

Callous–unemotional traits in conduct disorder in relation to salivary cortisol level

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Objectives

To show the correlation between items of Callous Unemotional Inventory (CUI) and Conduct Disorder and to assess correlation between salivary cortisol and Conduct Disorder.

Background

Emerging evidence suggests that low levels of cortisol may act as a biological marker for the Callous Unemotional traits (CU Traits) subgroup of Conduct Disorder.

Materials and methods

The current study tested the presence of items of Callous Unemotional Inventory (CUI) and the salivary cortisol level among group of patients with Conduct Disorder (Forty patients from 12 to 16 years old, diagnosed according to criteria of DSM IV and recruited from Kasr El Aini Psychiatric hospital) and group of control (Forty healthy volunteers). Both groups were subjected to Callous Unemotional traits Inventory and salivary cortisol level was assessed using ELISA.

Results

Patient group showed high levels of CU traits compared to control group. Patient group showed significant difference in salivary cortisol level (mean is 3.188 ± 1.1108) compared to control group (mean is 5.01 ± 1.846). This study found correlation between Callous traits and severity of Conduct Disorder.

Conclusion

The current findings build upon recent research in suggesting that low cortisol level may be a biological marker for patients with Conduct Disorder and high levels of CU traits.

Keywords:

callous–unemotional traits, conduct disorder, disruptive disorder, salivary cortisol

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Introduction

Conduct disorder (CD) is highly prevalent during childhood and early adolescence, characterized by a repetitive and persistent pattern of behavior that violates the rights of others or in which major age-appropriate societal norms or rules are violated (Sourander *et al.*, 2007).

Childhood-onset CD is distinguished by the presence of significant levels of callous–unemotional traits (CUI), characterized by a lack of guilt, lack of concern about the feelings of others, lack of concern about performance in important activities, and shallow or deficient affect (Hare and Neumann, 2006). The estimated prevalence of high CUI in youth with CD ranges from 10–46% in community samples to 21–59% in clinic samples (Kahn *et al.*, 2012).

Cortisol is an emotional or stress reactivity hormone that indexes activity in the hypothalamic–pituitary–adrenal (HPA) axis. A previous research revealed the relation between HPA-axis abnormalities and antisocial and aggressive behavior. Some evidence suggests that low cortisol levels may serve as a biological marker for a severe

antisocial subgroup with pronounced CUI (Loney *et al.*, 2006).

Aim

The aim of this study was to assess items of CUI and the salivary cortisol level in a group of patients with CD and a group of controls, to show the correlation between items of CUI and CD and to assess the correlation between salivary cortisol and CD.

Patients and methods

This is a cross-sectional case–control study. After taking approval from the hospital Scientific and Ethical Committee, forty patients having the diagnosis of Conduct Disorder diagnosed according to DSM IV, were recruited from the Child and Adolescent Psychiatric outpatient clinic Kasr el Aini hospitals

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through the period from September 2013 till March 2014. The participants were divided into two groups (groups A and B). Group A consisted of 40 patients diagnosed with CD according to *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. (DSM-IV) using a diagnostic tool Kiddie-SADS-Present and Lifetime (K-SADS-PL) from the Child and Adolescent Psychiatric outpatient clinic from Kasr El Aini University Hospitals (also specific learning disorder as a comorbid condition was diagnosed according to the criteria of DSM-IV because K-SADS-PL does not include the diagnosis of this disorder). Group B consisted of 40 controls (healthy volunteers among relatives of medical and paramedical personnel staff of Kasr Al-Aini University Hospital). All scales show absence of psychopathology in the control group. The control group was matched in age and sex to exclude their possible confounding effect on the cortisol level. Both sexes were included. Their ages ranged between 12 and 16 years. Informed oral and written consent were taken from parents of all participants included in this study. Patients with mental retardation and patients on corticosteroid therapy or other hormonal treatments were excluded. Substance abuse disorder comorbidity was excluded in the patient group as it may affect cortisol level and substance abuse may result in aggression.

When selecting controls, family members of patients, although available, were excluded so as to avoid the possibility of cortisol changes as possible biological factors in disruptive behavior disorder, as serum cortisol levels in the first-degree relatives were significantly higher than that in healthy controls.

The two groups were subjected to the following: (a) the K-SADS-PL, which is a semistructured diagnostic interview designed to assess current and past episodes of psychopathology in children and adolescents according to the DSM-IV criteria; (b) the inventory of callous-unemotional traits (ICU), for assessment of four items of CUI (careless, unemotional, uncaring, and callous traits); and (c) laboratory investigations: salivary samples for cortisol level assessment were collected and preserved at -20°C in the clinical laboratories of clinical pathology Department of Fayoum University Hospitals. Free cortisol levels were assessed using enzyme-linked immunosorbent assay DRG (DRG International, Inc., USA; 841 Mountain Ave, Springfield Township, (Newjersey) NJ07081, USA) Salivary Cortisol enzyme-linked immunosorbent assay.

Statistical analysis

Data were statistically described in terms of mean $\pm$ SD, median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical

variables between the study groups was made using Student's *t*-test for independent samples for comparing two groups when normally distributed and the Mann-Whitney *U*-test was used for independent samples when not normally distributed. Comparison of numerical variables between more than two groups was made using the Kruskal-Wallis test with post-hoc multiple two-group comparisons. For comparing categorical data, the χ^2 -test was performed. An exact test was used instead, when the expected frequency was less than 5. Correlation between various variables was made using Spearman's rank correlation equation. *P* values less than 0.05 were considered statistically significant. All statistical calculations were carried out using the statistical package for the social science (SPSS, version 15 for Microsoft Windows; SPSS Inc., Chicago, Illinois, USA) computer program.

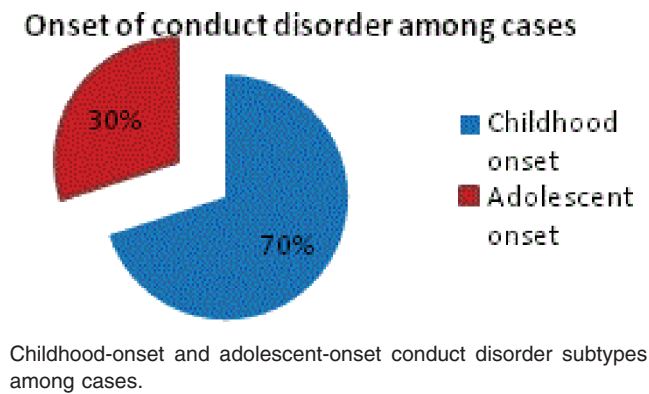
Results

The participants were divided into two groups, groups A and B. Group A consisted of 40 patients diagnosed with CD and group B consisted of 40 controls. Table 1 shows

Table 1 Some demographic data and clinical characteristics of the study participants

	Case (n=40)	Control (n=40)
Age (mean $\pm$ SD)	13.95 $\pm$ 1.568	13.18 $\pm$ 1.259
Sex [n (%)]		
Male	28 (70)	24 (60)
Female	12 (30)	16 (40)
Level of education		
Illiterate	6 (15)	0 (0)
Read and write	3 (7.5)	9 (22.5)
Primary school	4 (10)	4 (10)
Preparatory school	15 (37.5)	18 (45)
Secondary school	12 (30)	9 (22.5)
Nature of occupation		
Student	31 (77.5)	40 (100)
Skillful jobs	6 (15)	2 (5)
Nonskillful job	9 (22.5)	0 (0)
School achievement (mean $\pm$ SD)	45.6 $\pm$ 28.09	
Punishment [n (%)]		
Suspended	8 (20)	
Corporal punishment	28 (70)	
Never	4 (10)	
School attendance		
Going to school		
Regular	12 (30)	
Irregular	19 (47.5)	
Not enrolled in school	9 (22.5)	
Family history of externalizing disorder		
Antisocial personality disorder	12 (30)	
Attention deficit hyperactivity disorder	4 (10)	
Conduct disorder	9 (22.5)	
Oppositional defiant disorder	9 (22.5)	

Figure 1



some demographic data and clinical characteristics of the study participants as regards age, sex, educational level, occupation, school attendance, and family history of externalizing disorder.

On clinical assessment of cases using the K-SADS-PL, 70% ($n=28$) were diagnosed as having childhood-onset CD subtype, whereas 30% ($n=12$) were diagnosed as having adolescent-onset CD subtypes (Fig. 1). Summary of various symptoms of CD (present and past history of threshold symptoms diagnosed according to the K-SADS-PL) in the case group is presented in Table 2.

Items of ICU were compared between the case and control groups. Fig. 2 shows that the four items of ICU (careless traits, unemotional traits, callous traits, and unemotional traits) were statistically significantly higher in the case group than in the control group ($P \leq 0.000$). However, on comparing items of CUI between cases of childhood-onset CD and adolescent-onset CD, Fig. 3 shows that there was no significant difference in items of ICU between cases of childhood-onset type of CD and cases of adolescent-onset type of CD.

On comparing salivary cortisol level between the case and control groups, Fig. 4 shows that salivary cortisol level among participants of the case group was lower than that in the control group. The difference was statistically significant ($P \leq 0.000$). As regards sex differences in salivary cortisol level in the case group, Fig. 4 shows that there was no statistically significant difference between male (mean salivary cortisol level was 3.214 ± 1.1362) and female patients (mean salivary cortisol was 3.125 ± 1.095) ($P=0.896$).

As regards sex differences in items of ICU in the case group, Fig. 5 shows that there was no significant

Table 2 Summary of various symptoms of conduct disorder (present and past history of threshold symptoms diagnosed according to the Kiddie-SADS-Present and Lifetime in the case group)

Symptoms of conduct disorder (present and past history of threshold symptoms diagnosed according to the Kiddie-SADS-Present and Lifetime in the case group)	<i>n</i> (%)	Present history [<i>n</i> (%)]
Lies	30 (75)	38 (95)
Truant	28 (70)	34 (85)
Initiates physical fights	25 (62.5)	33 (82)
Bullies, threatens, intimidate other	23 (57.5)	31 (77.5)
Nonaggressive stealing	31 (77.5)	40 (100)
Vandalism	8 (20)	12 (30)
Breaking, entering	0 (0)	3 (7.5)
Aggressive stealing	2 (5)	2 (5)
Fire setting	16 (40)	27 (67.5)
Often stay out at night	16 (40)	25 (87.5)
Ran away over night	9 (22.5)	28 (70)
Use a weapon	1 (2.5)	9 (22.5)
Crutely to person	22 (55)	38 (95)
Forced sexual activity	0 (0)	2 (5)
Crutely to animals	11 (27.5)	22 (55)

Figure 2

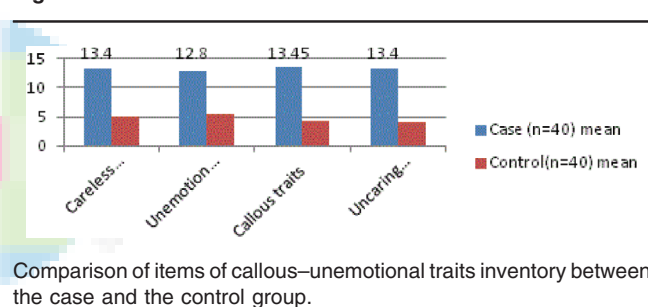
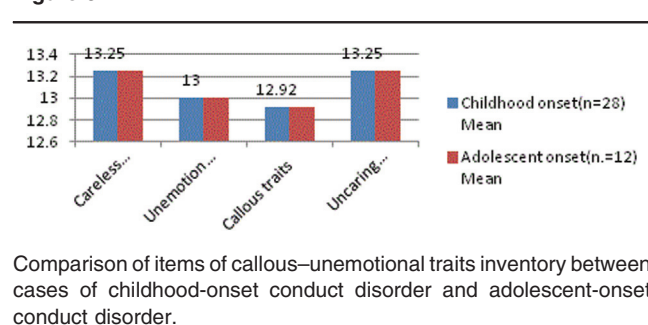


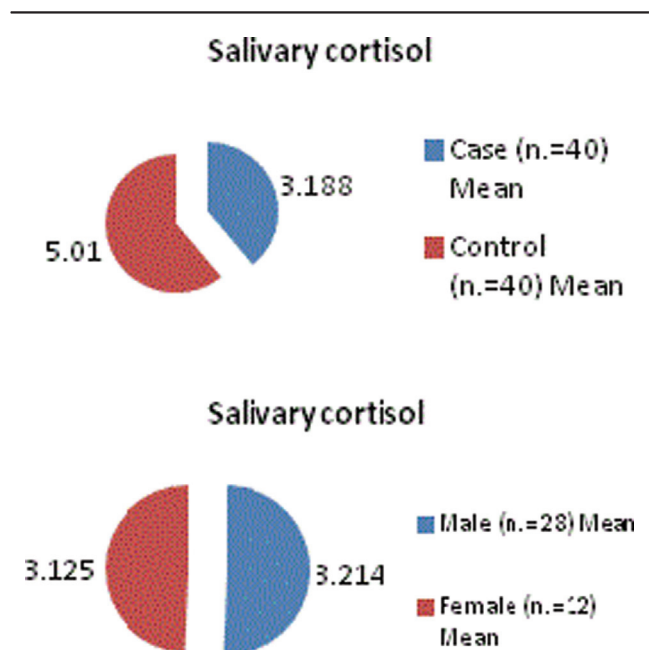
Figure 3



difference between male and female patients with respect to items of ICU.

On studying the correlation between items of ICU and age of onset of CD and salivary cortisol level, Table 3 shows that there was no significant correlation between items of CUI and age of onset of CD. Moreover, there was no significant correlation between items of CUI and salivary cortisol level.

Figure 4



Comparison of salivary cortisol between both the case and the control group and sex difference in salivary cortisol level in the case group.

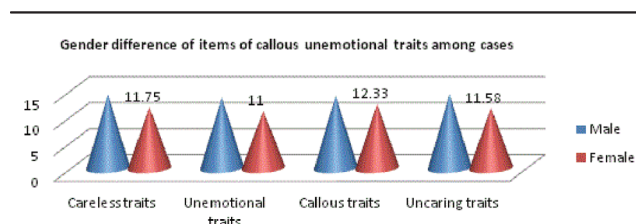
Discussion

In this study, participants between 12 and 16 years of age were selected. This is guided by studies in the literature that studied aggression in adolescents with conduct problems (Waldman *et al.*, 2011), and studies using the self-report of ICU (Forsman *et al.*, 2008). The factor structure of ICU has been tested in a large community sample of German adolescents between 12 and 18 years of age (Essau *et al.*, 2006) and a moderately sized sample of juvenile offenders between 12 and 20 years of age in the USA (Kimonis and Frick, 2011).

In total, 70% of patients were male and 30% were female (Table 1). This is consistent with the findings of Keith and Kathleen (2005), who found that boys show approximately three to four times higher rates of CD compared with girls. The sex difference can be attributed to the more consistent parental expectations and reinforcement of girls and more unresponsive and rejective parenting of boys; in addition, greater predispositions toward responding in more aggressive ways to boys' behavior compared with girls' behavior may be a contributing factor.

In this study, 70% ($n=28$) of cases were diagnosed as having childhood-onset CD subtype, whereas 30% ($n=12$) of cases were diagnosed as having adolescent-onset subtype. Such subtyping was supported by the research by Moffitt *et al.* (2008), who defined meaningful groups of CD according to age as follows: childhood-onset CD, characterized by the presence of at least one

Figure 5



Sex difference in items of callous-unemotional traits in the case group.

Table 3 Correlation between the items of callous-unemotional traits inventory and the age of onset of conduct disorder and salivary cortisol level)

Callous-unemotional traits	Age of onset of conduct disorder	
	<i>R</i>	<i>P</i> value
Careless traits	-0.250	0.197
Unemotional traits	-0.113	0.489
Callous traits	-0.248	0.123
Uncaring traits	-0.209	0.195

Callous-unemotional traits	Salivary cortisol	
	<i>R</i>	<i>P</i> value
Careless traits	-0.0118	0.468
Unemotional traits	-0.13	0.423
Callous traits	-0.045	0.782
Uncaring traits	-0.19	0.239

symptom before the age of 10 years, and adolescent-onset CD, characterized by appearance of symptoms after the age of 10 years.

The finding of this study supported that there was an increase in the percentage of symptoms from past to present history, which may indicate the progressive course of CD. It is in line with the findings of Moffitt *et al.* (2002), who found that children often begin showing mild conduct problems as early as preschool or early elementary school and their behavioral problems tend to increase in rate and severity throughout childhood and into adolescence, and that they continue to show antisocial and criminal behavior into adulthood. Conduct problems can also be aggravated by interpersonal problems within family and school and poor outcome in school achievement, which may be a cause and a result for symptom progression.

This study found that the case group showed significantly higher values in the four items of ICU compared with the control group. It is consistent with the findings of Frick and Dickens (2006), who reviewed 24 published studies using child or adolescent samples in which either psychopathic traits in general, or CUI

specifically, were associated with more severe conduct problems.

CUI were important for designating a more severe (Christian *et al.*, 1997) and stable (Frick *et al.*, 2005) pattern of antisocial behavior within children who showed serious conduct problems. Moreover, Kahn *et al.* (2012) suggested that the proposed callous-unemotional (CU) specifier would designate between 10 and 32% of children with CD in the community sample. Further, the base rates of the CU specifier and the individual CU symptoms were fairly low in children without CD.

This is consistent with the findings of Frick (2012), who indicated that between 20 and 50% of children with serious conduct problems exhibit non-normative levels of CUI. This subgroup of youths with severe conduct problems and elevated CUI seem to exhibit a more severe and stable pattern of antisocial behavior compared with other youths.

In a national representative sample ($n=5326$) of children between 5 and 16 years of age, Rowe *et al.* (2009) reported that 46% of children with CD had high rates of CUI, and those with CUI showed a more stable pattern of CD.

It is consistent with the findings of Larson and Lochman (2003), Taylor *et al.* (2003), Viding *et al.* (2007), Bezdjian *et al.* (2011), and Waldman *et al.* (2011), who found an association between CUI and conduct problems, and also found that unique genetic influences both constructs and supports partially distinct etiological underpinnings.

Accumulating evidence indicates that youth with elevated CUI are at risk for exhibiting severe and persistent antisocial behavior, even after controlling for co-occurring disruptive behavior disorder symptoms (Pardini and Fite, 2010).

In this study, difference in salivary cortisol level between cases and controls was statistically significant ($P \leq 0.000$) (in the case group salivary cortisol level ranged from 1.9 to 6.2, with a mean of 3.188 ± 1.1108 , whereas in the control group salivary cortisol level ranged from 2 to 8.5, with a mean of 5.01 ± 1.846).

This finding is consistent with that of Alink *et al.* (2008), who examined data from 82 studies conducted between 1978 and 2006. The results supported an inverse relationship between cortisol and antisocial behavior – that is, the development of antisocial behavior is associated with low cortisol levels.

The finding of this study is not consistent with that of Sondejker *et al.* (2007), who indicated that, in a large representative general population sample of preadolescent boys and girls, the association between disruptive behaviors and indices of the basal HPA-axis functioning were weak, and not always in the direction expected. To explain discrepancies with previous studies, the severity of problems in high-risk groups versus general population samples could be of importance. In clinical samples, problems are more severe and likely to have persisted for several years before referral to mental health services takes place. Hence, the HPA-axis may have become less sensitive to stress. As a result, in these individuals, much more stress may be needed to activate the HPA-axis, which would result in decreased basal levels of cortisol (underarousal) in individuals with severe disruptive behaviors. Such a phenomenon might play a less important role in the general population (Van de Wiel *et al.*, 2004).

This study found that there was no significant correlation between items of CUI and age of onset of CD. It is not consistent with the findings of Pardini *et al.* (2006), who found that CUI seem to further delineate childhood-onset CD cases that are more likely to persist in their antisocial behavior into adulthood. There also appears to be unique causal factors underlying the conduct problems found in children with CUI, such as low temperamental fear. This may be attributed to the small sample size of this study and usage of the self-report of the ICU, and not only the teacher-reported or the parent-reported ICU.

The presence of CUI seems to be more highly associated with the childhood-onset conduct problems (Silverthorn *et al.*, 2001). However, these traits seem to designate a more severe, chronic, and aggressive subgroup within this trajectory, and a subgroup with distinct temperamental characteristics (Frick, 2006).

It is not in line with other studies that reported that CUI were more common in youths with childhood-onset to their antisocial behavior compared with those with an adolescent-onset type (Dandreaux and Frick, 2009).

In this study, there was no correlation between items of ICU and salivary cortisol. It is not consistent with the findings of Stadler *et al.* (2011), who found that CU+ patients with disruptive behavior problems showed a blunted cortisol reactivity to stress. The strengths of latter study were the large sample size, use of multiple informants to assess disruptive behaviors, and

assessment of three cortisol measures on relevant time points during the day.

This is not in line with previous results reporting blunted HPA-axis function in a nonreferred adolescent sample with high CUI, which was not observed in those without high CUI (Loney *et al.*, 2006). This can be attributed to the small sample size of this study and assessment of only one sample of salivary cortisol without stress provocation. Barry *et al.* (2003) explained that stress sensitivity may be a key factor in the link between HPA-axis functioning and disruptive behaviors.

In this study, there was no significant difference in cortisol level between male and female patients in the case group. This is contradictory to the findings of Bryan *et al.* (2006), who reported the absence of a statistically significant CU-low cortisol relation for female participants (in contrast to male CUI with conduct problems) and that female CUI with conduct problems may not be associated with cortisol abnormalities. It is important to note that it would not entirely rule out an emotional under-reactivity component to female psychopathy, which may be attributed to various biological, cognitive, emotional, and behavioral responses that subsume a fear response, and it is possible that male psychopathy is simply more robustly tied to low emotional reactivity (i.e. across a number of indices such as passive avoidance impairment, heart rate, hormone, and skin conductance findings).

It is not consistent with the findings of Keith and Kathleen (2005), who found that girls had higher cortisol levels compared with boys. Netherton *et al.* (2004) suggested that gonadal steroids might play an important role in this finding. Gonadal steroids, and estrogens in particular, are known to interact with the HPA-axis. Increased HPA-axis activity in girls might be related to the direct effect of estrogens on corticotropin-releasing hormone Vanyukov *et al.* (1993).

According to Sondejker *et al.* (2007), sex interaction effects were found, indicating that associations between cortisol levels and disruptive behaviors were different in boys versus girls.

Higher rates of CD problems were associated with higher morning cortisol levels in girls and lower cortisol levels in boys. The finding that lower cortisol levels in boys were associated with higher levels of CD problems

is in accordance with previous studies (McBurnett *et al.*, 2000).

For instance, estrogens, which are known to influence HPA-axis activity, might play a role (Vanyukov *et al.*, 1993).

The small sample size of the participants and the small number of female participants could support this inconsistency.

Future research could compare and contrast resting hormone levels to hormone levels assessed following perceived threat or emotional provocation. This provocation might exacerbate group differences and/or suggest important contextual variables related to underlying emotional impairments (Bryan *et al.*, 2006).

In this study there was no significant difference in items of ICU between male and female patients in the case group. It is not consistent with the findings of Essau *et al.* (2006), who found that boys had significantly higher scores on ICU, both for total and subscale scores. Moreover, the finding of this study is not consistent with past research indicating that men tend to score higher than women on all dimensions of psychopathy, including the CU dimension (Vitacco *et al.*, 2006). The small sample size of the participants and the small number of female participants could support this inconsistency.

Conclusion

It is important to study items of CUI in patients with CD and its relation with cortisol level. The patients with CD show high levels of CUI compared with normal children and adolescents. The level of cortisol is lower in patients with CD than in the control group. There was no correlation between cortisol level and items of CUI. There was no correlation between the age of onset of CD and items of CUI.

Limitations of the study

The data collection was confined to specific age group among cases of CD (aged 12–16) in whom the ICU could be applied. The number of participants interviewed was small, as the patients who met the inclusion criteria (cases of CD aged 12–16) were few as their parents consider that their treatment would not be promising and so do not seek medical advice. Another obvious limitation of the study was the use of only self-reported inventory, and so data may not be enough to generalize the current results into larger scale. The cross-sectional study together with number of

participants may not be enough to generalize the current results to the population-based cases.

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Conflicts of interest

There are no conflicts of interest.

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