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The associations of hair cortisol and DHEA with posttraumatic stress disorder symptoms in refugees

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ABSTRACT

Background: Exposure to traumatic events, ongoing adversity, and posttraumatic stress disorder (PTSD) are associated with altered activity of the hypothalamic-pituitary-adrenal (HPA) axis, but findings are mixed. This may be explained in part by heterogeneity in PTSD symptom profiles.
Aim: The aim of this study was to investigate the complex relationships between the number of traumatic events and post-displacement stressors, individual symptoms of PTSD, and HPA-axis hormones cortisol and dehydroepiandrosterone (DHEA) in refugees.
Methods: Adult (18+ years) Syrian refugees with increased levels of distress participating in a randomized controlled trial completed baseline measures to assess traumatic events (trauma checklist), post-displacement stressors (Post-Migration Living Difficulties checklist), symptoms of PTSD (PTSD Checklist for DSM-5; PCL-5), and provided a hair sample for additional stress hormone analyses. We used R-packages *qgraph* and *bootnet* to perform network analysis on the number of traumatic events and post-displacement stressors, individual symptoms of PTSD, and HPA-axis hormones cortisol and DHEA. The final network model was corrected for depression severity.
Results: 115 (53% male, *M* age = 36.9, *SD* = 12.7) of 206 participants provided a hair sample. A higher number of traumatic events was directly associated with three symptoms of the PTSD cluster arousal and reactivity, i.e., sleep disturbance, hypervigilance and physiological reactivity, and with three other PTSD symptoms, namely flashbacks, avoidance of reminders, and self-destructive behavior. A higher number of post-displacement stressors was associated with four symptoms of the PTSD cluster cognition and mood, i.e., trauma-related amnesia, negative beliefs, blaming of self/others, and detachment, as well as with intrusive thoughts, sleep disturbance, hypervigilance, and exaggerated startle response. The number of traumatic events and post-displacement stressors were not associated with cortisol or DHEA. Cortisol was positively associated with two symptoms of the PTSD cluster cognition and mood, i.e., negative beliefs and negative trauma-related emotions, and negatively associated with avoidance of reminders. DHEA was positively associated with restricted affect and with three symptoms of the PTSD symptom cluster arousal and reactivity, i.e., irritability/anger, sleep disturbance, and self-destructive behavior, and negatively associated with avoidance of thoughts.
Conclusions: This study demonstrated that exposure to traumatic events and post-displacement stressors is not related to cortisol and DHEA, but that cortisol and DHEA are differentially related to individual symptoms of PTSD. While lower levels of both cortisol and DHEA were associated with increased avoidance, higher levels of cortisol were mostly associated with symptoms of the PTSD cluster cognition and mood and higher levels of

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DHEA were mostly associated with symptoms of the PTSD cluster arousal and reactivity. These findings contribute to explaining the variability of findings in the literature on HPA-axis activity in PTSD.
Ethics: The study was approved by the Research Ethics Review Committee at VU Medical Center, the Netherlands (Protocol ID: NL61361.029.17, 7 September 2017) and prospectively registered online (https://www.trialregister.nl/trial/6665).

1. Introduction

Refugees may be exposed to a range of potentially traumatic and adverse experiences prior to, during and after displacement, including violence, combat, insecurity about their asylum status, and lack of employment opportunities [1]. Trauma and adversity are associated with an increased risk of mental disorders, including the development of a posttraumatic stress disorder (PTSD) and overall PTSD symptomatology [1,2]. PTSD is a highly disabling disorder, significantly impacting a person's functioning [3]. Globally, the lifetime prevalence of PTSD in the general population is 3.9% and in the trauma-exposed 5.6% [4], while PTSD is estimated to affect as many as one-third of refugees [5].

It has been hypothesized that dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis may act as a mechanism connecting trauma exposure and ongoing adversity to psychopathology [6,7]. The HPA-axis is a complex system of neuroendocrine pathways and feedback loops that regulates homeostasis in the body by adaptively responding to internal and external stressors [8]. In response to acute stress, the HPA-axis is activated and secretes various steroid hormones including cortisol and dehydroepiandrosterone (DHEA) which regulate different (mostly opposing) physiological functions. Higher concentrations of cortisol lead to various physiological processes such as enhanced release of glucose to allow for a 'fight or flight' response and suppressed immune function. When sufficient circulating cortisol concentrations have been reached, a negative feedback loop is triggered that downregulates HPA-activity again and avoids the systemic dysfunction caused by prolonged cortisol exposure. DHEA has neuroprotective and anti-glucocorticoid effects and may help counteract some of the negative effects of excessive cortisol (e.g., long-term immune suppression). A sensitive balance between cortisol and DHEA are thus important to regulate the body's homeostasis [7].

Chronic stress due to exposure to a traumatic event or ongoing adversity such as discrimination or economic hardship is associated with altered HPA-axis activity (or: HPA-axis dysregulation) [9]. Higher levels of cortisol and DHEA have been observed in trauma-exposed individuals relative to non-exposed controls [10,11], although there are also studies showing no significant association [12]. Among trauma-exposed samples, cortisol levels have been found to be elevated in individuals with recent exposure but blunted in individuals with non-recent exposure (e.g., among adults with childhood trauma) [13,14]. Furthermore, trauma-exposed individuals with recent/ongoing stress (e.g., unemployment) have higher cortisol levels compared with trauma-exposed individuals with past/absent stress [15].

The current literature on abnormalities in cortisol and DHEA in relation to PTSD symptoms is inconsistent. Meta-analytic studies comparing individuals with PTSD to exposed and/or non-exposed controls report lower levels of cortisol [16,17] or no relation between PTSD and cortisol [12]. Lower hair cortisol has been observed in police officers with PTSD compared to trauma-exposed police officers without PTSD [18], whereas no difference in hair cortisol levels has been found between asylum seekers with and without PTSD [19]. Furthermore, higher cortisol levels have been observed in internally displaced individuals reporting worse PTSD symptoms [20]. Similarly, meta-analytic studies on DHEA measured in saliva/urine/plasma samples have reported higher levels of DHEA in PTSD patients compared to non-exposed controls, but no differences between PTSD patients and trauma-exposed healthy controls [11,17].

These variable findings could be due to confounding influences from the type of measurement method [21]. Urine, saliva or plasma samples allow for the investigation of acutely (plasma, saliva) or short-term (urine) circulating cortisol and DHEA levels, but are also susceptible to factors such as circadian rhythm, contraceptive use and reactivity to acute transient stress [21]. Hair samples provide a retrospective index of integrated long-term hormone secretion and are less susceptable to these typical confounds [22]. Other factors that may (partly) explain these inconsistent findings include trauma exposure factors such as number of events, severity, and recency [10,11,16,21,23], and comorbidity with other conditions such as depression [24]. Yet another explanation could be heterogeneity in PTSD symptomatology.

PTSD as classified in DSM-5 consists of 20 symptoms organized in four symptom clusters: intrusions, avoidance, alterations in cognition and mood, and alterations in arousal and reactivity [3]. These 20 symptoms together make up 636,120 possible presentations of PTSD [25], leading to considerable symptom heterogeneity. Furthermore, some of these symptoms – such as symptoms of fear (e.g., intrusive symptoms, avoidance symptoms), dysphoria (e.g., negative affect) and distress (e.g., alterations in arousal and reactivity) – are shared with other disorders such as anxiety disorders and depression [26]. Heterogeneity in PTSD presentations or symptom profiles may lead to inconsistencies in research on the underlying biology of the diagnosis PTSD [25] including inconsistencies in findings on HPA-axis activity in relation to different symptom profiles.

Several studies demonstrated associations between cortisol levels and specific PTSD symptom clusters. For example, a study among earthquake survivors found that hair cortisol levels were negatively associated with avoidance but not with other PTSD clusters [27]. Another study reported a negative association (at trend level) of hair cortisol with the avoidance and intrusion clusters [23]. Salivary cortisol was also found to be negatively associated with intrusions among air-disaster exposed first-responders [28]. In the same sample, hyperarousal symptoms were positively associated with cortisol [28]. This is in contrast with a study that demonstrated a negative association of the hyperarousal symptom cluster with salivary cortisol and a positive association of the hyperarousal symptom cluster with salivary DHEA in primary care patients with PTSD [24]. Lastly, serum cortisol was found to be lower in PTSD patients scoring high on dissociation than in healthy controls and in PTSD patients scoring low on dissociation [29].

These studies provide evidence that cortisol and DHEA may be differently associated with PTSD symptom clusters but do not provide any insight on the association between cortisol and DHEA with individual PTSD symptoms. Network analysis mathematically analyzes and visually represents the complex interconnections of *individual* symptoms and can thus be useful for the investigation of the heterogeneity in PTSD symptomatology [30]. There is a growing number of studies on network models of PTSD among conflict-affected and displaced populations [31–33]. Network analysis can also incorporate other variables that may play an important role in the etiology and maintenance of PTSD, such as exposure to trauma and ongoing stressors. Two studies among conflict-affected populations modeled different types of traumatic events, ongoing stressors, and distress symptoms and found that compared to traumatic events, ongoing stressors were more strongly related to symptoms of depression and anxiety [34,35]. To the best of our knowledge, no studies have yet used network analysis to investigate the relationship of HPA-axis hormones cortisol and DHEA with individual symptoms of PTSD. The advantage of network analysis in this respect is

that it allows to identify the complex interplay between each of these variables. This may provide a more complete picture of how cortisol and DHEA are related to trauma and post-displacement stressor exposure, and to different individual PTSD symptoms. By more adequately addressing the issue of heterogeneity within PTSD, this strategy may explain previous contradictory findings regarding the relationship between stress hormones, PTSD and exposure to trauma and other stressors.

The overall aim of this study was to investigate the complex relationships between the number of traumatic events and post-displacement stressors, the 20 DSM-5 PTSD symptoms (clusters B to E), and HPA-axis hormones cortisol and DHEA assessed in hair samples in Syrian refugees with elevated psychological distress and impaired functioning. We first estimated the network structure of the number of traumatic events, the number of post-displacement stressors, and individual symptoms of PTSD. In a next step, we expanded the network by adding hair cortisol and DHEA. In a last model we also corrected for depression severity.

2. Methods

2.1. Setting

This neuroendocrine study was part of the STRENGTHS project. The aim of the STRENGTHS project was to evaluate the effectiveness and cost-effectiveness of brief, transdiagnostic, psychological interventions for Syrian refugees in Europe and the Middle East and North Africa [36]. For the current study, we used the baseline pre-randomization data of a randomized controlled trial (RCT) that was carried out by the Vrije Universiteit Amsterdam in the Netherlands [37,38]. The RCT was approved by the Research Ethics Review Committee at VU Medical Center, the Netherlands (Protocol ID: NL61361.029.17, 7 September 2017) and prospectively registered online (https://www.trialregister.nl/trial/7552).

2.2. Study design and participants

Participants in the single-blind RCT were enrolled between March 2019 and December 2021. Participants were recruited from community centers, non-governmental organizations, reception centers, language schools and social media. Adult Arabic-speaking Syrian refugees of 18 years and older, with elevated psychological distress (scoring >15 on Kessler Psychological Distress Scale) [39] and impaired daily functioning (scoring >16 on the WHO Disability Assessment Schedule 2.0) [40] were eligible to participate. Participants were excluded if they had acute medical conditions, imminent suicide risk, expressed acute needs or protection risks, and any indication of severe mental disorders (e.g., psychotic disorders) or cognitive impairment (e.g., severe intellectual disability) as assessed with an observation checklist [37,41]. Participants with current receipt of specialized mental health care were also excluded [38].

2.3. Procedure

Oral and written informed consent was obtained from all participants before screening. A tiered informed consent process was adhered to, allowing participants to opt out of the hair sampling procedure. Included participants completed the baseline assessment with questionnaires on demographics, mental health, traumatic events, and post-displacement stressors. For participants who consented, hair samples were collected at the end of the baseline assessment. Hair samples were placed in aluminum foil, labeled, sealed inside an envelope, and stored in a dark cupboard at room temperature. The full procedure of the RCT is described elsewhere [37,38].

The assessments were carried out by Arabic-speaking assessors who received a 3-day training on questionnaire administration, general interview techniques, the use of the online questionnaire tool Survalyzer, common mental disorders, psychological first aid, and ethical research conduct. Participants completed the baseline questionnaires by themselves or were assisted by assessors in case of lower literacy.

2.4. Questionnaires

PTSD symptoms were assessed with the Arabic translation of the 20-item PTSD Checklist for DSM-5 (PCL-5) [42]. The 20 items of the PCL-5 correspond with the 20 PTSD symptoms in DSM-5, including five intrusion symptoms (cluster B: intrusive thoughts, nightmares, flashbacks, emotional cue reactivity, and physiological cue reactivity), two avoidance symptoms (cluster C: avoidance of thoughts, and avoidance of reminders), seven cognition and mood symptoms (cluster D: trauma-related amnesia, negative beliefs, blame of self or others, negative trauma-related emotions, loss of interest, detachment, and restricted affect), and six arousal and reactivity symptoms (cluster E: irritability/anger, self-distructive/reckless behavior, hypervigilance, exaggerated startle response, difficulty concentrating, and sleep disturbance) (see Table 2) [3]. The PCL-5 items are scored on a 0–4 scale. The instrument has been validated in Arabic and Kurdish displaced populations in Iraq [42]. Depression severity was assessed with the Arabic translation of the 15-item subscale of the Hopkins Symptom Checklist (HSCL-25) [43]. Items are scored on a 1–4 scale and the total score is calculated by taking the mean of all items. The instrument has been validated in Arabic-speaking women in Lebanon [43]. Reliability of the PCL-5 and HSCL-25 depression subscale in the current sample were Cronbach's $\alpha = 0.93$ and $\alpha = 0.90$, respectively (and $\alpha = 0.93$ and $\alpha = 0.90$ in the full RCT sample).

The number of traumatic events was assessed through a checklist [44] adapted for the STRENGTHS project, indexing 27 potentially traumatic events. The items were translated and back-translated by Arabic-speaking members of the research team. Each item was scored 1 (yes) or 0 (no) and summed for analysis (total range 0–27) [37]. Post-displacement stressors were scored using the Arabic-language version of the Post-Migration Living Difficulties checklist [44], a list of 17 post-displacement challenges scored on a 0–4 scale. Items with at least a score of 2 (moderately serious problem) were considered positive responses and summed for analysis (total range 0–17).

2.5. Hair samples

Cortisol and DHEA concentrations were measured through hair samples. Hair samples have the advantage of providing a retrospective index of integrated long-term cortisol and DHEA secretion with low susceptibility to typical confounds such as circadian rhythm and contraceptive use [21]. We collected ~100 strands of hair as close as possible to the scalp at the vertex posterior. Scalp-near 3-cm hair segments, allowing for the examination of cumulative cortisol levels over a 3-month period [45] were analyzed by the laboratory at the Technical University of Dresden to determine cortisol and DHEA content at baseline. All hair samples were analyzed as one batch using an established liquid chromatography-tandem mass spectrometry (LC-MS/MS) protocol [22].

Hair characteristics (i.e., natural hair color), cosmetic hair care practices in the prior 3 months (i.e., chemical hair treatment including coloring, bleaching, perming; frequency of hair washing), use of hair products on the day of assessment, and use of corticosteroids in the prior 6 months were assessed at the time of the hair sample collection.

2.6. Statistical analysis

Statistical analyses were conducted with the statistical package R version 4.1.2. First, descriptive statistics were calculated using mean (*M*) and standard deviations (*SD*) for continuous variables, and frequencies (*N*/%) for categorical variables. Cortisol and DHEA were strongly

skewed, and therefore log-transformed for analysis which resulted in a normal distribution. Second, socio-demographic and clinical characteristics of participants who provided hair samples were compared with participants who did not, using *t*-tests for continuous variables (i.e., age, time in the Netherlands, symptoms of PTSD, functional impairment, psychological distress, number of traumatic events, and number of post-displacement stressors) and Pearson chi-square tests for categorical variables (i.e., gender, educational level, marital status). Third, we estimated the PTSD network model. We first estimated the network structure including one variable for the number of traumatic events (sum score), one variable for the number of post-displacement stressors (sum score), and the 20 DSM-5 PTSD symptoms of the PCL-5. In a second step, we added two more variables: hair cortisol (pg/mg) and DHEA (pg/mg). In a final step, we added a depression severity score to control for the potential confounding effect of depression. The R analytic code used to estimate the network model has been provided in Supplement 1.

In the visualization of a network model, each variable is represented by a node, and connections between the variables are represented by edges. Edge weights can range from −1 (negative relationship, indicated by a red edge) to 1 (positive relationship, indicated by a blue edge), with thicker and more saturated edges representing stronger connections. Only when an edge weight is exactly zero (i.e., in the absence of a connection between two nodes), no edge is drawn.

We used the R-package *qgraph* [46] to estimate Gaussian Graphical Models (GGM) based on partial correlations (*r*). The *cor_auto* function was used to compute polychoric correlations for ordinal variables (i.e., PTSD symptoms) and Pearson correlations for interval variables (i.e., the number of traumatic and post-displacement events, HPA-axis hormones, and depression severity score). GGM includes pairwise association parameters between all nodes. To reduce the number of likely spurious connections, we applied the EBIC graphical LASSO regularization technique in which only relevant edges in the network are retained by

Table 1
Participant characteristics.

	Participants with hair sample ($n = 115$)	Participants without hair sample ($n = 91$)	Comparison
Gender, male *n* (%)	61 (53.0%)	66 (72.5%)	$\chi^2 = 8.157^{**}$, $p = .004$
Age, *M* (*SD*) [range]	36.9 years (12.7) [18–69]	36.1 years (10.4) [18–62]	$t = 0.505$, $p = .614$
Refugee status			$\chi^2 = 0.330$, $p = .954$
Request for asylum ongoing	8 (7.0%)	8 (8.8%)	
Resident permit	85 (73.9%)	65 (71.4%)	
Dutch citizenship	14 (12.2%)	12 (13.2%)	
Other	1 (0.9%)	1 (1.1%)	
Missing	7 (6.1%)	5 (5.5%)	
Time (months) in the Netherlands [a], *M* (*SD*) [range]	45.5 (22.9) [1–97]	42.2 (23.4) [2–113]	$t = 0.878$, $p = .381$
Marital status, *n* (%)			$\chi^2 = 0.818$, $p = .976$
Never married	38 (33.0%)	32 (35.3%)	
Currently married	55 (47.8%)	44 (48.4%)	
Separated/divorced	16 (13.9%)	12 (13.2%)	
Widowed	3 (2.6%)	2 (2.2%)	
Cohabiting	3 (2.6%)	1 (1.1%)	
Work status, *n* (%)			$\chi^2 = 6.696$, $p = .570$
Paid work	18 (15.7%)	18 (19.8%)	
Non-paid work	16 (13.950	14 (15.4%)	
Student	50 (43.5%)	31 (34.1%)	
Keeping house	5 (4.3%)	2 (2.2%)	
Unemployed	20 (17.4%)	20 (22.0%)	
Other	4 (3.5%)	6 (6.6%)	
Educational level, *n* (%)			$\chi^2 = 8.5^{*}$, $p = .014$
None/basic education	11 (9.6%)	19 (20.9%)	
Secondary education	17 (14.8%)	20 (22.0%)	
Tertiary education	87 (75.7%)	52 (57.1%)	
PTSD symptoms, *M* (*SD*)	34.3 (17.0)	34.5 (16.9)	$t = -0.056$, $p = .955$
Probable PTSD [b], *n* (%)	60 (52.2%)	49 (53.8%)	$\chi^2 = 0.057$, $p = .811$
Depression, *M* (*SD*)	2.49 (0.67)	2.43 (0.71)	$t = -0.672$, $p = .502$
Probable depression [c], *n* (%)	82 (71.3%)	60 (66.0%)	$\chi^2 = 0.684$, $p = .408$
Number of traumatic events, *M* (*SD*) [range *n*]	9.6 (5.0) [0–26]	9.6 (5.2) [0–21]	$t = 0.006$, $p = .995$
Most reported traumatic events, *n* (%)			
Being a civilian in a war zone	93 (80.9%)	78 (85.7%)	
Having been in danger during the flight	82 (71.3%)	74 (81.3%)	
Unnatural death of family member/friend	75 (65.2%)	52 (57.1%)	
Forced separation from family member	74 (64.3%)	52 (57.1%)	
Serious accident, fire or explosion	69 (60.0%)	54 (59.3%)	
Number of post-displacement stressors, *M* (*SD*) [range *n*]	6.4 (3.6) [0–15]	7.6 (3.4) [2–16]	$t = -2.311^{*}$, $p = .022$
Most reported post-displacement stressors, *n* (%)			
Worries about family back home	82 (71.3%)	79 (86.8%)	
Loneliness, boredom, isolation	73 (63.5%)	65 (71.4%)	
Difficulties learning Dutch language	67 (58.3%)	62 (68.1%)	
Separation from family	65 (56.5%)	59 (64.8%)	
Unable to return home in case of emergency	67 (58.3%)	54 (59.3%)	
Sample collected by assessor, *n* (%)	101 (87.8%)	N/A	N/A
HPA-axis hormones, *Median* (*IQR1–3*)			
Cortisol (pg/mg) [d]	4.59 (3.21–7.44)	N/A	N/A
DHEA (pg/mg) [d, e]	10.37 (7.32–16.09)	N/A	N/A

* $p < .05$, ** $p < .01$, *** $p < .001$
[a] $n = 200$.
[b] based on a cut-off score of ≥32.
[c] based on a cut-off score of ≥2.10.
[d] before log-transformation.
[e] $n = 113$; PTSD = posttraumatic stress disorder.

setting very small edge coefficients to zero [47]. We used a less conservative EBIC hyperparameter of $\gamma = 0.25$ to recover more edges than the default $\gamma = 0.50$, as this suits the explorative design of our study and because it improved the stability of the networks.

Accuracy of the networks was evaluated using the R-package *bootnet* [48]. We first bootstrapped (1000 iterations) the 95% confidence intervals (CIs) of the edge weights, providing an indication of the variability among edges. To examine whether edges are also significantly different from each other, we performed bootstrapped difference tests between the edge weight estimates.

3. Results

Of the 206 participants included in the RCT, 115 (55.8%) baseline hair samples were collected. The reasons for not providing a hair sample were not giving consent ($n = 44$, 48.4%), short hair length ($n = 26$, 28.6%), suspension of in-person assessments due to COVID-19 lockdown ($n = 20$, 22.0%), or unclear ($n = 1$, 1.0%). Due to COVID-19 restrictive measures, 14 hair samples (12.2%) were collected by the participants themselves and sent by post. Descriptive data of the sample are presented in Table 1. The subset of participants who provided a hair sample were less often male ($\chi^2 = 8.157$, $p = .004$), higher educated ($\chi^2 = 8.5$, $p = .014$), and reported significantly less post-displacement stressors ($t = -2.311$, $p = .022$). Participants did not differ on any of the other variables (see Table 1).

Of the participants who provided a hair sample ($n = 115$), 61 (53.0%) were male and the average age was 36.9 years (range 18–69, $SD = 12.7$). Almost half of the sample were currently married (47.8%), and the majority of participants had entered at least a bachelor's degree (75.7%). Participants were on average 46 months in the Netherlands (with a range of 1 to 97 months). Hair characteristics are presented in Supplement 2. The median cortisol level was 4.59 pg/mg (interquartile range [IQR] 3.21–7.44) and the median DHEA level was 10.37 pg/mg (IQR 7.32–16.09). Overall symptom severity was 34.3 ($SD = 17.0$) on the PCL-5. Sixty participants (52.2%) had a score of at least 33 on the PCL-5, indicative of likely PTSD. Table 2 presents the mean levels and standard deviations of the individual PTSD symptoms. The highest overall means were observed for difficulty concentrating ($M = 2.45$, $SD = 1.28$), emotional cue reactivity ($M = 2.28$, $SD = 1.29$), and sleep disturbance ($M = 2.25$, $SD = 1.4$). Self-destructive behavior ($M = 0.84$, $SD = 1.17$) had the lowest mean.

Table 2
Average Symptom Levels for Different DSM-5 PTSD Symptoms (N = 115).

Item	Symptom	*M*	*SD*
Cluster B. Intrusions			
B1	Intrusive thoughts	2.11	1.24
B2	Nightmares	1.41	1.34
B3	Flashbacks	1.42	1.27
B4	Emotional cue reactivity	2.28	1.29
B5	Physiological cue reactivity	1.34	1.31
Cluster C. Avoidance			
C1	Avoidance of thoughts	2.04	1.31
C2	Avoidance of reminders	1.91	1.28
Cluster D. Cognition and mood alterations			
D1	Trauma-related amnesia	1.00	1.13
D2	Negative beliefs	1.55	1.33
D3	Blame of self or others	1.76	1.38
D4	Negative trauma-related emotions	1.58	1.29
D5	Loss of interest	1.99	1.32
D6	Detachment	2.09	1.29
D7	Restricted affect	1.99	1.40
Cluster E. Arousal and reactivity alterations			
E1	Irritability/anger	1.32	1.21
E2	Self-destructive/reckless behavior	0.84	1.17
E3	Hypervigilance	1.75	1.36
E4	Exaggerated startle response	1.32	1.36
E5	Difficulty concentrating	2.45	1.28
E6	Sleep disturbance	2.25	1.40

Participants reported a variety of traumatic experiences, including being a civilian in a war zone (80.9%), having been in danger during the flight (71.3%), unnatural death of a family member or friend (65.2%), forced separation from family member (64.3%) and a serious accident, fire or explosion (60.0%). The most frequently reported post-displacement stressors included worries about family back home (71.3%), loneliness, boredom and isolation (63.5%), difficulties learning the Dutch language (58.3%), separation from family (56.5%) and unable to return home in case of emergency (58.3%) (Table 1).

3.1. Associations between the number of traumatic and post-displacement stressors and individual symptoms of PTSD

The (regularized) network structure of the number of traumatic events, the number of post-displacement stressors and the 20 PTSD symptoms is presented in Fig. 1 (Network 1). The edge weights (denoted as *r*) of the direct connections between nodes in the network are presented in Supplement 3.

The number of traumatic events and post-displacement stressors were associated with different symptoms of PTSD, having only the associations with sleep disturbance (E6) and hypervigilance (E3) in common. The number of traumatic events had direct associations with six PTSD symptoms. These included avoidance of reminders (C2) ($r = 0.12$), sleep disturbance (E6) ($r = 0.09$), physiological cue reactivity (B5) ($r = 0.05$), hypervigilance (E3) ($r = 0.02$), self-destructive behavior (E2) ($r = 0.01$), and flashbacks (B3) ($r = 0.01$). The number of post-displacement stressors was directly connected with eight PTSD symptoms. These included sleep disturbance (E6) ($r = 0.21$), trauma-related amnesia (D1) ($r = 0.19$), hypervigilance (E3) ($r = 0.12$), intrusive thoughts (B1) ($r = 0.09$), exaggerated startle response (E4) ($r = 0.04$), blame of self/others (D3) ($r = 0.04$), detachment (D6) ($r = 0.02$), and negative beliefs (D2) ($r = 0.02$).

Apart from these direct associations, the number of traumatic events and post-displacement stressors were also indirectly associated with other symptoms of PTSD. For example, both the number of traumatic events and post-displacement stressors were related to sleep disturbance (E6), and sleep disturbance was related to several other PTSD symptoms such as nightmares (B2) and restricted affect (D7). In contrast, while the number of post-displacement stressors was positively connected with trauma-related amnesia (D1), amnesia was not or only weakly related to other PTSD symptoms.

The PTSD symptoms were strongly connected with each other (i.e., 89 connections out of 190 potential connections). The strongest connections between symptoms are observed within the PTSD symptom clusters, such as between avoidance of thoughts (C1) and avoidance of reminders (C2) ($r = 0.46$) and between nightmares (B1) and emotional cue reactivity (B4) ($r = 0.38$). There were also strong links between symptoms from different clusters, such as between nightmares (B2) and sleep disturbance (E6) ($r = 0.24$) and loss of interest (D5) and difficulty concentrating (E5) ($r = 0.21$).

The bootstrapped 95% CIs of the edge weights to investigate robustness of the edge weights can be found in Supplement 4. The mean of the bootstrapped edge weights largely overlapped with that of the full sample, suggesting adequate network estimation. The bootstrapped difference test showed that edges with weights $\geq$0.30 (i.e., C1-C2, B1-B4, D6-D7 and D5-D6) did not significantly differ from each other but were significantly larger than most of the edges in the network. There were very few edges connected to the number of traumatic events and post-displacement stressors that were significantly larger than other edges in the network. However, although edge weights were small, it must be noted that these are partial correlations in a regularized network (i.e., small coefficients that are likely to represent spurious relationships have been set to zero), which means that all connections in the network are corrected for all other connections in the network and can thus be regarded meaningful.

The network structure for the full sample ($N = 206$) was comparable,

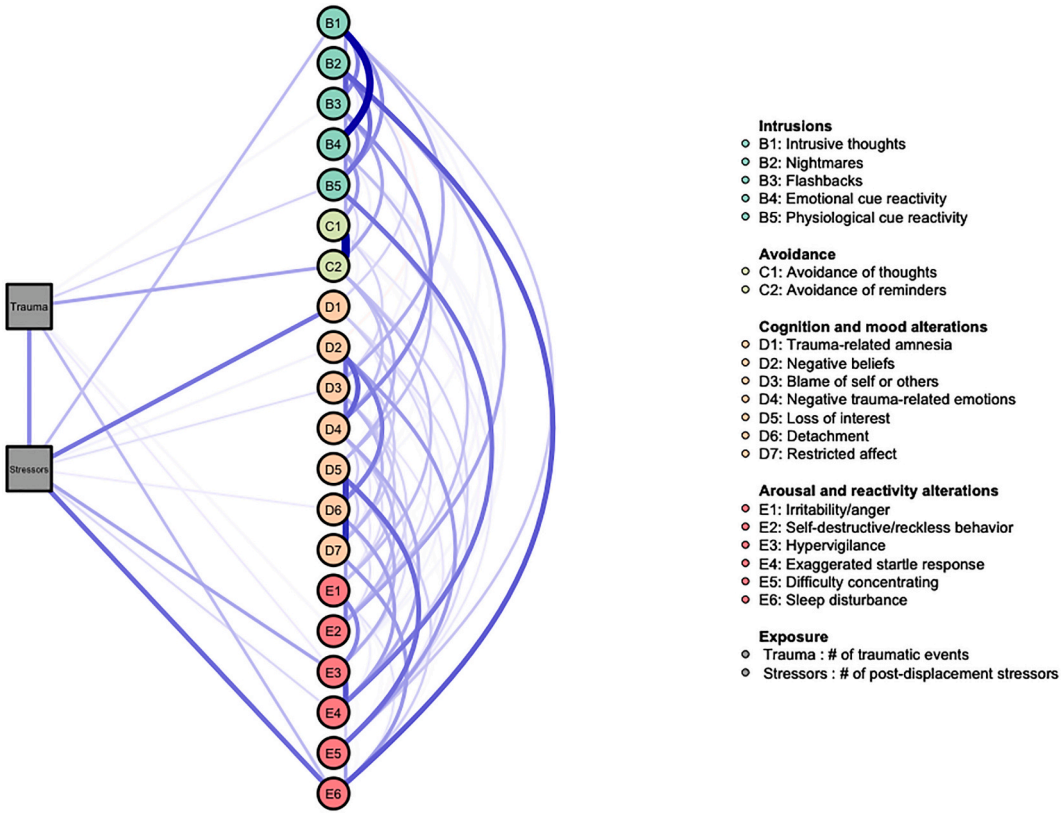

Fig. 1. Network of Number of Traumatic Events, Number of Post-Displacement Stressors, and Symptoms of PTSD (Network 1).
Nodes represent symptoms and edges represent the partial correlations (i.e., controlled for the other correlations between nodes in the network) between nodes.

but with a few more connections between the number of traumatic events and PTSD symptoms (9 instead of 6 connections) and between the number of post-displacement stressors and PTSD symptoms (14 instead of 8 connectsion) (see Supplement 3).

3.2. The role of HPA-axis hormones

We then re-estimated the network structure by adding cortisol and DHEA (see Network 2 in Fig. 2, and Supplement 3). Neither the number of traumatic events nor the number of displacement stressors were directly connected with cortisol or DHEA, indicating that participants with higher numbers of traumatic events and/or post-displacement stressors did not have different levels of cortisol and DHEA.

Cortisol and DHEA had few and small connections with individual PTSD symptoms and were not related to each other. Cortisol had small positive connections with symptoms of the PTSD cognition and mood cluster. Higher levels of cortisol were related to negative beliefs (D2) ($r = 0.03$) and negative trauma-related emotions (D4) ($r = 0.01$). Cortisol had one small negative connection with avoidance of reminders (C2) ($r = -0.02$), indicating that lower levels of cortisol were related to avoidance. DHEA had small positive connections with symptoms of the cluster alterations in arousal and reactivity. Higher levels of DHEA were related to irritability/anger (E1) ($r = 0.07$), sleep disturbance (E6) ($r = 0.07$), and self-destructive behavior (E2) ($r = 0.05$). DHEA also had a positive connection with restricted affect (D7) ($r = 0.03$), and a small negative connection with avoidance of thoughts (C1) ($r = -0.04$).

The bootstrapped 95% CIs of the edge weights can be found in Supplement 4. Cortisol and DHEA did not have any edges that were significantly stronger than other edges in the network.

Adding the depression severity score to the network did not change the strength of the connections of cortisol and DHEA with individual symptoms of PTSD, nor was the severity of depression associated with cortisol and DHEA (see Supplement 3).

4. Discussion

In this paper, we investigated the complex relationships of the number of traumatic events and post-displacement stressors with individual symptoms of PTSD in a Syrian refugee sample and additionally considered the role of HPA-axis hormones herein. Participants were part of a RCT evaluating a transdiagnostic, non-trauma-focused intervention and reported elevated levels of distress, with over half meeting severity levels of probable PTSD.

The main finding of this study was that the number of traumatic events and post-displacement stressors were not related to cortisol and DHEA, but that cortisol and DHEA were differentially related to individual symptoms of PTSD. Cortisol and DHEA did not have any associations in common, except that both were weakly associated with avoidance symptoms. Lower levels of cortisol were related to avoidance of reminders and lower levels of DHEA to avoidance of thoughts. This is in line with an earlier study that demonstrated a negative association between hair cortisol and the avoidance symptom cluster among earthquake survivors [27], but in contrast with a study among female primary care attendees with PTSD that did not demonstrate a correlation between salivary cortisol or DHEA and the avoidance cluster [24]. These different findings might be explained by the use of hair (long-term index) [27] versus salivary samples (short-term index) [24]. Furthermore, we found that higher levels of cortisol were (weakly) associated with more negative beliefs and negative trauma-related emotions (symptoms of the PTSD cluster cognition and mood), which adds to the meta-analytic evidence for hypercortisolism in depression [16,49]. For DHEA, we found that higher levels were associated with more irritability/anger, sleep disturbance, self-destructive behavior (symptoms of the PTSD cluster arousal and reactivity), and restricted affect. Gill et al. [24] also found that higher levels of salivary DHEA were associated with the DSM-IV hyperarousal cluster among female primary care attendees with PTSD. Our study findings and prior research may point to DHEA as

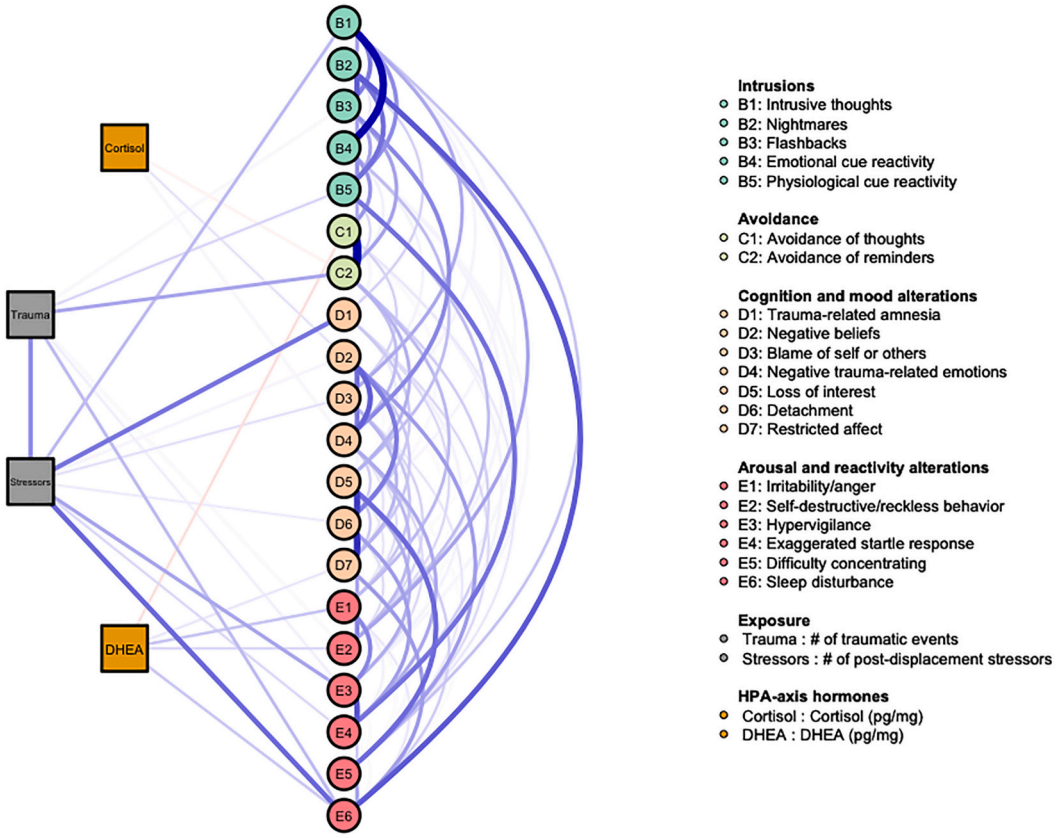

Fig. 2. Network of Number of Traumatic Events, Number of Post-Displacement Stressors, and Symptoms of PTSD with HPA-Axis Hormones (Network 2). Nodes represent symptoms and edges represent the partial correlations (i.e., controlled for the other correlations between nodes in the network) between nodes.

a biomarker of hyperarousal symptoms in PTSD. In contrast to earlier studies that also demonstrated an association of the hyperarousal cluster with lower [24] and higher levels [28] of salivary cortisol, we did not replicate this using hair cortisol samples. The network associations did not change after controlling for depression severity, which itself was not associated with cortisol or DHEA. It is possible that the relation between depression severity (a composite score) and cortisol was suppressed because the majority of the sample (71%) reported above cut-off levels of depression.

This study did not demonstrate direct associations between cortisol, DHEA and the number of traumatic events and post-displacement stressors. Cortisol and DHEA were, however, indirectly associated with the number of traumatic events and post-displacement stressors through specific symptoms of PTSD. For example, higher levels of DHEA were indirectly related to higher numbers of traumatic events and post-displacement stressors through sleep disturbance. Thus, in our distressed sample of Syrian refugees we did not replicate meta-analytic findings that higher DHEA levels are associated with trauma exposure, irrespective of the presence of a PTSD diagnosis [11]. Rather, we confirm the notion that HPA-axis hormones are related to PTSD (symptomatology) [16,17,20,23]. It should however be noted that we did not assess the recency of trauma exposure, while research has shown that the HPA-axis functions differently over time. Individuals with recent trauma exposure are more likely to display hyperactivity and individuals with past trauma exposure are more likely to display hypoactivity [10,50]. In addition, trauma-exposed individuals with ongoing adversity seem to show higher levels of hair cortisol than trauma-exposed individuals without ongoing adversity [15]. In this study, we found that Syrian refugees exposed to a higher number of traumatic events also reported a higher number of post-displacement stressors. So although one would expect a negative association of trauma exposure with cortisol, cortisol levels may have remained relatively elevated in the light of the presence of ongoing stressors in the post-displacement context.

Both the number of traumatic events and the number of post-displacement stressors were associated with sleep disturbance and hypervigilance but did not have any other direct associations in common. Although both had connections to symptoms of the PTSD symptom cluster arousal and reactivity, the number of traumatic events had more direct connections with trauma-related symptoms such as intrusions and avoidance, whereas the number of post-displacement stressors had more direct connections with symptoms of the PTSD symptom cluster cognition and mood. Both the number of traumatic events and post-displacement stressors were indirectly associated with other PTSD symptoms such as nightmares and restricted affect through sleep disturbance.

We also observed that PTSD symptoms were positively interconnected, with the strongest links within PTSD symptom clusters, a common finding across studies [31,32,51,52]. In line with meta-analytic evidence [30], we identified strong connections between the two avoidance symptoms, and within the cognition and mood symptom cluster.

This study has several strengths. Research on pathophysiology in refugee populations remains scarce, and there are no studies that have investigated the relationship between HPA-axis activity and individual symptoms of PTSD in a relatively homegeneous sample of refugees with a Syrian background. The use of hair samples has methodological advantages as it provides a long-term index and is less susceptible to diurnal changes [21]. Another strength is the representation of male participants given challenges with hair sampling in men (e.g., more often shorter hair). Lastly, a strength is the inclusion of trauma exposure and post-displacement stressors in the network model as both types of

experiences are highly relevant to this population.

Limitations include that participants were self-referred individuals with a Syrian refugee background and self-reported psychological distress and impaired functioning participating in a RCT, which may limit the generalizability of the current findings to the broader population of other refugees or other trauma and non-trauma exposed individuals. The current sample thus did not include any healthy controls, and the variance in levels of cortisol and DHEA in this study may as a result have been restricted. Second, our analyses relied on cross-sectional data which limits our understanding on causality within the networks. For example, it is unclear whether detachment caused restricted affect, or vice versa [54]. Third, no power analysis was carried out for this sub-study and so the accuracy of the network model estimates may have been affected by the relatively small sample size [48]. Fourth, we used sum scores for the presence or absence of a traumatic event or post-displacement stressor. Our study thus did not consider important factors such as type and duration, which may explain why we did not demonstrate a link with HPA-axis hormones [13,14,16,21]. Furthermore, this study relied on self-report, whereas the association between self-report measures of stress and hair cortisol concentrations remains questionable [15,16].

Notwithstanding the methodological concerns, this study provides granular insight on endocrine markers, traumatic events, post-displacement stressors and specific PTSD symptoms in a high-risk Syrian refugee sample. It furthermore provides clues to investigate whether there is a differential association between HPA-axis functioning and various PTSD symptom profiles. Studies on more homogeneous PTSD symptom profiles may find effects that may otherwise go undetected in heterogeneous samples with different presentations of PTSD.

4.1. Conclusion

This study demomstrated that traumatic event exposure and post-displacement stressors are not related to cortisol and DHEA, but that cortisol and DHEA are differentially related to individual symptoms of PTSD. While both lower levels of cortisol and DHEA were connected with avoidance, only higher levels of cortisol were connected with symptoms of the PTSD symptom cluster cognition and mood and higher levels of DHEA were associated with symptoms of the PTSD symptom cluster arousal and reactivity. These findings contribute to explaining the variability of findings in the literature on HPA-axis activity in PTSD.

Declaration of Competing Interest

None declared.

Data availability

The Vrije Universiteit Amsterdam (VU) will keep a central data repository of all data collected in the STRENGTHS project. The data will be available upon reasonable request to the STRENGTHS consortium. Data access might not be granted to third parties when this would interfere with relevant data protection and legislation in the countries participating in this project and any applicable EU legislation regarding data protection. Interested researchers can contact Prof. Dr. Marit Sijbrandij at e.m.sijbrandij@vu.nl to initiate the process.

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Supplementary material

Supplementary material to this article can be found online at https://doi.org/10.1016/j.comppsych.2023.152438.

References

[1] Li SSY, Liddell BJ, Nickerson A. The relationship between post-migration stress and psychological disorders in refugees and asylum seekers. Curr Psychiatry Rep 2016;18(9):0–9.
[2] Liu H, Petukhova MV, Sampson NA, Aguilar-Gaxiola S, Alonso J, Andrade LH, et al. Association of DSM-IV posttraumatic stress disorder with traumatic experience type and history in the World Health Organization world mental health surveysvol. 74. JAMA Psychiatry. American Medical Association; 2017. p. 270–81.
[3] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. 2013.
[4] Koenen KC, Ratanatharathorn A, Ng L, McLaughlin KA, Bromet EJ, Stein DJ, et al. Posttraumatic stress disorder in the world mental health surveys. In: Psychological Medicine. vol. 47. Cambridge University Press; 2017. p. 2260–74.
[5] Patanè M, Ghane S, Karyotaki E, Cuijpers P, Schoonmade L, Tarsitani L, et al. Prevalence of mental disorders in refugees and asylum seekers: a systematic review and meta-analysis. Global Mental Health [Internet] 2022 Jun 14:1–14.
[6] Zänkert S, Bellingrath S, Wüst S, Kudielka BM. HPA axis responses to psychological challenge linking stress and disease: What do we know on sources of intra- and interindividual variability?vol. 105. Psychoneuroendocrinology. Elsevier Ltd; 2019. p. 86–97.
[7] Kamin HS, Kertes DA. Cortisol and DHEA in development and psychopathology. Horm Behav [Internet] 2017;89:69–85.
[8] Sheng JA, Bales NJ, Myers SA, Bautista AI, Roueinfar M, Hale TM, et al. The hypothalamic-pituitary-adrenal Axis: development, programming actions of hormones, and maternal-fetal interactions. Front Behav Neurosci 2021;14(January):1–21.
[9] Hosseini-Kamkar N, Lowe C, Morton JB. The differential calibration of the HPA axis as a function of trauma versus adversity: a systematic review and p-curve meta-analyses. Neurosci Biobehav Rev [Internet] 2021;127(April):54–135.
[10] Luo H, Hu X, Liu X, Ma X, Guo W, Qiu C, et al. Hair cortisol level as a biomarker for altered hypothalamic-pituitary- adrenal activity in female adolescents with posttraumatic stress disorder after the 2008 Wenchuan earthquake. Biol Psychiatry 2012;72(1):65–9.
[11] van Zuiden M, Haverkort SQ, Tan Z, Daams J, Lok A, Olff M. DHEA and DHEA-S levels in posttraumatic stress disorder: a meta-analytic review. Psychoneuroendocrinology. 2017;84(June):76–82.
[12] Klaassens ER, Giltay EJ, Cuijpers P, van Veen T, Zitman FG. Adulthood trauma and HPA-axis functioning in healthy subjects and PTSD patients: a meta-analysis. Psychoneuroendocrinology [Internet] 2012;37(3):317–31. Available from: https://doi.org/10.1016/j.psyneuen.2011.07.003.
[13] Heller M, Roberts ST, Masese L, Ngina J, Chohan N, Chohan V, et al. Gender-based violence, physiological stress, and inflammation: a cross-sectional study. J Womens Health 2018;27(9):1152–61.
[14] Khoury JE, Bosquet Enlow M, Plamondon A, Lyons-Ruth K. The association between adversity and hair cortisol levels in humans: a meta-analysis. Psychoneuroendocrinology [Internet] 2019;103(January):104–17. Available from: https://doi.org/10.1016/j.psyneuen.2019.01.009.
[15] Stalder T, Steudte-Schmiedgen S, Alexander N, Klucken T, Vater A, Wichmann S, et al. Stress-related and basic determinants of hair cortisol in humans: a meta-analysis. Psychoneuroendocrinology [Internet] 2017;77:261–74. Available from: https://doi.org/10.1016/j.psyneuen.2016.12.017.
[16] Koumantarou Malisiova E, Mourikis I, Darviri C, Nicolaides NC, Zervas IM, Papageorgiou C, et al. Hair cortisol concentrations in mental disorders: A systematic review. Physiol Behav 2021;229(October 2020):113244 [Internet]. Available from: https://doi.org/10.1016/j.physbeh.2020.113244.
[17] Schumacher S, Niemeyer H, Engel S, Christopher J, Laufer S, Klusmann H, et al. HPA axis regulation in posttraumatic stress disorder: a meta-analysis focusing on potential moderators. Neurosci Biobehav Rev [Internet] 2019;100:35–57. Available from: https://doi.org/10.1016/j.neubiorev.2019.02.005.
[18] van Zuiden M, Savas M, Koch SBJ, Nawijn L, Staufenbiel SM, Frijling JL, et al. Associations among hair cortisol concentrations, posttraumatic stress disorder status, and amygdala reactivity to negative affective stimuli in female police officers. J Trauma Stress [Internet] 2019;32(2):238–48. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1002/jts.22395.
[19] Mewes R, Reich H, Skoluda N, Seele F, Nater UM. Elevated hair cortisol concentrations in recently fled asylum seekers in comparison to permanently settled immigrants and non-immigrants. Transl Psychiatry 2017;7(3):1–5.
[20] Buchmüller T, Lembcke H, Busch J, Kumsta R, Wolf OT, Leyendecker B. Exploring hair steroid concentrations in asylum seekers, internally displaced refugees, and immigrants. Stress. 2020;23(5):538–45.
[21] Steudte-Schmiedgen S, Kirschbaum C, Alexander N, Stalder T. An integrative model linking traumatization, cortisol dysregulation and posttraumatic stress disorder: insight from recent hair cortisol findings. Neurosci Biobehav Rev [Internet] 2016;69:124–35. Available from: https://doi.org/10.1016/j.neubiorev.2016.07.015.
[22] Gao W, Stalder T, Foley P, Rauh M, Deng H, Kirschbaum C. Quantitative analysis of steroid hormones in human hair using a column-switching LC-APCI-MS/MS assay.

J Chromatograph B [Internet] 2013;928:1–8. Available from: https://doi.org/10.1016/j.jchromb.2013.03.008.
[23] Steudte S, Kirschbaum C, Gao W, Alexander N, Schönfeld S, Hoyer J, et al. Hair cortisol as a biomarker of traumatization in healthy individuals and posttraumatic stress disorder patients. Biol Psychiatry 2013;74(9):639–46.
[24] Gill J, Vythilingam M, Page GG. Low cortisol, high DHEA, and high levels of stimulated TNF-α, and IL-6 in women with PTSD. J Trauma Stress 2008:530–9.
[25] Galatzer-Levy IR, Bryant RA. 636,120 ways to have posttraumatic stress disorder. Perspect Psychol Sci 2013;8(6):651–62.
[26] Zoellner LA, Pruitt LD, Farach FJ, Jun JJ. Understanding heterogeneity in PTSD: fear, dysphoria, and distress. Depress Anxiety 2014;31:97–106.
[27] Wang L, Cao C, Wang W, Xu H, Zhang J, Deng H, et al. Correspondence; linking hair cortisol levels to phenotypic heterogeneity of posttraumatic stress symptoms in highly traumatized chinese women. In: Biological Psychiatry. vol. 77. USA: Elsevier; 2015. e21–2.
[28] Witteveen AB, Huizink AC, Slottje P, Bramsen I, Smid T, van der Ploeg HM. Associations of cortisol with posttraumatic stress symptoms and negative life events: a study of police officers and firefighters. Psychoneuroendocrinology. 2010 Aug;35(7):1113–8.
[29] Lee HS, Min D, Baik SY, Kwon A, Jin MJ, Lee SH. Association between dissociative symptoms and morning cortisol levels in patients with post-traumatic stress disorder. Clin Psychopharmacol Neurosci 2022 May 31;20(2):292–9.
[30] Isvoranu AM, Epskamp S, Cheung MWL. Network models of posttraumatic stress disorder: a Meta-analysis [internet]. J Abnorm Psychol 2021;130.
[31] Spiller TR, Schick M, Schnyder U, Bryant RA, Nickerson A, Morina N. Symptoms of posttraumatic stress disorder in a clinical sample of refugees: a network analysis. Eur J Psychotraumatol [Internet] 2017;8(sup3):1318032. Available from: https://doi.org/10.1080/20008198.2017.1318032.
[32] Kangaslampi S, Garoff F, Golden S, Peltonen K. A network analysis of posttraumatic stress symptoms among help-seeking refugees in Kenya. J Anxiety Disord [Internet] 2021;78(January):102358.
[33] Ibrahim H, Neuner F. Network Structure of DSM-5 PTSD Symptoms: Results from Cross-National Survey Among Iraqi and Syrian Displaced People54. Asian Journal of Psychiatry Elsevier BV; 2020.
[34] Mootoo C, Fountain C, Rasmussen A. Formative psychosocial evaluation using dynamic networks: trauma, stressors, and distress among Darfur refugees living in Chad. Confl Health 2019 Jun 26;13(1).
[35] Jayawickreme N, Mootoo C, Fountain C, Rasmussen A, Jayawickreme E, Bertuccio RF. Post-conflict struggles as networks of problems: a network analysis of trauma, daily stressors and psychological distress among Sri Lankan war survivors. Soc Sci Med 2017 Oct 1;(190):119–32.
[36] Sijbrandij M, Acarturk C, Bird M, Bryant RA, Burchert S, Carswell K, et al. Strengthening mental health care systems for Syrian refugees in Europe and the Middle East: integrating scalable psychological interventions in eight countries. Eur J Psychotraumatol 2017;8:1388102.
[37] de Graaff A, Cuijpers P, Acarturk C, Bryant R, Burchert S, Fuhr D, et al. Effectiveness of a peer-refugee delivered psychological intervention to reduce psychological distress among adult Syrian refugees in the Netherlands: study protocol. Eur J Psychotraumatol 2020;11(1):1694347.
[38] de Graaff AM, Cuijpers P, Twisk JWR, Kieft B, Hunaidy S, Elsawy M, et al. Peer-provided psychological intervention for Syrian refugees: results of a randomised controlled trial on the effectiveness of Problem Management Plus. BMJ Mental Health 2023 Feb;26(1):e300637.
[39] Kessler RC, Andrews G, Colpe LJ, Hiripi E, Mroczek DK, Normand SLT, et al. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. Psychol Med [Internet] 2002;32(6):959–76.
[40] WHO. In: Üstun TB, Kostansjek N, Chatterji S, Rehm J, editors. Measuring health and disability: Manual for WHO disability assessment schedule WHODAS 2.0. Geneva, Switzerland: WHO; 2010.
[41] WHO. Problem Management Plus (PM+). Individual psychological help for adults impaired by distress in communities exposed to adversity [internet]. Generic fi. Geneva: WHO; 2016. Available from: http://www.who.int/entity/mental_health/emergencies/problem_management_plus/en/index.html.
[42] Ibrahim H, Ertl V, Catani C, Ismail AA, Neuner F. The validity of posttraumatic stress disorder checklist for DSM-5 (PCL-5) as screening instrument with Kurdish and Arab displaced populations living in the Kurdistan region of Iraq. BMC Psychiatry 2018;18:259.
[43] Mahfoud Z, Kobeissi L, Peters TJ, Araya R, Ghantous Z, Khoury B. The Arabic validation of the Hopkins symptoms Checklist-25 against MINI in a disadvantaged suburb of Beirut, Lebanon. Int J Educat Psychol Assess 2013;13(1):17–33.
[44] Nickerson A, Bryant RA, Schnyder U, Schick M, Mueller J, Morina N. Emotion dysregulation mediates the relationship between trauma exposure, post-migration living difficulties and psychological outcomes in traumatized refugees. J Affect Disord 2015;173:185–92.
[45] Wennig R. Potential problems with the interpretation of hair analysis results. Forensic Sci Int 2000;107(1–3):5–12.
[46] Epskamp S, Cramer AOJ, Waldorp LJ, Schmittmann VD, Borsboom D. Qgraph: network visualizations of relationships in psychometric data. J Stat Softw 2012;48(4):1–18.
[47] Epskamp S, Fried EI. A tutorial on regularized partial correlation networks. Psychol Methods 2018;23(4):617–34.
[48] Epskamp S, Borsboom D, Fried EI. Estimating psychological networks and their accuracy: a tutorial paper. Behav Res Methods 2018;50(1):195–212.
[49] Knorr U, Vinberg M, Kessing LV, Wetterslev J. Salivary cortisol in depressed patients versus control persons: a systematic review and meta-analysis. Psychoneuroendocrinology. 2010;35(9):1275–86.
[50] Staufenbiel SM, Penninx BWJH, Spijker AT, Elzinga BM, Van Rossum EFC. Hair cortisol, stress exposure, and mental health in humans: A systematic review. Psychoneuroendocrinology 2013;38:1220–35.
[51] Armour C, Fried EI, Deserno MK, Tsai J, Pietrzak RH. A network analysis of DSM-5 posttraumatic stress disorder symptoms and correlates in U.S. military veterans. J Anxiety Disord 2017;May 2013(45):49–59.
[52] Bryant RA, Creamer M, O'Donnell M, Forbes D, McFarlane AC, Silove D, et al. Acute and chronic posttraumatic stress symptoms in the emergence of posttraumatic stress disorder a network analysis. JAMA Psychiatry 2017;74(2):135–42.
[54] Fried EI, van Borkulo CD, Cramer AOJ, Boschloo L, Schoevers RA, Borsboom D. Mental disorders as networks of problems: A review of recent insights. In: Social Psychiatry and Psychiatric Epidemiology. Dr. Dietrich Steinkopff Verlag GmbH and Co. KG. vol. 52; 2017.