Notably, sexual dysfunction is greater in menopausal women with low socioeconomic status (SES).<sup>72</sup> As women in poverty overly engage in ruminative coping,<sup>73</sup> it is possible that poorer stress regulation contributes to disparities in sexual dysfunction related to SES.

Hypoactive sexual desire shares neurobiological underpinnings with depression<sup>4,74</sup>; i.e., insomnia disorder's most common comorbidity. Given that worry, rumination, and sleep reactivity are highly expressed and etiologically implicated in both insomnia and depression,<sup>30,34,35,75</sup> it is perhaps unsurprising that these forms of cognitive-emotional and sleep system-related forms of stress dysregulation appear to link menopausal insomnia to low sexual desire. Indeed, the inability to inhibit worrisome and ruminative thoughts is common among those with low sexual desire and high sexual distress.<sup>4,64,74</sup>

### Study limitations

The present study should be interpreted in light of certain limitations. The entire sample comprising only subjects with insomnia limits our study in three key ways: First, we have no group of postmenopausal good sleepers for comparison of sexual health. Although we cited rates of sexual distress in other postmenopausal samples in the Discussion section for comparison of sexual distress rates, having a group of good sleepers would have been a preferable comparison. Second, because all subjects had clinical insomnia with sleep disturbance verified by PSG, we undoubtedly experienced the restriction of range of insomnia symptoms. Restriction of range would have (at its most benign) produced underestimated effect sizes and may have even (at its most harmful) produced type II errors due to reduced statistical power. Third, observed associations between stress dysregulation and sexual health may not be generalizable to postmenopausal women without insomnia; e.g., it is possible that fatigue is unrelated to sexual health in good-sleeping postmenopausal women. A critical methodological limitation of the present study is its cross-sectional design. Consequently, we were unable to investigate temporal directionality of associations.

Another limitation may concern subjective reports on vaginal pain during sexual activity. Recent research shows that >50% of postmenopausal women suffer in silence with vulvovaginal atrophy and associated pain during sex, yet <10% of postmenopausal women receive pharmacotherapy for this condition.<sup>76</sup> It is possible that postmenopausal women in our study may have underreported these symptoms out of reluctance or perhaps even out of lack of education regarding vulvovaginal atrophy and sexual pain.<sup>77</sup> Lastly, large prospective studies are needed to

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characterize changes in mood, sleep, and sexual health across the menopause transition to better delineate disease processes involved in menopause-related insomnia, depression, and sexual dysfunction. Such investigations should also account for the effects of important age-related medical conditions such as cardiovascular and metabolic disorders (e.g., hypertension, diabetes type II), which have been linked to insomnia, depression, and sexual dysfunction<sup>78–81</sup> and may contribute to or be affected by changes in mood, sleep, and sexual function in peri- and postmenopausal women.

# Conclusion

Our data indicate that nearly half of postmenopausal women with chronic insomnia are sexually distressed. Although prior research has shown that poor sleep itself leads to poor sexual function,<sup>13</sup> findings in the present study also suggest that stress dysregulation common to insomnia in the forms of cognitive-emotional dysregulation, sleep reactivity, and somatic hyperarousal could potentially underlie co-occurring insomnia and impaired sexual function. Broadly, insomnia symptoms were most closely tied to impairments in sexual arousal and orgasmic function. Interestingly, low sexual desire is a common sexual complaint among postmenopausal women,4,27 but menopausal insomnia did not directly correspond to low sexual desire. Rather, low desire was associated with dysregulated stress responses like high worry, rumination, sleep reactivity, and depression. Along these lines, vaginal pain during sexual activity was not associated with insomnia itself, but rather with worry, rumination, and nighttime hot flashes. Prospective research is needed to clarify the associations among insomnia, stress dysregulation, and sexual health. Importantly, while both pharmacologic and non-pharmacologic interventions can improve marital intimacy and sexual health in peri- and postmenopausal women,<sup>82,83</sup> future clinical trials may evaluate whether augmenting currently supported therapies with interventions improving sleep and emotion regulation to enhance treatment outcomes.

# **Abbreviations**

BDI-II, Beck Depression Inventory, 2nd edition; CBTI, cognitive-behavioral therapy for insomnia; DBAS, Dysfunctional Beliefs and Attitudes about Sleep scale; DSM-5, Diagnostic and Statistical Manual of Mental Disorders, 5th edition; FIRST, Ford Insomnia Response to Stress Test; FSDS-R, Female Sexual Distress Scale – revised; FSFI, Female Sexual Function Index; ISI, Insomnia Severity Index; PSAS, Presleep Arousal Scale; PSG, polysomnography; PSWQ, Penn State Worry Questionnaire; SES, socioeconomic status; WASO, wake after sleep onset.

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# **Author contributions**

All authors contributed to data analysis, drafting or revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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