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Depressive symptoms linked to 1-h plasma glucose concentrations during the oral glucose tolerance test in men and women with the metabolic syndrome

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Abstract

Aims—The addition of the 1-h plasma glucose concentration measure from an oral glucose tolerance test to prediction models of future Type 2 diabetes has shown to significantly strengthen their predictive power. The present study examined the relationship between severity of depressive symptoms and hyperglycaemia, focusing on the 1-h glucose concentration vs. fasting and 2-h oral glucose tolerance test glucose measures.

Methods—Participants included 140 adults with the metabolic syndrome and without diabetes who completed a baseline psychobiological assessment and a 2-h oral glucose tolerance test, with measurements taken every 30 min. Depressive symptoms were assessed using the Beck Depression Inventory.

Results—Multivariate linear regression revealed that higher levels of depressive symptoms were associated with higher levels of 1-h plasma glucose concentrations after adjusting for age, gender, ethnicity, BMI, antidepressant use and high-sensitivity C-reactive protein. Results were maintained after controlling for fasting glucose as well as for indices of insulin resistance and secretion. Neither fasting nor 2-h plasma glucose concentrations were significantly associated with depressive symptoms.

Conclusions—Elevated depressive symptoms in persons with the metabolic syndrome were associated with greater glycaemic excursion 1-h following a glucose load that was not accounted for by differences in insulin secretory function or insulin sensitivity. Consistent with previous findings, this study highlights the value of the 1-h oral glucose tolerance test plasma glucose measurement in the relation between depressive symptoms and glucose metabolism as an indicator

of metabolic abnormalities not visible when focusing on fasting and 2-h post-oral glucose tolerance test measurements alone.

Introduction

A recent meta-analysis has shown the clinical significance of glucose dysregulation as a potential pathogenic pathway in the link between depression and Type 2 diabetes [1]. Baseline depressive symptomatology predicts impaired glucose control over time in asymptomatic individuals [2]. Experimental studies in individuals with depression have also shown that impaired insulin sensitivity and hyperinsulinaemia, which play a role in glycaemic control, improve after recovery from depression [3,4]. However, the direction of the relationship between depression and hyperglycaemia remains controversial [5–9].

In studies examining the relationship between depression and hyperglycaemia, impaired glucose metabolism has been commonly characterized by elevated levels of fasting glucose or impaired glucose tolerance 2 h following an oral glucose tolerance test [10]. Models based on measurements taken during the fasting state cannot incorporate an assessment of β -cell function based on a defective acute secretory response, which is considered a prerequisite in the development of hyperglycaemia and the overall pathophysiology of Type 2 diabetes [11]. The addition of the 1-h plasma glucose concentration to prediction models of future Type 2 diabetes has shown to significantly strengthen their predictive power [12]. Recent research suggests that 1-h plasma glucose concentration during an oral glucose tolerance test is associated with risk for future Type 2 diabetes and is more strongly associated with β -cell function and with indices of insulin secretion and resistance than fasting and 2-h plasma glucose concentrations [13,14]. Notably, a 1-h plasma glucose response of 8.5 mmol/l (155 mg/dl) to the oral glucose tolerance test has been shown to stratify adults without diabetes into high and low future risk for Type 2 diabetes, independent of glucose tolerance [15]. Physiologically, the period 30–60 min after the ingestion of a meal represents the peak point of metabolic and digestive events [14] and may thus be a better time in the oral glucose tolerance test to examine the psychobiological connection between depression and metabolic dysfunction, specifically glucose dysregulation.

This study aims to examine the association between depressive symptoms and measures of plasma glucose concentrations from an oral glucose tolerance test at three different time points (fasting, 1- and 2-h). The oral glucose tolerance test can be regarded as a physiological challenge in which the body needs to process an excessive amount of glucose. In this study, we ask whether the metabolic response at the peak of this challenge (the 1-h measurement point) is associated with severity of depressive symptoms in individuals with the metabolic syndrome. The metabolic syndrome constitutes a high-risk state in which a series of clinical manifestations of insulin resistance and excessive weight have developed, namely abdominal obesity, glucose intolerance, elevated blood pressure and dyslipidaemia, directly increasing the risk of developing cardiovascular disease and Type 2 diabetes [16]. The metabolic syndrome precedes the clinical manifestation of disease and provides a facilitative context to study possible mechanisms that link depression and diabetes in a pre-diabetic stage.

Participants and methods

Results for this study were based on participants who completed a baseline assessment as part of a randomized controlled trial, Biobehavioral Bases and Management of Metabolic Syndrome, approved by the Institutional Review Board. The 140 study participants were recruited from Miami community clinics. Eligible participants received a full explanation of the study and provided informed consent. Study eligibility criteria were: men or women aged 30–70 years, with at least sixth grade education and at least three of five features of the modified National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP)-III criteria for classifying the metabolic syndrome [16]: impaired fasting glucose but not diabetes (i.e. fasting glucose 5.6–6.9 mmol/l), abdominal obesity measured as waist circumference > 102 cm/> 88 cm (men/women), triglyceride levels > 2.83 mmol/l, HDL cholesterol < 1 mmol/l/< 1.3 mmol/l (men/women) or a blood pressure > 130 mmHg/> 85 mmHg or treated hypertension. Participants with fasting glucose greater than 7 mmol/l, previously diagnosed cardiovascular, endocrine or renal conditions, body weight over 159 kg and pregnant women were excluded from the study. Fasting blood samples were obtained, followed by a 2-h oral glucose tolerance test, after which participants underwent a standard assessment measuring social, psychological and behavioural characteristics. Participants also completed a medical history form, underwent an anthropometric examination, took a sub-maximal exercise stress test and were given a 24-h dietary recall assessment. All questionnaires and interview forms were administered in English or Spanish as per the participant's language preference.

Severity of depressive symptoms was assessed using the 21-item Beck Depression Inventory (BDI) [17]. The Beck Depression Inventory is well validated and has been used extensively in previous research with internal reliability between $\alpha = 0.85$ and 0.93 [18]. The Beck Depression Inventory total score has been shown to be significantly associated with standard clinical measures of depression severity [18]. Based on total Beck Depression Inventory score, severity of depressive symptoms was categorized as follows: 0–13 = minimal range, 14–19 = mild, 20–28 = moderate and 29 = severe depressive symptoms.

For the oral glucose tolerance test, blood was drawn at –15 min and time 0 to obtain an estimate of fasting glycaemia. Participants then consumed a 75-g oral glucose load over 5 min (Orange-Dex, Custom Laboratories, Baltimore, MD, USA). Blood specimens were obtained at 30, 60, 90 and 120 min later and stored for plasma glucose and serum insulin assay. Plasma glucose was measured by the hexokinase method (Roche Diagnostics, Indianapolis, IN, USA) and plasma insulin was assayed by an automated immunoassay with electrochemiluminescence detection (Roche Diagnostics) using the Roche Cobas 6000 Analyzer. Baseline insulin (I_0) and glucose (G_0) concentration were calculated averaging results from the –15 and 0 time points. The homeostasis model was used to estimate insulin resistance (HOMA-IR index) and β -cell function (HOMA-B) [19]. The $ISI_{0,120}$, an index of insulin sensitivity, was calculated using the formula proposed by Gutt and colleagues, which uses both fasting and 2-h post-oral glucose insulin and glucose concentrations [20]. The insulinogenic index (IGI) and the corrected insulin response at 30 min post-load (CIR_{30}) were also used as indices of insulin secretion [21]. Area under the glucose curve (AUC_g) was calculated with the trapezoid rule using measurements from all time points obtained

from the oral glucose tolerance test (i.e. -15, 0, 30, 60, 90 and 120 min). Total cholesterol, triglycerides, HDL cholesterol and high-sensitivity C-reactive protein (hs-CRP) were measured on a Roche 6000 Auto-Analyzer (Roche Diagnostics) following the manufacturers' instructions. Automated chemistry and immunoassays exhibit interassay coefficients of variation consistently less than 5%. LDL cholesterol was calculated by the Friedewald equation [22].

Age, gender, marital status, educational level, former or current smoker status and antidepressant medication use were obtained by self-report. Physical activity was assessed by adding the average number of minutes of light, moderate and vigorous physical activity reported per day. Weight and height were used to derive BMI as kg/m². Waist circumference was measured horizontally midway between the iliac crest and the lowest portion of the rib cage to the nearest 0.5 cm and the average of the two measures was used.

Statistical analyses

Of the 140 participants who completed the baseline assessment, three participants had missing data for glucose values, three for insulin values and one for depression score. Multiple imputation was used to deal with the missing data [23]. Descriptive statistics were computed and the distribution of each variable examined. Sensitivity analyses were performed on extreme outliers. Pearson correlation coefficients were estimated to assess univariate associations. A significance level of $\alpha = 0.05$ was used for all tests. Three multivariate linear regression models were fitted to three different outcomes: fasting, 1- and 2-h plasma glucose concentration in mg/dl obtained from the oral glucose tolerance test. Severity of depressive symptoms as assessed by the Beck Depression Inventory was used as the predictor. Covariates that relate to depression were selected a priori and included in the model. Each model included age, gender, ethnicity, BMI, antidepressant medication use and hs-CRP as covariates. Based on the results of these regression models, sensitivity analyses were conducted on the model, with 1-h plasma glucose as outcome. Specifically, fasting glucose, commonly used indices of insulin resistance (i.e. I_0 , HOMA-IR, $ISI_{0,120}$) and insulin secretion (i.e. CIR_{30} , insulinogenic index and HOMA-B), area under the glucose curve, and health behaviours (i.e. physical activity, smoking) were added in separate models to determine whether the observed relation could be explained by any of these factors.

Results

Sample characteristics are presented in Table 1. The sample included 67 men and 73 women of predominantly Hispanic origin with an average age of 51 years. The majority of the sample (93%) had abdominal obesity, 72% had a BMI ≥ 30 kg/m² and almost half the sample (42%) was physically inactive. Twenty-nine per cent of the participants had depression scores above the minimal range (BDI score > 13), with 14% ranging in the mild depression range (BDI 14–19), 10% in the moderate depression range (BDI 20–28) and 5% in the severe depression range (BDI ≥ 29). Average fasting and 2-h glucose levels were in the normal range, but 7% of participants had fasting glucose concentrations in the impaired range, 36% had impaired glucose tolerance (elevated 2-h glucose only) and 10% of participants a combination of impaired fasting glucose and impaired glucose tolerance.

According to 1-h plasma glucose values, 47% of participants were in the low-risk group (< 8.5 mmol/l) and 53% of participants were in the high-risk group (≥ 8.5 mmol/l) for future Type 2 diabetes.

Initial analyses indicated that severity of depressive symptoms (Beck Depression Index) did not differ between participants with normal glucose levels, impaired fasting glucose, impaired glucose tolerance, or impaired fasting glucose and impaired glucose tolerance combined ($P > 0.10$). Correlational analyses for the entire sample revealed that Beck Depression Inventory scores were positively and significantly associated with antidepressant use, age, ethnicity, BMI and hs-CRP. Depressive symptom severity was significantly higher in women (mean 12.4; SD 1.19) than in men (mean 8.6; SD 1.07). Higher 1-h plasma glucose concentrations were significantly associated with being older ($r = 0.25$, $P < 0.05$) and having higher BMI ($r = 0.19$, $P < 0.05$). As shown in Table 2, depressive symptom severity was significantly correlated with greater area under the glucose curve, higher levels of hs-CRP and significantly higher 1-h plasma glucose levels ($r = 0.22$, 0.24 and 0.26 , respectively; all $P < 0.01$). Participants with higher fasting, 1- and 2-h plasma glucose levels had lower insulin sensitivity and secretion as measured by the $ISI_{0,120}$ and the insulinogenic index, respectively. Although 1-h plasma glucose levels were significantly correlated with fasting ($r = 0.42$, $P < 0.001$) and 2-h post-load ($r = 0.61$, $P < 0.001$) plasma glucose concentrations, Beck Depression Inventory scores were not significantly associated with fasting plasma glucose levels ($P > 0.10$) and only marginally associated with 2-h post-load plasma glucose concentrations ($r = 0.17$; $P > 0.05$).

As shown in Table 3, multivariate linear regression controlling for age, gender, ethnicity, BMI, antidepressant use and hs-CRP demonstrated that severity of depressive symptoms remained associated with peak 1-h glucose levels after controlling for these factors ($\beta = 0.22$, $P = 0.02$). The multivariate model accounted for 18% of the variance in peak plasma glucose concentration. For every additional point increase in Beck Depression Inventory total score there was a 0.31-mmol/l increase in 1-h plasma glucose levels. When fasting plasma glucose levels and 2-h plasma glucose levels were used as outcomes in multivariate regression models with age, gender ethnicity, BMI, antidepressant use and hs-CRP as covariates, the association with depressive symptoms was not significant ($P > 0.10$ for both fasting and 2-h glucose levels).

Sensitivity analyses showed that, when introduced in the regression model as an additional covariate, fasting plasma glucose did not change the significant association between depression and 1-h plasma glucose ($\beta = 0.20$, $P < 0.05$). Further analyses demonstrated that the association of depressive symptoms with 1-h glucose was not accounted for by differences in fasting insulin levels, or indices of insulin resistance or insulin secretion (all $P < 0.01$). Results were also not explained by health behaviours, including physical activity and smoking ($P < 0.01$). Only when the area under the glucose curve, a more comprehensive index that uses data from all measurement time points obtained from the oral glucose tolerance test, was entered as a covariate, the relationship between depressive symptoms and 1-h glucose levels became non-significant ($\beta = 0.06$, $P > 0.10$).

Despite differences in Beck Depression Inventory scores for men and women, no gender interactions were observed for the reported associations. More than 80% of participants with moderate depressive symptomatology had a 1-h plasma glucose concentration above the 8.5 mmol/l (155 mg/dl) proposed cut-off, indicating worse glucose control and higher risk for Type 2 diabetes ($P < 0.01$). For each depressive symptom subgroup, Fig. 1 shows the proportion of participants classified in the low- vs. high-risk groups for future Type 2 diabetes according to their peak 1-h plasma glucose concentration ($<$ or ≥ 8.5 mmol/l). The majority of participants with moderate depressive symptoms fall in the high-risk group in contrast to those with no depressive symptoms.

Discussion

In this study we were able to demonstrate significant direct relationships between depressive symptomatology and 1-h hyperglycaemia in a sample of predominately Hispanic adults with the metabolic syndrome. The strong residual association between depressive symptoms and 1-h post-oral glucose tolerance test plasma glucose concentrations following adjustment of age, gender, ethnicity, BMI, antidepressant use and hs-CRP, suggest an independent association between depressive symptoms and poor glucose control. Severity of depressive symptoms remained associated with 1-h plasma glucose levels, even after accounting for fasting plasma glucose levels and commonly used indices of insulin sensitivity and secretion. It is possible that, as they are not direct measurements of these processes, the indices used to assess insulin secretion or action may not have the power to reduce the association between depressive symptoms and 1-h plasma glucose levels. Nonetheless, data still suggest that the association between depressive symptoms and hyperglycaemia may be related to impairment in the ability to control the glycaemic excursion after a glucose load as depressive symptomatology becomes more severe. This finding is consistent with the hypothesis that the body's ability to respond to a glucose challenge becomes impaired as depressive symptomatology becomes more severe. However, the cross-sectional nature of this study precludes any assumption of causality.

We provide novel data assessing the value of 1-h plasma glucose levels when evaluating the relationship between depression and hyperglycaemia and show that they provide metabolic information not captured by the fasting and 2-h glycaemia alone. Results show that 1-h plasma glucose levels can be comparable with using more comprehensive indices that use all measurements time points from an oral glucose tolerance test, such as the area under the glucose curve, while being parsimonious and practical. Previous studies on the relationship between depression and glucose metabolism have only examined fasting glucose or insulin levels or used indices based on these time points and results have been inconsistent [9,24] and small in magnitude [1]. For instance, the HOMA-IR, a widely used method to assess insulin sensitivity, is calculated using only the product of fasting insulin and glucose concentration [19]. Results from a meta-analysis on the association between depression and insulin resistance showed that the method used to assess insulin resistance has an impact upon findings [1].

These results might help explain previous negative findings of studies that investigate the association between markers of glucose metabolism and depression [6–9]. Studies using

only fasting plasma glucose levels may have missed critical information in support of the idea that depressive symptomatology can affect glucose metabolism. For example, in one of the few studies that provided oral glucose tolerance test 1-h data, 1-h plasma glucose concentrations were significantly lower after antidepressant treatment even although fasting glucose levels showed no differences before and after recovery from depression [3]. One-hour plasma glucose measures may identify changes in post-prandial glycaemia that precede changes in fasting glucose and overt hyperglycaemia [14], making the association with depressive symptoms more prominent.

It is well established that progressive β -cell failure is the primary factor responsible for the development of hyperglycaemia and overt Type 2 diabetes [13]. While models based on measurements taken during the fasting state cannot incorporate any measure of stimulated β -cell activity [11], the plasma glucose concentration at 1 h during the oral glucose tolerance test has shown stronger correlations with surrogate measures of β -cell dysfunction compared with the 2-h plasma glucose values [12]. Furthermore, exaggerated 1-h plasma glucose excursion has been suggested to reflect a progressive decline in β -cell glucose sensitivity and in the ability of β -cells to respond to changes in glucose concentration [25]. Future studies focusing on depression would benefit from looking at 1-h plasma glucose levels in addition to other markers of glucose metabolism.

Previous findings in at-risk individuals show lower insulin secretion in individuals with untreated depression compared with non-depressed or treated persons [4]. In individuals with already diagnosed Type 2 diabetes, daily negative mood has been shown to affect fasting glucose the following day [26]. The association between the metabolic syndrome and depression has been well documented [27]. Results from this study suggest that the metabolic syndrome may be a facilitative context to evaluate the link between depression and the metabolic abnormalities that lead to Type 2 diabetes. Furthermore, these findings have clinical relevance as these participants are already at an elevated risk for developing diabetes and cardiovascular disease. However, the current sample was small and predominantly comprised of US Hispanics, which limits the generalizability of findings. While Hispanics tend to have higher prevalence of the metabolic syndrome compared with non-Hispanic white people [28], the group of metabolic risk components that define the metabolic syndrome have been shown to occur across ethnic groups [29].

The lack of a diagnostic interview to assess depressive symptoms, and the preponderance of Beck Depression Inventory scores that fall below the criteria for significant depression limit conclusions that can be drawn from these data regarding the relation of clinical depression to impaired glucose metabolism. However, previous studies suggest that the health risk of depressive symptoms is best represented by a continuum of severity [30]. Worse glucose control was seen in participants with moderate depressive symptomatology, with most (> 80%) having 1-h glucose values above the 155-mg/dl cut-off, indicating higher risk for Type 2 diabetes.

Conclusions

In summary, results from this study support previous findings pointing to the value of using 1-h plasma glucose concentrations and further expand previous results showing a link with depressive symptomatology, particularly among Hispanics with the metabolic syndrome. Adding 1-h plasma glucose markers to commonly used indices of glucose metabolism in future studies may shed new light into the mechanisms that link depression and Type 2 diabetes.

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What's new?

- Findings highlight the value of examining the 1-h plasma glucose concentration from an oral glucose tolerance test in addition to fasting and 2-h assessments when investigating the link between depression and hyperglycaemia.
- This study further expands previous findings highlighting the 1-h plasma glucose concentration from an oral glucose tolerance test as an indicator of metabolic abnormalities in the pre-diabetes stage and shows a link between 1-h plasma glucose and depressive symptomatology.
- Results suggest that the metabolic syndrome may be a facilitative context to study the mechanisms that link depression and Type 2 diabetes.

Figure 1.

Proportion of participants classified in the high- vs. low-risk group for future Type 2 diabetes based on their 1-h plasma glucose concentration (< or ≥ 8.5 mmol/l) for each depressive symptom subgroup. The majority of participants with moderate depressive symptoms fall in the high-risk group in contrast to those with minimal depressive symptomatology.

Table 1Participant Characteristics characteristics ($Nn = 140$).

	Mean (SD _{SD})/ Nn (%)
Age (years)	51.2 (8.8)
Gender	73 (52%)
Women	67 (48%)
Men	3 (2%)
Ethnicity	14 (10%)
Caucasian	123 (88%)
African American	63 (45%)
Hispanics	77 (55%)
Education (%)	
> > High school	
High school	
Beck Depression Inventory Total total score	10.6 (9.0)
Using antidepressant medication	16 (11%)
Abdominal obesity (men > 102 cm., women > 88 cm.)	130 (93 %)
Weight (kg)	89.1 (16.5)
BMI (Kg/m ²)	32.6 (3.7)
Triglycerides (mmol/L)	2.8 (1.24)
Total Cholesterolcholesterol, (mmol/L)	5.3 (0.90)
HDL Cholesterolcholesterol, (mmol/L)	1.01 (0.24)
Fasting Insulin insulin (pmol/L)	112.9 (78.4)
Fasting Glucose glucose (mmol/L)	5.0 (0.53)
1-hour Glucose glucose (mmol/L)	8.8 (2.0)
2-hour Glucose glucose (mmol/L)	7.4 (2.3)
Glucose Concentrations concentrations	65 (47.8%)
Normal	9 (6.6 %)
Impaired Fasting glucose glucose(IFG)	49 (36 %)
Impaired Glucose glucose Tolerance tolerance(IGT)	13 (9.6%)
IFG Impaired fasting glucose + + IGT impaired glucose tolerance	3.7 (2.9)
HOMA _{IR} (units)	24.6 (11.5)
ISI _{0,120}	230.7 (149.5)
HOMA _B (units)	1.9 (1.5)
Insulinogenic indexGI	49.4 (37.9)
CIR ₃₀	16864.8 (3247.3)
Area under the glucose curveUC g	33.3 (48.4)
hs ₋ CRP (mmol/L) ^a	64 (46%)
Current or former smokers	60.1 (120.3)
Physical Activity activity (min/day)	

^aM

* Median reported and hs-CRP.

CIR₃₀, corrected insulin response at 30 min post-load; HOMA-B, homeostasis model assessment of β -cell function; HOMA-IR, homeostasis model assessment of insulin resistance; hs-CRP, high-sensitivity C-reactive protein; ISI_{0,120}, index of insulin sensitivity.

Table 2

Pearson correlations of Beck Depression Inventory/DI scores and biomarkers of glucose, insulin, and inflammatory activity.

	Beck Depression Inventory	Ins_0	Glu_0	Glu_1	Glu_2	AUCg	Area under the glucose curve	HomaIR	HOMA-IR	HomaB	Insulinogenic index	IGI	ISI_0,120	CIR_30	hs-CRP
Beck Depression Inventory/BDI	—														
Ins_0		0.02	0.14	0.26**†	0.17	0.22**†		0.03		−0.04	−0.09		−0.15	0.05	0.24**†
Glu_00		—	0.34**†	0.11	0.09	0.16		0.99**†		0.62**†	0.15		−0.23**†	0.51**†	0.15
Glu_1			—	0.42**†	0.24**†	0.51**†		0.44**†		−0.38**†	−0.22**†		−0.21*	0.17*	0.19
Glu_2				—	0.61**†	0.92**†		0.15		−0.12	−0.46**†		−0.52**†	0.07	0.16
Area under the glucose curveUCg					—	0.76**†		0.10		0.04	−0.26**†		−0.85**†	0.03	0.25**†
HomaHOMA_IR						—		0.20*		−0.12	−0.48**†		−0.65**†	0.12	0.18
HomaHOMA_B								—		0.53**†	0.10		−0.23**†	0.49**†	0.18
Insulinogenic indexIGI										—	0.31**†		−0.15	0.35**†	0.07
ISI_0,120											—		0.14	0.46**†	0.04
CIR_30													—	−0.16	−0.27**†
hs-CRP														—	0.03
															—

* *p* < 0.05
**† *p* < 0.01.

CIR₃₀, corrected insulin response at 30 min post-load; HOMA-B, homeostasis model assessment of β -cell function; HOMA-IR, homeostasis model assessment of insulin resistance; hs-CRP, high-sensitivity C-reactive protein; ISI(0, 120), index of insulin sensitivity.

Table 3
Depressive symptoms as predictor of fasting, 1-hr, and 2 2-hr plasma glucose levels

	Fasting Glucose glucose ($R^2 = 0.08$)			1-hour Glucose glucose ($R^2 = 0.18$)			2-hour Glucose glucose ($R^2 = 0.21$)		
	B (SE _{SE})	Beta β	pP	B (SE _{SE})	β Beta	pP	B (SE _{SE})	β Beta	pP
Age	0.01 (0.01)	0.19	0.03	0.03 (0.02)	0.22	0.01**†	0.07 (0.02)	0.27	0.00***†
Gender	0.13 (0.10)	0.13	0.16	0.16 (0.34)	0.09	0.29	0.07 (0.36)	0.02	0.85
Ethnicity	0.10 (0.08)	0.12	0.20	0.20 (0.29)	0.22	0.01**†	0.60 (0.31)	0.16	0.06
BMI (Kg/m ²)	0.01 (0.01)	0.05	0.56	0.56 (0.05)	0.10	0.25	0.16 (0.05)	0.28	0.00***†
Depression Medication	--0.16 (0.16)	--0.09	0.31	0.31 (0.55)	--0.12	0.18	--0.78 (0.59)	--0.11	0.19
Use use									
hs-CRP	0.01 (0.01)	0.08	0.40	0.40 (0.03)	0.12	0.18	0.06 (0.04)	0.13	0.12
Beck Depression InventoryBDI	0.01 (0.01)	0.10	0.31	0.31 (0.02)	0.22	0.02**†	0.02 (0.02)	0.06	0.52
Total total Scorescore									

*p P 0.05

**† pP 0.01

***† p P 0.001.

hs-CRP, high-sensitivity C-reactive protein.