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Research Article

Functional Magnetic Resonance Imaging Brain Study in Children with Conduct Disorder: An Observational Case-Control Study

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Abstract
Background: Conduct disorder (CD) is a psychological condition characterized by a persistent and recurrent pattern of violating the basic rights of others, along with disregarding important social norms or rules during the developmental stages of childhood or adolescence. This study aimed to compare functional magnetic resonance imaging (FMRI) brain scans of children diagnosed with conduct disorder to those of a matched control group, to determine whether any observed changes correlate with developmental or sociodemographic factors, and to explore the relationship between these changes and the symptom profiles of the patients.
Methods: This Observational Case-Control Study involved 50 male participants, comprising 25 children with conduct disorder and 25 controls, all aged between 7 and 12 years, who were recruited consecutively. The subjects were categorized into two equal groups: the Conduct Disorder group, children without comorbidities, specifically those exhibiting at least one symptom indicative of CD prior to reaching the age of 10, while the control group consisted of healthy children who had no previous occurrences of neurological or psychiatric conditions.
Results: Comparison patients with control showed that degree of activation in the regions of interest (ROI) showed significant increase activation in Bilateral Amygdala and Rt insula while Lt insular was non-significant. Additionally, there was significant increase in activations in ROI while both orbitofrontal cortex activities were non-significant. Fractional Anisotropy (FA) of examined tracts showed significant ($P< 0.05$) decrease in all examined tracts. Multiple linear regression analysis was done to test if the changes in brain activation and the tract integrity could predict the degree of callous unemotional traits. Both amygdala, insula, prefrontal cortex (both ventromedial and dorsolateral) and anterior cingulate cortex activities exhibited strong negative correlations with the severity of Callous Unemotional traits. Regarding DTI, both uncinate fasciculus integrity measured by FA affection showed strong negative correlations with the severity of Callous unemotional traits.
Conclusions: A positive correlation between Callous Unemotional Traits scores and duration of illness was found in patients' group. The higher callous unemotional traits were, the less brain activity in Regions of Interest and the less tracts integrity were detected.

Keywords: Functional Magnetic Resonance Imaging Brain, Children, Conduct Disorder, Regions of Interest, Fraction Anisotropy

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Introduction:

Conduct disorder (CD) is a psychological condition marked by a consistent and ongoing pattern of infringing upon the fundamental rights of others as well as significant societal norms or regulations during the developmental stages of childhood or adolescence. Those affected by CD may display aggressive behavior towards individuals or animals, engage in the destruction of property, demonstrate deceitful conduct, commit theft, and violate important rules[1].Conduct disorder (CD) is recognized as one of the most prevalent psychiatric conditions in children, posing significant societal and economic challenges, while also increasing the risk of developing antisocial personality disorder in adulthood [2]. The societal ramifications of CD are profound, as it is often associated with a range of negative mental and physical health outcomes, in addition to a reduced quality of life[3].

An expanding array of research has uncovered a neurobiological basis for conduct disorder, particularly focusing on brain areas involved in emotional processing [4]. Individuals diagnosed with CD exhibit deficits in fear conditioning and facial expression recognition, as well as diminished startle responses [5]. Subsequent research has linked these deficits to the amygdala and prefrontal cortex[6]. Additionally, functional magnetic resonance imaging (FMRI) studies reveal that male adolescents diagnosed with conduct disorder (CD) exhibit abnormal neural responses in these regions when presented with emotional facial expressions [4]or emotional imagery [7]. In alignment with these findings, structural MRI investigations have shown diminished gray matter volumes in the amygdala, anterior insula, and orbitofrontal cortex (OFC) in adolescents with CD relative to their healthy counterparts [8].

Studies have demonstrated that the uncinate fasciculus (UF), which serves as the principal fiber tract connecting the amygdala and the adjacent anterior temporal lobe to the orbitofrontal cortex (OFC), displays microstructural irregularities in both adults diagnosed with psychopathy [9] and adolescents with conduct disorder (CD) [10]. A comprehensive review of the functional neuroimaging studies pertaining to CD has uncovered unusual activation patterns in populations exhibiting antisocial behavior[11] , particularly in the medial temporal lobe (notably the amygdala) and prefrontal areas (such as the anterior cingulate)[12, 13], in addition to the orbitofrontal cortex [14, 15].

We hypothesized that the brain of children with CD is different from normal individuals, moreover, we hypothesize that connection among brain regions is also different.

The aim of this work was to compare Functional MRI Brain study of children with CD with matched control group and to see if these changes is associated with any developmental or sociodemographic variables and to see the association of these changes with the symptoms profile of patients.

Methods:

This observational, case control study was carried out on 50 male children (25 children with Conduct Disorder and 25 controls), aged between 7 and 12 years, The individuals in the Conduct Disorder group displayed at least one symptom characteristic of Conduct Disorder (CD) prior to the age of 10, indicating childhood-onset traits. and without any comorbid conditions. The sample of our study are recruited consecutively through convenient sampling from the children population of Gharbia governate catchment area of approximately 500000 children, in which those with conduct disorder represents about 8% [16]. EPI INFO Calculator assuming confidence level was 80 %, with 5% accepted margin of error (MOE) and design effect was 1. This gives sample size of 48 children from which 25 continued to the end of the study. The other 23 due to different reasons (10 children refused to complete the MRI examination and 13 children gave unreliable psychometric information. These 25 control cases were recruited from family member of the studied patients this makes them motivated to share in the study after explaining to the nature and aim of the study. Acceptance of parents to preform MRI was not easy and we spent a lot of time to explain the nature of the procedure to the parents and to assure the children. Also, the parents gave a written informed consent after they showed their willingness to perform the procedure.

They underwent a task-based Functional BOLD MRI and Diffusion Tensor Imaging examination.

Inclusion criteria were Age: 7-12 years, all persons included in this study are males, child must be able to comprehend and perform study related information or tasks and child parents have a willingness to complete study procedures and able to provide written informed consent.

Exclusion criteria were history of hypoxic-ischemic events, central nervous system infections, children with other comorbid psychiatric disorders, unstable serious medical illness like epilepsy, congenital anomalies, cerebrovascular diseases, and autoimmune diseases, evidence of structural brain injury detected on MRI, intellectual disability (IQ less than 70) and relative and absolute contraindications to MRI examinations.

This research was carried out from October 2021 to October 2023, after receiving approval from the Ethical Committee at Tanta University Hospitals in Tanta, Egypt.

All participants underwent a series of assessments, which included:

1. A detailed psychiatric history and mental status examination, complemented by a comprehensive physical and neurological assessment. A clinical evaluation for Conduct Disorder (CD) was conducted utilizing a validated Arabic version of the Mini International Neuropsychiatric Interview for Children and Adolescents, referred to as "M.I.N.I-Kid" [16, 17]. This assessment aimed to collect clinical data and to exclude any psychiatric disorders in the control group participants. The diagnosis was made according to the DSM-5 criteria for Conduct Disorder.

2. **Psychometric tools were used to assess the following:**

a. Socioeconomic status (SES) by El-Gilany and EL-Wasify scale [18].

b. The intelligence quotient (IQ) was evaluated using the validated Arabic version of the Stanford-Binet test, specifically the fourth edition [19, 20]. This assessment was employed to gauge the IQ of participants, thereby establishing their overall intelligence level and excluding individuals with intellectual disabilities from both the patient and control groups.

c. Child behaviors by the Arabic version of CBCL Questionnaire For ages 6-18years were used to evaluate child psychopathology [21, 22].

d. The Inventory of Callous Unemotional Traits (ICU), developed by Frick [23] and subsequently validated in Arabic by Azzam [24], measures callous and unemotional characteristics through a 24-item questionnaire. This instrument aims to deliver an in-depth evaluation of such traits.

3. Radiological Imaging: all participants examined by FMRI in Radiology Department -Tanta University by using a 1.5 Tesla machine (GE HealthCare, Sigma HDX., WI) including task based FMRI using visual stimuli material and Diffusion Tensor Imaging. To mitigate any possible influences of medication, the fMRI experiment was conducted promptly following the confirmation of the diagnosis of CD. All patients examined by Functional MRI paradigm using block design (alternating action and rest tasks) were used to explore brain regions activity in response to viewing negative emotional pictures to explore functional alteration in CD. Prior to the implementation of functional imaging techniques, negative images were standardized in terms of their content, complexity, luminance, color schemes, and the presence of human figures, faces, and animals. Pictures included represent symptoms of CD in the form of initiates physical fights, violence against others, stealing with confronting a victim, truancy from school, using a weapon that can cause serious physical harm to others and engaged in fire setting. Participants were informed that the purpose of the study was to examine brain activity associated with the observation of the images shown to them, and they were directed to focus intently on all presented images. During the scanning process, participants were secured with bitemporal pressure pads and viewed images from the Open Affective Standardized Image Set (OASIS). The images were displayed on a screen positioned three meters away from the scanner and were observed through a mirror mounted above the head coil.

Statistical analysis

The data collected were systematically organized, tabulated, and subjected to statistical analysis utilizing IBM® SPSS statistical software, version 27 (Statistical Package for Social Studies), developed by IBM in Chicago, Illinois, USA. To evaluate the normality of the dataset, the one-sample Kolmogorov—Smirnov test was utilized, which confirmed the parametric nature of the data. For the numerical variables, we computed the range, means, and standard deviations. The independent Student's t-test was employed to assess the differences between two mean values, while One-way ANOVA was applied for comparisons involving more than two groups. For categorical variables, we calculated the counts and percentages, and the differences among subcategories were analyzed using chi-square test. To assess the correlation between variables, Pearson's correlation coefficient (r) was used. Additionally, linear regression analysis was performed to estimate risk and identify predictor variables, with a significance threshold established at $p<0.05$. Multiple linear regression analysis is a statistical method that examines the relationship between a dependent variable and one or more independent variables, offering insights into the strength of these relationships.

Results

Sociodemographic data of our sample showed non-significant differences between patient and control group in age, residence, father 's occupation, parents' education. However there are statistically significant differences between studied groups regarding, mother 's occupation, and child abuse by their family ($p<0.05$). (Table 1)

Clinical assessment reported that the IQ of children with conduct disorders is lower that of control group with significant differences in IQ between patient and control group (p= 0.001*) (Table2).

There was 25(100%) of the patients complained of repeated lying and the majority of the patients 22(88%) complained of physical assault, 20(80.0%) complained of breaking the rules, truancy and stealing without confronting a victim, 17(68%) running from home, 14(56%) complained of property destruction,11(44%) had physical cruel to animals 9(36%) use a weapon and 6(24%) had force sexual offence. The mean duration of illness was 3.68± 1.030 years (Table 3).

Inventory of Callous Unemotional traits (ICU) score of patients and control groups showed that significantly higher score in patients than control (p= 0.001*), this is positively correlated with the duration of illness. (Table 3)

Psychometric evaluation of children's behaviour by CBCL showed statistically significant lower scores in CD children regarding social competence, school competence, total competence and scholastic achievement. ($p<0.05$). scores of exeternalizing problems including breaking rules, aggressive behavior and social problems were more in patients than control group which means that Patients with conduct disorder were complaining about externalizing problems rather than internalizing problems. Patients with conduct disorders had poor relationships with others than control as shown from were statistically significant differences in relations to teachers & school mates and parents & siblings (p<0.001).

The degree of activation in all regions of interest (ROI) is higher in patients with conduct disorder than control cases. The observed increase in activation was statistically significant in the right and left amygdala, the right insula, both hemispheres of the ventromedial prefrontal cortex, the dorsolateral prefrontal cortex, and both anterior cingulate cortices (see Table 4). A negative correlation was found between the activation levels of the ROI and the degree of callous-unemotional traits (refer to Table 6). Additionally, the investigation into fasciculus anisotropy indicated a significant reduction (P < 0.05) in both the left and right uncinate fasciculus, the inferior longitudinal fasciculus, and the inferior fronto-occipital fasciculus (illustrated in Table 5) Fig 1. Significant negative correlation between the degree of tracts integrity affection measured by Fractional Anisotropy (FA) with the mean of Inventory of Callous Unemotional traits (ICU) score among patients' group (Table 6).

Multiple linear regression analysis was done to test if the changes in brain activation and the tract integrity could predict the degree of callous unemotional traits. We applied model in which the score of the inventory of callous unemotional traits score is a dependent variable and the ROI activity and FA of examined tracts mentioned before as independent variable. Sociodemographic data as cofounding variables. The model summary for the predictor factors affecting the severity of Callous Unemotional Traits indicated that the regression model accounted for approximately 15.7% of the variance in the severity of the traits, as evidenced by the R^2 value of 0.157 (Table 6).

The results of the analysis showed the negative significant associations with several brain regions and tracts, highlighting their potential roles in influencing these callous unemotional traits. Notably, both amygdala, insula, prefrontal cortex regions (both ventromedial and dorsolateral) and anterior cingulate cortex activities exhibited strong negative correlations with the severity of Callous unemotional traits. Regarding DTI, both uncinate fasciculus integrity measured by FA affection showed strong negative correlations with the severity of Callous unemotional traits. This suggests that reduced activity in these areas and decreased FA of both uncinate fasciculus might be linked to heightened severity of these traits (Table 7).

In contrast, both orbitofrontal cortex and several tracts integrity (specifically for the inferior longitudinal and fronto-occipital fasciculi) did not demonstrate significant relationships with the severity of these traits. This implies that these regions and tracts might not play as critical a role in this context (Table 7).

Discussion

Conduct disorder (CD) is a psychiatric condition marked by a consistent and repetitive pattern of infringing upon the fundamental rights of others, as well as breaching significant societal norms or regulations during the developmental stages of childhood or adolescence. Those diagnosed with CD may display behaviors such as aggression towards individuals or animals, destruction of property, deceit, theft, and serious rule violations [1]. This disorder ranks among the most common psychiatric issues in children and is linked to considerable economic burdens on society, alongside an elevated risk of developing antisocial personality disorder in later life [26].

A notable negative correlation was observed between the activation levels in the specified brain regions and the mean ICU score, except the right and left orbitofrontal cortex, where no significant correlation was found. This suggests that patients diagnosed with conduct disorder (CD) who exhibit high levels of callous-unemotional traits demonstrate little to no activation in the targeted brain areas, whereas those with low levels of such traits show pronounced activation in these regions.

This finding aligns with previous research on CD, which indicates an inverse relationship between callous-unemotional traits and neural responses in affective-motivational areas [27].

Additionally, individuals exhibiting reactive aggression (RA) display heightened responses in these regions compared to those with lower aggression levels [7]. Supporting this notion, a preliminary investigation by Decety et al. [28] revealed that patients with early-onset CD lacking callous-unemotional traits exhibited increased activation in the relevant brain regions.

Callous unemotional traits were also shown to be associated with a reduced treatment response and poorer clinical outcomes. Moreover, CU traits are linked to impaired empathy and neurocognitive dysfunctions in emotion [29].

The functioning of brain regions is inherently interconnected, as they are components of broader brain systems. Therefore, it is essential to explore the white-matter pathways that link various brain regions in individuals with conduct disorder (CD). Our hypothesis posits that the neurological architecture of children diagnosed with CD differs from that of typically developing individuals, and we further suggest that the interconnections among brain regions are also altered. We focused on three specific tracts: the uncinate fasciculus, the inferior longitudinal fasciculus, and the inferior fronto-occipital fasciculus, to evaluate the integrity of these pathways by measuring Fractional Anisotropy (FA). In comparison to the control group, the patients exhibited a significant reduction in FA across all assessed tracts, including the uncinate fasciculus, inferior longitudinal fasciculus, and inferior fronto-occipital fasciculus (P < 0.001*). This research focused on three specific neural tracts due to the observation that individuals diagnosed with conduct disorder (CD), who largely exhibited no other psychiatric disorders, showed deficits in FA within the primary pathways that connect the frontal and temporal lobes. These pathways are often reported as abnormal in functional neuroimaging studies involving both adolescent and adult populations exhibiting antisocial behavior, such as the uncinate fasciculus. Furthermore, we hypothesized that FA irregularities would also be present in tracts that connect the frontal lobe to other brain regions, such as the inferior fronto-occipital fasciculus, as well as in those linking the temporal lobe to various areas, including the inferior longitudinal fasciculus.

Additional research corroborates our hypothesis, revealing that the uncinate fasciculus displays microstructural abnormalities in adults diagnosed with psychopathy [30].

The observed reduction in FA values may be attributed to accelerated atypical maturation processes, which could also account for the diminished FA values within the same white matter tract [30]. Conversely, efforts to replicate these findings in individuals diagnosed with Conduct Disorder through tractography techniques have either revealed no abnormalities in the uncinate fasciculus or indicated an increase in FA [31]. The uncinate fasciculus is particularly susceptible during the early stages of life; factors such as premature birth, early social deprivation, and elevated levels of parental verbal abuse have been linked to lower FA in white matter pathways, which may have long-term implications for the development of antisocial behavior starting in childhood [32]. The relationship between the FA values of the examined tracts and the mean score on the Inventory of Callous-Unemotional Traits (ICU) revealed a significant negative correlation. This suggests that patients with Conduct Disorder exhibiting pronounced callous-unemotional traits demonstrate a substantial decrease in the integrity of these tracts (indicated by the lowest FA values), whereas those with Conduct Disorder and lower callous-unemotional traits show less impairment in tract integrity (characterized by intact or mildly attenuated tracts). This finding aligns with the work of Haney-Caron et al. [33] which indicated that higher counts of Conduct Disorder symptoms corresponded with lower FA, suggesting increased microstructural disorganization within white matter.

A multiple linear regression analysis was conducted to examine whether variations in brain activation and tract integrity could serve as predictors for the extent of callous-unemotional traits. In this model, the score from the inventory measuring callous-unemotional traits was designated as the dependent variable, while the activity in regions of interest (ROI) and fractional anisotropy (FA) of the previously mentioned tracts were treated as independent variables. Sociodemographic factors were included as confounding variables. The findings revealed that the functional activity of the right and left amygdala, the right and left insula, both the ventromedial and dorsolateral prefrontal cortex regions, as well as the right and left anterior cingulate cortex, exhibited significant negative correlations with the intensity of callous-unemotional traits. In agreement with Aggensteiner et al., [34] who showed that increased CU traits were associated with amygdala hypoactivation, and that only patients with low CU traits showed increased amygdala activity to negative faces and Jiang et al., [35] showed that male adolescents with CU traits exhibited reduced amygdala efficiency compared to controls.

It was found that decreasing activity with increasing CU traits has also been observed in the anterior cingulate cortex (ACC) [36].

Furthermore, diffusion tensor imaging (DTI) results indicated that the FA of the uncinate fasciculus also showed strong negative correlations with the severity of these traits. This suggests that reduced activity in these specific brain regions, along with lower FA in the uncinate fasciculus, may be linked to a heightened severity of callous-unemotional traits. Additionally, Fairchild et al. [8] found that regression analyses performed on individuals with conduct disorder indicated a negative correlation between conduct disorder symptoms and the volume of the right insula. One of the recent structural MRI studies showed that both types of aggression negatively correlated with the left amygdala volume [37]. In agreement with Naaijen et al., [38] who found that amygdala volumes have been reported to negatively correlate with proactive aggression but positively with reactive aggression [39].

Limitations of this study: the sample size in this study was relatively limited, consisting solely of male children, which may restrict the applicability of our findings to female children. The diversity among participants concerning sociodemographic and clinical characteristics could potentially influence the outcomes. Additionally, the constraints of our facilities, such as utilizing a 1.5 Tesla MRI rather than a 3 Tesla MRI, may have affected the results. In some instances, functional MRI examinations were repeated due to participants' mild movements after reassurance. Some participants experienced panic attacks during the MRI scans, as the machine used was a closed type rather than an open MRI. Some children were dropped during our study for different reasons, as a result of their phobia from closed MRI device, their excessive movement which unavoidable and difficult dealing with them. Our research did not explore whether the observed differences in brain activation are indicative of the patients' current conditions or represent long-term traits, a limitation attributed to the extensive follow-up time required and the funding necessary for repeated imaging after symptom resolution. We employed a passive viewing paradigm, which has been shown to more consistently activate the amygdala compared to paradigms that incorporate cognitive elements. For instance, it remains unclear whether the images elicited stronger aversive associations and memories in children with conduct disorder (CD) compared to the control group. Furthermore, while poor performance and low motivation in children with CD cannot be entirely dismissed, this interpretation does not align with our findings of heightened activation in limbic regions. Lastly, there was a noted trend indicating a discrepancy in intelligence, with boys diagnosed with CD displaying lower IQ scores than their healthy counterparts, which may influence our results.

Conclusions:
A significant positive correlation was identified between Callous Unemotional Traits scores and the duration of illness within the patient group. Specifically, as the levels of callous unemotional traits increased, a corresponding decrease in brain activity in Regions of Interest and reduced integrity of neural tracts was observed.

List of abbreviations
CD: Conduct disorder
DTI: Diffusion Tensor Imaging
FA: Fractional Anisotropy
ICU: Inventory of Callous Unemotional Traits
MRI: Magnetic Resonance Imaging
OASIS: Standardized Image Set
OFC: Orbitofrontal Cortex
ROI: Regions of Interest
UF: Uncinate Fasciculus

Declaration

Ethics approval and consent to participate
This research was carried out from October 2021 to October 2023, after receiving approval from the Ethical Committee at Tanta University Hospitals in Tanta, Egypt.

Consent for publication
An informed written consent was obtained from all patients.

Availability of data and material
Data and material are available on a reasonable request from the author.

Competing interests
The authors have no financial or proprietary interests in any material discussed in this article.

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Authors' contributions
RAE, EAG and AAM supervised the study; KEAEE and AEH were responsible for data collection. RAE analyzed and interpreted the data. All authors provided comments on the manuscript at various stages of development. All authors read and approved the final manuscript.

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Table 1: Socio demographic data of studied groups

		Patient group (n=25)	**Control group (n=25)**	P
Age (years)		10.72±1.275	10.48±1.388	0.52
Residence	**Rural**	19(70.0%)	13(52.0%)	0.07
	Urban	6(24.0%)	12(48.0%)	
SES	**Very low**	6(24.0%)	1(4.0%)	**0.001***
	Low	12(48.0%)	3(12.0%)	
	Intermediate	6(24.0%)	15(60.0%)	
	High	1(4.0%)	6(24.0%)	
Father's occupation	**Unemployed**	7(28.0%)	2(8.0%)	0.081
	Governmental Job	9(36.0%)	16(64.0%)	
	Self-employed	7(28.0%)	7(28.0%)	

	Died	2(8.0%)	0(0.0%)	
Mother's occupation	**Housewife**	16(64.0%)	7(28.0%)	**0.013***
	Governmental Job	5(20.0%)	15(60.0%)	
	Self employed	4(16.0%)	3(12.0%)	
Parents Education	**Illiterate**	7(28.0%)	3(12.0%)	0.31
	Intermediate institutes	13(52.0%)	14(56.0%)	
	High education	5(20.0%)	8(32.0%)	
Family Type	**Nuclear**	15(60.0%)	24(96.0%)	**0.002***
	Extended	10(40.0%)	1(4.0%)	
Marital status of parents	**Married**	15(60.0%)	24(96.0%)	**0.001***
	Divorced	8(32.0%)	1(4.0%)	
	Widowed	2(8.0%)	0(0.0%)	
Child abuse by their families	**No abuse**	4(16.0%)	20(80.0%)	**0.001***
	Physical	12(48.0%)	5(20.0%)	
	Psychological	5(20.0%)	0(0.0%)	
	Sexual	2(8.0%)	0(0.0%)	
	Neglected	2(8.0%)	0(0.0%)	

Data are presented as mean ± SD or frequency (%). * Significant p value < 0.05, SES: Socioeconomic status.

Table 2: Intelligence Quotient (IQ) of the patients and the control groups.

		Patient group (n=25)	**Control group (n=25)**	P
IQ	**Borderline**	14(56.0%)	1(4.0%)	**0.001***
	Low Average	6(24.0%)	5(20.0%)	
	Average	5(20.0%)	16(64.0%)	
	High Average	0(0.0%)	3(12.0%)	

IQ: Intelligence Quotient. Data are presented as frequency (%). * Significant p value < 0.05.

Table 3: The mean of duration of illness and symptoms of CD group

		N=25	
Duration of illness (years)		3.68± 1.030	
Symptoms of CD	**Force Sexual offence**	6(24.0%)	
	Breaking the rules	20(80.0%)	
	Property destruction	14(56.0%)	
	Repeated lying	25(100.0%)	
	Truancy	20(80.0%)	
	physically cruel to animals	11(44.0%)	
	Physical Assault	22(88.0%)	
	Run away from home	17(68.0%)	
	Use of a weapon	9(36.0%)	
	Stealing without confronting a victim	20(80.0%)	
Inventory of Callous unemotional traits score (ICU)	**Patient group (n=25)**	**Control group (n=25)**	P
	47.28±14.438	22.64±1.753	**0.001***
Duration of illness			
Callous Unemotional Traits	**Pearson Correlation ®**	**0.844******	
	P	**0.001***	
	N	**25**	

Data are presented as mean ± SD or frequency (%), CD: Conduct disorder, ICU: Inventory of Callous Unemotional traits. * Significant p value < 0.05.

Table 4: Comparison of mean degree of regions of Interest in patients and control groups

Mean degree of Regions of Interest (ROI) activity	Patient (n=25)	Control (n=25)	T Test for equality of means			95% CI	
			T	P	Mean difference	Lower	Upper
Rt Amygdala	0.32±0 .217	0.14±0.05	2.863	**0.009***	0.18	0 .162	0.270
Lt Amygdala	0 .34±0 .23	0.17±0.103	3.210	**0.002***	0.16	0.062	0.270
Rt insula	0 .17±0.25	0.10±0.10	2.830	**0.007***	0.158	0.045	0.271
Lt insula	0.23±0.27	0.07±0.11	1.325	0.191	0.068	-0.03-	0.173
Rt VM prefrontal cortex	0 .31±0 .22	0 .20±0.08	2.15	**0.003***	0.10	0.006	0.199
Lt VM prefrontal cortex	0 .30±0 .22	0 .15±0 .12	2.84	**0.007***	0.14	0.04	0.248
Rt DL prefrontal cortex	0 .38±0 .17	0 .15±0 .11	5.41	**0.001***	0.22	0.14	0.313
Lt DL prefrontal cortex	0 .40±0 .19	0 .16±0.11	5.47	**0.001***	0.24	0.15	0.338
Rt OFC	0.04±0.09	0.08±0.12	1.49	0.14	-0.04	-0.10-	0.015
Lt OFC	0.04±0.09	0.08±0.12	1.51	0.13	-.004-	-0.10-	0.015
Rt Anterior cingulate cortex	0.35±0.19	0.08±0.12	5.62	**0.001***	0.026	0.16	0.355
Lt Anterior cingulate cortex	0.40±0.17	0.09±0.12	7.08	**0.001***	0.31	0.22	0.399

Data are presented as mean ± SD. *Significant p value< 0.05, Lt: left, Rt: right, CI: confident interval, ROI: Regions of Interest, OFC: orbitofrontal cortex.

Table 5: Comparison of Fractional Anisotropy of examined tracts in patients and control groups

Fractional Anisotropy (FA) of examined tracts	Patient (n=25)	Control (n=25)	T Test for equality of means			95% CI	
			T	P	Mean difference	Lower	Upper
Right Uncinate Fasciculus	0 .35± 0.04	0 .44±0.01	-8.85	**0.001***	-0.09	-0.11	-0.07
Left Uncinate Fasciculus	0 .35±0.05	0.44±0.01	-9.01	**0.001***	-0.09	-0.11	-0.07
Right inferior longitudinal fasciculus	0.38±0.05	0.47±0.01	-8.06	**0.001***	-0.09	-0.11	-0.06
Left inferior longitudinal fasciculus	0 .37±0.05	0.47±0.01	-9.24	**0.001***	-0.10	-0.12	-0.08
Right inferior Fronto occipital fasciculus	0 .38±0.04	0.49±0.01	-10.2	**0.001***	-0.108	-0.129	-0.08
Left inferior Fronto occipital fasciculus	0 .39±0.04	0.49±0.01	10.17	**0.001***	-0.097	-0.116	-0.07

Data are presented as mean ± SD. *Significant p value< 0.05, CI: confident interval, LT: left, Rt: right, FA: Fraction Anisotropy, UF: uncinate fasciculus.

Table 6: Model summery of predictor factors affecting the severity of Callous Unemotional Traits

ROI	R Square	F	P
Model	0.157	9.66	**0.001***

* Significant p value < 0.05.

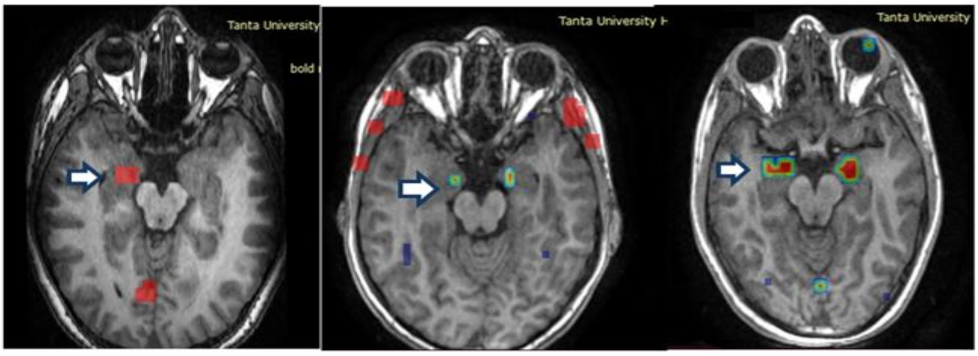
Table 7: Multiple linear regression of the predictor factors affecting the severity of Callous Unemotional Traits

	Unstandardized Coefficients		Standardized Coefficients	T	Sig.
	B	Std. Error	Beta		
Rt Amygdala	-6.442	18.921	-0.097	-3.340	0.001*
Lt Amygdala	-4.839	19.314	-0.721	-2.270	0.001*
Rt insula	-5.402	5.258	-0.087	-4.027	0.002*
Lt insula	-.129	8.003	-0.106	-3.766	0.006*
Rt VM prefrontal cortex	-2.171	36.212	-0.453	-4.806	0.016*
Lt VM prefrontal cortex	-2.388	41.947	-0.410	-3.629	0.034*
Rt DL prefrontal cortex	-2.913	37.566	-0.310	-4.663	0.003*
Lt DL prefrontal cortex	-2.689	42.336	-0.359	-4.630	0.003*
Rt orbitofrontal cortex	1.624	62.736	0.071	0.169	0.874
Lt orbitofrontal cortex	2.162	65.933	0.194	0.442	0.681
Rt Anterior cingulate cortex	-0.319	8.492	-0.004	-5.038	0.002*
Lt Anterior cingulate cortex	-4.206	16.284	-.052	-5.258	0.001*
RT Uncinate Fasciculus	-3.432	47.589	-0.109	-7.660	0.05*
LT Uncinate Fasciculus	-6.502	67.922	-.0242	-5.023	0.04*
RT inferior longitudinal Fasciculus	-7.744	41.686	-0.289	-1.841	0.139
LT inferior longitudinal Fasciculus	-6.365	63.323	-0.229	-0.953	.394
RT inferior Fronto occipital Fasciculus	-4.800	128.841	-0.161	-0.363	.735
LT inferior Fronto occipital Fasciculus	-1.389	155.119	-0.050	-0.099	.926

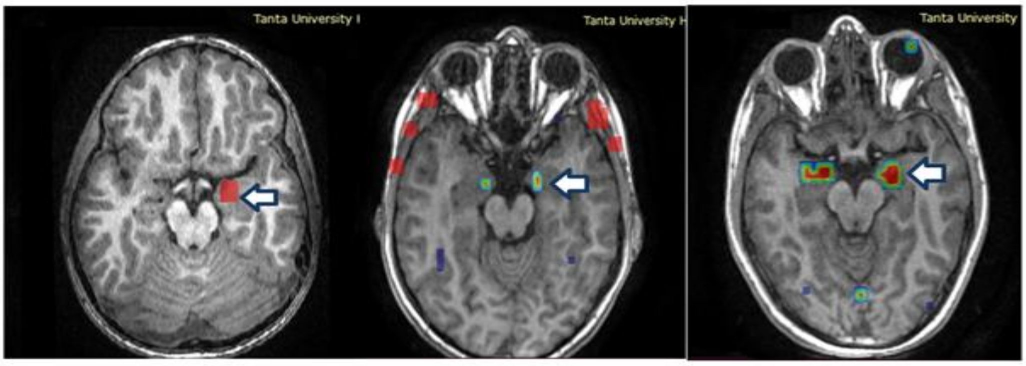
Rt: right, Lt left, DL: Dorsolateral, VM: ventromedial. * Significant p value < 0.05.

Figure legends

Figure 1: Example for Functional Bold MRI and DTI (FA) results: Rt and Lt Amygdala activity and both uncinate fasciculus.

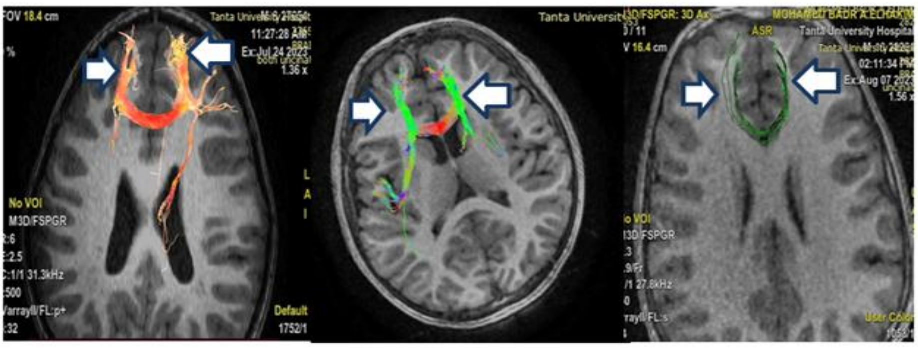


Control group CD patient with high ICU score CD patient with low ICU score



Control group CD patient with high ICU score CD patient with low ICU score

NB: Both uncinate fasciculus tracts in the same figure:



Intact both UF tracts Control group | Mild attenuated both UF tracts CD patient with low ICU score | Marked attenuated both UF tracts CD patient with high ICU score

Figure 2: Functional Bold MRI and DTI (FA) results: Rt and Lt Amygdala activity and both uncinate fasciculus