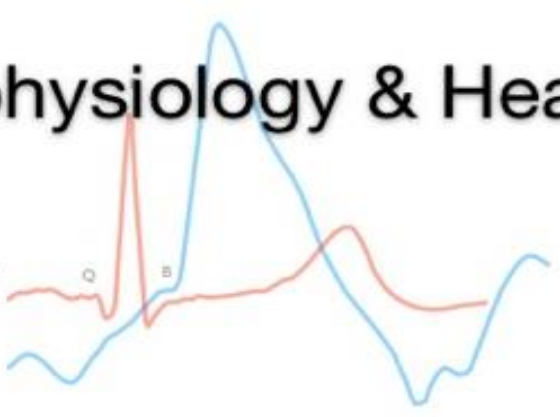


Blood sugar metabolism and stress reactivity predict depressive symptoms during pregnancy

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Significance

- The prevalence rate of **perinatal depression** is estimated to be 9-16% (Schmied et al., 2013; Woody et al., 2017).
- Antenatal depression** has been found to increase the risks of preterm birth, low birth weight, and intrauterine growth restriction (Ghimire et al., 2020).
- Depression** and **diabetes** are highly comorbid (Robinson et al., 2018). The association between depression and gestational diabetes mellitus has a less well-established link.
- Stress responses** have been shown to moderate blood glucose levels during pregnancy and blood glucose levels have been associated with depressive symptoms (Horsch et al., 2016).

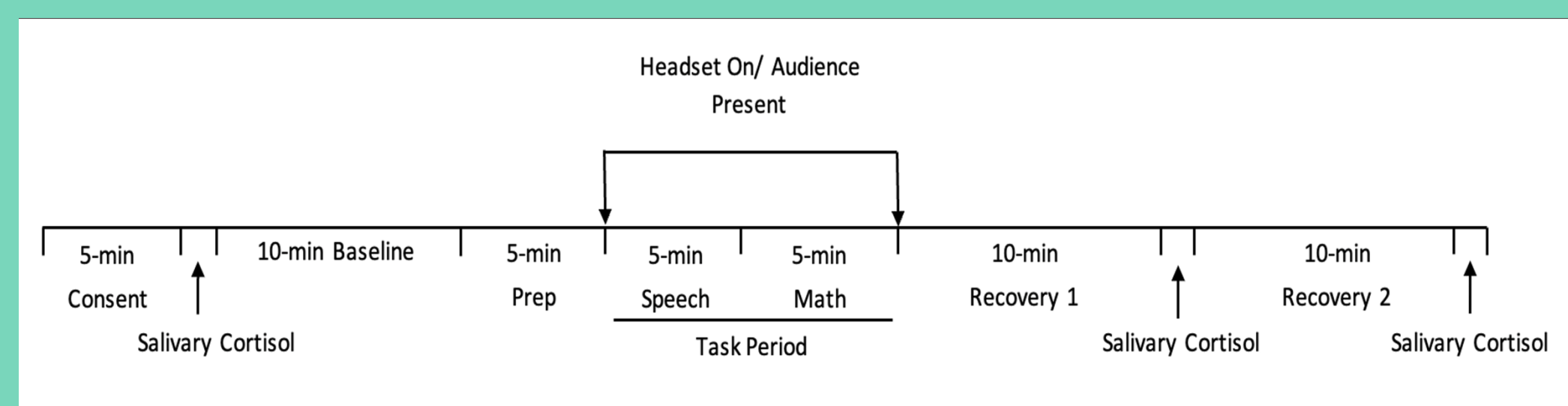
Hypothesis: Cortisol stress responses may moderate the association between blood sugar metabolism and depressive symptoms during pregnancy.

Methods

Participants: N = 101 pregnant women recruited from Sanford Health OB/GYN departments.

Procedure: Participants completed an assessment of depressive symptoms (Center for Epidemiological Studies – Depression, CES-D) at:

- Time 1: 24 to 28 weeks gestation
 - Time 2: 30 to 32 weeks gestation
 - Time 3: 36 to 38 weeks gestation
- Cortisol stress reactivity** was assessed using the Virtual Reality - Trier Social Stress Test (VR-TSST) at about 28 weeks gestation.
 - VR-TSST:** Participants performed a speech and oral arithmetic task while viewing a pre-recorded virtual audience of 200 individuals.
 - Blood Sugar Metabolization:** An Oral Glucose Tolerance Test (OGTT) was performed by Sanford Health between 24-28 weeks gestation. Results of this test were obtained from medical records.
 - Outcome:** Depressive symptoms measured with the CES-D.



VR-TSST Lab Protocol: participants provided saliva to measure resting cortisol. Then they performed speech and math tasks while viewing a 200-person audience in virtual reality. A second saliva sample was then taken.

Table 1: Demographics

Demographic	Percent
Age	
18-23	8.9
24-29	40.6
30-35	40.6
36-41	9.9
BMI	
19-26	59.3
27-34	31.4
35-42	5.8
43-50	3.5
Education	
< Some College	19.6
> College	80.4
Income	
\$10,000 - \$35,000	22.0
\$45,000 - \$75,000	25.2
\$85,000 - \$150,000	52.7
Nulliparity	
Had previous pregnancies	62.9
Nulliparous	37.1
Race	
White	88.8
Black	2.0
Asian	4.1
American Native	3.1
Latino	2.0

Figure 1. Depressive Symptoms (CESD) During Pregnancy

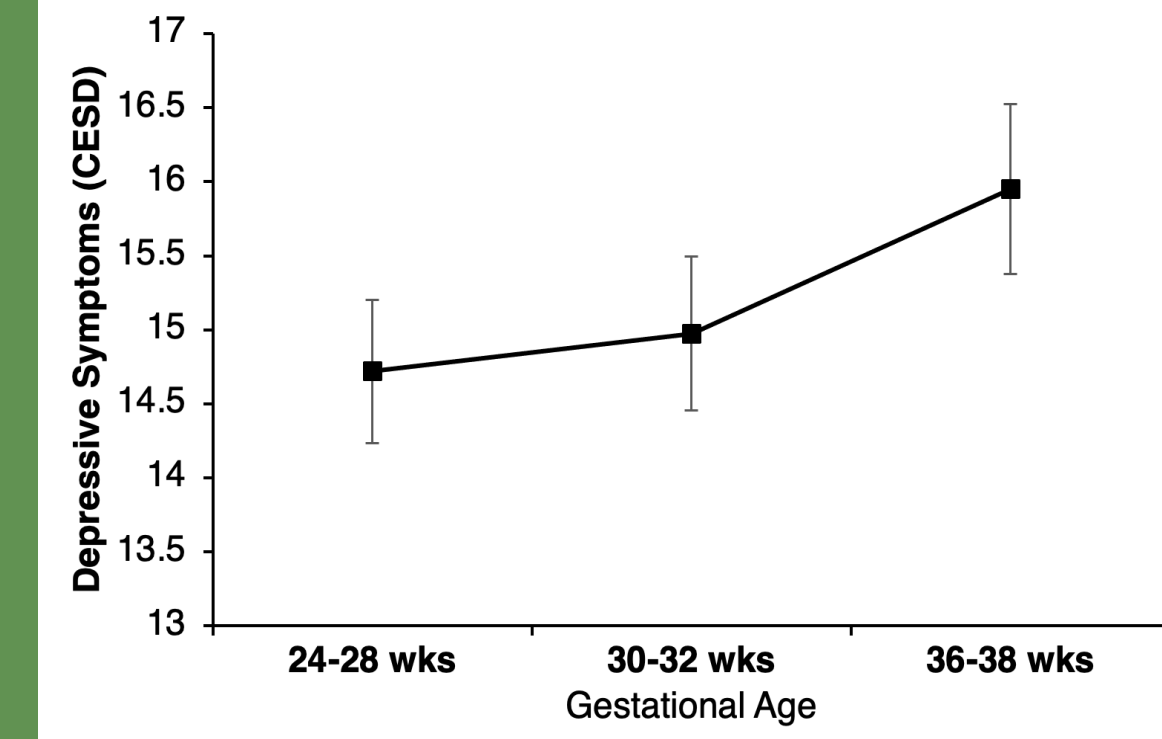


Figure 2. Cortisol Response to Lab Stress Task (TSST)

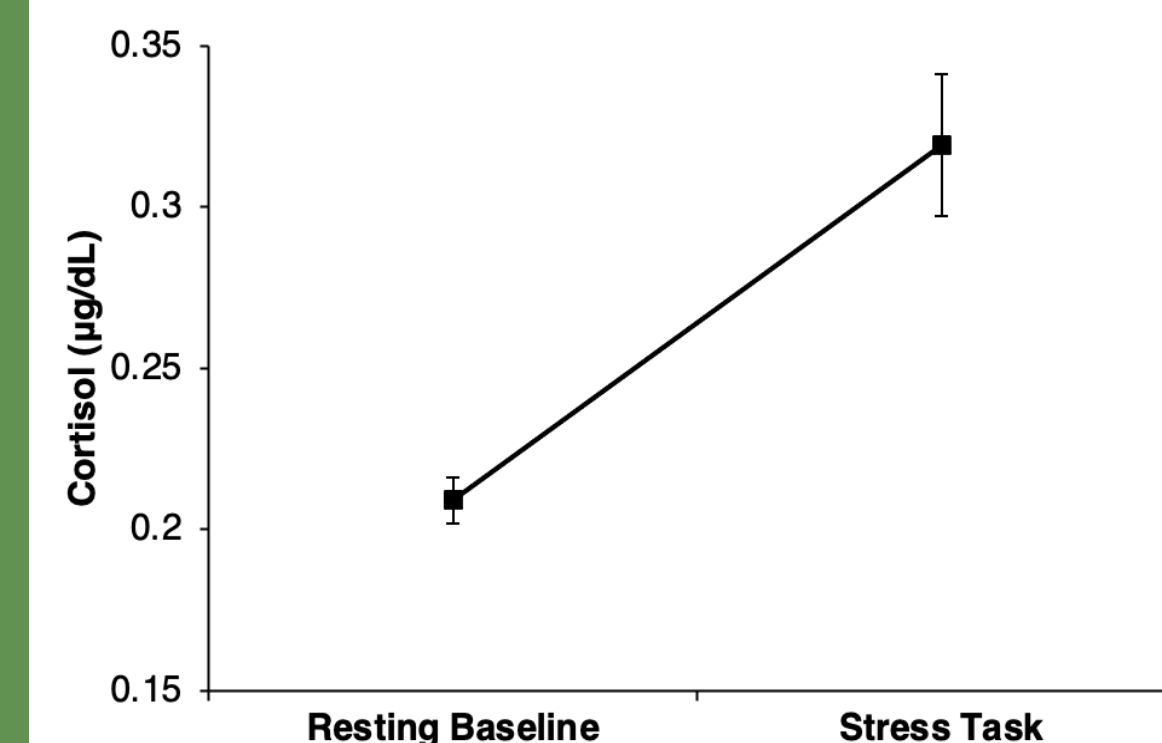


Figure 3. Blood Sugar Metabolization (OGTT) Moderates an Association Between Cortisol Responses and Depressive Symptoms

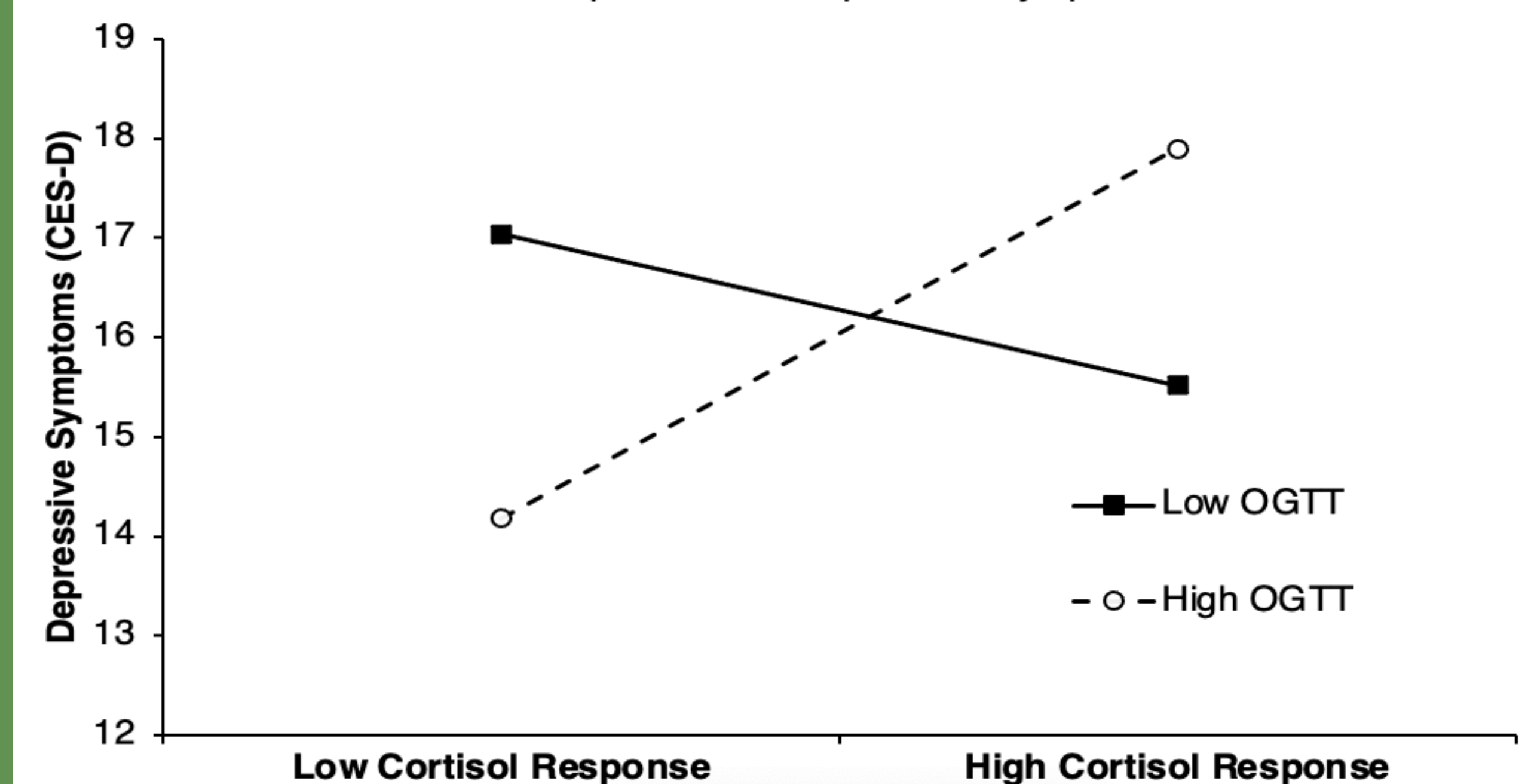


Table 2: Correlations Between Demographic, Stress, Physical, and Psychological Variables

	1	2	3	4	5	6	7	8	9	10	11
1. Age at time of Lab	1										
2. BMI Kg/M ²	-.052	1									
3. SES ^A	.359**	-.044	1								
4. Nulliparity (0=null)	-.392	-.171	.281	1							
5. Baseline Cortisol	-.198*	-.113	-.155	.148	1						
6. Task Cortisol	.014	-.019	.135	.140	.365**	1					
7. Recovery Cortisol	-.002	-.004	.018	.100	.400**	.927**	1				
8. Blood Sugar (OGTT)	.195	.063	.085	.076	.021	.048	.032	1			
9. 24-28 wks CESD	-.266*	.174	-.345**	.060	.218*	.022	-.011	.129	1		
10. 30-32 wks CESD	-.267*	.060	-.273*	.065	.019	-.065	-.094	.106	.698**	1	
11. 36-38 wks CESD	-.197	.049	-.218*	.070	.020	-.059	-.034	.011	.622**	.721**	1

**Correlation is significant at the 0.01 level (2-tailed)

*Correlation is significant at the 0.05 level (2-tailed)

^ASES is the combination of education and adjusted income.

Results

Correlations

Correlation coefficients are shown in Table 2. Notably, Baseline Cortisol was significantly, positively associated with depressive symptoms at Time 1.

Preliminary Analyses

Repeated measures ANOVA revealed that there was a significant effect of Time on Depressive Symptoms (CESD), $F(2, 154) = 4.78, p < .05, \eta^2 = .06$. Post hoc comparisons revealed that Time 3 CESD scores were significantly higher than Time 1 or Time 2 scores, $p < .05$ (Figure 1). Repeated measures ANOVA revealed that there was a significant effect of the stressor task on cortisol reactivity, $F(1, 83) = 27.48, p < .001, \eta^2 = .25$ (Figure 2).

Primary Analyses

A hierarchical mixed-model regression was used to predict depressive symptoms (CESD).

STEP 1: control variables (age, BMI, nulliparity, and SES) and baseline cortisol

STEP 2: Task cortisol and OGTT (Blood Sugar Metabolization) results

STEP 3: Task Cortisol by OGTT Interaction

STEP 3, Interaction results

The interaction between cortisol reactivity and OGTT was significant at all three timepoints, $\beta = .32, .25, .24$, respectively, all $ps < .05$.

Predicted values for Time 2 CESD are depicted in Figure 3. Similar patterns were found for Times 1 and 3.

Discussion

The findings of this study supported the hypothesis: that blood sugar metabolism during pregnancy moderated an association between cortisol stress reactivity and depressive symptoms.

- The depressive symptoms of women who had relatively low blood sugar metabolism (high OGTT results) were positively associated with cortisol reactivity. This was not the case for women with more effective blood sugar metabolism (low OGTT results).
- The established link between diabetes and depression may be moderated by individual's stress responses. Specifically, it may be that those with poor blood sugar metabolism (high OGTT) are especially prone to experience depressive symptoms when they also respond to stress with large cortisol concentrations.

Knowing women's cortisol stress reactivity and OGTT results may help us identify those at greatest risk for depression during pregnancy.

Future research should consider blood sugar metabolism at different points in pregnancy as this may fluctuate. In addition, future studies should consider the combined impact of blood sugar metabolism and cortisol stress reactivity on other pregnancy outcomes, such as length of gestation (e.g., preterm birth) and birth weight.