Hair cortisol, allostatic load, and depressive symptoms in Australian Aboriginal and Torres Strait Islander people

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ABSTRACT

Chronic stress and adversity are associated with poor mental health and are thought to contribute to the existing mental health gap between Aboriginal and Torres Strait Islander people and other Australians. Hair cortisol and allostatic load (AL) are indices of sustained stress and may be mediators of the effects of stress on health. The aim of this study was to examine the relationship between hair cortisol, AL, and depressive symptoms. This cross-sectional study comprised 329 Aboriginal and Torres Strait Islander adolescents and adults recruited at two health screening programs operating in three communities in north Queensland. We measured hair cortisol and calculated an AL index from 10 biomarkers. We assessed depressive symptoms with a version of the Patient Health Questionnaire-9 adapted for Aboriginal and Torres Strait Islander people (aPHQ-9). We found differences in cortisol and AL between the screening programs and communities, which were not explained by depressive symptoms. Overall aPHQ-9 scores were unrelated to hair cortisol (p = .25 and p = .94) and AL (p = .30 and p = .88) when age, gender and smoking were taken into account. However, anhedonia (p = .007) and insomnia (p = .006) sub-scores were each significantly associated with AL in one study site. Our present data did not demonstrate overall associations of stress biomarkers and multisystem dysregulation with depressive symptoms, which suggests that the relationship between cumulative stress and depression may be better explained by other factors in this population. The specific association between anhedonia and insomnia with AL indicates that chronic multisystem dysregulation plays a role in these features of depression in this population.

Lay summary

Our study investigated the relationship between symptoms of depression and two biological pathways thought to mediate depression risk – the stress hormone cortisol and allostatic load (AL) – in an Australian Aboriginal and Torres Strait Islander population. Overall, cortisol and AL were unrelated to depression. However, AL was selectively associated with anhedonia (lack of motivation or drive) and sleep disturbances. These results suggest that metabolic dysregulation measured as AL may be relevant to the depression risk in this population.

KEYWORDS Aboriginal and Torres Strait Islander; depression; allostatic load; hair cortisol; screening; PHQ-9

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Introduction

Chronic or repeated stress is among the best-established risk factors for depression and is thought to mediate in part the effects of social determinants and environmental adversity on mental health. For example, adverse events during childhood and socioeconomic disadvantage increase the vulnerability for mood disorders in adulthood (Danese et al., 2009; Green et al., 2010; Kessler et al., 2010). The hypothalamic-pituitary-adrenal (HPA) axis is considered a key system in mediating the link between stress and depression through the excessive release of glucocorticoids (Lupien, McEwen, Gunnar, & Heim, 2009). Over time, sustained exposure to adversity and high levels of glucocorticoids is thought to adversely affect areas of the developing brain relevant to depression (Anacker, O'Donnell, & Meaney, 2014; McEwen, 2000). The effects of stress may be particularly relevant in the context of mental health disparities affecting indigenous people across the globe, who are often confronted with social challenges that likely converge on stress and may contribute to existing health disparities (Berger, Juster, & Sarnyai, 2015; Sarnyai, Berger, & Jawan, 2016).

Australian Aboriginal and Torres Strait Islander people suffer from a multitude of diseases at higher rates compared with the non-Indigenous population, including common and severe mental disorders (Anderson et al., 2016; Australian Institute of Health and Welfare, 2015). While prevalence rate estimates vary, depression is thought to affect approximately 13–23% of Aboriginal and Torres Strait Islander people (Luke et al., 2013; Paradies & Cunningham, 2012), 1.5–2.3 times more than in the general Australian population. Recently, Harriss et al. (2018) noted high rates of depressive symptoms in a community-based study of Aboriginal youth with 18% experiencing moderate or severe depressive symptoms while another study in the Torres Strait found comparatively low depression rates in Torres Strait Islander people with diabetes (12%) (Taylor, McDermott, Thompson, & Usher, 2016).[AQ3] Similarly, self-reported psychological distress is common, with approximately a third of Aboriginal and Torres Strait Islander adolescents and adults reporting high or very high levels of distress (Australian Institute of Health and Welfare, 2015; Azzopardi et al., 2018) and hospitalization rates for mental illnesses are approximately twice as high than in the non-Indigenous population (Australian Institute of Health and Welfare, 2015). The lasting effects of colonialization and dispossession, including racial discrimination, separation, trauma and other sequelae, contribute to these health inequalities, partly through chronic effects of stress (Berger & Sarnyai, 2015; Berger et al., 2015; Sarnyai et al., 2016). We have recently shown that chronic self-reported distress and discrimination are associated with an altered pattern of diurnal cortisol production in young Aboriginal adults and depression is associated with the biological response to acute stress (Berger et al., 2017). Similar observations of altered stress processing have been made in other minority groups, suggesting that this mechanism may be suited to explain health disparities in different contexts (Akdeniz et al., 2014). Consequently, stress hormones and other mediators of chronic exposure to stress might contribute to explaining higher depression rates in at-risk groups.

Over time, stress and the release of stress mediators contribute to detrimental physiological processes known as allostasis, a concept that recognizes the long-term consequences of stress and maladaptation (McEwen, 1998). Sustained allostatic states may lead to increased AL, characterized by immune, endocrine and metabolic dysregulation and indexed by a set of routinely used markers including glycosylated hemoglobin, cortisol, c-reactive protein (CRP), interleukin-6 (IL6), triglycerides, cholesterol, and blood pressure (Juster, McEwen, & Lupien, 2010; Seeman, McEwen, Rowe, & Singer, 2001). This set of markers has significant predictive value for adverse health outcomes later in life (Barboza Solis et al., 2015; Karlamangla, Singer, & Seeman, 2006) and together these markers appear to reflect metabolic changes and future risk better than individual risk biomarkers (Juster et al., 2010). Several studies also support a link between elevated AL and depression (Juster et al., 2011; Kobrosly, Seplaki, Cory-Slechta, Moynihan, & van Wijngaarden, 2013; Kobrosly, van Wijngaarden, Seplaki, Cory-Slechta, & Moynihan, 2014), suggesting that

heightened AL might contribute to depression risk. However, not all studies support this hypothesis (Rodriquez et al., 2018). Importantly, ethnic minority status as well as socioeconomic disadvantage might be moderators in the link between inflammation/immune activation and depression (Stewart, 2016).[AQ4] Consequently, AL might be well suited to investigate the higher rates of depression in this population (Berger et al., 2015; Sarnyai et al., 2016).

The aim of the present study was to explore the relationship between hair cortisol as well as the AL index and depressive symptoms in three Indigenous communities. We hypothesized that higher levels of cortisol and elevated AL are associated with more severe depressive symptoms. In addition, we aimed to conduct an exploratory analysis examining the relationship between hair cortisol and AL and specific aspects of depression.

Methods

Setting and study design

Two ongoing health-screening programs delivered to Aboriginal and Torres Strait Islander communities in north Queensland are the basis for the present study. The Torres and Cape Hospital and Health Service (TCHHS) delivers the Well Persons Health Check (WPHC) program throughout remote communities in the Torres Strait Islands. Gurriny Yealamucka Health Services Aboriginal Corporation (GYHSAC) in Yarrabah delivers the Young Persons Check (YPC). Briefly, the aims of these annual programs are to provide health promotion, screening and follow-up management for a range of chronic and communicable diseases to all eligible members of the communities. In 2016, researchers from James Cook University participated in both these health programs in collaboration with the TCHHS and GYHSAC. The TCHHS WPHC program (Zenadth Kes Health Partnership) was delivered in the remote island communities of Waiben (Thursday Island) and Mer (Murray Island) located north of Cape York in the Torres Strait. The GYHSAC YPC (Looking after your mates) was located in the community of Yarrabah, situated 52 km south-east of Cairns by road. A brief depression screening tool was added to the health assessments to estimate the prevalence of moderate to severe depressive symptoms in these communities and to identify participants to whom further mental health care should be offered. Using short screening tools in primary healthcare settings is aimed at improving the recognition of depression with subsequent stepped care for individuals with a need for further assessment or care (Haswell et al., 2009; Reynolds & Patel, 2017). The project was endorsed by the GYHSAC Board of Directors, the TCHHS and the local Community Councils and was approved by the Human Research Ethics Committee of James Cook University (H6404) and the Far North Queensland Human Research Ethics Committee (HREC/16/QCH/70-1059).

Participants

The study recruited participants from all individuals aged 15–24 years who attended the YPC in March/April 2016 and all individuals aged 15 years or older who attended the WPHC in Waiben and Mer in October/November/December 2016, representing approximately 54% (Yarrabah), 6.5% (Waiben), and 29.3% (Mer) of the local Aboriginal and/or Torres Strait Islander population in the age range targeted by the health checks, respectively. Participants were recruited via announcements in local media, posters and peer recruiting. For the present analysis, participants were considered eligible if they identified as Aboriginal and/or Torres Strait Islander, were aged 15–24 years (YPC) or 15 years or older (WPHC) and provided written informed consent or verbal consent (n = 1) if written consent could not be obtained (participant and parent/guardian consent for participants aged 17 years or younger). In Yarrabah, 350 members of the community were initially approached and 122 completed the depression screening and consented to their participation in the present research. In Waiben and Mer, a total of 214 individuals were approached and 107 participants from Waiben and 100 from Mer consented and were included in the present analysis.

Data collection

After providing informed consent, each participant was asked to undergo a series of questionnaires and assessments in addition to the routine health screening. Variables relevant to the present analysis included demographic information (gender, age), diet and other health behaviors (smoking), depressive symptoms, a hair sample for hair cortisol analysis, and blood samples for several routine and research blood tests.

Depressive symptoms were measured with the adapted Patient Health Questionnaire 9 (aPHQ-9), a screening instrument designed to measure depressive symptoms in primary care patients that has been adapted for Aboriginal

people in central Australia (Brown et al., 2013) and is currently undergoing validation (Hackett et al., 2016). The aPHQ-9 measures depressive symptoms as a score, ranging from 0 (absence of depressive symptoms) to 27 (severe depressive symptoms). A score of 10 or higher in the original PHQ-9 had a sensitivity of 88% and specificity of 88% for a DSM-IV diagnosis of major depression in a validation study of over 6000 primary care patients (Kroenke, Spitzer, & Williams, 2001). This cutoff has been adapted for the present study to distinguish between "no/mild" and "moderate/severe" depressive symptoms.

Biomarker assessment/allostatic load

Cortisol was analyzed from 3 cm hair sections, which were cut as closely to the scalp as possible from the posterior vertex region to assess cumulative cortisol concentrations of the past three months. Sample preparation and analysis was based on the protocol by Stalder et al. (2017) with minor modifications. Briefly, the hair samples were washed three times for 3 min with 2.5 mL isopropanol and left to dry for 12 h. The hair samples were then weighed, frozen and subsequently ground in a bead beater with 3.2 mm zirconium oxide beads in stainless steel micro vials for 2 min. The samples were then incubated with 1.5 mL methanol at room temperature for 24 h prior to centrifugation at 10,000 rpm for 2 min. One mL supernatant was transferred into a new micro vial and evaporated under a constant stream of nitrogen at 50 °C until completely dry. Then, 0.4 mL phosphate-buffered saline was added, the samples were vortexed for 15 s and stored at –20 C before being analyzed with a commercial immunoassay (Salimetrics, Carlsbad, CA). Inter- and intra-assay coefficients were below 3% for all assays. The analysis was carried out at our laboratory (James Cook University, Cairns, Australia).

Cytokines were analyzed using a Procarta 8-plex panel (Procarta Biosystems, Norwich, UK). CRP was measured with a high-sensitivity assay (Procarta Biosystems, Norwich, UK). Glucose, triglycerides, lipoproteins and cholesterol were analyzed at a commercial pathology service (Sullivan Nicolaides, Cairns, Australia).

Biomarkers for the AL index were selected based on (i) representation of several physiological systems including, neuroendocrine, immune, metabolic, and cardiovascular parameters, (ii) use in previous AL research (Juster et al., 2011; Seeman et al., 2001), and (iii) associations with disease risk. Cardiovascular markers included heart rate, systolic blood pressure and diastolic blood pressure. Neuroendocrine markers included hair cortisol. Immune markers were IL-6, tumor necrosis factor alpha (TNFα), and high sensitivity (hs) CRP. Metabolic markers included triglycerides, high-density lipoprotein, low-density lipoprotein, total cholesterol, glucose, glycosylated hemoglobin (HbA1c), and body mass index (BMI).

For the computation of the AL index, the risk cutoff for each individual biomarker was determined based on clinical reference ranges published by the Royal College of Pathologists of Australasia (triglycerides, high-density lipoprotein, low-density lipoprotein, total cholesterol) and the 75th percentile as determined based on the distribution in each study sample for all other markers. We then used a "scaling" approach previously described by our group and others to calculate the AL index (Berger et al., 2018; Chen, Miller, Lachman, Gruenewald, & Seeman, 2012). Briefly, for each individual, every marker with values above the cutoff (below for HDL) was defined as "1", and the sum of all markers in each category (cardiovascular, immune, neuroendocrine, metabolic) was divided by the number of markers in each category to allow for equal weighting of the four categories. For those markers where the distribution differed between male and female controls, gender-specific cutoffs were calculated and used to compute the index (Juster et al., 2016).

Statistical analysis

Prior to statistical analysis, the distribution of the data was assessed for normality assumptions and outliers. Normality of the data was ascertained by assessing the skewness of data distribution and the associated standard errors. A range of <3 was used as the cutoff for the use of parametric tests. Variables with greater skewness (cortisol) were log-transformed. Cross-sectional differences in demographic characteristics, biological variables and depression scores were tested with independent-sample *t*-tests and rank-sum tests for parametric and non-parametric continuous data, and with Chi2 tests for categorical data. The aPHQ-9 scores were dichotomized using a cutoff of 10 and the strata moderate/severe and no/mild depressive symptoms were created to group study participants for subsequent analyses. To test the association of biomarker levels and AL with depressive symptoms, logistic regression models using hair cortisol and AL as independent variables and depressive symptoms as dependent variable were fitted. Logistic regres-

sion models were adjusted for potential confounding variables including age, gender, and smoking, which correlated with the AL index and are common covariates in the AL literature (Juster et al., 2010). The Hosmer–Lemeshow test was used to test model calibration. All tests were two-sided, a p value of <.05 was considered statistically significant. Stata 13.0 (Stata Corp, College Station, TX) was used for all analyses.

Results

Demographic results

Descriptive results for demographic variables and aPHQ-9 scores across the three sites are presented in Table 1. A total of 122 people participating in the YPC and 207 people participating in the WPHC were included in the present analysis. Twenty-two (18%) participants of the YPC had aPHQ-9 scores above the cutoff for probable depression compared with 19 (9.2%) in the WPHC. The mean age of YPC participants was 19.1 years for participants above the cutoff for probable depression and 19.4 years for those below. A larger proportion of participants of with YPC with probable depression were female, though this was not significant. Participants of the YPC above the cutoff were more likely to smoke although this did not reach statistical significance ($\chi^2 = 2.96$, $p = .09$).

Table 1. Characteristics of 329 Aboriginal and Torres Strait Islander people attending the 2016 Well Persons Health Check (WPHC) and Young Persons Check (YPC), Queensland, Australia.Table Layout

	YPC ($n = 122$)				WPHC ($n = 207$)			
	No/mild depressive symptoms ($n = 100$)	Moderate/severe depressive symptoms ($n = 22$)	Total ($n = 122$)	p Value	No/mild depressive symptoms ($n = 188$)	Moderate/severe depressive symptoms ($n = 19$)	Total ($n = 207$)	p Value
Age								
Mean (SD)	19.44 (3.22)	19.18 (2.30)	19.39 (3.07)	.72[a]	41.14 (17.22)	32.00 (10.68)	40.30 (16.92)	.02[a]
Age group								.08[b]
12–25 years, n (%)	100 (100.0)	22 (100.0)	122 (100.0)		46 (24.5)	6 (31.6)	52 (25.1)	
26–45 years, n (%)	0 (0.0)	0 (0.0)	0 (0.0)		67 (35.6)	11 (57.9)	78 (37.7)	
46–65 years, n (%)	0 (0.0)	0 (0.0)	0 (0.0)		59 (31.4)	2 (10.5)	61 (29.5)	
66–85 years, n (%)	0 (0.0)	0 (0.0)	0 (0.0)		16 (8.5)	0 (0.0)	16 (7.7)	
Gender				.22[b]				.79[c]
Female, n (%)	54 (54.0)	15 (68.2)	69 (56.6)		105 (55.9)	10 (52.6)	115 (55.6)	
Male, n (%)	46 (46.0)	7 (31.8)	53 (43.4)		83 (44.1)	9 (47.4)	92 (44.4)	
Smoking, dichotomized				.09[c]				.48[c]
Yes, n (%)	62 (62.6)	18 (81.8)	80		83 (44.1)	10 (52.6)	93	
Household size								.56[b]
Number of people, median (IQR)	N/A	N/A			4 (2–6)	4.5 (3–8)	4 (2–6)	
Education								.27[b]
Some primary	N/A	N/A			16	0	13	

aPHQ-9: adapted Patient Health Questionnaire-9; BMI: body mass index; IQR: interquartile range; SD: standard deviation.

[a]Independent samples t-test.

[b]Mann–Whitney U test.

[c]Chi^2-$t$est.

	YPC (n = 122)				WPHC (n = 207)			
	No/mild depressive symptoms (n = 100)	Moderate/ severe depressive symptoms (n = 22)	Total (n = 122)	p Value	No/mild depressive symptoms (n = 188)	Moderate/ severe depressive symptoms (n = 19)	Total (n = 207)	p Value
Some secondary	N/A	N/A			55	5	60	
Completed secondary	N/A	N/A			60	6	66	
Completed tertiary	N/A	N/A			56	7	63	
BMI, mean (SD)	24.89 (6.60)	26.39 (8.21)	25.16 (6.91)	.36[a]	31.73 (7.19)	29.65 (7.15)	31.54 (7.19)	.23[a]
aPHQ-9								
Total score, mean (SD)	4.18 (2.82)	16 (4.34)	5.95 (4.91)	<.001[a]	2.76 (2.56)	14.36 (3.93)	3.82 (4.31)	<.001[a]
Total score, median (IQR)	4 (2–7)	12.5 (10–16)	5 (2–9)	<.001[b]	2 (0–4)	14 (11–15)	3 (1–5)	<.001[b]
aPHQ-9: adapted Patient Health Questionnaire-9; BMI: body mass index; IQR: interquartile range; SD: standard deviation.								
[a]Independent samples t-test.								
[b]Mann–Whitney U test.								
[c]Chi^2-$t$est.								

Hair cortisol

Hair cortisol levels were significantly higher among participants of the WPHC relative to participants of the YPC ($t(250) = –2.16$, $p < .001$). Hair cortisol was not correlated with age among participant of the WPHC ($p = .08$) and participants of the YPC ($p = .25$). Hair cortisol was not different between male and female participants of the YPC ($t(92) = –0.65$, $p = .67$) or WPHC ($t(156) = –0.90$, $p = .75$). Hair cortisol was not different between participants above and below the cutoff for depression in participants of the YPC ($t(92) = –0.05$, $p = .91$) and the WPHC ($t(156) = –0.23$, $p = .96$; Table 2).

Table 2. Allostatic load biomarkers of 329 Aboriginal and Torres Strait Islander people attending the 2016 Well Persons Health Check (WPHC) and Young Persons Check (YPC), Queensland, Australia.Table Layout

	YPC (n = 122)				WPHC (n = 207)			
	No/mild depressive symptoms (n = 100)	Moderate/ severe depressive symptoms (n = 22)	Total (n = 122)	p Value[a]	No/mild depressive symptoms (n = 188)	Moderate/ severe depressive symptoms (n = 19)	Total (n = 207)	p Value[a]
	Mean (SD)	Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)	Mean (SD)	
Heart rate (bpm)	79.16 (13.52)	85.77 (17.62)	80.35 (14.49)	.05	71.61 (11.60)	70.42 (10.05)	71.50 (11.45)	.67
CRP: c-reactive protein; HbA1c: glycosylated hemoglobin; HDL: high density lipoprotein; LDL: low density lipoprotein; IL-6: interleukin-6; SD: standard deviation.								
[a]Independent samples t-test.								

	YPC (n = 122)				WPHC (n = 207)			
	No/mild depressive symptoms (n = 100)	Moderate/ severe depressive symptoms (n = 22)	Total (n = 122)	p Value[a]	No/mild depressive symptoms (n = 188)	Moderate/ severe depressive symptoms (n = 19)	Total (n = 207)	p Value[a]
Systolic blood pressure (mmHg)	117.26 (12.60)	118.27 (12.37)	117.44 (12.51)	.73	124.55 (18.01)	122.05 (19.70)	124.32 (18.14)	.57
Diastolic blood pressure (mmHg)	74.03 (7.76)	75.27 (10.78)	74.25 (8.35)	.53	78.10 (12.47)	79.73 (10.96)	78.25 (12.32)	.58
Hair cortisol (ng/mg)	7.79 (9.61)	7.91 (7.40)	7.81 (9.26)	.91	14.04 (28.48)	15.74 (21.84)	14.21 (27.83)	.96
CRP (µg/mL)	0.56 (0.54)	0.44 (0.29)	0.54 (0.51)	.36	0.97 (0.89)	0.58 (0.44)	0.94 (0.87)	.06
IL-6 (pg/mL)	9.18 (10.36)	6.86 (4.01)	8.79 (9.62)	.34	4.25 (6.53)	3.70 (2.08)	4.20 (6.25)	.72
TNFa (pg/mL)	1.31 (2.16)	1.13 (0.65)	1.28 (1.99)	.71	0.61 (2.12)	0.41 (0.79)	0.59 (2.03)	.68
Glucose (mmol/L)	4.95 (1.09)	4.61 (0.62)	4.89 (1.02)	.18	6.21 (3.34)	5.18 (2.26)	6.10 (3.26)	.19
HbA1c (%)	5.21 (0.69)	5.11 (0.20)	5.19 (0.63)	.51	6.08 (1.51)	5.75 (1.59)	6.05 (1.52)	.36
Triglycerides (mmol/L)	1.60 (1.33)	1.67 (0.84)	1.61 (1.25)	.80	1.97 (1.08)	2.21 (2.44)	1.99 (1.28)	.45
Total cholesterol (mmol/L)	4.13 (0.85)	4.19 (1.11)	4.14 (0.90)	.76	4.74 (1.06)	4.92 (4.40)	4.76 (1.06)	.50
HDL (mmol/L)	1.08 (0.24)	1.04 (0.26)	1.07 (0.24)	.47	1.17 (0.36)	1.16 (0.27)	1.17 (0.35)	.93
LDL (mmol/L)	2.33 (0.65)	2.38 (0.95)	2.34 (0.71)	.77	2.66 (0.86)	2.86 (0.75)	2.68 (0.85)	.35
Allostatic load index	2.52 (1.95)	2.74 (1.62)	2.56 (1.89)	.63	3.42 (1.95)	2.80 (1.84)	3.36 (1.94)	.19

CRP: c-reactive protein; HbA1c: glycosylated hemoglobin; HDL: high density lipoprotein; LDL: low density lipoprotein; IL-6: interleukin-6; SD: standard deviation.

[a]Independent samples t-test.

Allostatic load

Allostatic load was significantly higher in participants of the WPHC compared with participants of the YPC ($t(327) = -3.66$, $p < .001$). Allostatic load was correlated with age among participants of the WPHC ($r = 0.276$, $p < .001$) but not among participants of the YPC ($r = 0.035$, $p = .71$). Allostatic load was not different between male and female participants of the YPC ($t(120) = 0.19$, $p = .85$) or WPHC ($t(205) = 0.89$, $p = .38$). Of the AL biomarkers,

heart rate was higher in participants above the cutoff for moderate-severe depressive symptoms in the YPC at trend level ($t(120) = –1.96$, $p = .05$) but not in the WPHC ($t(201) = 0.43$, $p = .67$; Table 2). CRP was lower among participants above the cutoff in the WPHC at trend level ($t(204) = 1.89$, $p = .06$). Levels of the other AL biomarkers did not differ between participants above or below the cutoff in the YPC (all $p>.47$) and the WPHC (all $p>.18$).

Associations between biomarkers/AL and depressive symptoms

Adjusted for age, gender and smoking, hair cortisol was not associated with increased odds for moderate/severe depressive symptoms in the YPC ($\chi^2(62) = 7.64$, OR = 1.74 (95%CI = 0.80–3.78), $p = .16$) or WPHC ($\chi^2(76) = 3.59$, OR = 1.10 (95%CI = 0.54–2.24), $p = .78$; Table 3). Similarly, AL was not associated with moderate/severe depressive symptoms in the YPC ($\chi^2(80) = 5.67$, OR = 1.04 (95%CI = 0.74–1.48),$p = .79$) or WPHC ($\chi^2(93) = 3.86$, OR = 1.02 (95%CI = 0.69–1.52), $p = .88$).

Table 3. Odds ratios (95%CIs) for the association between selected characteristics and moderate/severe depressive symptoms in 339 Aboriginal and Torres Strait Islander people attending the 2016 Well Persons Health Check (WPHC) and Young Persons Check (YPC), Queensland, Australia.Table Layout

	Model 1[a]		Model 2[b]		Model 3[c]	
	OR (95%CI)	*p* Value	OR (95%CI)	*p* Value	OR (95%CI)	*p* Value
All participants (*n* = 329)						
Hair cortisol[d]	0.93 (0.66–1.30)	.70	1.31 (0.80–2.13)	.28	1.10 (0.54–2.24)	.78
Allostatic load	0.91 (0.76–1.08)	.30	0.98 (0.82–1.18)	.91	1.06 (0.82–1.37)	.62
Age	0.96 (0.93–0.98)	.004				
Gender	1.26 (0.64–2.47)	.49				
Smoking	1.00 (0.96–1.05)	.69				
YPC (*n* = 122)						
Hair cortisol[d]	0.97 (0.56–1.65)	.91	1.57 (0.77–3.21)	.21	1.74 (0.80–3.78)	.16
Allostatic load	1.06 (0.83–1.34)	.63	1.16 (0.87–1.54)	.30	1.04 (0.74–1.48)	.79
Age	0.97 (0.83–1.13)	.72				
Gender	1.82 (0.68–4.86)	.23				
Smoking	0.99 (0.92–1.07)	.89				
WPHC (*n* = 207)						
Hair cortisol[d]	0.98 (0.62–1.57)	.96	1.05 (0.64–1.72)	.83	1.10 (0.54–2.24)	.78
Allostatic load	0.83 (0.63–1.09)	.19	0.90 (0.68–1.19)	.49	1.02 (0.69–1.52)	.88
Age	0.96 (0.93–0.99)	.03				
Gender	0.87 (0.34–2.26)	.79				
Smoking	1.04 (0.97–1.11)	.21				

[a]Odds ratios unadjusted.

[b]Odds ratios adjusted for age and gender.

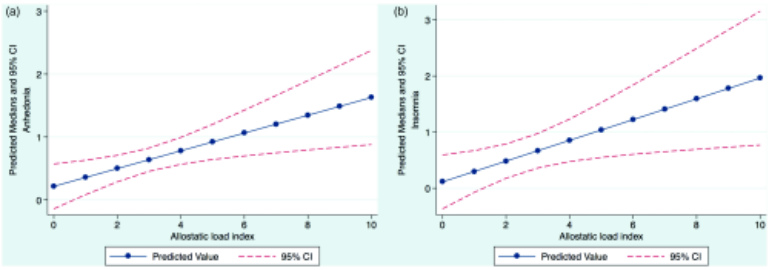
[c]Odds ratios adjusted for age, gender, and smoking.

[d]Log transformed values.

Next, we investigated if AL and hair cortisol are associated with individual sub-domains of the aPHQ-9. Adjusted for age, gender and smoking, AL was significantly associated with item 1 (anhedonia) of the aPHQ-9 in Waiben and Mer ($\chi^2(93) = 24.47$, adj. Beta = 0.312 (95%CI = 0.085–0.539), $p < .007$) and with item 3 (insomnia) in Yarrabah ($\chi^2(80) = 11.11$, adj. Beta = 0.312 (95%CI = 0.085–0.539), $p < .007$; Figure 1). In Yarrabah, a trend-level association

with item 8 (psychomotor retardation) was found ($\chi^2(79) = 9.49$, adj. Beta = 0.301 (95%CI = –0.003–0.607), $p = .05$). No associations were found of cortisol with any of the sub-domains.

Figure 1. Ordered logistic regression analysis of allostatic load (AL) and anhedonia in participants of the Well Persons Health Check aged 15 years an above (WPHC) (a) and of allostatic load and insomnia in participants of the Young Persons Check aged 15–24 years (YPC) (b). Regression analyses are adjusted for age, gender and smoking.



Discussion

The aim of the present study was to explore associations of hair cortisol and AL with depressive symptoms in two cohorts of Aboriginal and Torres Strait Islander people taking part in an annual community health check. Contrary to our hypothesis, no association was seen between hair cortisol levels, AL and aPHQ-9 scores. However, anhedonia and insomnia were each significantly positively correlated with AL in one of the study sites.

Cortisol measured from hair was unrelated to depressive symptoms in our study. Cortisol is believed to be relevant to the pathological mechanisms seen in depression for several reasons. For example, a plethora of studies provided evidence for altered cortisol levels in patients with major depressive disorder, although the findings are inconsistent. One of the largest studies to date to address this question found a significant but modest elevation of cortisol in patients with major depressive disorder irrespective of symptom severity (Vreeburg et al., 2009).[AQ5] Other evidence includes findings of down regulation of glucocorticoid receptors, believed to be secondary to chronic hypercortisolism, and decreased glucocorticoid receptor function (Pariante & Miller, 2001). While some studies found hair cortisol to be higher in patients with depression (Pochigaeva et al., 2017), more recent studies investigating hair cortisol do not support consistently elevated levels in patients with depression (Stalder et al., 2017), including in children and adolescents (Milam, Slaughter, Verma, & McConnell, 2014; Ouellette et al., 2015; Simmons et al., 2016).[AQ6] However, there is evidence for higher hair cortisol in individuals experiencing chronic stress (Stalder et al., 2017) and low socio economic status (Ursache, Merz, Melvin, Meyer, & Noble, 2017), suggesting that hair cortisol levels are related to key risk factors for depression.[AQ7]

An important observation was that cortisol was higher in the participants of the WPHC compared with those of the YPC. Clearly, age is a potential confounder in addition to other systematic differences between the communities (Stalder et al., 2017). The relationship between age and hair cortisol is heterogeneous though, particularly in adolescents (Gray et al., 2018), and age was not correlated with cortisol levels in our study. In addition, BMI is known to be positively correlated with hair cortisol (Gray et al., 2018; Stalder et al., 2017) but similarly was not correlated in the YPC and WPHC cohorts ($p = .884$ and $p = .985$, respectively). Differences in hair cortisol between the two cohorts may be due to factors not measured as part of this study, such as socio-economic differences or other stressors (Stalder et al., 2017).

To our knowledge, this is the first investigation of AL in relation to a mental health outcome in an Aboriginal and Torres Strait Islander population and one of few studies to investigate a potential biological mediator of the effects of stress on mental health. AL is commonly conceptualized as a multisystem indicator of the cumulative effects of chronic stress and adversity. In a population that has both high rates of mental ill-health including depression and suicide and a high prevalence of trauma (Calma, Dudgeon, & Bray, 2017), biological stress mediators and AL may contribute to sustain health inequalities. Populations living under high levels of stress – in particular children – are at increased risk for poor mental health and are consequently a priority in mental health research (Herrman, 2017). Our data support a relationship between AL and two features of depression in this group.

Previous studies in other populations have provided mixed results concerning the relationship between AL and depression. Juster et al. (2011) conducted a follow-up study in 58 adults (mean age = 67 years) and observed prospective associations of increased AL with depressive symptoms in the same year and three years later, although the latter was reduced to a trend when sex and age were included as covariates. Similarly, another study reported associations of depressive symptoms with a multisystem index similar to the AL used here in a Taiwanese cohort (n = 958) (Seplaki, Goldman, Weinstein, & Lin, 2004).[AQ8] In contrast, a recent large (n = 12,272) cross-sectional study investigated AL and depressive symptoms in an ethnically diverse sample and found no significant associations irrespective of ethnicity (Rodriquez et al., 2018). A question raised by these reports is if AL is relevant only in older populations. However, our data neither support a role for AL in older adult or adolescent participants.

The association of AL with anhedonia and sleep disturbances may suggest that AL is selectively related to specific aspects of depression, in particular motivation, psychomotor drive and sleep. Recently, data from the National Health and Nutrition Survey (NHANES) demonstrated selective and robust associations of elevated levels of CRP with fatigue, sleep disturbance, and altered appetite (Stewart, 2016). There is preclinical and clinical evidence to suggest that inflammation and oxidative stress – as seen in allostatic states – impair motivation through effects on striatal dopaminergic reward processing (Felger & Treadway, 2017). Two recent studies support that peripheral inflammation is selectively associated with anhedonia in adult patients with depression (Jha, Miller, Minhajuddin, & Trivedi, 2018) and across diagnostic categories in young people with psychiatric disorders (Freed et al., 2018). Additionally, the link between immune activation and depressive symptoms was missing in some but not all ethnic groups in this study, suggesting that ethnicity may be a moderator of the hypothesized effects of inflammation on depression (Stewart, 2016). Together, these data provide support for the notion that AL may be related to deficits in motivation, psychomotor drive and sleep disturbance.

There are several limitations to this study. First, our study was cross-sectional and inferences cannot be made about the temporal dynamic of hair cortisol or AL and depressive symptoms. Second, several health behaviors and social determinants relevant to AL have not been taken into account comprehensively. Our study was thus unable to investigate which factors determine AL. Third, while AL is conceptualized as the biological traces or chronic stress, perceived stress itself was not assessed. Fourth, cortisol was measured from hair and reflects cumulative cortisol concentrations over the past three months, while depressive symptoms were assessed within two weeks preceding the assessment. Therefore, the timing of the assessment may have contributed to the negative findings. Finally, it is possible that severely depressed individuals were less likely to attend the health check and underreporting of depression may consequently affect our results. The study setting in a community health check setting may also imply a perceived lack of privacy and some study participants may have perceived this as a barrier to disclosing depressive symptoms due to the perceived associated stigma. The study sample may thus not be representative of the wider community. Strengths of the study include the large sample, the diverse age range and the use of hair cortisol, which is not sensitive to the diurnal variation and sampling bias that can be problematic when measuring cortisol from saliva or plasma.

These shortcomings highlight the need for future research in several domains. For example, it seems necessary to elucidate to what extent the previously found role of AL in depression depends on illness severity, study setting (population-based vs. clinical) or ethnicity. Similarly, inconsistencies in the operationalization of the AL index open up the possibility that different findings are attributable to the weighting of the AL markers. Finally, conditions characterized by chronic low-grade inflammation such as obesity or type-2-diabetes mellitus are more common in patients with depression and this relationship may be partially attributable to allostatic mechanisms.

In conclusion, our findings add to the few studies on the relationship between hair cortisol, AL and depressive symptoms in a population affected by considerable social and environmental stressors and putatively higher rates of depression. The relationship between these factors and anhedonia and psychomotor drive may indicate that chronic multisystem dysregulation plays a role in specific features of depression in this population.

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Disclosure statement

The authors report no conflict of interest in relation to this study.[AQ9]

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