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Associations between adverse home environments and appetite hormones, adipokines, and adiposity among Chilean adolescents

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Summary

Little is known regarding the relationship between adverse home environments and hormones important in regulation of appetite and their impact on obesity in children and adolescents. In this study, we examined the impact of socioeconomic economic status, family stress and maternal depressive symptoms on appetite hormones, adipokines and adiposity. To determine whether adverse home environments in childhood and adolescence relate to adiposity in adolescence and disruptions in appetite hormones and adipokines, specifically lower levels of adiponectin and ghrelin and elevated levels of leptin and orexin. Adversity in the home (maternal depressive symptoms, family stress, socioeconomic disadvantage) was measured in the households of 593 Chilean youth at age 10 years (52.3% male) and in 606 youth at 16 years. At 16 years, participants provided fasting blood samples for assessment of adipokines and appetite hormones. Waist-to-height ratio was used to assess central adiposity. Correlational analyses examined associations between continuous levels of adversity in childhood and adolescence and appetite hormones and adiposity in adolescence. Multinomial logistic regressions compared hormone levels by tertiles of adversity. Participants were 52% male, with average age at the 16 years hormone assessment being 16.8 ($n = 606$, SD = 0.26). Those with highest maternal depression at age 10 had lower adiponectin OR = 0.95 [95% CI: 0.91, 0.99], $p = 0.005$) and ghrelin levels (OR = 0.98 [95% CI: 0.98, 1.00), $p = 0.022$) than those in the lowest maternal depression group at age 16. Those with the highest family stress at 16 years had lower adiponectin levels (OR = 0.93 [95% CI: 0.89, 0.98), $p = 0.004$) and higher central adiposity (OR = 1.05 [1.01, 1.08], $p = 0.009$) than the lowest family stress group. There were no significant associations found between socioeconomic status at either 10 or 16 years and appetite hormones. Results add new evidence regarding the relationship between household adversity to appetite hormones and adipokines, with the most consistent results for adiponectin. Current findings suggest that the relationship between home environment and adipokines and appetite hormones may play a role in altered adiposity in children and adolescents.

1 | INTRODUCTION

Childhood adversity, psychosocial stress and an unsupportive home environment are known to predict a higher risk of obesity and adverse cardiometabolic outcomes.[1–3] Adversity can include a broad spectrum of environmental stressors, including family stress, financial strain, impoverished environs, maternal depression and child neglect, all of which have been previously shown to be risk factors for adiposity through alteration of neurobiological systems.[1–4] It is well known that these stressors can affect chronic disease prevalence in later life,[2] but not much is known about the underlying mechanisms by which these relationships exists.

One mechanism may be explained by alteration of appetite hormones, such as ghrelin, orexin, leptin and adipokines (i.e. adiponectin), which communicate with the central nervous system about energy homeostasis and are essential to eating patterns in humans. As such, they contribute to adiposity, metabolic syndrome and other adverse cardiometabolic outcomes, by their hormonal dysregulation of hunger and satiety.[5] Aspects of the home environment are known to be associated with the production of leptin and adiponectin,[5] biologically active markers of obesity, and it has been hypothesized that the effects of chronic stress increase food cravings via alteration of these specific hormones, which then contributes to chronic diseases such as obesity and diabetes.[5–6] Ghrelin, a neuropeptide hormone that is released from cells in the stomach and small intestine and increases appetite, has been shown to be a persistent biomarker for chronic stress exposure in rats as well as in humans.[7,8] Leptin, on the other hand, regulates energy balance by inhibiting hunger via actions on the hypothalamus and is directly correlated with the amount of fat in an individual's body.[8] A number of studies have shown associations between leptin levels, early life stress, and depressive symptoms in adulthood, such that the total amount of leptin secreted is higher in adults from poorer home environments.[9] In contrast, one prospective study found that leptin levels were lower in children who experienced physical maltreatment,[10] suggesting inconsistent evidence to support the relationship between leptin and various forms of adversity and stress.

Adiponectin is also secreted from adipose tissue and is involved in glucose regulation, insulin sensitization and fatty acid oxidation, though it does not have a direct effect on appetite. Lower levels of adiponectin have been shown to be an independent risk factor for developing diabetes and metabolic syndrome and coronary artery disease.[11] During times of depression, however, pro-inflammatory cytokines can prevent adiponectin from functioning as an anti-inflammatory agent.[12] Importantly, higher self-reported measures of an early adverse home environment, including abuse, neglect and stress, have been associated with significantly lower adiponectin levels.[13] Furthermore, lower adiponectin levels have

been seen in adults with depression,[12] but it is currently not known whether parental depression has any influence on a child's adiponectin levels.

Lastly, orexin is another important hormone involved in the sleep–wake cycle as well as a potent activator of increased cravings for food. It has additionally been shown to be inhibited by leptin but activated by ghrelin, indicating that it is a hormone that may be integrally tied to eating that can also be disturbed if other important feeding hormones are disrupted in the presence of stress.[14] One study conducted on stress-induced rats showed that orexin regulated cardiovascular responses,[14] while another study showed that in individuals with obesity, regardless of stress exposure, orexin was significantly reduced.[15]

There are several studies that have shown that early-life adversity have strong, positive associations with mid-life leptin and marginal negative associations with mid-life adiponectin.[13] Yet, after adjusting for various demographic variables and lifestyle factors, the associations with adiponectin were attenuated.[13] Additionally, The Center for the Health Assessment of Mothers and Children of Salinas California (CHAMACOS) study found significant negative associations between the home environment (e.g. sociodemographic factors, health status of family members, maternal depression, home learning environment) in childhood and adiponectin levels at ages 9 and 14 among Mexican-American youth with obesity.[16] Most studies have focused on an independent stressor or hormone. No study to our knowledge has comprehensively examined the associations between various forms of adversity and adipokines and appetite hormones, particularly across age, and specifically in children through adolescence, and these are current gaps in literature that this study hopes to address.

The aim of this study was to examine the association between adversity experienced in childhood and adolescence and appetite hormones and adiposity in adolescence. Three types of adversity were studied, maternal depressive symptoms, family stress, and socioeconomic disadvantage, and each type was divided into tertiles of low-to-none, moderate, or high. Based on the available literature and the scientific understanding that stressors link to obesity by altering hunger and feeding hormones,[1,3,17] we hypothesized that those with both moderate and high stressors during childhood and adolescence will be associated with higher levels of leptin and orexin, lower levels of adiponectin and ghrelin, and higher waist-to-height ratio (WHtR) at adolescence. We also sought to determine whether appetite hormones, adipokines and WHtR differ between levels of low-to-absent home adversity variables and adversity at the moderate or high levels. These analyses will reveal whether hormones and adiposity are affected specifically by moderate to high levels of adversity, and we do not expect that stressors in childhood will have less of an effect on hormones than stressors in adolescence.

2 | METHODS

Participants were drawn from the Santiago Longitudinal Study, which originally involved 1790 Chilean infants in a randomized controlled trial to prevent iron deficiency anaemia.[18,19] Infants were recruited from community clinics serving low-to-middle income families (1991–1996) and assessed at the Institute of Nutrition and Food Technology (INTA), University of Chile. Eligible infants were healthy, singleton, full term, weighing ≥3.0 kg at birth. Infants were randomized to receive iron-fortified formula, low-iron formula or unmodified cow milk (a no-added iron condition), from 6 to 12 months.

Participants were followed up at ages 5, 10 and 16 years. We focus here on data from the 10- and 16-year follow-up assessments, during which mothers completed questionnaires and were interviewed about their home and family. When participants were 16 years old, we began a study of obesity and cardiovascular risk ($n = 679$). These individuals participated in a half-day assessment including measurement of blood pressure, height and weight. Fasting laboratory studies were also drawn to assess leptin, ghrelin, adiponectin, and orexin (Table 1). This study's analytic sample includes participants who had appetite hormone data at 16 years and at least one measured adversity variable at age 10 and age 16, for a total sample of 606 youths. Indices of adverse home conditions were available for 585–595 children at age 10 and 515–606 youth at age 16. The full study protocol was approved by the relevant university Institutional Review Boards in the USA and Chile.

3 | MEASURES

3.1 | Adversity in the home environment

At child age 10 and 16, mothers completed the 20-item Center for Epidemiologic Studies-Depression Scale (CES-D)[20] to assess mothers' depressed mood. The CES-D questionnaire asks about the frequency of depressed mood within the past week (such as 'I could not get going' or 'I had crying spells'), with response options ranging from 'rarely or none of the time' (0) to 'most or all the time' (3). Responses were summed across items so that scores ranged from 0 to 60. In clinical practise, scores 16–23 indicate mild to moderate depression, and scores 24–60 indicate severe depression.[20] The Cronbach alphas of the CES-D items ranged between 0.83 and 0.91 at the two study time points.

At both the 10- and 16-year follow-ups, mothers completed the 30-item Social Readjustment Rating Scale questionnaire,[21] which assesses family conflict, family financial strain, and chronic illnesses of family members. Items were coded as 0 (not present) or 1 (present) within the past year, with higher scores indicating greater family stress (range: 0–30).[21]

Mother ratings on the 13-item Graffar Social Classification instrument was used to assess the family socioeconomic disadvantage at child age 10 and 16.[22] The Graffar is a widely used measure of disadvantage in developing countries. Items ask about the housing conditions (quality of house construction, crowding), material belongings (own a refrigerator, washing machine, car, etc.), and parents' occupations, job stability and educational level. Scores range from 13 to 65, with higher scores indicating greater disadvantage.[22]

3.2 | Hormones

After an overnight fast, a morning blood sample (between 8 and 10 ml) was provided by adolescent participants at age 16 for the measurement of appetite hormones at INTA. Fasting serum leptin concentration (1 ng/ml sensitivity) was measured using the Sandwich Enzyme Immunoassay kit (DRG International, Inc., USA) and adiponectin was measured using ELISA R&D Systems (Minneapolis, MN, USA). Commercial radioimmunoassay kits were used to measure ghrelin (Phoenix Pharmaceuticals, Inc., Burlingame, CA, USA).

3.3 | Anthropometric measurements

At age 16, with minimal clothing, waist circumference (WC) was measured with nonelastic flexible tape and recorded to 0.1 cm. Height was measured to the nearest 0.1 cm using a Holtain stadiometer. WHtR was calculated by dividing waist size by height. WHtR is considered a reliable index of central adiposity,[23] and a more accurate predictor of risk of developing obesity and cardiometabolic disease than BMI, waist circumference, or other anthropometric measures.[24,25]

4 | COVARIATES

Initial analyses showed differences by sex in adipokine, appetite hormones, and WHtR or central adiposity (Table 1). We controlled for sex in all analyses except for those involving leptin. Given the highly different leptin levels for males and females, we stratified the logistic regressions involving leptin by sex, and there is research to support that there are sex differences in the relation between adversity and leptin levels.[16] Since child age and BMI at the 16-year assessment were also associated with several of the appetite hormones, we adjusted for age and 16-year BMI in analyses involving the appetite hormones. BMI z scores were used using World Health Organization standards adjusted for age and sex. BMI Z-score cut-points of >1.0, >2.0, >3.0 are recommended to define at risk of overweight and obesity.

In addition, given the significant association between family socioeconomic disadvantage and mothers' depressed mood and family stress, we controlled for socioeconomic disadvantage in the regressions involving maternal depression and family stress.

5 | STATISTICAL ANALYSES

Multinomial logistic regressions were used to examine whether levels of adipokines, appetite hormones, and central adiposity vary by level

	N	M or % (SD)	Range
Participants			
Sex			
Male	317	52.3%	
Female	289	47.7%	
Age at 10 years assessment	595	10.0 (0.50)	9.9–10.4
Age at 16 years assessment	606	16.8 (0.26)	16.4–17.7
Male BMI z score (10 years)		1.20 (1.21)	
Male BMI z score (16 years)		0.60 (1.21)	
Female BMI z score (10 years)		0.97 (1.13)	
Female BMI z score (16 years)		0.76 (1.16)	
Adverse home conditions (10 years)			
Mothers' depressive symptoms	595	17.3 (12.9)	0–57
Family stress	593	4.8 (2.6)	0–15
Family socioeconomic disadvantage	585	29.2(7.2)	19–63
Adverse home conditions (16 years)			
Mothers' depressive symptoms	515	18.8 (14.2)	0–60
Family stress	515	4.4 (2.58)	0–13
Family socioeconomic disadvantage	606	20.6 (2.58)	18–54

	Total (N = 606)	Male (n = 317)	Female (n = 289)	
	M (SD)	M (SD)	M (SD)	p
Outcomes (16 years)				
Leptin (ng/ml)	12.2 (13.7)	5.93 (9.2)	19.1 (14.6)	**0.001**
Ghrelin (pg/ml)	238 (145)	226 (137)	250 (154)	**0.003**
Adiponectin (μg/ml)	11.3 (5.4)	10.3 (4.9)	12.4 (5.6)	**0.001**
Orexin (pg/ml)	16.5 (4.2)	16.6 (4.2)	16.5 (4.2)	0.858
Waist-to-height ratio (WHtR)	0.49 (0.01)	0.47 (0.01)	0.51 (0.01)	**0.001**

TABLE 1 Descriptive statistics of participants and study variables (N = 515–606)

Note: Bolded *p* values indicate significant sex difference in 16-year appetite hormones and WHtR.

of adversity (using SPSS v. 23). Each individual adversity variable (maternal depressive symptoms, family stress and socioeconomic disadvantage) was categorized into tertiles of high, moderate, and low-to-none, with statistical cutoffs created by having approximately 33% of the sample in each adversity level for each adversity variable. We then compared levels of each adipokine and hormone by adversity level, using the low-to-none adversity group as the reference. That is, contrasts were made between the low-to-none adversity group compared to those with moderate adversity and, separately, those with high adversity. By using tertiles, we are investigating whether very high or moderate levels of adversity potentially disrupt appetite hormone balance compared to low to no levels of adversity. Odds ratios and 95% confidence intervals are reported for statistically significant contrasts.

Prior to conducting analyses, we assessed normality of the dependent variables. All showed normal distribution. T-tests were conducted to assess sex differences in appetite hormones, adipokines, and WHtR. We also conducted correlations to examine linear relations between the adversity variables and appetite hormones.

6 | RESULTS

Table 1 is a summary of the characteristics of the study sample. A total of 606 adolescents were included for the hormone analysis (289 female, 47.7%). At the 10-year assessment, children ranged from 9.9 years to 10.4 years (mean [M] = 10.0, SD = 0.50). At the 16-year assessment, participants ranged from 16.4 years to 17.7 years (mean [M] = 16.8, SD = 0.26). All participants were of Hispanic/Latino origin. Results of t-tests indicated that girls had significantly higher levels of leptin, ghrelin, adipokines, and WHtR than boys (Table 1).

Results of the correlational analyses (Table 2) show that lower adiponectin related to more frequent maternal depressive symptoms at child age 10 and more family stress at child age 16. Higher central adiposity related to more frequent maternal depressive symptoms at child age 16, more family stress at child age 16, and greater socioeconomic disadvantage at age 10.

Results of the logistic regressions for maternal depression (Table 3) showed that, compared to participants in the lowest maternal depression tertile at age 10 (T1), those in the highest maternal

TABLE 2 Correlations between the adversity variables and 16-year appetite hormones and waist-to-height ratio

16 years	Maternal depression		Family stress		Socioeconomic disadvantage	
	10 years	16 years	10 years	16 years	10 years	16 years
Leptin	0.02	**0.04**	0.01	**0.01**	0.08	−0.02
Ghrelin	−0.07	−0.06	0.05	−0.01	−0.07	−0.07
Adiponectin	−**0.09**[*]	−0.02	−0.06	**-0.10**[*]	0.03	0.01
Orexin	−0.02	0.02	−0.01	0.07	−0.00	−0.01
WHtR	0.02	0**.11**[**]	0.04	**0.12**[**]	**0.11**[**]	0.07

Note: Socioeconomic disadvantage was coded such that high scores indicate greater disadvantage. Analyses involving appetite hormones were adjusted for sex, age at the16-year assessment, and 16-year BMI; analyses involving WHtR controlled for sex and age.
Abbreviation: WHtR, waist-to-height ratio.
[*]*p* < 0.05. [**]*p* < 0.01.

TABLE 3 Appetite hormones, adipokines and anthropometric values at adolescence (16 years) by tertiles of maternal depressive symptoms during childhood (10 years) and adolescence (16 years)

	10-year tertiles			16-year-tertiles		
	T1 M (SE) 95% CI	T2 M (SE) 95% CI	T3 M (SE) 95% CI	T1 M (SE) 95% CI	T2 M (SE) 95% CI	T3 M (SE) 95% CI
Leptin (ng/ml)						
Male	6.93 (1.20)	5.58 (1.11)	5.79 (1.17)	4.51 (1.08)	5.92 (1.06)	7.94 (1.33)
	4.57, 9.29	3.41, 7.76	3.49, 8.09	2.39, 6.61	3.84, 7.97	5.30, 10.5
Female	16.5 (1.97)	19.8 (1.85)	20.6 (2.05)	19.4 (2.05)	17.8 (1.98)	19.6 (1.82)
	12.6, 20.3	16.2, 23.4	16.5, 24.6	15.4, 23.4	13.9, 21.7	16.1, 23.2
Ghrelin (pg/ml)	**259 (9.68)**	243 (11.1)	**223 (10.9)**	249 (9.88)	232 (11.4)	221 (10.6)
	234, 272	213, 256	**209, 252**	229, 268	209, 254	200, 242
Adiponectin (ug/ml)	**11.9 (0.40)**	11.3 (0.38)	**10.3 (0.35)**	11.4 (0.36)	10.9 (0.39)	10.9 (0.39)
	11.1, 12.7	10.6, 12.1	**9.56, 11.1**	10.9–12.9	10.1, 11.6	10.1, 11.6
Orexin (pg/ml)	16.4 (0.28)	16.9 (0.32)	16.3 (0.31)	16.6 (0.29)	17.1 (0.35)	16.5 (0.32)
	15.9, 16.9	16.2, 17.5	15.7–16.9	15.9, 17.2	16.4, 17.7	15.9, 17.1
WHtR	0.493 (0.006)	0.491 (0.006)	0.497 (0.006)	**0.489 (0.006)**	0.485 (0.006)	**0.503 (0.006)**
	0.481, 0.505	0.477, 501	0.481, 0.507	**0.479, 0.504**	0.474, 0.496	**0.493, 0.514**

Note: Analyses involving appetite hormones were adjusted for sex, age at the16-year assessment, SES, and 16-year BMI; analyses involving WHtR controlled for sex, age, and SES. Bolded values in the same row were statistically different (*p* < 0.05).
Abbreviations: T1, low-to-none adversity tertile; T2, moderate adversity tertile; T3, high adversity tertile; WHtR, waist-to-height ratio.

depression tertile (T3) had lower ghrelin (OR = 0.98 [95% CI: 0.98, 1.00), *p* = 0.022) and lower adiponectin (OR = 0.95 [95% CI: 0.91, 0.99], *p* = 0.005) at age 16. When considering mothers' depressive symptoms at child age 16, compared to participants in the lowest maternal depression tertile (T1), those in the highest tertile (T3) had higher central adiposity (OR = 1.03 [95% CI: 1.00, 1.06], *p* = 0.033).

Results for family stress (Table 4) showed that, compared to participants in the lowest tertile for family stress, those in the highest tertile for family stress at age 16 had lower adiponectin levels (OR = 0.93 [95% CI: 0.89, 0.98], *p* = 0.004) and higher central adiposity (OR = 1.05 [1.01, 1.08], *p* = 0.009). There were no differences in 16-year appetite hormones or central adiposity by 10-year family stress tertile.

Results for socioeconomic disadvantage (Table 5) show that youth in the low disadvantage tertile (T1) at age 10 had lower central adiposity at adolescence than those in the moderate socioeconomic disadvantage tertile (T2) at age 10 (OR = 0.96 [CI: 0.94, 0.99], *p* = 0.01).

7 | DISCUSSION

The goal of the current study was to examine the associations between various adversities in childhood and adolescence with adipokines, appetite hormones and adiposity at adolescence. Correlations were computed to examine associations using continuous levels

TABLE 4 Appetite hormones, adipokines and anthropometric values at adolescence (16 years) by tertiles of family stress during childhood (10 years) and adolescence (16 years)

	10-year tertiles			16-year-tertiles		
	T1 *M (SE)* 95% CI	**T2** *M (SE)* 95% CI	**T3** *M (SE)* 95% CI	**T1** *M (SE)* 95% CI	**T2** *M (SE)* 95% CI	**T3** *M (SE)* 95% CI
Leptin (ng/ml)						
Male	6.62 (0.962)	6.75 (1.18)	4.93 (1.32)	5.33 (1.39)	5.61 (0.934)	7.37 (1.13)
	4.74, 8.51	4.44, 9.06	2.35, 7.52	2.61, 8.06	3.78, 7.44	5.14, 9.59
Female	20.7 (1.57)	18.6 (1.97)	17.5 (2.47)	15.9 (2.24)	19.8 (1.60)	21.1 (1.99)
	17.7, 23.8	14.7, 22.5	12.6, 22.3	11.6, 20.4	16.6, 22.9	17.2, 25.0
Ghrelin	230 (10.5)	233 (10.7)	255 (10.2)	235 (12.4)	235 (8.58)	227 (11.2)
	209, 251	212, 254	235, 275	211, 259	218, 253	205, 249
Adiponectin	11.2 (0.370)	11.8 (0.377)	10.9 (0.451)	**11.8 (0.523)**	11.2 (0.331)	**10.3 (0.412)**
	10.5, 11.9	11.1, 12.6	9.99, 11.8	**10.9–12.9**	9.43, 11.0	**9.43, 11.0**
Orexin	16.6 (0.305)	16.7 (0.309)	16.3 (0.296)	16.0 (0.369)	16.8 (0.267)	16.6 (0.335)
	15.9, 17.1	16.1, 17.3	15.7–16.8	15.3, 16.8	16.3, 17.4	15.9, 17.3
WHtR	0.493 (0.006)	0.489 (0.006)	0.497 (0.006)	**0.482 (0.004)**	0.489 (0.004)	**0.514 (0.004)**
	0.481, 0.505	0.477, 0.501	0.485, 0.509	**0.470, 0.494**	0.480, 0.497	**0.496, 0.521**

Note: Analyses involving appetite hormones were adjusted for sex, age at the 16-year assessment, SES, and 16-year BMI; analyses involving WHtR controlled for sex, age, and SES. Bolded values in the same row were statistically different ($p < 0.05$).
Abbreviations: T1, low-to-none adversity tertile; T2, moderate adversity tertile; T3, high adversity tertile; WHtR, waist-to-height ratio.

TABLE 5 Appetite hormones, adipokines and anthropometric values at adolescence (16 years) by tertile of socioeconomic disadvantage during childhood (10 years) and adolescence (16 years)

	10-year tertiles			16-year-tertiles		
	T1 *M (SE)* 95% CI	**T2** *M (SE)* 95% CI	**T3** *M (SE)* 95% CI	**T1** *M (SE)* 95% CI	**T2** *M (SE)* 95% CI	**T3** *M (SE)* 95% CI
Leptin (ng/ml)						
Male	4.69 (1.13)	7.32 (1.06)	6.31 (1.26)	7.62 (1.29)	5.45 (1.12)	5.24 (1.06)
	2.46, 6.92	5.22, 9.40	3.84, 8.77	5.08, 10.2	3.26, 7.64	3.15, 7.33
Female	18.5 (2.15)	21.4 (1.81)	16.9 (2.34)	20.1 (2.13)	18.4 (2.01)	18.3 (2.15)
	14.3, 22.7	17.9, 24.9	12.3, 21.5	15.9, 24.2	14.5, 22.4	14.1, 22.6
Ghrelin	247 (10.1)	243 (11.2)	232 (10.6)	251 (10.3)	231 (10.4)	225 (9.67)
	227, 266	221, 265	212, 253	231, 271	211, 251	207, 245
Adiponectin	11.0 (0.44)	10.7 (0.38)	11.6 (0.45)	10.9 (0.36)	11.2 (0.37)	11.2 (0.34)
	10.4, 11.8	9.88, 11.4	11.0, 12.5	10.2, 11.6	10.5, 11.9	10.5, 11.9
Orexin	16.4 (0.29)	16.6 (0.32)	16.6 (0.30)	16.9 (0.29)	16.2 (0.29)	16.5 (0.28)
	15.8, 16.9	15.9, 17.2	16.0, 17.2	16.4, 17.5	15.7, 16.8	15.9, 17.0
WHtR	**0.483 (0.004)**	**0.505 (0.004)**	0.486 (0.005)	0.489 (0.005)	0.498 (0.005)	0.489 (0.005)
	0.474, 0.493	**0.495, 0.514**	0.475, 0.496	0.479, 0.499	0.488, 0.508	0.480, 0.498

Note: Analyses involving appetite hormones were adjusted for sex, age at the 16-year assessment, and 16-year BMI; analyses involving WHtR controlled for sex and age. Bolded values in the same row were statistically different ($p < 0.05$).
Abbreviations: T1, low-to-none adversity tertile; T2, moderate adversity tertile; T3, high adversity tertile; WHtR, waist-to-height ratio.

of adversity, and logistic regressions were computed to identify whether appetite hormones and adiposity differ by level of adversity. Results were generally comparable between the two types of analyses, with both analyses uncovering associations between more frequent maternal depressive symptoms and higher family stress with lower adiponectin and higher central adiposity, and between greater

socioeconomic disadvantage and higher central adiposity. In the tertile analyses, we additionally observed that more frequent maternal depressive symptoms at child age 10 years were associated with lower ghrelin levels at adolescence.

Our findings corroborate results from other studies that have found relations between childhood adversities and adiponectin levels.[13,17] Because adiponectin is known to have beneficial immunologic and metabolic properties that play a protective role in the development of obesity, lower levels are not ideal and are risk factors for diabetes mellitus and metabolic syndrome.[26] Prior research in this sample has also identified higher ratios of leptin/adiponectin directly and indirectly related to increased risk factors metabolic syndrome by worsened insulin resistance.[27] Future study of this cohort could determine whether lower adiponectin levels seen at 16 years have any effect on prevalence of other physical manifestations of obesity in adulthood.

As stated earlier, adolescents in the highest tertiles for family stress had lower adiponectin and higher central adiposity. As an anti-inflammatory adipokine, adiponectin inhibits the function of macrophages and increase cytokines such as IL-10 and IL-1 receptor antagonist, which attenuate the immune response.[26] However, constant stress can prevent adiponectin from providing an attenuating response.[28]

There is conflicting literature on the effect of glucocorticoids on adiponectin expression, with some studies showing that glucocorticoids decrease adiponectin expression in tissues, whereas others show that it enhances expression.[28,29] Therefore, it is uncertain whether increased circulating glucocorticoids in the higher family stress groups are facilitating lower adiponectin expression. However, it is known that glucocorticoids cause hyperglycemia and dysregulated lipid metabolism within skeletal, hepatic and adipose tissue, which can promote visceral adipose mass and could explain the increased central adiposity in the higher stress group, in addition to conferring skeletal and hepatic insulin resistance.[26,29] Furthermore, increased intrabdominal fat mass has been shown to be inversely related to adiponectin.[8] Thus, the current findings may elucidate and corroborate the role of adversity in central adiposity and development of insulin resistance via specific appetite hormones and adipokines.

The negative associations seen between maternal depressive symptoms and adiponectin corroborate results from the CHAMACOS study,[16] which found negative associations which were strongest when comparing maternal depression when participants were young and adiponectin when they were older. In addition, maternal depression and family stress could impact the well-being of youth via mechanisms not currently considered. For example, previous studies show associations between parental stress and depression with increased risk of adolescent obesity as mediated by adverse parenting or parent–child interactions.[30,31] Given that lower adiponectin levels may indicate risk for metabolic and cardiovascular disease, identifying maternal depression could provide a potential avenue for intervention.

Lastly, the negative association between maternal depressive symptoms and ghrelin corroborates evidence from studies using rodent models that show that early-life psychological stress results in increased ghrelin response.[7] In that study, the rat models were also shown to display aberrant eating behaviour and binge eating. Using the current Chilean sample, ghrelin was found to be negatively associated with insulin resistance, which in turn related to an increase in metabolic risk factors.[27] Additionally, leptin/adiponectin ratios were related to insulin resistance and metabolic syndrome.[27] Knowing these points, it is important once again, to consider the effect that maternal depression and other adversities can have, not only on adipokines, but on feeding hormones such as ghrelin and indications for metabolic disturbance which in turn influence feeding patterns and behaviours.[32-33]

As for leptin, no association was found with maternal depression, family stress, or socioeconomic disadvantage for either sex, and, thus, we are unable to corroborate previous studies that found either higher or lower leptin levels in relation to exposure to a specific adversity.[8,9,33] Similarly, for orexin, we found no significant relations to differing levels of adversity. The adversity measures in the current study did not include serious, chronic stressors, which may partly explain the lack of associations in our study. However, it may be valuable to reassess the relationships between adversity and leptin adiponectin and ghrelin in participants as young adults.[8]

Study strengths and limitations should be considered when interpreting the findings. An important strength of this study is the use of longitudinal data to assess the relation between early-life adversities with adipokine and hormone levels in a relatively large study cohort. In addition, adversities were measured at childhood and adolescence, providing the ability to assess across-time trends in adversity.

Several study limitations include attrition of the study group over time, that participants were from low- to middle-income communities, which would affect generalizability beyond this income group. Another limitation is that the present study did not measure adipokines at childhood, thus hormonal developmental trends were not able to be studied. Additionally, since the report was conducted by mothers, it is unclear how children perceived stressful environments directly, and that additionally children vary in terms of resilience and how they process stress. Finally, when using BMI z scores, the countries' growth curves were not utilized, which is another limitation. It is important to note that this paper looked as specifically three types of adversities as a part of adverse home environment, although there are many others that have been known to affect a child's stress levels including neglect, absence of a parental figure, parental warmth, parental education, and food insecurity.[34]

This research has health implications for the general population and for populations at risk for obesity. Findings inform how various childhood stressors may relate to adipokines, metabolic hormones, and adiposity. Such findings are important as feeding hormones and adiposity are known to relate to the development of chronic disease.[4,11,26] Results also add new information on how adverse environments relate to hormones and cycles essential for normal child and adolescent development. Additionally, these findings could contribute to public health initiatives regarding prevention and education regarding childhood stressors in the role of risk for obesity and obesity-related morbidity.

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