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Short report

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Do depressive symptoms correlate with oxidative stress in a sample of healthy college students?

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ABSTRACT – *Background and Objectives*: Major depression and sub-threshold depressive symptoms are associated with health crisis. Oxidative stress may be a mechanism for major depression. In the present study, we examined the relationship between the degree of depressive symptoms and oxidative status using a reliable and inexpensive method that evaluates endogenous hydroperoxides.

Methods: We conducted a cross-sectional study in 54 non-smoking college students and measured serum reactive oxygen metabolites (ROMs) and the biological antioxidant potential (BAP) as an index of oxidative status. Depressive symptoms were assessed by the Beck Depression Inventory (BDI).

Results: The concentrations of ROMs did not differ between the lower BDI group (BDI < 14) and the higher BDI group (BDI ≥ 14) (282.7 ± 59.84 U.CARR vs 307.7 ± 67.51 U.CARR, z = -1.19, P = 0.239). We did find a significant relationship between ROM concentration values and higher BDI scores (*rho* = 0.30, P = 0.042). BAP levels in the higher BDI group were not significantly greater than those in the lower BDI group (z = -0.108, P = 0.287). There was no significant correlation between BAP and depressive symptoms (*rho* = 0.22, P = 0.140). Moreover, we conducted a multiple regression analysis to control for gender difference and difference in sleep perception of the previous night between the two BDI groups. However, depressive symptoms were not significantly predicted by ROM concentrations (β = 0.28, P = 0.076).

Conclusions: While results of the present study demonstrated a slight correlation between depressive symptoms and oxidative stress, this linkage could not be confirmed after controlling for significant confounding factors. This result should be verified in a larger sample.

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Introduction

Major depression is serious public health problems that increase the risk of comorbid diseases such as cardiovascular disease[1-3], stroke[4], cancer[5-7] and diabetes[8-10]. Oxidative stress has gained attention in psychiatric medicine, and various markers of oxidative stress have been identified[11]. Recently, reactive oxygen metabolites (ROMs) and the biological antioxidant potential (BAP) were used to evaluate oxidative status, and their significance as clinical markers has been reported in various medical fields[12-15]. Although the increase in lipid peroxidation products and elevated oxidative DNA damage have been demonstrated in depressed subjects[16-18], the ROMs and BAP have not been examined. We, therefore, aimed to examine the relationship between depressive symptoms and oxidative stress, using the ROMs and BAP.

Methods

Participants and procedure

Participants were 54 non-smoking students. These volunteers were excluded from analysis if they reported a history of psychiatric disorders, an irregular sleep-wake rhythm, taking a supplement, or drinking alcoholic beverages almost daily. None of those included in the analysis had sought medical care in the month previous to the study. Female participants were excluded from analysis if they were menstruating. Forty-seven participants were included in the data analysis.

We asked participants to maintain regular hours for bedtime and awakening, and to abstain from eating and drinking except for water and tea after the usual dinner hour. On the following day between 9:00 am and 12:00 noon we obtained a fasting blood sample and assessed depressive symptoms.

Subjects were asked to complete self-administered questionnaires, and answered items on the lifestyle as well as other characteristics such as age, gender, menstrual state, height and weight, and history of psychiatric disorders. Depressive symptoms were assessed by the Beck Depression Inventory-II (BDI), which consists of 21 items. Scores were scaled from 0 to 63, with higher scores indicating greater depressive symptoms. Total scores can be classified as indicating four severity categories: minimal (0-13), mild (14-19), moderate (20-28), and severe (29-63)[19]. Participants were classified into two groups according to BDI scores: a lower BDI group (0-13) and a higher BDI group (14-39). Questions were also asked regarding personality and anxiety. These findings are to be reported in a separate paper.

Table I
Characteristics of the study subjects

	Lower BDI group $n = 31$	Higher BDI group $n = 16$	P value
Age years	20.7 ± 0.70	20.8 ± 0.91	0.859
Male, *n* (%)	17 (54.8)	4 (25.0)	0.068
Body mass index	21.5 ± 2.96	20.8 ± 2.87	0.262
Sleep time, previous night (hour)	6.7 ± 0.77	6.2 ± 1.28	0.265
Perception of sleep, previous night, *n* (%)			
Soundly	26 (83.9)	8 (50)	0.020*
Poor	5 (16.1)	8 (50)	
Alcohol consumption, *n* (%)$^{+}$			
Sometimes	6 (19.4)	5 (31.3)	0.472
Never	25 (80.6)	11 (68.8)	
Engages in exercice, *n* (%)$^{+}$			
Sometimes	9 (29.0)	6 (37.5)	0.742
None	22 (71.0)	10 (62.5)	

Note: $^{+}$ No one asnswered “almost every day”.
* $P < 0.05$.

Assay of oxidative status

ROMs were evaluated by the d-ROMs test (Diacron International, Grosseto, Italy) as an index of oxidative stress, which estimates endogenous hydroperoxide. The 10μl of Blood was collected from all participants by finger puncture with disposable lancets and analyzed with the free radical analysis system (FRAS) immediately after collection. The results of the d-ROM test are expressed in arbitrary units called “Carratelli Units” (U.CARR).

The BAP test was performed by the FRAS system, which includes both a photometric device and an incorporated thermostatic mini-centrifuge. This test measures the blood concentration of antioxidants as agents able to reduce iron from its ferric (Fe^{3+}) to ferrous form (Fe^{2+}). We estimated the intensity of this chromatic change photometrically. The results are expressed as μmol/l.

Statistical analysis

In this study, we used the Mann-Whitney *U* test, chi-square test, and Spearman’s correlation analysis. Additionally, if we found a significant linkage, multiple regression analysis was applied to assess the association of the depressive symptoms with potential confounding factors.

Results

The demographic data and results are summarized in Table I. There was a difference in perception of the previous night’s sleep. Regarding the possible effects of gender differences in results of assessment of ROMs and BAP, female students had a higher value for ROMs compared to males ($z = -3.18$, $P = 0.001$), but there was no difference in the BAP value ($z = -0.77$, $P = 0.438$).

Participants in the higher BDI group had a mean ROM level of 307.7 ± 67.51 U.CARR and those in the lower BDI group had a mean ROM level of 282.7 ± 59.84 U.CARR (Table II), with no significant difference between the two groups. Likewise, the mean BAP level in the higher BDI group was not significantly higher than that in the lower group, and no significant correlation was observed between the BDI score and BAP (*rho* = 0.22, *P* = 0.140). However, we found a weak correlation between the BDI score and the ROM concentration (*rho* = 0.30, *P* = 0.042). Figure 1 shows a scatter plot of the relationship between oxidative stress and depressive symptoms. Only in female participants there was a statistically slight relationship between depressive symptoms and ROMs. Because between-groups differences in gender and the perception of sleep were found, we applied multivariate analysis to control the effect for of these differences statistically. As shown in Table III, although the BDI score appeared to have a relationship with the ROM value after control for the confounding factors, the probability did not reach the 5% level of statistical significance.

Table II
Comparisons of oxidative indexes in lower and higher BDI groups

	Lower BDI group		Higher BDI group	*P* value	
Oxidative indexes					
ROMs	282.7 ± 59.84	*vs*	307.7 ± 67.51	0.239	*n.s*
BAP	1890.7 ± 703.93	*vs*	2210.1 ± 857.18	0.287	*n.s*

Note: ROMs, Reactive Oxygen Metabolites; BAP, Biological Antioxidant Potential.
Values express mean and standard deviation.

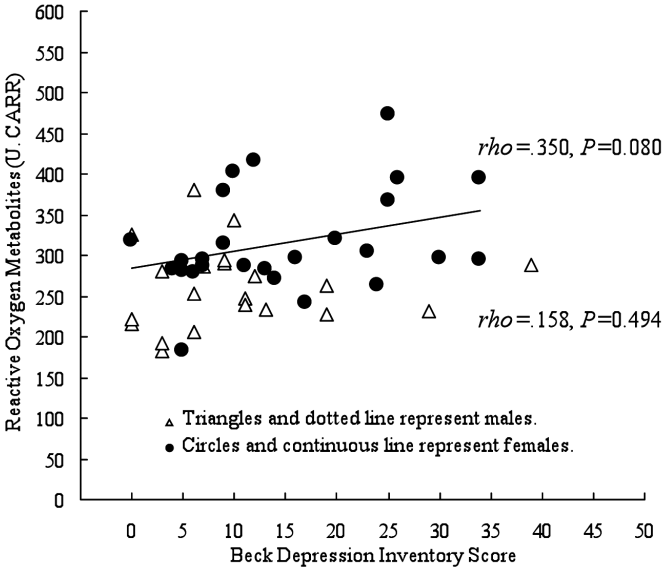

Figure 1. Correlations between reactive oxygen metabolites and the Beck depression inventory score according to gender were shown separately.

Conclusions

In this study, we found that depressive symptoms had a slight correlation with the increased concentration of ROMs, although no significant differences in the levels of ROMs and BAP between the two BDI groups were observed. Previous studies have demonstrated a significant correlation between oxidative stress and depression[16-18, 20, 21]. Furthermore, Bilici *et al.* reported that lipid peroxidation and antioxidative enzyme levels were significantly decreased to normal levels after selective serotonin reuptake inhibitor therapy for 12 weeks[22]. However, our results showed no clear correlation between depressive symptoms and oxidative status. This may be due to the relatively mild depressive symptoms in our subjects.

There is a possible mechanism that links the oxidative state with depressive symptoms. Hypothalamic-pituitary-adrenal (HPA) axis overactivity is frequently observed in those with major depression[23]. A HPA axis stimulated by psychological stress may enhance the production of reactive oxygen species relevant to cytotoxicity[24]. Moreover, depression has been related to increased immune activity. Leukocytes, monocytes, T helper cells, and interleukin are immune inflammatory markers that are increased in depressive disorders[25-28].

The d-ROMs and BAP tests, which are minimally invasive, easy and inexpensive, provide information on the general wellness state of the body for the clinician. To our knowledge, this study is the first attempt to examine an association between depressive symptoms and ROMs. Additional studies that include a larger number of participants and subjects with major depression disorders are needed.

Table III
Multiple linear regression analysis predicting depresive smptoms

	β	t	P
Gender (male = 0, female = 1)	0.07	0.45	0.652
Perception of previous night's sleep (soundly = 0, poor = 1)	0.20	1.40	0.169
Reactive Oxygen Metabolites	0.28	1.82	0.076

Note: ROMs, Reactive Oxygen Metabolites; BAP, Biological Antioxidant Potential.
Values express mean and standard deviation.

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