Sex Hormones and Sleep in Men and Women from the General Population: A Cross-Sectional Observational Study

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Background Sleep is a complex vital state and a highly active and dynamic process occupying one third of human's lifetime. The prevalence of insomnia worldwide is estimated to be 10-30% and insomnia is associated with a higher risk of hypertension, obesity, metabolic syndrome and depression (2). To date, associations between sex hormones and sleep were mainly investigated in connection with hormone replacement therapy (1), menopausal status (4) and menstrual cycle (5) in women and obstructive sleep apnoea in men (6). Thus, we examined a comprehensive panel of sex hormones and various sleep characteristics in a population-based sample of healthy men and women from the general population.

METHODS

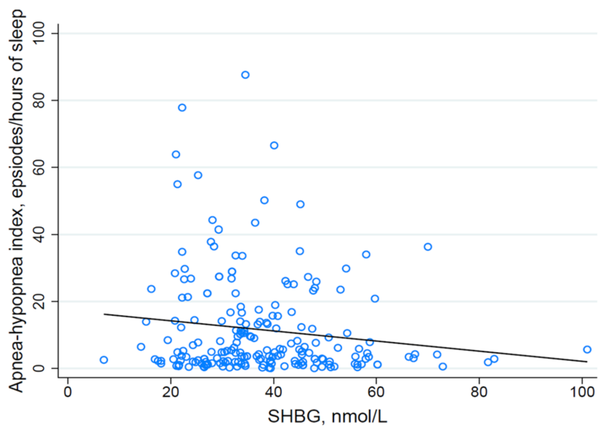
- We used data from 204 men and 213 women of the Study of Health in Pomerania TREND, who underwent cardiorespiratory polysomnography.
- Associations of total and free testosterone (TT, fT), androstenedione (ASD), estrone (E1), and estradiol (E2) measured by liquid chromatography-tandem mass spectrometry, and sex hormone-binding globulin (SHBG), dehydroepiandrosterone-sulphate (DHEAS) and E2/TT ratio with sleep measures were investigated.
- Sleep measures include total sleep time (TST), sleep efficiency, wake after sleep onset (WASO), apnea-hypopnea index (AHI), Insomnia severity index (ISS), Epworth sleepiness scale (ESS), and Pittsburgh sleep quality index (PSQI).
- Sex-specific multivariable regression models were adjusted for age, waist circumference, hypertension, smoking, physical inactivity, and alcohol consumption. Sensitivity analyses were performed with stratification by diagnosis of depression and menopausal status (women).

RESULTS

- In men, associations of TT, fT, SHBG, and E2/TT ratio with AHI in age-adjusted analyses were rendered non-significant after multivariable adjustment **(Figure 1A, Table 1)**. In multivariable analyses, ASD was associated with ESS **(Table 1)**.
- In women, only age-adjusted models showed an inverse association of SHBG with AHI (**Figure 1B, Table 1)**. Multivariable analyses showed positive associations of DHEAS with WASO and of E2 and E2/TT ratio with ESS **(Figure 1C, Table 1)**.
- Additionally, fT and SHBG were associated with AHI in multivariable models in pre-menopausal women.

Figure 1: Scatterplot of

A) AHI by SHBG in men



B) AHI by SHBG in women

C) ESS by E2 in women

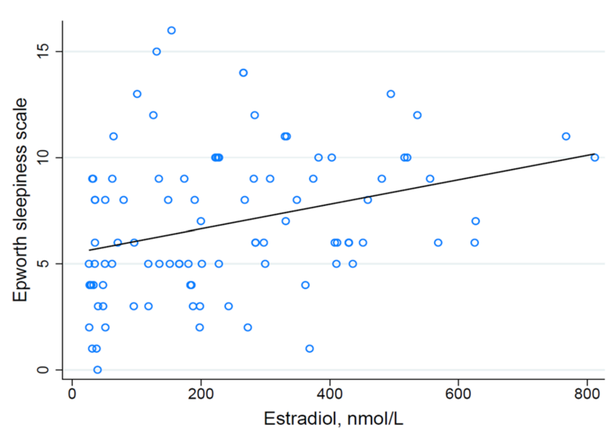


Table 1: Sex-specific, cross-sectional associations of sex hormones and SHBG with sleep measures in linear regression models.

		Beta coefficient (95% CI)						
		TT	Androstenedione	Free Testosterone	DHEAS	E2	Ratio E2/TT	SHBG
					Men			
WASO	age-adjusted	0.08 (-0.007; 0.17)	0.10 (-0.001; 0.20)	0.02 (-0.10; 0.14)	0.03 (-0.11; 0.17)	-0.08 (-0.21; 0.03)	**-0.15 (-0.27; -0.02)***	**0.11 (0.01; 0.21)***
	mv-adjusted	0.07 (-0.02; 0.17)	0.07 (-0.02; 0.18)	0.02 (-0.10; 0.15)	0.02 (-0.10; 0.16)	-0.06 (-0.19; 0.06)	-0.12 (-0.25; 0.001)	0.08 (-0.01; 0.19)
ESS	age-adjusted	-0.33 (-0.74; 0.07)	**-0.68 (-1.13; -0.23)***	-0.26 (-0.77; 0.24)	0.05 (-0.50; 0.60)	-0.39 (-0.88; 0.09)	-0.03 (-0.52; 0.45)	-0.33 (-0.79; 0.13)
	mv-adjusted	-0.36 (-0.85; 0.11)	**-0.71 (-1.18; -0.25)***	-0.30 (-0.86; 0.26)	0.01 (-0.52; 0.56)	-0.39 (-0.89; 0.09)	-0.12 (-0.69; 0.44)	-0.33 (-0.82; 0.16)
PSQI	age-adjusted	-0.27 (-0.74; 0.19)	-0.25 (-0.75; 0.24)	-0.39 (-0.87; 0.09)	-0.19 (-0.90; 0.51)	-0.36 (-0.80; 0.07)	0.01 (-0.48; 0.51)	-0.05 (-0.65; 0.55)
	mv-adjusted	-0.20 (-0.74; 0.32)	-0.31 (-0.84; 0.21)	-0.37 (-0.88; 0.13)	-0.20 (-0.90; 0.49)	-0.39 (-0.82; 0.03)	-0.21 (-0.76; 0.34)	0.09 (-0.59; 0.78)
					Women			
WASO	age-adjusted	0.08 (-0.01; 0.18)	0.03 (-0.11; 0.17)	0.04 (-0.05; 0.14)	**0.13 (0.01; 0.25)***	0.11 (-0.08; 0.31)	0.05 (-0.13; 0.24)	0.05 (-0.05; 0.15)
	mv-adjusted	0.07 (-0.01; 0.17)	0.04 (-0.01; 0.18)	0.03 (-0.06; 0.13)	**0.16 (0.03; 0.28)***	0.13 (-0.06; 0.33)	0.08 (-0.11; 0.28)	0.08 (-0.03; 0.20)
ESS	age-adjusted	0.003 (-0.40; 0.40)	-0.20 (-0.67; 0.27)	-0.15 (-0.57; 0.25)	0.05 (-0.45; 0.56)	**0.99 (0.33; 1.64)***	**0.95 (0.23; 1.68)***	0.17 (-0.24; 0.60)
	mv-adjusted	0.03 (-0.35; 0.43)	-0.17 (-0.64; 0.29)	-0.15 (-0.57; 0.27)	0.04 (-0.45; 0.53)	**1.04 (0.37; 1.72)***	**0.98 (0.24; 1.73)***	0.28 (-0.22; 0.79)
PSQI	age-adjusted	-0.07 (-0.60; 0.45)	-0.03 (-0.70; 0.62)	-0.17 (-0.69; 0.35)	0.48 (-0.10; 1.07)	**-0.83 (-1.59; -0.07)***	**-0.82 (-1.62; -0.02)***	0.06 (-0.50; 0.63)
	mv-adjusted	-0.12 (-0.67; 0.41)	-0.04 (-0.73; 0-64)	-0.23 (-0.81; 0.33)	0.52 (-0.08; 1.12)	-0.66 (-1.42; 0.09)	-0.63 (-1.44; 0.16)	0.06 (-0.54; 0.67)
					Odds ratio (95% CI)			
					Men			
AHI	age-adjusted	**0.62 (0.46; 0.83)***	0.80 (0.59; 1.08)	**0.71 (0.51; 0.99)***	0.94 (0.66; 1.33)	1.21 (0.89; 1.64)	**1.69 (1.24; 2.28)***	**0.65 (0.49;0.88)***
	mv-adjusted	0.78 (0.56; 1.08)	0.90 (0.65; 1.22)	0.85 (0.59; 1.21)	0.99 (0.69; 1.41)	1.06 (0.77; 1.46)	1.29 (0.91; 1.83)	0.82 (0.59; 1.14)
					Women			
AHI	age-adjusted	1.05 (0.77; 1.41)	0.95 (0.67; 1.35)	1.31 (0.96; 1.78)	1.03 (0.74; 1.42)	0.80 (0.45; 1.43)	0.76 (0.42; 1.39)	**0.55 (0.38; 0.78)***
	mv-adjusted	1.15 (0.84; 1.58)	1.04 (0.71; 1.53)	1.21 (0.87; 1.69)	1.14 (0.79; 1.65)	1.40 (0.64; 3.06)	1.24 (0.51; 3.00)	0.78 (0.53; 1.15)

Table 1: Data are β-coefficients or odds ratios and their 95% confidence interval with $p < 0.05$ marked as *. The multivariable model was adjusted for age, waist circumference, smoking status (three categories), physical inactivity, alcohol consumption, and hypertension. DHEAS, dehydroepiandrosterone-sulphate; SHBG, sex hormone-binding globulin; TT, total testosterone; E2, estradiol; CI, confidence interval; mv, multivariable; WASO, wake after sleep onset; ESS, Epworth sleepiness scale; PSQI, Pittsburgh sleep quality index; AHI, apnea-hypopnea index.

Conclusion Consistent with previous findings, the present cross-sectional population-based study observed sex-specific associations of testosterone, SHBG, and estrogen with sleep disturbances and poor sleep quality. However, multivariable-adjusted analyses confirmed the relative impact of body composition, health-related lifestyle, and comorbidity on the association between sex hormones and sleep.

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