Recurrence of depression in relation to history of childhood trauma and hair cortisol concentration in a community based sample

Roman Duncko*[1, 2], Susanne Fischer*[4, 5], Stephani L. Hatch[1], Souci Frissa[6], Laura Goodwin[7], Andrew Papadopoulos[5], Anthony J. Cleare[3, 5], Matthew Hotopf[1, 3]

*shared first authorship

[1]Department of Psychological Medicine, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, SE5 8AF, UK

[2]Camden & Islington NHS Foundation Trust, St Pancras Hospital, 4 St Pancras Way, London, NW1 0PE, UK

[3]South London and Maudsley NHS Foundation Trust, Maudsley Hospital, Denmark Hill, London, SE5 8AF, UK

[4]University of Zurich, Institute of Psychology, Clinical Psychology and Psychotherapy, Binzmuehlestrasse 14 / Box 26, 8050 Zurich, Switzerland

[5]Centre for Affective Disorders, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, SE5 8AF, UK

[6]Health Service and Population Research, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, SE5 8AF, UK

[7]Department of Psychological Sciences, University of Liverpool, Liverpool, L69 7ZA, UK

Corresponding author: Dr Roman Duncko, PhD MRCPsych, Department of Psychological Medicine, Weston Education Centre, 10 Cutcombe Road, London, SE5 9RJ, United Kingdom, Tel.: +44 (0)7454832939, Email: roman.duncko@kcl.ac.uk

Abstract

Background: Childhood trauma represents a risk factor for developing depression with increased rates of recurrence. Mechanisms involved include a disturbed regulation of the hypothalamic-pituitary-adrenocortical (HPA) axis. Hair cortisol concentration (HCC) is a measure of long-term HPA axis activity with less interference from circadian and confounding factors. However, no study has so far used HCC to investigate the role of childhood trauma in recurrent pattern of depressive symptoms.

Methods: A community based sample of 500 participants was recruited and depression was assessed at three time points using the Revised Clinical Interview Schedule. The Childhood Trauma Questionnaire was administered to identify a history of childhood trauma. Hair samples were obtained from 144 participants for analysis of cortisol.

Results: Patients with Recurrent depression had higher rates of childhood trauma compared to participants with No depression. Participants with Current-only depression had increased HCC compared to the No depression group, while this was absent in participants with Recurrent depression. Within the depressed group (both Current-only and Recurrent depression), those with a history of childhood physical abuse had lower HCC when compared to those with no such history.

Conclusions: Our findings show that retrospectively reported childhood trauma is associated with protracted trajectories of depression and a distinct pattern of long-term HPA axis activity.

Keywords: childhood trauma; hair cortisol; life events; recurrent depression

Introduction

Depressive disorders are amongst the most common psychiatric disorders and remain one of the leading causes of disability worldwide [1]. To reduce patients' suffering as well as the economic burden, increasing emphasis has been given to risk factors associated with unfavourable outcomes of depression, such as chronicity or the high recurrence of depressive symptoms.

It is now widely accepted that trauma and stressful life events are strongly associated with the development of depression (see [2] for a recent review). Such associations have been documented in studies with retrospective assessment of childhood trauma [3] but also in studies using a prospective cohort design [4]. Increasing research interest has focused on links between childhood trauma and longitudinal characteristics of depression, such as chronicity and recurrence (see [5] for review and meta-analysis). A strong relationship has been reported between childhood trauma and earlier age of onset and greater number of depressive episodes [6], as well as chronicity of symptoms [7]. Together, these findings indicate that childhood trauma may be one of the risk factors involved in unfavourable outcomes of depression.

Extensive research has focused on neurobiological mechanisms linking childhood trauma and adult depression with emphasis on a disturbed regulation of the hypothalamic-pituitary-adrenocortical (HPA) axis [8]. Only a limited number of studies has investigated abnormalities of HPA axis regulation in subjects with an objective report of childhood trauma showing elevated salivary cortisol levels in children adopted from Romanian orphanages [9], as well as reduced basal and CRH stimulated HPA axis activity in girls with previously reported sexual abuse [10]. Studies investigating the association between retrospective reports of childhood trauma and HPA axis activity reported increased HPA axis activation during psychosocial stress but lower basal activity in depressed women [11], while others did not detect any difference in basal cortisol secretion in non-clinical groups with versus without a history of childhood trauma [12, 13]. One explanation for such discrepant findings may be methodological, in that different specimen were used to determine basal concentrations of cortisol (e.g., plasma, saliva, urine).

Most recently, hair cortisol concentrations (HCC) have gained interest in studying HPA activity in depression. Measurement of cortisol levels in hair reflects long-term levels of free plasma cortisol and is currently seen as a measure suitable to investigate the baseline HPA axis activity in mental disorders [14]. Only limited information is available on the relationship between hair cortisol concentrations and diagnosis of depression, with some reports showing increased hair cortisol levels [15, 16], others showing a lack of association with depression [17, 18], and yet others reporting attenuated levels of hair cortisol in depressed patients [19]. A possible explanation for such inconsistency is the hypothesized effect of childhood trauma on baseline HPA axis activity. Thus, a different proportion of patients with depression and history of childhood trauma in the comparison group could result in varying levels of hair cortisol concentrations in different studies. To date, there is only one published study evaluating this effect by measuring hair cortisol concentrations, reporting lower concentrations in depressed patients with a history of childhood trauma when compared to patients without reported childhood trauma [20]. This finding is in accordance with another study reporting an inverse relationship between hair cortisol concentrations and retrospective report of adverse childhood experiences [21], but more research is needed to replicate these findings in community based samples to support their generalizability.

Another important question is whether the change in HPA axis activity in subjects with a history of childhood trauma is associated with specific clinical outcomes, such as chronicity or recurrence of

depressive symptoms. To date, the only study investigating the association between longitudinal characteristics of depression and hair cortisol reported increased hair cortisol concentration in patients with a first episode of depression, but not in patients with recurrent depression [22]. No Information is available as to the rates of childhood adversity in the two depressed groups, so it remains unknown whether the observed difference in hair cortisol in recurrent depression might be related to a history of childhood adversity.

The aim of the present study was to test in a community-based sample whether a history of childhood trauma is associated with recurrence of depression identified through longitudinal follow-up. Hair cortisol concentrations were measured in a subsample of our participants to explore the role of altered HPA axis activity in moderating associations between childhood trauma and an unfavourable outcome of depression. Based on the above literature, we expected that participants with a history of childhood trauma would be more likely to experience a recurrent pattern of depression and that such a pattern would be linked to an absence of the increased hair cortisol concentrations.

Methods

Participants

Participants were recruited during phase 3 of the South East London Community Health (SELCoH) study. SELCoH was a community survey investigating the mental and physical comorbidity in participants from randomly selected households in the south London boroughs of Southwark and Lambeth. Participants aged 16 and over were recruited during phase 1 as described previously [23] and participated in clinical interviews including the assessment of common mental disorders (CMD). The follow-up for phase 2 was organized 8 months later and included a re-assessment of CMD (detailed in [24]). Nine months after participating in phase 2, a purposive subsample of 500 participants was recruited for phase 3 and participants attended further interviews to obtain information on sociodemographic and physical characteristics as well as a re-assessment of CMD. Participants in phase 3 were also interviewed regarding their history of traumatic life events and childhood trauma, and a proportion (144 participants) provided biological samples for analysis of hair cortisol concentrations. Of these, four participants were excluded due to reported use of systemic corticoid medication, one was excluded due to hair cortisol concentration beyond three standard deviations from the average without acceptable explanation and two participants did not complete all questionnaires required for the clinical characterisation and were excluded from the analyses. The study was approved by the King's College London research ethics committee, reference CREC/07/08-152 (phase 1) and King's College London Psychiatry, Nursing and Midwifery Research Ethics Committee, reference (PNM/10/11-106 for phase 2 and PNM/12/13-152 for phase 3).

Health and sociodemographic characteristics

Symptoms of depression and ICD-10 diagnoses were assessed using the Revised Clinical Interview Schedule (CIS-R, [25]). The CIS-R is a standardized interview designed for assessment of CMD indicated by the score ≥12 and algorithm allowing the ICD-10 diagnosis of depression and anxiety disorders. The diagnosis of depression by CIS-R during SELCoH phases 1, 2 and 3 was used to establish the longitudinal character of depression and assignment to 1 of the 4 groups: 1) No depression - no diagnosis of

depression at any of the 3 phases, 2) Past depression - history of depression at phase 1 or 2 but no current diagnosis of depression at phase 3, 3) Recurrent depression - diagnosis of depression at phases 1 or 2 as well as current diagnosis at phase 3, 4) Current-only depression - current diagnosis of depression at phase 3 but not at phases 1 or 2. Diagnosis of a comorbid anxiety disorder for evaluation of co-morbidity was assessed with the CIS-R administered at phase 3.

Presence of psychotic symptoms at phase 3 was assessed with the Psychosis Screening Questionnaire (PSQ, [26]). The PSQ is a 12-item questionnaire developed for screening of psychosis with a reported sensitivity and specificity of 96.9% and 95.3%.

Hazardous use of alcohol was assessed with the Alcohol Use Disorders Identification Test [27]. The AUDIT is a well-established 10-item questionnaire measuring alcohol consumption, dependence, and problematic behaviours related to alcohol use. The maximum attainable score is 40, with a cut-off of eight or more indicating hazardous drinking.

The presence of illicit drug use was screened with questions asking about the use of drugs during the previous twelve months including: cannabis, cannabis with tobacco, amphetamines, cocaine, ecstasy, hallucinogens, tranquilizers, opiates, khat, metamphetamine and legal highs. Current use of steroids, hormonal contraceptives and anxiolytic or antidepressant medications was assessed with the medication questionnaire designed for the SELCoH study. This was done by study personnel after participants had written down the names of their medication at home and brought this information to the study appointment. Fair or poor general health was self-rated with a single item question and presence of specific physical symptoms during the past four weeks was assessed with the Patient Health Questionnaire (PHQ-15, [28]. The PHQ-15 is a 15-item questionnaire developed for assessment of physical symptoms, with a Cronbach's alpha of 0.8. The presence of long-standing health problems was established with individual questions asking about asthma, chronic bronchitis, diabetes, stomach or other digestive disorder, liver disease, rheumatic disorder or arthritis, heart trouble, HIV, stroke, high blood pressure, migraine, epilepsy, gynaecological problem, cancer, kidney problem. Utilization of health services was assessed by asking about the number of visits for treatment or check-ups during the past twelve months.

Sociodemographic information was obtained using a computer assisted interview schedule administered by trained interviewers as described previously [23]. This included information on employment status, educational attainment, age, gender and ethnicity. Educational attainment was divided into no school qualifications or up to GCSE levels, A levels or vocational, and higher qualifications (three categories). Employment status was indicated as "not in regular employment" versus "in regular employment". Ethnicity was recorded based on UK Census categories: White British, Black African, Black Caribbean, Asian, and Other.

Childhood trauma and stressful life events

The short version of the Childhood Trauma Questionnaire [29] was used to ask about past experiences of abuse and neglect. The questionnaire distinguishes between five domains of trauma: emotional neglect, physical neglect, emotional abuse, physical abuse, and sexual abuse. Responses are indicated on a five-

point Likert scale (score range from 25-125). The mean of severity scores of childhood trauma was calculated from severity scores of the five domains of trauma.

Stressful life events were assessed by a list of 22 items that were based on Turner and Lloyd's 20 item list [30], the Life Events Questionnaire, and the List of Threatening Events. The list contained both traumatic and other life events. Participants indicated whether they had ever experienced the life event in question and whether this had been the case in the past twelve months. The count of traumatic and other life events during lifetime and past twelve months was calculated for each person.

Hair cortisol concentration (HCC)

Hair strands were taken from the posterior vertex of all consenting participants with a hair length of at least 3cm. Samples were stored in aluminium foil at room temperature. Three centimetres representing the past three months were cut off each sample and processed as described previously [31]. The Immulite Immunoassay analyser (www.diagnostics.siemens.com) was used to conduct immunoassays, as previously described [32]. The inter- and intra-assay variance of this assay is below 10%.

Data preparation and statistical analysis

Participants were assigned to one of the four diagnostic groups as described above (No depression, Past depression, Recurrent depression, Current-only depression). Differences in **sociodemographic as well as physical and mental health** variables were tested with univariate ANOVA (for continuous variables) or X^2 (for categorical variables). To test for differences between the Current-only and Recurrent depression group, Post-hoc tests were performed for dependent variables showing a statistically significant overall effect. Bonferroni correction was used to adjust the p level for multiple post-hoc comparisons. Variables with statistically significant or marginally significant effects ($p<0.1$) were used as confounders in subsequent analyses.

The mean score of **childhood trauma** was stratified into three categories (none, low, moderate to severe) according to published cut-off scores [29]. The association with current depressive symptoms and number of depressive episodes was initially tested with multiple regression adjusted for confounders identified in our study (age, education level, employment status) and reported in the literature (sex, ethnicity). To test the hypothesized association between reported childhood trauma and a recurrent pattern of depression, we designed a dummy variable combining the variables of current depression and past depression into the categories of No depression, Past depression, Recurrent depression, Current-only depression and used this as a predictor variable in the multinomial logistic regression adjusted for confounders identified in our study (age, education level, employment status) and reported in the literature (sex, ethnicity). To specifically test for the effect of recurrent depression , the Recurrent depression group was selected as the comparison group in the model.

Stressful life events variables were stratified into two categories: less than 5 versus 5 or more for lifetime occurrence; 0 versus 1 or more for occurrence during the past 12 months. The association of stressful life

events with the recurrent pattern of depression was tested with multinomial logistic regression adjusted for confounders as described above.

Due to a non-normal distribution, the **HCC** values were log-transformed for the purpose of statistical analyses, but untransformed values were used for presentation of results in the graph and table. The association with current depressive symptoms and number of depressive episodes was initially tested with a linear regression adjusted for confounders identified in the same sample and described previously (age, ethnicity, use of analgesic medications and hormonal contraceptives, season and use of heat-based hair treatments; [31]). To test the hypothesized association between HCC and recurrent pattern of depression, a dummy variable combining the variables of current depression and number of depressive episodes into the categories of No depression, Past depression, Recurrent depression, Current-only depression was used as a predictor variable in the multivariate linear regression.

To test the hypothesized association between **HCC and depression in context of reported childhood trauma**, we designed a predictor variable combining the childhood trauma and current-depression. For this analysis, the history of childhood trauma was dichotomized into 2 categories (no reported childhood trauma and low to severe reported childhood trauma) resulting in four categories: 1) No current depression and no childhood trauma, 2) no current depression and reported history of childhood trauma, 3) current depression and no childhood trauma, 4) current depression and reported history of childhood trauma.

Results

Sociodemographic characteristics according to diagnostic group

Participants with Current-only depression tended to be younger (mean age 40.6±14.82) than participants with No depression (48.34±15.96, ($F(3)=2.5$, $p=0.059$). There was no significant association between sex ($x^2(3)=3.78$, $p=0.29$) or ethnicity ($x^2(6)=2.37$, $p=0.88$) and diagnostic group. There was a significant overall effect of the level of education of participants ($x^2(6)=19.54$, $p=0.003$). Post hoc analysis revealed that the group with Recurrent depression ($x^2(2)=14.05$, $p=0.001$) but not the groups with Past depression ($x^2(2)=4.42$, $p=0.11$) or Current-only depression ($x^2(2)=5.11$, $p=0.078$) had lower educational attainment compared to the No depression group. There was a significant association between employment status and diagnostic group ($x^2(3)=11.74$, $p=0.008$). Participants with Recurrent depression were less likely to be employed compared to the No depression group ($x^2(1)=10.50$, $p=0.001$), but no such difference was observed for participants with Current-only ($x^2(1)=1.1$, $p=0.29$) or Past depression ($x^2(1)=1.93$, $p=0.16$, Table 1). None of the sociodemographic characteristics showed a difference between the Recurrent depression and Current-only depression group.

Clinical characteristics according to diagnostic group

There was a significant overall effect of group assignment on rates of depressive symptoms ($F(3)=314.9$, $p<0.001$), total CISR score ($F(3)=280.0$, $p<0.001$), rates of diagnosed anxiety disorder ($x^2(3)=216.81$, $p<0.001$), psychotic symptoms ($x^2(3)=70.34$, $p<0.001$), history of illicit drug use ($x^2(3)=9.32$, $p=0.025$) as

well as use of antidepressant and anxiolytic medication ($x^2(3)=73.12$, $p<0.001$) (Table 2). Post hoc analyses revealed that participants with Recurrent depression had overall higher rates of depressive symptoms (p=0.024) compared to participants with Current-only depression and this difference was most pronounced for the frequency of suicidal thoughts ($x^2(1)=3.64$, p=0.056) and depressive thoughts ($x^2(1)=3.33$, p=0.068). Participants with Recurrent depression also had a higher total CIS-R score reflecting their symptoms of depression and anxiety (p=0.013), higher rates of a comorbid anxiety disorder ($x^2(1)=3.39$, p=0.047) and positive screening for psychosis ($x^2(1)=9.71$, p=0.002) compared to participants with Current-only depression. There was no significant difference in the history of illicit drug use and use of antidepressant and anxiolytic medication between the Current-only and Recurrent depression group.

There was a significant overall effect of the diagnostic group on ratings of poor general health ($x^2(3)=67.46$, $p<0.001$), longstanding physical illnesses ($F(3)=18.48$, $p<0.001$), health care visits ($x^2(9)=34.22$, $p<0.001$) and overall physical problems (PHQ-15; $F(3)=52.8$, $p<0.001$) but not BMI (Table 3). Post hoc analyses showed that participants with Recurrent depression had more frequent self-reported poor general health ($x^2(1)=5.55$, p=0.018) and higher rates of long-standing physical illnesses (p=0.037) compared to participants with Current-only depression. There was no significant difference in number of health care visits and PHQ-15 score between the Current-only and Recurrent depression group.

Childhood trauma and stressful life events

The initial multiple regression showed significant association between childhood trauma and current depressive symptoms (β=0.05, p=0.006) and number of depressive episodes (β=0.15, p=0.005; R^2=0.14, $F(7, 468)=10.9$, p=0.0000). The multinomial logistic regression using the predictor variable combining current and past depression variables showed that participants in Past depression and Recurrent depression groups but not those in the Current-only depression group had higher multinomial odds ratios of childhood trauma than participants with No depression (Table 4) and this was most pronounced in the moderate to severe category. The Recurrent depression group also had higher multinomial odds ratio than participants with Current-only depression in the moderate to severe childhood trauma category.

A greater proportion of participants with Past depression or Recurrent depression reported stressful life events during lifetime compared to participants with No depression (Table 4). In addition, multinomial odds ratio of stressful life events during lifetime was higher in the Recurrent depression group when compared to the Current-only depression group. Ratio of stressful life events during the past year was elevated in participants with Recurrent as well as Current-only depression compared to the No depression group.

Hair cortisol concentration

The initial regression analysis showed only marginally significant association between HCC and current depression (β=0.61, p=0.07; R2=0.23, $F(9, 118)=3.93$, p=0.0002). The analysis using the predictor variable combining current and past depression variables showed that HCC was higher in the Current-only compared to the No depression group (β=0.87, p=0.034, R^2=0.23, $F(9,125)=4.23$, $p<0.0001$, Figure 1).

To allow analysis of the effect of self-reported childhood trauma and depression on HCC, participants were assigned to groups based on their depression status during the last assessment and the history of childhood trauma. The group with current depression with no history of childhood trauma but not the group with both current depression and history of childhood trauma had higher HCC than the group without current depression and no self-reported childhood trauma (β=0.94, p=0.032; R^2=0.24, F(9, 118)=4.18, p<0.0001).

Discussion

The present study reports that self-reported history of childhood trauma was associated with a pattern of recurring depressive symptoms in adulthood. These individuals with Recurrent depression did not exhibit the increased HCC levels seen in individuals with Current-only depression. Furthermore, individuals with both depression and reported history of childhood trauma did not have the increased HCC observed in the group with depression without history of childhood trauma.

The high proportion of recurrent depression in our sample is in line with the current understanding of the recurrent nature of depressive disorder in the majority of patients [33]. Demographic, physical and psychosocial characterisation of the current sample showed that recurrent depression was associated with lower educational attainment, higher unemployment and poorer general health with a larger number of longstanding physical illnesses. These findings are in agreement with reports of lower educational level in participants with chronic depression [7], as well as higher social and physical dysfunction predicting the recurrence of depressive symptoms [34]. Similar associations observed in a young adult sample were explained by family background and illness related experiences [35]. This indicates that the lower education level and higher unemployment may contribute to the pathogenesis and lead to recurrent problems but can also be a consequence of recurrence and/or chronicity of depression. The higher rates of depressive symptoms and comorbidity with anxiety disorders observed in our group with recurrent depression are in accordance with the literature [35, 7] and have previously been identified as risk factors for recurrence of symptoms [34]. Similarly, the trend for a higher frequency of suicidal thoughts and depressive thoughts in our participants with recurrent depression is in line with reports in younger adults and indicates a higher risk of self-harm in this subgroup [35].

Our findings also show a significant association between a reported history of childhood trauma and recurrent depression, with a dose-response relationship. These findings add to the literature describing the cumulative effect of childhood trauma on depression [36] and contribute to the very limited information available on association between childhood trauma and recurrent or chronic depression [7, 37].

Our study reports a significant association between recent stressful life events and current depression which is in accordance with the well-established effect of life events on occurrence of depressive episodes (see [38] for review). A significant amount of research has been dedicated to the differentiation of dependent and independent life events. It has been demonstrated that the presence of depressive symptoms and genetic risk factors can contribute to behaviours increasing the risk of so-called dependent life-events [39] and events that do not seem to be causally related to subsequent depressive episodes [40]. The lack of association between lifetime stressful events and Current-only depression observed in our study may be related to the fact that lifetime stressful events reported by our participants are likely

to include both dependent (i.e., events that are linked with depressive symptoms) and independent events. While new onset depression is expected to be associated with mainly independent events, recurrent depression is more likely to be associated with both dependent and independent events. This conclusion is supported by our finding that lifetime stressful events were associated with a history of depression in the past. Higher rates of lifetime stressful life events in the recurrent depression group may also reflect the chronicity of stressful experiences in accordance with the reported relationship between life events and severity and chronicity of depressive symptoms [41].

Our study is the first report of HCC in a community based sample of participants longitudinally assessed for depression. Our finding of higher HCC in the Current-only depression group is in line with the previous report from a clinical sample [22] and is likely reflecting the increased overall HPA axis activity. This is in support of the available literature on increased HPA axis activity in depression and may be due to the stressful effect of experienced symptoms as well as the hypothesized abnormal HPA axis feedback mechanisms [42]. In contrast to the group with Current-only depression, HCC in the group with Recurrent depression did not differ from participants with No depression. The fact that this group exhibited an absence of the increase in HPA axis activity despite the significant long-term psychological distress documented by high rates of symptoms and life events, is indicative of aberrant mechanisms regulating HPA axis activity. The design of our study allowed analysis of association with reported childhood adverse experiences and we found higher hair cortisol concentrations in participants with depression and no history of childhood trauma but not in those with depression and a history of childhood trauma. Our finding of absence of increased hair cortisol concentrations in this group is in support of the theory that childhood trauma during a sensitive age period can interfere with the HPA hyporesponsive period with subsequent abnormal basal or stress related HPA axis activity [43]. This can be related to a specific disturbance of mechanisms regulating stress response with an increase in central HPA activity followed by a subsequent peripheral desensitisation at the pituitary or adrenocortical level. Increased central HPA axis activity with higher expression of CRH has been reported in women with a history of childhood abuse [8]. The hypothesized peripheral hypocortisolism is in accordance with findings in animal models of early life stress [44], findings of reduced cortisol secretion in groups with history of early life stress [45, 46], reports of reduced adrenocortical activation during psychological stress [47, 48, 49] or pharmacological challenge [50]. Such mechanism could explain a more recent report of reduced hair cortisol in patients with depression [51] and the role in mediating the effects of childhood trauma on development of externalizing symptoms [52]. Such counter-regulatory changes at the peripheral level could further enhance the disinhibition of central CRH pathways interfering with the regulation of emotions and contributing to the occurrence and persistence of depressive symptoms [42].

The findings reported in our study need to be interpreted in the context of several limitations. Our study employed a prospective follow-up design to ascertain the longitudinal course of depressive symptoms. In contrast, the history of childhood trauma was assessed retrospectively, using the standardized Childhood Trauma Questionnaire and was therefore subject to possible recall bias likely to be present in patients with current depressive symptoms [53]. Such bias could have affected comparison between groups with and without depression, as well as between the Current-only and Recurrent depression groups due to the higher severity of depressive symptoms in the latter group. However, our results also showed higher rates of reported childhood trauma in participants with past history of depression but no current diagnosis identified at the time of completing the Childhood Trauma Questionnaire. This indicates that our finding of higher rates of reported childhood trauma in participants with recurrent depression cannot be fully attributed to their higher severity of depression. Furthermore, the Childhood Trauma

Questionnaire has been extensively tested for validity and reliability. This included studies using an independent source of information about trauma [54], as well as follow-up repeated assessment [55]. The number of participants included in the hair cortisol analyses was not sufficient for evaluating the combined effect of childhood trauma and recurrence of depression on hair cortisol concentrations and further research is needed to confirm and expand our findings. As discussed previously [31], participants providing the hair sample for HCC analysis were mostly of White British ethnicity, female gender and middle to older age group, which may have affected some of the associations between age, gender, ethnicity and HCC. To identify the impact on the associations between childhood trauma/stressful events and depression the analyses reported in Table 4 were repeated for the subsample of participants providing the hair sample and the associations were of same direction and similar effect size (data not shown) as reported in this study.

In conclusion, this is the first study investigating the role of long-term HPA axis activity in the relationship between childhood trauma and unfavourable outcomes of depression. Our findings show an association between specific etiological factors (childhood trauma), time course of depressive symptoms (chronicity or recurrence) and physiological profile (relative peripheral hypocortisolism). While the community character of our sample allows some degree of generalization of our results, further research is needed to provide more detail on possible neuroendocrine mechanisms involved and their impact on response to treatment.

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Table 1: Sociodemographic characteristics of participants.

Diagnostic groups	**No depression**	**Past depression**	**Recurrent depression**	**Current-only depression**
	N=359 (73.9%)	N=55 (11.3%)	N=46 (9.5%)	N=26 (5.4%)
Age				
mean (SD)	48.34 (15.96)	49.42 (15.82)	45.65 (13.52)	40.62 (14.82)
Gender				
female N (%)	197 (55%)	32 (58.2)	32 (69.6)	16 (61.5)
Ethnicity:				
White	255 (71)	37 (67.3)	32 (71.1)	21 (80.8)
Black	67 (18.7)	10 (18.2)	9 (20)	3 (11.5)
Other	37 (10.3)	8 (14.6)	4 (8.9)	2 (7.7)
N (%)				
Education attainment:				
Up to GCSEs	75 (20.9)	17 (30.9)	19 (41.3)	10 (38.5)
A level/vocational	75 (20.9)	14 (25.4)	13 (28.3)	6 (23.1)
Higher education	209 (58.2)	24 (43.6)	**14 (30.4)***	10 (38.5)
N (%)				
No paid employment				
N (%)	116 (32.3)	23 (41.8)	**26 (56.5)***	11 (42.3)

Statistical significance of post-hoc tests: * - $p<0.05$ compared to participants with No depression.

Table 2: Clinical characteristics of participants.

Diagnostic groups	**No depression**	**Past depression**	**Recurrent**	**Current-only**
Depressive symptoms Total				
Mean (SD)	0.71 (1.11)	1.74 (1.59)	5.87 (1.3)	**5 (1.65) #**
Total CISR score				
Mean (SD)	3.55 (4.24)	8.73 (6.51)	24.89 (9.08)	**20.85 (7.55) #**
Diagnosis of anxiety disorder				
N (%)	18 (5)	9 (16.4)	38 (82.6)	**16 (61.5) #**
Positive screening for psychosis				
N (%)	13 (3.6)	3 (5.45)	17 (37)	**1 (3.8) #**
Hazardous use of alcohol				
N (%)	78 (21.7)	17 (30.9)	10 (21.7)	7 (26.9)
History of illicit drug use				
N (%)	73 (20.3)	16 (29.1)	14 (30.4)	11 (42.3)
Use of antidepressant or anxiolytic medication				
N (%)	24 (6.7)	13 (23.6)	22 (47.8)	9 (34.6)

Statistical significance of post-hoc tests: # - $p<0.05$ comparing the Current-only depression group with Recurrent depression group.

Table 3: Physical health characteristics of participants.

Diagnostic groups	**No depression**	**Past depression**	**Recurrent**	**Current-only**
BMI				
Mean (SD)	29.92 (5.18)	27.73 (6.13)	28.69 (6.89)	28.58 (6.96)
Poor general health				
N (%)	3 (0.8)	4 (7.27)	12 (26.1)	**1 (3.8)#**
Number of long-standing physical illnesses				
Mean (SD)	0.98 (1.4)	1.58 (1.8)	2.7 (2.4)	**1.65 (1.6)#**
Number of places visited for checkup or treatment during last 12 months				
0	83 (23.1)	11 (20)	3 (6.5)	3 (11.5)
1-2	228 (63.5)	32 (58.2)	27 (58.7)	14 (53.8)
3-4	38 (10.6)	5 (9.1)	11 (23.9)	8 (30.8)
5 or more	10 (2.8)	7 (12.7)	5 (10.9)	1 (3.8)
N (%)				
Physical problems during past 4 weeks (PHQ-15 score)				
Mean (SD)	4.44 (3.5)	7.05 (4.5)	11.04 (5.7)	9.88 (4.4)

Statistical significance of post-hoc tests: # - $p<0.05$ comparing the Current-only depression group with Recurrent depression group.

Table 4: Childhood trauma and stressful life events. Multinomial odds ratios (MOR) from a logistic regression model adjusted for age, gender, ethnicity, education level and employment status.

	Past depression	**Recurrent**	**Current-only**	**Recurrent vs. Current-only**
	MOR (95% CI)	MOR (95% CI)	MOR (95% CI)	MOR (95% CI)
CTQ Mean Severity Score				
low	1.8 (0.8-4.1)	**5.2 (2.3-11.8)***	2.5 (0.9-6.6)	2.1 (0.7-6.6)
moderate to severe	**5.9 (2.4-14.6)***	**10.6 (4.1-27.5)***	0.8 (0.1-7.1)	**12.4 (1.4-109.1)#**
Stressful Life Events - lifetime				
5 or more	**1.89 (1.05-3.4)***	**3.58 (1.8-7)***	1.25 (0.5-2.9)	**2.85 (1.03, 7.9)#**
Stressful Life Events – last year				
1 or more	1.75 (0.98-3.1)	**2.64 (1.3-5.2)***	**2.62 (1.1-6.2)***	1.01 (0.4-2.8)

Statistical significance: * - $p<0.05$ compared to No depression group, # - $p<0.05$ Current-only group compared to Recurrent depression group.

Table 5: Hair cortisol concentrations (pg/mg) by current depression and history of childhood trauma.

Diagnostic groups		**No current depression**		**Current depression**	
		No childhood trauma	**History of childhood trauma**	**No childhood trauma**	**History of childhood trauma**
CTQ Mean Severity Score	N,	85,	28,	8,	9,
	Mean±SD	386.7±450	231.8±241.1	**790.8±733***	458.2±506.2

Statistical significance from a linear regression model adjusted for age, season, ethnicity, use of analgesic medications and contraceptives and use of heat based hair treatments: * - $p<0.05$ compared to the group with no current depression and no history of childhood trauma, # - $p<0.05$ compared to participants with current depression without the history of childhood trauma.

Figure 1: Hair cortisol concentrations in pg/mg analyzed by diagnostic group. Data shown as mean ± SEM. Statistical significance from a linear regression model adjusted for age, season, ethnicity, use of analgesic medications and contraceptives and use of heat based hair treatments: * - $p<0.05$ compared to the No depression group.