Exploring hair steroid concentrations in asylum seekers, internally displaced refugees, and immigrants

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Exploring hair steroid concentrations in asylum seekers, internally displaced refugees, and immigrants

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ABSTRACT
The study of physiology in response to war and forced displacement can yield insight into the origin of stress-related mental health disorders. Previous studies found alterations in hair cortisol concentrations (HCC) in refugees. However, the direction of this alteration in HCC, as well as the association between HCC and psychological stress, remain unclear. Mixed findings can potentially be explained by the lack of contextual factors that have been taken into account. In this explorative study, we investigated HCCs in three female refugee samples (N = 89) in different contexts. Samples were i) asylum seekers from Syria, who sought protection in Germany two years ago (n = 37), ii) internally displaced persons (IDPs), who fled a genocide and lived in conditions of ongoing insecurity in Iraq (n = 14), and iii) Kurdish immigrants and former asylum seekers, who resettled to Germany 18 years ago and were used as reference group (n = 38). HCC was assessed in the scalp-nearest 6 cm of hair (2/3 cm segments). Data on mental and physical health, exposure to traumatic events, and time between immigration and HCC assessments were collected. Syrian asylum seekers had lower HCC than immigrant controls (g^2 = .06). PTSD symptoms and perceived stress were associated with elevated cortisol levels in IDPs (r = .66 and r = .56), while time since immigration was associated with cortisol levels only in immigrant controls (r = .38). We discuss our findings with regard to the importance of contextual factors, particularly time since displacement and ongoing insecurity, when studying physiological reactions in refugees.

LAY SUMMARY
Female Syrian asylum seekers had lower levels of hair cortisol concentration than Kurdish immigrants in Germany. Hair cortisol concentration was associated with post-traumatic stress symptoms only in internally displaced women who were exposed to ongoing stress and insecurity in Iraq.

Introduction
Refugees are exposed to multiple stressors before, during and after forced displacement, making them prone to develop mental health problems (e.g., Fazel et al., 2005; Lindert et al., 2009). The role of stress as a risk factor for mental health problems is well established (Chrousos, 2009), whereas the underlying biological mechanisms are still being elucidated. Refugees offer a possibility to study the physiological effects of chronic adversities during adulthood otherwise often investigated in childhood (Khoury et al., 2019).

A large body of research has focused on the hypothalamic-pituitary-adrenal (HPA) axis with its main downstream endocrine effector, the glucocorticoid cortisol (e.g., Wolf, 2008). Whereas short-term fluctuations of cortisol levels can be reliably assessed through sampling in saliva or blood, human hair cortisol concentration (HCC) offers the possibility to study cortisol release over longer time intervals. HCC represents an index of the cumulative cortisol secretion of the past months and is robust to situational and circadian variations (Dettenborn et al., 2010; Yamada et al., 2007), which makes it suitable to study physiological responses to chronic stressors.

As of today, research on HCC alterations in refugees is scarce. Two studies found elevated HCC in war-affected populations with posttraumatic stress disorder (PTSD) as compared to traumatized controls (Shaheen et al., 2018; Steudte et al., 2011), while two did not find any effects (Mewes et al., 2017; Sierau et al., 2019). Two studies compared HCC levels in refugees to non-refugee groups and found evidence for elevated HCC levels in refugees (Mewes et al., 2017) or similar HCC levels between the groups (Dajani et al., 2018). Initial hypercortisolism after the exposure to adversities may turn into hypocortisolism in the long-term (Steudte-Schmiedgen...
et al., 2016). Moreover, the degree of on-going stress can moderate effects of chronic stress on HCC (Stalder et al., 2017). As refugees differ in the time since they experienced forced displacement-related adversities and on the degree of on-going stress, both could potentially account for inconsistent findings.

In the present study, we assessed HCC in three different samples of women affected by forced displacement to explore if the time since forced displacement, perceived stress, trauma and PTSD could potentially explain previously mixed findings. Participants were (a) internally displaced persons (IDPs) in a refugee camp in Iraq, who lived in conditions of on-going stress; (b) asylum seekers from Syria, who arrived in Germany relatively recently; and (c) former (Kurdish) asylum seekers and (Kurdish) immigrants, respectively, who both came to Germany more than a decade ago. We expected elevated HCC in IDPs and lower HCC in asylum seekers compared to immigrants. Furthermore, we explored associations between HCC and stress-related variables within samples (PTSD symptoms, traumatic events, perceived stress level, time since displacement, perceived physical health). There is evidence that other steroid hormones, for instance dehydroepiandrosterone (DHEA), are involved in the physiological response following traumatic events (van Zuiden et al., 2017). Thus, we conducted exploratory analyses on group differences in DHEA and cortisone concentrations to investigate if these steroids are useful biomarkers for chronic stress in the context of forced displacement.

Methods

Participants

A total of 92 women participated in our study (age 18–70 years). Exclusion criteria were Cushing’s syndrome, Addison’s disease, asthma and obesity. (Notably, IDPs in Iraq might be unaware of the respective diseases due to a lack of medical supply). Pregnant women (n = 1) and women beyond the age of 59 years (n = 2) were excluded. We compared HCC of two refugee samples and used an immigrant sample as reference group (see Table 1 for demographic information). All participants were born in adjacent geographical regions (boarder regions of Iraq, Syria and Turkey).

The first sample consisted of internally displaced women living in refugee camps in Northern Iraq, who fled organized violence of the terror group “Islamic State” around August 2014 (n = 14). The second sample consisted of Syrian asylum seekers, who came to Germany to apply for asylum, on average, two years ago (n = 37). The third sample were (Kurdish) immigrants and asylum seekers, who have had been living in Germany, on average, for 18 years (n = 38).

Measurements

Symptoms of PTSD were assessed according to DSM-IV criteria using the 16 item PTSD-scale of the Harvard Trauma Questionnaire (HTQ; Mollica et al., 1992). We used the Arabic and Kurdish version of the HTQ (Mollica et al., 2004). Physical and mental health were assessed using the short form health survey (SF-12) (Jenkinson et al., 1997) in Arabic (Steel et al., 2006). To measure the level of perceived stress we used Cohen’s Perceived Stress Scale obtaining 10 items (PSS-10) (Cohen et al., 1983) in Arabic (Almadi et al., 2012). Time since immigration was measured as the time (in years) between the interview and the arrival in Germany or the refugee camp, respectively.

We created a scale to assess the experience of traumatic events which unlike other trauma scales does not ask for specific events, but broad event types (“Refugee Adversity and Traumatic Events Rating Scale” [RATERS], see Supplementary materials Appendix I to III for German, English and Arabic Version). This was necessary, as we did not want to trigger PTSD symptoms by asking for specific events. The 3-item rating scale was constructed with support of a clinical psychologist and double translated into Arabic. Three types of traumatic events were assessed by the scale: Having been “captured, intimidated or threatened,” “physically hurt or humiliated by another person” and “not having sufficient food, water or shelter.” Participants responded on a 4-point scale if they had not experienced those events (1), heard from someone about those events (2), had a close friend /family member who had experienced the events (3) or had experienced the events themselves (4). A sum score of the three items was obtained.

Most questionnaires had very good internal consistency in our sample (HTQ-PTSD: $\alpha=.87$, SF-12: $\alpha=.95$, PSS-10: $\alpha=.81$), the consistency of the trauma-scale was acceptable ($\alpha=.72$).

Hair sample collection

Hair strands were collected from a posterior vertex position as close to the scalp as possible. Hair strands were tied together, sealed airtight and stored in a dry and dark place in a safe. Hair steroid analysis were carried out in an external laboratory (Technical University Dresden, Germany). In the lab, hair strands were cut into two 3 cm segments. Human hair is growing with an average of 1 cm per month (Dettenborn et al., 2012), thus the proximal segment (Segment 1) reflected the previous 3 months, while the distal segment (Segment 2) reflected months 4–6 prior to the assessments. Steroid concentrations of cortisol, cortisone and DHEA were determined using liquid chromatography tandem mass spectrometry (LC-MS/MS) following the protocol of Gao et al., 2013. We assessed potential confounders of HCC, notably hair-related treatments (wearing a headscarf; washing frequency; natural curls; use of conditioner; hair coloration), use of hormonal contraceptives and pregnancy. Demographic variables included age, education, number of children and time since (forced) displacement.

Procedure

The study was conducted between May 2017 and October 2018. Recruitment of asylum seekers was done by word of mouth, in local mosques and local refugee camps with the help of NGOs, and social workers. Immigrants were recruited by
Table 1. Demographic information, stress-related and control variables.

<table>
<thead>
<tr>
<th>Demographic information</th>
<th>Asymmetry seekers (n = 37)</th>
<th>Immigrant controls (n = 38)</th>
<th>Test statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic information</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age M (±)</td>
<td>34.34 (11.71)</td>
<td>30.04 (5.25)</td>
<td>34.63 (9.39)</td>
</tr>
<tr>
<td>Number of children Median (Range)</td>
<td>1 (0–5)</td>
<td>2 (1–4)</td>
<td>3 (0–8)</td>
</tr>
<tr>
<td>Education (years) M (±)</td>
<td>5.07 (6.32)</td>
<td>13.72 (3.22)</td>
<td>7.84 (4.76)</td>
</tr>
<tr>
<td>Years since displacement M (±)</td>
<td>1.75 (0.00)</td>
<td>1.72 (0.94)</td>
<td>17.75 (5.65)</td>
</tr>
<tr>
<td>Psychological variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Above PTSD cutoff in % (n)</td>
<td>92.9 (13)</td>
<td>57.1 (20)</td>
<td>13.2 (5)</td>
</tr>
<tr>
<td>HTQ-PTSD scale M (±)</td>
<td>2.68 (0.59)</td>
<td>2.04 (0.49)</td>
<td>1.47 (0.36)</td>
</tr>
<tr>
<td>PSS-10 sum score M (±)</td>
<td>24.50 (6.12)</td>
<td>20.12 (6.80)</td>
<td>16.79 (6.65)</td>
</tr>
<tr>
<td>SF-12 Mental T-Score M (±)</td>
<td>38.70 (7.87)</td>
<td>47.39 (8.47)</td>
<td>47.46 (9.19)</td>
</tr>
<tr>
<td>SF-12 Physical T-Score M (±)</td>
<td>29.85 (13.19)</td>
<td>40.00 (12.18)</td>
<td>49.59 (8.73)</td>
</tr>
<tr>
<td>RATERS M(±)</td>
<td>7.43 (3.18)</td>
<td>4.84 (2.30)</td>
<td>3.27 (2.46)</td>
</tr>
<tr>
<td>Control variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head scarf in % (n)</td>
<td>100 (14)</td>
<td>75.70 (28)</td>
<td>76.3 (29)</td>
</tr>
<tr>
<td>Hair-washing per week M (±)</td>
<td>-</td>
<td>3.03 (1.01)</td>
<td>3.14 (0.87)</td>
</tr>
<tr>
<td>Natural curls in % (n)</td>
<td>-</td>
<td>53.30 (16)</td>
<td>39.50 (15)</td>
</tr>
<tr>
<td>Use of conditioner % (n)</td>
<td>-</td>
<td>60.00 (18)</td>
<td>44.70 (17)</td>
</tr>
<tr>
<td>Hair colorationin % (n)</td>
<td>-</td>
<td>73.30 (22)</td>
<td>34.20 (13)</td>
</tr>
<tr>
<td>Hormonal contraceptives % (n)</td>
<td>-</td>
<td>17.90 (5)</td>
<td>15.80 (6)</td>
</tr>
<tr>
<td>M: Mean; ±: Standard deviation; n: number; IDP: Internally displaced persons; PTSD: Post-traumatic stress disorder. *p &lt;.05.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>aHarvard Trauma Questionnaire cutoff according to Mollica et al. (2004).</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bSF-12 scale.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cRefugee Adversity and Traumatic Event Rating Scale (see Supplementary materials Appendix I, II, III).</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>dThe hair-related questions were omitted in Iraq to limit the length of the interview.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data preparation

Data were processed in SPSS® 25.0 for Windows (IBM Corporation, Armonk, NY, USA). HCC values below the detection limit were set at 50% of the thresholds proposed by Gao et al., 2013 (2 participants on HCC, 2 on DHEA, 1 on cortisone). Steroid data were log-transformed to normalize the skewness of the distribution. Samples were compared running separate analyses of covariance (ANCOVA) for each steroid (HCC, Cortisone, DHEA) including age as covariate. In case of missing items within instruments, we replaced items by the scales mean if less than 13 of 16 items were missing for the HTQ (19 cases) and less than 9 out of 10 items were missing for the PSS-10 (3 cases) as recommended by the manuals. Missing values were deleted pairwise in the statistical analysis.

Statistical analysis

In a first step, preparatory analyses were conducted: Samples were compared regarding possible confounding factors on HCC (age, hair-related variables) using the respective test (ANOVA, Chi-square test, p < .05). If groups differed, associations between the variables and HCC were checked using Pearson’s bivariate correlation (p < .05). If case variables were associated with HCC they were used as covariates in the main analysis. Samples were compared on stress-related variables using ANOVAs (PTSD symptoms, traumatic events, mental and perceived physical health, time since forced migration). Moreover, the association of HCC in segment 1 and segment 2 was checked using Pearson’s bivariate correlation.

Due to heterogeneity of variances in HCC data caused by a high variance in Asymmetry (Levene’s test p < .05), we (1) ran ANCOVAs without the IDP sample and (2) conducted separate non-parametric analyses with the IDP sample (Kruskal-Wallis-test on independent samples). Non-parametric analyses were performed on untransformed steroid values as normality is not required. In case of significant group differences, t-tests or corresponding non-parametric tests (Mann-Whitney U-tests) were conducted using immigrants as reference group.

Explorative analyses included correlations between steroids (Pearson’s bivariate correlations, two-sided, p > .05). The associations between HCC and stress-related variables (SF-12, PSS-10, PTSD-HTQ, Traumatic events, Time since migration) were tested using Pearson’s bivariate correlations (two-sided, p > .05). Bootstrapping was applied to increase the robustness of the test in a relative small sample with non-normal distributed variables (500 iterations, Bias-corrected 95% confidence interval).

Results

Preparatory analysis

The Kurdish immigrant control sample encompassed two sub-samples, namely former asylum seekers seeking...
protection in Germany, on average, 20 years ago \((n = 13)\) as well as non-refugee immigrants \((n = 25)\) who came to Germany, on average 16 years ago. We conducted a preliminary analysis to test if the latter two groups differed on HCCs, symptoms of PTSD and demographic variables. This was not the case \((p > .2)\), hence the two groups were merged to increase the statistical power \((n = 38)\).

The three remaining samples (immigrant controls, IDPs, asylum seekers) differed on PTSD rates, perceived stress, on their perceived physical and mental health, as well as on traumatic events (see Table 1). IDPs had the highest level of PTSD symptoms, the highest level of perceived stress and the highest trauma load, whereas immigrants scored lowest on the respective scales.

Group comparisons revealed that samples differed on three possible confounding variables, namely age, hair coloration and wearing a headscarf (see Table 1). However, only age was correlated with HCC \((r = .22, p = .04)\), while neither hair coloration \((t (73) = -1.25, p = .21)\) nor wearing a headscarf \((t (87) = -1.1, p = .29)\) were associated with HCC. Thus, only age was included as covariate in the subsequent main analysis.

HCC decreased significantly from segment 1 to segment 2, \(t (88) = 5.38, p < .001\). Due to this fact and the high correlation between HCC in both segments \((r = .83, p < .001)\) we focused on segment 1 (analysis of segment 2 can be found in Supplementary materials). HCC and cortisone (segment 1, log-transformed) were significantly correlated \((r = .82, p < .001)\), while DHEA was not associated with either \((p > .2)\).

**Group differences in steroid concentrations**

Asylum seekers had lower levels of HCC compared to immigrant controls, \(F (1, 70) = 4.70, p < .034, partial \eta^2 = .06\) (see Table 2 and Figure 1). The non-parametric analysis revealed group differences on hair cortisol as well, \(H (2) = 8.94, p < .01\). Again, asylum seekers had lower HCC than immigrant controls, \(U = 411.00, p < .01\), while IDPs did not differ from immigrants \((p > .2)\). Compared to immigrants, IDPs had a significantly lower cortisone concentration, whereas the DHEA concentration of IDPs was marginally higher than those of immigrants (see Table 2). Group differences for the measured steroids showed a similar pattern in segment 2 (see Supplemental Table 1).

**Exploratory analysis of association between HCC and stress-related variables**

Different associations between HCC and stress-related variables became apparent within samples (Table 3). Symptoms of PTSD were positively associated with HCC in IDPs \((p = .01)\) (see Figure 2). Similarly, perceived stress was positively associated with HCC in IDPs \((p = .04)\). Notably, PTSD symptoms were strongly associated with perceived stress \((r = .64, p < .001)\). Time since immigration was positively associated with HCC in immigrants \((p = .03)\). Moreover, the perceived physical health of asylum seekers was negatively associated with HCC on trend level \((p = .06)\). All other associations between HCC and stress-related variables were not significant \((p > .10)\).

**Discussion**

The aim of our study was to assess the usefulness of hair cortisol as a measure of chronic stress in populations affected by forced displacement. In order to account for different stress levels, we chose to compare two refugee samples—asylum seekers in Germany and internally displaced persons in Iraq with an immigrant sample in Germany from a similar region of origin. Two findings seem of particular relevance for the growing literature on biomarkers in chronically stressed populations: Lowered HCC in asylum seekers compared to immigrants, and a positive association between PTSD symptoms and HCC in internally displaced persons.

Our finding that HCC was lower in asylum seekers than in immigrants is in contrast to the findings by Mewes et al. (2017), who found elevated HCC in asylum seekers compared to native residents / immigrants in Germany. However, while both studies looked at asylum seekers and an immigrant control group, it is possible that the inconsistent findings can be explained by the time since immigration. The asylum seekers in the sample by Mewes et al. (2017) had arrived, on average, seven months ago, while the asylum seekers in our study had lived in Germany for almost two years. According to meta-analytic findings, the time passed since a major stressor occurred affects the cortisol reaction with elevated cortisol levels likely to occur shortly after the stressor (relative hypocortisolism) and to fall gradually below baseline thereafter (relative hypocortisolism) (Miller et al., 2007). A bi-phasic response might be caused by a hyper-sensitization of HPA-axis negative feedback loops due to chronically elevated cortisol levels, which could lead to a diminished cortisol secretion over time (Steudte-Schmiedgen et al., 2016). However, in the case of asylum seekers it is not easy to disentangle the time since the occurrence and the duration of experienced distress. For asylum seekers, not only the stressor before and during flight but also post-migration living circumstances (e.g., uncertainties regarding residence status) can severely affect their mental health (Müller et al., 2019; Porter & Haslam, 2005). These feelings of insecurity can in turn affect the cortisol secretion, as was shown for war-affected adolescents (Dajani et al., 2018). Interestingly, HCC was positively associated with time since immigration in our control group. This supports the notion that migration-related stress affects HCC, but it also points toward the capability of the HPA axis to recover from chronic stress and eventually return to baseline level. In our research design, the time since arrival is systematically entangled with experiencing stressful events. For instance, former asylum seekers are unlikely to experience the amount of insecurity associated with a recent asylum claim. Another factor which is confounded with time since immigration is the prevalence of PTSD. PTSD symptoms in traumatized individuals often remit decades after traumatic events (Chapman et al., 2012). Hence, it remains unclear whether relatively lower cortisol values in asylum seekers were caused by a more recent temporal distance to a series...
of traumatic events, by elevated PTSD rates, or by higher levels of perceived insecurity (or a mix of these factors).

To date, there is inconsistent evidence as to whether HCC is a valid biomarker for PTSD. To address this question, traumatized control groups are commonly compared to PTSD groups. While research on victims of a natural disaster indicate a specific PTSD effect on the HPA axis (Luo et al., 2012), studies on displaced populations are less conclusive. In line with our findings of higher HCC levels with a higher number of PTSD symptoms in internally displaced persons two studies on adolescents in war-affected populations reported elevated HCC in persons with PTSD (Steudte et al., 2011; Shaheen et al., 2018), whereas PTSD had no effect on HCC in asylum seekers (Mewes et al., 2017). A plausible explanation for this pattern is that the HPA axis might reflect psychological stress only in case of ongoing stress exposure—an interpretation supported by meta-analytic findings (Stalder et al., 2017). However, there are several reasons to question the specificity of HCC as a biomarker for PTSD. In one study on asylum seekers, HCC was associated with emotional problems but not with PTSD symptoms (Sierau et al., 2019). Similarly, we found that HCC was also associated with perceived stress. This lack of specificity of HCC as a biomarker might have its root in the broad detrimental effects of chronic stress on mental health (e.g., McEwen, 1998). Instead of representing a specific biomarker for PTSD, HCC

### Table 2. Cortisol, cortisone and DHEA concentration in hair of segment 1.

<table>
<thead>
<tr>
<th></th>
<th>IDP</th>
<th>Asylum seekers</th>
<th>Immigrant controls</th>
<th>Test-statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisol</td>
<td>7.54 (±9.82)</td>
<td>5.67 (±4.68)</td>
<td>8.64 (±7.91)</td>
<td>H (2) = 8.94, p = .01&lt;sup&gt;AI&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cortisone</td>
<td>9.63 (±6.64)</td>
<td>17.65 (±14.57)</td>
<td>24.31 (±21.93)</td>
<td>H (2) = 12.51, p = .002&lt;sup&gt;IC&lt;/sup&gt;</td>
</tr>
<tr>
<td>DHEA</td>
<td>17.91 (±11.31)</td>
<td>19.37 (±24.85)</td>
<td>10.66 (±4.49)</td>
<td>H (2) = 5.92, p = .05&lt;sup_IC&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Sample means of the cortisol, cortisone and dehydroepiandrosterone (DHEA) concentrations in pg/mg (Standard deviation). The first segment consists of the head-nearest 3 cm of hair and reflects the cumulative steroid concentrations of the previous 3 months. Test statistic refers to non-parametric Kruskal-Wallis test, upper letter indicate significant post-hoc pairwise comparison with immigrant sample as reference group. IDP: Internally displaced persons; n: number; AI: significant contrast between asylum seekers and immigrants; IC: significant contrast between IDPs and immigrants.

### Table 3. Bivariate correlations between HCC in segment 1 and stress-related variables within respective samples.

<table>
<thead>
<tr>
<th>Time since immigration (years)&lt;sup&gt;a,b&lt;/sup&gt;</th>
<th>HCC of IDPs</th>
<th>HCC of asylum seekers</th>
<th>HCC of immigrant controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>.66&lt;sup&gt;**&lt;/sup&gt;</td>
<td>−</td>
<td>.11</td>
<td>.38&lt;sup&gt;*&lt;/sup&gt;</td>
</tr>
<tr>
<td>.56&lt;sup&gt;**&lt;/sup&gt;</td>
<td>.11</td>
<td>.01</td>
<td>−.03</td>
</tr>
<tr>
<td>−.43</td>
<td>−.01</td>
<td>−.22</td>
<td>−.01</td>
</tr>
<tr>
<td>−.41</td>
<td>−.32</td>
<td>−.25</td>
<td></td>
</tr>
<tr>
<td>Traumatic events&lt;sup&gt;f&lt;/sup&gt;</td>
<td>−.22</td>
<td>−.25</td>
<td></td>
</tr>
</tbody>
</table>

HTQ-PTSD: Post Traumatic Stress Disorder scale of the Harvard Trauma Questionnaire; HTQ-Culture: PTSD-Scale of the HTQ supplemented by culturally adapted items; SF-12: short form health survey. Based on Pearson’s correlations (two-sided) with bootstrapped standardized errors (500 iterations, Bias-corrected 95% CI) *p < .05; **p < .01.

<sup>a</sup>Note that correlation cannot be calculated for IDPs as they arrived in the camp at the same time. Missing values were deleted list-wise. The respective number of pairwise deleted cases is indicated by uppercase numbers. <sup>b</sup>9 cases; <sup>c</sup>4 cases; <sup>d</sup>4 cases; <sup>e</sup>7 cases; <sup>f</sup>5 cases.

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**Figure 1.** Group differences in hair cortisol concentrations (HCC, log-transformed, pg/mg) in segment 1 (1.1–3 cm, on the left) and in segment 2 (4.6 cm, on the right) of immigrant controls, asylum seekers and internally displaced persons. Asylum seekers show lowered HCC in both segments compared to immigrant controls.
alterations could increase the risk to subsequently develop a PTSD (Steudte-Schmiedgen et al., 2015). Longitudinal studies on war-affected populations are needed here to address the question of whether and how alterations of the HPA axis functioning can set the stage for subsequent mental health problems. The fact that we assessed adults, whereas the majority of HCC studies with war-affected population encompassed children or adolescents, limits the comparability of the findings. Early life stress in war-affected populations was shown to alter the physiological stress-response system, e.g., by affecting the methylation pattern of genes (Perroud et al., 2014) or by affecting HPA axis reactivity (Schalinski et al., 2015). Future studies should aim at disentangling the effects of early life stress and later traumatic events in war-affected populations.

We also explored the feasibility of cortisone and DHEA as biomarkers for chronic stress, which have rarely been investigated in chronically stressed populations. In contrast to cortisol we found significantly lowered cortisone concentration in internally displaced persons compared to immigrants. While definite explanations are yet unclear, one interpretation is that extreme stress could affect the enzymatic process converting cortisone to cortisol (Poór et al., 2004). In line with a recent study on war-affected youth (Schindler et al., 2019) we found a trend for higher DHEA levels in internally displaced persons compared to immigrants. DHEA potentially has neuroprotective and antiglucocorticoid effects (e.g., Wolf & Kirschbaum, 1999) and might play a role in trauma recovery (Yehuda et al., 2006). The role of cortisone and DHEA as a reaction to chronic stress and their possible interference with the etiology of specific disorders need to be addressed in future studies.

Our study has a number of limitations. Firstly, the results need to be interpreted with care due to unclear migration-related effects. Immigrants showed lowered HCC in previous studies (Fischer et al., 2017; Mewes et al., 2017), which might be due to the living difficulties accompanying migration, e.g., discrimination, increased risk of poverty, or lack of social support. While our results suggest that the physiological effects of forced migration go beyond stressors of migration, consideration of a group of nonimmigrant residents would enable researchers to disentangle migration-related effects from traumatic experience in the context of forced displacement. A second concern refers to the unclear effect of physical health on HCC, as the variability between samples could also be explained by differences in the physical health status. Generally, somatic illness is not associated with HCC (Stalder et al., 2017). However, several diseases–most notably Cushing’s syndrome–severely affect the HCC (e.g., Wester & van Rossum, 2015). As far as we know, our samples did not include persons suffering from those diseases. However, our exclusion criteria were based on self-reports and should thus be treated with caution, particularly for internally displaced persons in Iraq, as they might be unaware of the disease due to limited access to medical care. The perceived physical health status we assessed was markedly lower in internally displaced persons. This is in line with studies showing a high comorbidity of PTSD and physical health in refugees (e.g., Berthold et al., 2014). The definite reasons for this association are still unclear, but one reason could be that the symptoms of PTSD to some extent overlap with subjective measures of physical health (e.g., shortness of breath). This might explain the negative association between perceived physical health and HCC in asylum seekers in our study (on trend level).

Figure 2. Association of PTSD symptoms (HTQ-PTSD scale) with HCC (log, pg/mg) in internally displaced women in Iraq. The PTSD scale represents the participants’ average score on the 16-items PTSD scale with a minimum value of 1 and a maximum value of 4. Values higher than two indicate a risk for PTSD. Higher PTSD symptoms were accompanied by higher HCC.
Instead of a somatic, stress-related effect, this association could reflect links between states of hyperarousal and HCC. Future studies should explore the relationship between physical diseases, mental disorders and chronic stress in vulnerable populations.

Apart from these limitations our study has a number of considerable strengths. It is among the few studies assessing HCC and its association with PTSD symptoms in war-affected populations, and to our knowledge the first to directly compare cortisol levels of different displaced groups, thereby enabling us to shed light on the effects of ongoing stress on HPA axis alterations. Moreover, our samples were culturally and ethnically less diverse than samples in previous studies, which minimizes the risk of cultural biases, e.g., eating habits or differences in hair growth between ethnic groups (Loussouarn, 2001).

To conclude, we found lowered HCC in asylum seekers compared to immigrants. Moreover, PTSD symptoms were positively associated with HCC in IDPs who were exposed to ongoing stress. Our findings illustrate the severe psychological consequences of forced displacement accompanied by HPA axis alterations even years after seeking protection in a secure host country. Novel insights into the biological underpinnings of mental health problems can help to identify groups which are at high risk for psychopathology, may make it possible to differentiate between biological subgroups underlying similar phenotypic psychopathologies, and could help to choose appropriate treatment strategies. The fact that experiences of forced migration leave long-term biological traces is a wake-up call to improve the psychological support for one of the most vulnerable groups in our societies.

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Disclosure of interest

No potential conflict of interest was reported by the author(s).

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