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REGULAR ARTICLE

Inverse association of des-acyl ghrelin with worksite blood pressure in overweight/obese male workers

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Abstract
Background Job strain, defined as a combination of high job demands and low job control, has been reported to elevate blood pressure (BP) during work. Meanwhile, a recent experimental study showed that ghrelin blunted the BP response to such mental stress. In the present study, we examined the hypothesis that des-acyl ghrelin may have some beneficial effects on worksite BP through modulating the BP response to work-related mental stress, i.e., job strain.
Methods Subjects were 34 overweight/obese male day-shift workers (mean age 41.7 ± 6.7 years). No subjects had received any anti-hypertensive medication. A 24-h ambulatory BP monitoring was recorded every 30 min on a regular working day. The average BP was calculated for Work BP, Morning BP, and Home BP. Job strain was assessed using the short version of the Japanese Job Content Questionnaire.
Results Des-acyl ghrelin showed significant inverse correlations with almost all BPs except Morning SBP, Morning DBP, and Home DBP. In multiple regression analysis, des-acyl ghrelin inversely correlated with Work SBP after adjusting for confounding factors. Des-acyl ghrelin was also negatively associated with BP changes from Sleep to Morning, Sleep to Work, and Sleep to Home.
Conclusions Des-acyl ghrelin was inversely associated with Worksite BP, suggesting a unique beneficial effect of des-acyl ghrelin on Worksite BP in overweight/obese male day-shift workers.

Keywords Worksite blood pressure · Des-acyl ghrelin · Job strain · Obesity · Ambulatory blood pressure monitoring

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Introduction

High job strain, defined as a combination of high job demands and low job control at work [1], has been reported to elevate blood pressure (BP) during work [2, 3]. This association between high job strain and high worksite BP is rather remarkable in obese workers compared with non-obese workers [3, 4]. In addition, BP elevation by mental stress through the autonomic nervous system (ANS) activity [5] was strengthened by obesity [6–8], insulin resistance [6], and metabolic syndrome (Mets) [9].

Ghrelin, originally known as a growth hormone (GH)-releasing peptide from the stomach [10], circulates in acylated and des-acylated forms [11]. Des-acyl ghrelin, which is the most abundant form (about 90 %), is devoid of GH releasing capacity and does not stimulate food intake [11]. However, it has been indicated that relatively low levels of des-acyl ghrelin [12] might contribute to obesity, insulin resistance, and Mets [13–16]. Yano et al. [15, 17] indicated, in recent epidemiological studies, that low circulating des-acyl ghrelin levels are involved in arteriosclerosis and cardiovascular disease events in elderly hypertensive people. Des-acyl ghrelin might have additional beneficial effects on the cardiovascular system [12] through different mechanism, such as improving

endothelial function [18], ANS activity [19], and BP [20]. A recent experimental study also showed that ghrelin blunted the BP response to mental stress [21].

Based on these findings, we hypothesized that des-acyl ghrelin might have some beneficial effects on worksite BP through modulating the BP response to work-related mental stress, i.e., high job strain. In this study, we focused on the relations of plasma des-acyl ghrelin levels with worksite BP and BP change to worksite BP.

Methods

Subjects

Fifty-five overweight/obese [body mass index (BMI) $\geqq$25 kg m^{-2}] male workers who participated in a weight reduction program conducted by Aichi Medical University Institute of Physical Fitness, Sports Medicine and Rehabilitation, were enrolled. The protocol of the study, which was approved by the Ethical Committee at Aichi Medical University, was explained in detail, and written informed consent was obtained from each subject. All of them were regular employees at several small- and medium-sized enterprises, with 10–300 employees. Ten subjects with incomplete measurements of their 24-h ambulatory BP monitoring (ABPM), one subject who worked under a shift work system including a night shift, 8 subjects receiving anti-hypertensive medication, and 2 subjects with poor recording of Holter electrocardiogram were excluded. Finally, 34 subjects, aged from 27 to 58 years (mean age, 41.7 $\pm$ 6.7 years), were examined.

Procedure

Subjects had physical examinations including blood sampling in the morning after an overnight fast. Height and weight were measured, and BMI was calculated as weight (kg)/height $(m)^2$. After subjects had been sitting quietly for 5 min, BP was measured 3 times with a fully automated sphygmomanometer (TM-2655; A&D, Tokyo, Japan). The average of the 3 BP measurements was calculated as Rest BP. Medical history, current therapeutic regime, smoking state, and alcohol consumption were queried using a self-reporting questionnaire. Smoker was defined as current smokers. Alcohol drinker was defined as a subject drinking alcohol of more than 20 g/day.

Twenty-four hour ABPM and 2-channel 24-h ambulatory electrocardiographic (ECG) were conducted on a regular working day. BP was automatically recorded every 30 min with a portable BP measuring device (TM-2431; A&D, Tokyo, Japan). The methods of ABPM measurement and the criteria for identifying BP measurement errors complied with the Guidelines for the Clinical Use of 24 Hour ABPM by the Japanese Circulation Society [22]. Subjects were also asked to record their activities in a diary throughout the BP measurement. Based on these activity logs, we calculated Worksite BP, Morning BP, and Home BP as follows: Worksite BP was the average during work, Morning BP was the average during the first 2 h after waking up, and Home BP was the average from getting home in the evening to going to bed.

The heart rate variability (HRV) was analyzed on a Holter analysis system (ML analyzer; Medi Link, Toyota, Japan). The digitized R–R intervals were recorded and stored, and the power spectral densities were computed using the maximum entropy method (MEM). The power spectral densities were analyzed in 3 areas of concentration of spectral power by means of MEM. In these 2 areas, low-frequency power (LF: 0.04–0.15 Hz) was analyzed as an index of sympathetic and parasympathetic nervous system activity, and high-frequency power (HF: 0.15–0.4 Hz) was analyzed as an index of parasympathetic nervous system activity. The ratio of LF to HF (LF/HF), an indirect index of sympathetic nervous system activity [23], was calculated for each data set.

Plasma glucose was analyzed in duplicate using the hexokinase method. Serum insulin was measured using the chemiluminescence enzyme immunoassay method. Hemoglobin A1c (HbA1c) was measured by the latex agglutination method.

To measure the des-acyl ghrelin level, a fasting venous sample was collected into a syringe containing EDTA-2Na (1.25 mg ml^{-1}) and aprotinin. Plasma was obtained by centrifuging the whole blood for 15 min at 4 °C, and was immediately frozen and stored at −40 °C until analysis. Des-acyl ghrelin levels were measured using a two-site sandwich enzyme-linked immunosorbent assay (ELISA) kit (Mitsubishi Chemical Medience, Tokyo, Japan) according to the manufacturer's instructions. The Homeostasis Model Assessment score of insulin resistance (HOMA-R) was calculated with the following formula: fasting insulin (mU ml^{-1}) × fasting glucose (mmol l^{-1})/405. All blood sample analyses were performed in the same laboratory (SRL, Nagoya, Japan).

Job strain, as defined by the job demands/control model [1], was measured by the Japanese short version of the Job Content Questionnaire (JCQ). The short version of JCQ measured three job demand items (work hard, demands for extra work, and insufficient time to perform work) and three items of job control (work at own pace, personal choice in the approach to work, and being able to incorporate one's own opinions to the workplace policies). All questions were scored on a Likert scale of 1–4. Job demand and job control scores were calculated by the sums of those item's scores. Each score for job demands and job control was

dichotomized by the median split into two groups (high and low). The high job strain group was defined as having both a score above the median for job demands (high job demands) and below the median for job control (low job control). Physical activity at work was classified into 'sedentary work' or 'not sedentary work' according to the self-reported behavior description diary. Sedentary work was defined as more than 80 % of working time doing desk work. Sleep state was assessed using the Japanese version of the Pittsburgh Sleep Quality Index (PSQI) [24, 25]. Poor sleep condition was defined as PSQI >5.5 [24, 25].

Statistical analysis

Data are expressed as mean ± SD. After examining the normality of distribution in all numerical variables using Shapiro–Wilk test, plasma des-acyl ghrelin levels, LF, HF, LF/HF, and HOMA-R were logarithmically transformed. Spearman's correlation coefficients were calculated to determine associations of des-acyl ghrelin with the other variables including BPs. We used unpaired *t* test to compare differences in variables including BPs and des-acyl ghrelin between subjects with or without job strain. Correlations between des-acyl ghrelin and BP in the 3 individual activities, i.e., Work, Home, and Morning were examined using multiple linear regression analysis adjusting for awake value of LF/HF and rest BP. To evaluate the effect of des-acyl ghrelin on BP changes, we examined the associations of des-acyl ghrelin with BP differences [22] calculated by subtracting Sleep BP from Work, Home, and Morning BPs, and by subtracting Work BP from Home and Morning BPs, using multiple linear regression analysis. Statistical significance was defined as $P < 0.05$. SPSS 21.0 for Windows (SPSS Tokyo, Japan) was used for the statistical analysis.

Results

The characteristics of subjects are presented in Table 1. The median job demand score was 9, and the median job control score was also 9. The high job strain group, therefore, had job demand scores above 9 and job control scores below 9. Twenty-four subjects were overweight, defined as 30 kg m^{-2} > BMI ≥25 kg m^{-2}, and ten subjects were obese, defined as BMI ≥30 kg m^{-2}; twelve subjects had hypertension, defined as rest BP ≥140/90 mm Hg; and two subjects had diabetes mellitus, defined as HbA1c ≥6.5 % or fasting glucose ≥126 mg dl^{-1}. None of the subjects had anti-diabetic treatment.

Table 2 shows Spearman's correlation coefficients between des-acyl ghrelin and the other variables. Des-acyl ghrelin was negatively correlated with waist circumference, and positively correlated with 24 h of LF, awake value of LF, and awake value of HF. It also showed significant inverse correlations with almost all BPs except Morning SBP, Morning DBP, Work DBP, Home DBP, and Sleep SBP.

Table 3 presented the comparison of physiological parameters between the two job strain groups, i.e. with and without job strain. There were no significant differences between the two groups both in BPs and in plasma des-acyl ghrelin levels.

Table 1 Descriptive characteristics of study subjects

Characteristics	$n = 34$
Age (years)	41.7 ± 6.7
Weight (kg)	84.8 ± 12.6
BMI (kg m^{-2})	29.0 ± 3.4
Waist circumference (cm)	96.3 ± 8.2
Rest SBP (mmHg)	134.5 ± 18.7
Rest DBP (mmHg)	84.8 ± 13.8
24-h SBP (mmHg)	139.1 ± 14.2
24-h DBP (mmHg)	85.2 ± 11.4
Morning SBP (mmHg)	140.3 ± 16.5
Morning DBP (mmHg)	88.0 ± 14.0
Worksite SBP (mmHg)	147.4 ± 15.5
Worksite DBP (mmHg)	90.5 ± 12.6
Home SBP (mmHg)	145.4 ± 18.3
Home DBP (mmHg)	87.9 ± 12.5
Sleep SBP (mmHg)	120.9 ± 16.8
Sleep DBP (mmHg)	75.6 ± 12.6
24-h average heart beat (bpm)	80.5 ± 6.3
24-h LF	544.6 ± 423.1
24-h HF	186.2 ± 205.2
24-h LF/HF	3.8 ± 2.5
Awake value of LF	508.0 ± 407.5
Awake value of HF	125.3 ± 171.6
Awake value of LF/HF	5.5 ± 2.8
Des-acyl ghrelin (pmol l^{-1})	179.3 ± 87.4
Glucose (mg dl^{-1})	100.2 ± 13.0
Insulin (μU ml^{-1})	9.8 ± 4.6
HOMA-R	2.5 ± 1.3
HbA1c (%)	5.2 ± 0.6
Current smoker, *n* (%)	11 (32.4)
Alcohol drinker, *n* (%)	10 (29.4)
Job demand score	9.2 ± 2.0
Job control score	8.9 ± 2.2
Job strain, *n* (%)	8 (23.5)
Sedentary work, *n* (%)	15 (44.1)
Poor sleep condition, *n* (%)	14 (41.2)

BMI body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *LF* low-frequency power, *HF* high-frequency power, *LF/HF* ratio of low- to high-frequency power, *HOMA-R* the homeostasis model assessment of insulin resistance, *HbA1c* hemoglobin A1c

Table 2 Spearman's correlation coefficients (*r*) between des-acyl ghrelin and other anthropometric, hemodynamic, heart rate variability, and metabolic parameters

	r	*P*
Age	−0.325	0.061
Weight	−0.225	0.201
BMI	−0.300	0.085
Waist circumference	−0.376	0.028
Rest SBP	−0.429	0.011
Rest DBP	−0.409	0.016
24-h SBP	−0.437	0.010
24-h DBP	−0.428	0.012
Morning SBP	−0.258	0.141
Morning DBP	−0.231	0.189
Worksite SBP	−0.474	0.005
Worksite DBP	−0.312	0.073
Home SBP	−0.393	0.021
Home DBP	−0.186	0.291
Sleep SBP	−0.268	0.125
Sleep DBP	−0.348	0.044
24-h LF	0.378	0.028
24-h HF	0.308	0.076
24-h LF/HF	0.053	0.768
Awake value of LF	0.360	0.037
Awake value of HF	0.362	0.035
Awake value of LF/HF	0.043	0.808
HOMA-R	−0.168	0.342

r means Spearman's correlation coefficients

BMI body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *LF* low-frequency power, *HF* high-frequency power, *LF/HF* ratio of low- to high-frequency power, *HOMA-R* the homeostasis model assessment of insulin resistance

In multiple regression analysis, des-acyl ghrelin was significantly correlated with Work SBP after adjusting for awake value of LF/HF and Rest SBP (Table 4).

Table 5 shows multiple regression analysis for evaluating the effect of des-acyl ghrelin on BP changes from Sleep to Work, from Sleep to Home, and from Sleep to Morning. After adjusting variables, a significant inverse association was observed between des-acyl ghrelin and SBP change from Sleep to Work. There were no significant associations between des-acyl ghrelin and the other BP changes from Sleep. Table 5 presents significant negative correlations of des-acyl ghrelin with SBP changes from Morning to Work, and from Work to Home in multiple regression analysis.

Discussion

A significant inverse correlation of plasma des-acyl ghrelin levels with Worksite SBP was observed in Japanese overweight/obese male day-shift workers (Tables 2, 3). Des-acyl ghrelin was also negatively associated with the difference subtracting Sleep BP from Work BP (Table 5). In addition, significant inverse correlations between des-acyl ghrelin and SBP changes from Morning to Work, and from Work to Home (Table 5). These results suggested that des-acyl ghrelin might have some beneficial effects on BP during work.

Des-acyl ghrelin was positively correlated with awake value of HF (Table 2), which is considered an index of parasympathetic nervous system activity. This result is in agreement with an animal experimental study which indicated that des-acyl ghrelin affected parasympathetic nervous system activity [19]. Lambert et al. [21] showed, in their experimental study, that ghrelin administration blunted BP response to mental stress with task load. It is therefore probable that des-acyl ghrelin has a sort of buffering effect on BP elevation caused by mental stress, such as job strain during work.

In this study, des-acyl ghrelin was not associated with Home SBP, while it inversely correlated with Work SBP. Home SBP might be strongly affected by a variety of home-related stressors [26], resulting in such an insignificant correlation as found in the study.

We measured des-acyl ghrelin but not acyl ghrelin in this study for a technical reason. It is well known that the acyl ghrelin level is parallel to that of des-acyl ghrelin [27], and that acyl ghrelin has unique beneficial cardiovascular effects [28, 29], such as improving ANS (sympathetic nervous system) and BP. Thus, the results of our study might have been confounded by the effect of acyl ghrelin. In this regard, future study should clarify the effects of the two types of ghrelin separately.

Recent studies have indicated that mental stress could affect circulating levels of ghrelin and the acylated enzyme of ghrelin, ghrelin-*O*-acyltransferse [30, 31]. On the other hand, it has been suggested that ghrelin affects the psychological state, such as anti-depressive symptoms [30]. Rouach et al. [32] showed, in their experimental study in humans, that the stress-induced increase in ghrelin was associated with the increase in cortisol, but not the increase in BP. This result suggests that ghrelin is not influenced by stress-induced BP changes directly. Further research is warranted to examine these complex relationships among mental stress, including job strain, BP, and acyl or des-acyl ghrelin.

In several interventional studies, regular exercise programs without caloric restriction raised levels of the total and the des-acyl ghrelin [33, 34], a reaction which in turn might prevent BP elevation at work. This positive effect could partially explain the hypothesis proposed by Hamer [35] that physical activity may alleviate the harmful effects of mental stress on cardiovascular disease.

Table 3 Comparison of mean values between subjects with and without job strain

	With job strain ($n = 8$)	Without job strain ($n = 26$)	P
Age (years)	43.3 ± 6.7	41.3 ± 6.8	0.474
BMI (kg m^{-2})	29.2 ± 2.9	29.0 ± 3.6	0.866
Waist circumference (cm)	95.2 ± 7.8	96.6 ± 8.5	0.671
Rest SBP (mmHg)	135.5 ± 9.2	134.2 ± 20.9	0.869
Rest DBP (mmHg)	85.0 ± 7.2	84.7 ± 15.3	0.655
24-h SBP (mmHg)	134.0 ± 14.0	140.7 ± 14.1	0.244
24-h DBP (mmHg)	83.6 ± 9.6	85.7 ± 12.0	0.653
Morning SBP (mmHg)	131.8 ± 19.2	142.8 ± 15.0	0.100
Morning DBP (mmHg)	82.7 ± 14.3	89.6 ± 13.7	0.229
Worksite SBP (mmHg)	142.5 ± 14.7	149.0 ± 15.6	0.310
Worksite DBP (mmHg)	88.2 ± 9.5	91.2 ± 13.5	0.557
Home SBP (mmHg)	143.4 ± 17.7	146.1 ± 18.8	0.723
Home DBP (mmHg)	84.9 ± 14.8	88.8 ± 11.8	0.443
Sleep SBP (mmHg)	115.7 ± 12.6	122.6 ± 17.7	0.319
Sleep DBP (mmHg)	73.6 ± 9.3	76.2 ± 13.6	0.624
Log 24-h of LF	6.3 ± 0.8	6.0 ± 0.6	0.369
Log 24-h of HF	4.8 ± 1.2	4.9 ± 0.7	0.727
Log 24-h of LF/HF	1.5 ± 0.7	1.1 ± 0.5	0.114
Log awake value of LF	6.2 ± 0.7	5.9 ± 0.6	0.331
Log awake value of HF	4.5 ± 1.0	4.4 ± 0.7	0.846
Log awake value of LF/HF	1.7 ± 0.7	1.5 ± 0.5	0.383
Log des-acyl ghrelin	2.2 ± 0.2	2.2 ± 0.2	0.820
Log HOMA-R	0.4 ± 0.2	0.3 ± 0.2	0.742

P were calculated using unpaired *t* test

BMI body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *LF* low-frequency power, *HF* high-frequency power, *LF/HF* ratio of low- to high-frequency power, *HOMA-R* the homeostasis model assessment of insulin resistance

Table 4 Results of multiple linear regression analysis with the Morning BP, Work BP, and Home BP as the dependent variables and des-acyl ghrelin as the independent variables, controlling for awake value of LF/HF and Rest BP

	B (95 % CL)	β	P	Model	
				R^2	ANOVA p
Morning BP					
SBP	−12.71 (−41.03 to 15.62)	−0.159	0.364	0.472	0.023
DBP	−8.30 (−32.47 to 15.87)	−0.123	0.486	0.464	0.027
Work BP					
SBP	−54.00 (−78.65 to −29.34)	−0.718	>0.001	0.549	0.005
DBP	−28.56 (−51.26 to −5.85)	−0.467	0.016	0.422	0.055
Home BP					
SBP	−49.12 (−83.81 to −14.42)	−0.555	0.007	0.356	0.140
DBP	−13.50 (−36.50 to 9.51)	−0.223	0.238	0.392	0.087

Model was adjusted for log-transformed awake value of LF/HF and Rest BP

BP blood pressure, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *LF/HF* ratio of low- to high-frequency power

Helicobacter pylori infection, which is a gram-negative bacterium associated with gastric diseases, might be related with ghrelin and ghrelin acylation. Plasma total, acyl, and des-acyl ghrelin of Helicobacter pylori infection-positive subjects was lower than those of negative subjects [31, 36]. However, Ando et al. [36] showed, in their clinical intervention study, that Helicobacter pylori eradication decreased plasma des-acyl ghrelin.

In human and animal experimental studies, injection of lipopolysaccharide, which is an innate defense response and is considered a hypothalamic–pituitary–adrenal axis activation, induced a rapid decrease in plasma des-acyl ghrelin levels [37].

In animal studies, abdominal surgery reduced plasma acyl and des-acyl ghrelin levels. However, the effects of abdominal surgery on des-acyl ghrelin in human are difficult to evaluate [31].

Table 5 Results of multiple linear regression analysis with the (A) BP changes from Sleep BP as the dependent variables and des-acyl ghrelin as the independent variables, controlling for awake value of LF/HF and Sleep BP (B) BP changes from Morning BP or Home BP to Work BP as the dependent variables and des-acyl ghrelin as the independent variables, controlling for awake value of LF/HF and Morning BP or Home BP

Model was adjusted for log-transformed awake value of LF/HF and (A) Sleep BP (B) Morning BP or Home BP

BP blood pressure, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *LF/HF* ratio of low- to high-frequency power

	B (95 % CL)	β	P	Model	
				R^2	ANOVAp
(A) BP changes from Sleep BP					
Morning–Sleep BP change					
SBP	4.72 (−17.89 to 27.45)	0.075	0.674	0.175	0.119
DBP	−2.10 (−22.85 to 18.66)	−0.040	0.838	0.055	0.630
Work–Sleep BP change					
SBP	−22.20 (−40.45 to −3.95)	−0.379	0.019	0.383	0.002
DBP	−6.75 (−26.96 to 8.47)	−0.165	0.372	0.165	0.138
Home–Sleep BP change					
SBP	−10.05 (−31.91 to 11.81)	−0.176	0.355	0.075	0.500
DBP	8.62 (−5.66 to 22.90)	0.225	0.227	0.162	0.145
(B) BP changes from Morning BP or Home BP to Work BP					
Work–Morning BP change					
SBP	−30.20 (−48.75 to −11.64)	−0.447	0.002	0.477	>0.001
DBP	−15.63 (−29.20 to −2.05)	−0.325	0.025	0.449	>0.001
Work–Home BP change					
SBP	−19.70 (−36.82 to −2.59)	−0.343	0.026	0.447	>0.001
DBP	−15.70 (−29.35 to −2.04)	−0.374	0.026	0.268	0.023

Many epidemiological studies have indicated that workers with high job strain have unhealthy lifestyles, such as excess alcohol consumption [38, 39], undesirable eating habits [38, 40–42], and fewer physical activities [38, 42, 43], and therefore tend to be obese [44, 45] and have Mets [46]. Thus, job strain might directly elevate Worksite BP, and obesity, or Mets with increased insulin resistance or low des-acyl ghrelin might also contribute to BP elevation.

Clinical implications

High Worksite BP or worksite (stress-induced)-masked hypertension, in which blood pressure increases during work in spite of being normotensive in a clinic, leads to target organ damage [47, 48] and is a risk for cardiovascular disease. In addition, BP variability, even awake time BP variability, also correlates with target organ damage [49]. It is therefore clinically important to manage stress-induced BP elevation during work. From this aspect, ghrelin could help control excessive BP elevation due to mental stress. Of the two types of ghrelin, however, acyl ghrelin is not suitable for subjects with obesity or Mets, because of its stimulating effect on food intake and reducing effect on insulin sensitivity. Des-acyl ghrelin might be a better candidate for the treatment of stress-induced hypertension in subjects with obesity-related diseases [50]. In addition, while des-acyl ghrelin infusion does not change plasma acyl ghrelin levels, it increases plasma des-acyl ghrelin levels [51]. However, there are few studies about the pharmacokinetics of ghrelin.

Limitations

Our study has several limitations. First, because of the cross-sectional nature of our data, we could not infer any causality. Second, because our study was conducted only among overweight/obese male workers, caution should be used when applying its results to other groups. Third, all cardiometabolic parameters were measured only once. Finally, medication use may be potentially confounding, although our results were not changed after adjustment of these factors as covariates.

Conclusion

The plasma des-acyl ghrelin level was inversely correlated with Worksite BP. Negative associations of des-acyl ghrelin with SBP change from Sleep to Work were also observed. This preliminary study found a negative correlation between ambulatory blood pressure at work and plasma des-acyl ghrelin concentrations in obese male workers. Further studies are required to confirm these findings and to determine if raising plasma concentrations will favorably affect the blood pressure in workers.

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Conflict of interest The authors declare that they have no conflict of interest.

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