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# Social cognitive deficits in male children with attention deficit hyperactivity disorder in relation to salivary oxytocin level

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## Abstract

**Background:** There is evidence supporting a pathophysiological role of oxytocin in attention deficit hyperactive disorder (ADHD) especially hyperactive and combined subtypes. It is known that children with ADHD show a high rate of social cognitive problems regarding emotion recognition. Oxytocin was assumed to play a role in the emergence of social cognition deficits in ADHD. Aim of this study is to assess social cognition (emotion recognition) deficits in relation to oxytocin level in different subtypes of ADHD among the study group. Forty male patients with ADHD were recruited from psychiatric outpatient clinic of Fayoum University Hospital, were diagnosed according to DSM-5, and were assessed using Conner's parent rating scale-revised (L). Social cognition measured by CANTAB emotion recognition task (ERT) and the level of salivary oxytocin was measured by ELISA technique.

**Results:** Combined subtype had been lower in correctly detecting the emotions of fear and anger. Predominately, hyperactive impulsive ADHD subtype was more rapid while detecting the emotions of surprise and disgust. There was significant negative correlation between age of onset of ADHD and errors in detecting the emotion of anger and positive correlation between age of onset of ADHD and errors in detecting the emotion of surprise. Correct detection of the emotion of happiness was associated with increased oxytocin level but the correct detection of the emotion of fear was inversely related to oxytocin level. No statistically significant difference between different subtypes of ADHD regarding salivary oxytocin level.

**Conclusion:** Oxytocin may play a role in social cognitive deficits in ADHD. The presence of social cognitive deficits in ADHD prompts further investigations to focus on the specificity of these deficits and in turn identify ways of managing them. Studying oxytocin in this population and its relation to social cognitive deficits can support the notion that oxytocin is a biological marker for ADHD.

**Keywords:** ADHD, Oxytocin, Social cognition, Emotion recognition

## Background

Attention deficit/hyperactivity disorder (ADHD) is a common chronic psychiatric disorder, characterized by a pattern of developmentally inappropriate inattention, hyperactivity, and impulsivity, which affects between 5% of children and 2.5% of adults according to DSM-5 criteria [1]. ADHD can result in inappropriate social behavior, which may arise from a poorer social repertoire and

deficits in social cognitive abilities at different stages in social information processing [2, 3].

It is thought that deficits in face recognition, which may be due to structural abnormalities and delayed brain maturation, seen in ADHD could be one of the possible mechanisms underlying specific alterations in emotion recognition and social cognition abilities in individuals with ADHD [4, 5].

Oxytocin has been involved in the pathophysiology of different psychiatric disorder; one of them is ADHD [6, 7]. Impairment in OT level in ADHD shown to be related to DA receptor derangements [8]. Plasma OT levels were reported to be lower in boys with ADHD compared with

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healthy controls, and it was suggested that the decreased levels could result in difficulties in emotion regulation and recognition of emotion observed in ADHD [9].

The aim of this study was to assess social cognition (emotion recognition) deficits in relation to oxytocin level in different subtypes of ADHD among the study group.

## Methods

This was a cross-sectional study through the period from May 2017 till December 2017. Participants included in this study were 40 male patients, aged between 6–12 years old, were diagnosed with ADHD according to the DSM-5 [1] criteria, and were recruited from psychiatric outpatient clinic, Fayoum University Hospitals. This sample size was selected to give the study a statistical power of 95% and was calculated using Epi info 7 (Epi Info™ website (<http://wwwn.cdc.gov/epiinfo/>)) based on expected prevalence of ADHD and its subtypes and mean of oxytocin (OT) level among patients with ADHD obtained from previous studies, (with 95% confidence interval and precision of 5%) in order to get maximum sample size. Patients were selected on the basis of consecutive sampling, according to their complaints, age, and being clinically average as regard IQ; then patients were diagnosed for having ADHD according to DSM-5 after completing the clinical protocol to exclude main comorbidities, endocrinal illnesses, and hormonal replacement therapy. Excluding comorbidity was important because it is known that disorders such as autism and mood or anxiety disorder could affect OT levels independent from ADHD [10].

Also, Cotter et al., [11] suggested that social cognition is impaired among large scale of neuropsychiatric disorder, and it may serve as a general biomarker indicative of neurological abnormality across a range of clinical conditions.

The patients group was designed on the basis of the information that ADHD is more prevalent in males compared with females [1]. Furthermore, it was also aimed to eliminate the intersex differences in the effect of estrogen on OT levels [8, 12]. All patients were drug naive to avoid effect of medications on OT level [13] and also to avoid its effect on improving social cognition [14, 15].

First, semi-structured interview was administrated to all cases. Then, Conner's parent rating scale–revised long version CPRS-R-L [16] (Arabic version [17]) was administrated to be completed by parents to assist in determining whether children between the ages of 3 and 17 years might suffer from ADHD.

All cases were subjected to Stanford-Binet Intelligence Scales, 5th edition [18]: (Arabic version [19]) to detect IQ scales to limit the confounding influence of intellectual disability while detecting cognition. Cambridge cognition CANTAB® Emotion Recognition Task (ERT) <http://www.cambridgecognition.com> [20] in Arabic language was used

to detect facial affect recognition using cloud-based test paradigm that assesses recognition of six universal facial expressions: happiness, sadness, anger, disgust, fear, and surprise; task computer morphed images derived from the facial features of real individuals each showing a specific emotion.

## Biochemical analysis

Salivary oxytocin levels were measured using the double-antibody sandwich enzyme-linked immunosorbent assay ELISA (Human Oxytocin ELISA Kit, Beijing, China) (assay range 2 pg/ml → 600 pg/ml; sensitivity 1.06 pg/ml). All participants were asked to produce passive drool. Saliva samples were collected in plain plastic tubes from participants before breakfast (at least 2 h fasting) after they washed their mouths, and were stored on ice throughout the session. Samples were frozen as quickly as possible during testing at the hospital refrigerator at 2–8 °C for not more than few hours. Then samples were frozen at –20 °C to ensure that they remained stable during long-term storage at Laboratory of Clinical Pathology Department, Fayoum University, where the samples were assayed.

## Statistical analysis

Data were statistically described in terms of mean ± standard deviation (± SD), median and range or frequencies (number of cases), and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student's *t* test for the independent samples in comparing two groups when normally distributed and Mann-Whitney *U* test for the independent samples when not normally distributed. Comparison of numerical variables between more than two groups was done using Kruskal Wallis test with post hoc multiple 2-group comparisons. For comparing categorical data, Chi-square ( $\chi^2$ ) test was performed. Exact test was used instead when the expected frequency is less than five [21]. Correlation between various variables was done using Spearman rank correlation equation. *p* values less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

## Results

The demographic and clinical data in the study group are shown in Table 1. The age of the study group ranged from 6.3–12 years, and the mean was  $8.560 \pm 1.487$ . Regarding the school achievement, only 20% ( $N = 8$ ) was achievable in their schools. Among cases, 32.5% ( $N = 13$ ) had history of consanguinity. Only 30% ( $N = 19$ ) of cases had family history of ADHD. According to DSM-5's classification of ADHD, 37.5% ( $N = 15$ ) showed predominantly inattentive

**Table 1** Demographic data and clinical characteristics of the study participants

Some of demographic data and clinical characteristics of the study participants										
	No				%					
Subtypes of ADHD among case group according to DSM-5										
Predominantly inattentive	15				37.5%					
Predominantly hyperactive	6				15%					
Combined	19				47.5%					
School achievement										
Achievable	8				20%					
Non achievable	32				80%					
Consanguinity										
Positive	13				32.5%					
Negative	27				67.5%					
Family history (FH) of ADHD										
Positive FH	12				30%					
Negative FH	28				70%					
Data from Conner's parent rating scale-revised (L) items among case group										
	I		II		III		IV		V	
	No	%	I	%	No	%	No	%	No	%
L (Inattentive)	6	15%	1	2.5%	5	12.5%	7	17.5%	21	52.5%
M (Hyperactive-Impulsive)	9	22.5%	4	10%	0	0%	3	7.5%	24	60%
N (Total)	6	15%	3	7.5%	4	10%	5	12.5%	22	55%

/ average should not be a concern, // slightly atypical indicates significant problem, /// mildly atypical indicates significant problem, IV moderately atypical indicates significant problem, V markedly atypical indicates significant problem

presentation, 47.5% ( $N = 19$ ) showed combined presentation, and 15% ( $N = 6$ ) showed predominantly hyperactive presentation. Regarding classification of Conner's parent rating scale-revised (L) items among cases, 52.5% ( $N = 21$ ) of cases with predominantly inattentive ADHD subtype, 60% of cases with predominantly hyperactive impulsive ADHD subtype ( $N = 24$ ), and 55% of cases with combined subtype ( $N = 22$ ) were markedly atypical indicating a significant problem.

There was no significant difference between different subtypes of ADHD regarding salivary oxytocin level ( $P = 0.279$ ) (Table 2).

There were statistically significant differences between ADHD subtypes as regard their mean scores in the emotion recognition task ERT (total hits fear and total hits anger) in which cases with combined subtype had the least score in correctly detecting fear and anger. However, there was no statistically significant difference

regarding their mean scores in the ERT (total hits happiness, sadness, surprise, disgust). Also, there were no statistically significant differences between different subtypes of ADHD regarding their mean scores in the ERT (false alarm of the six emotions) (Table 3).

Cases with hyperactive impulsive subtype showed a significant negative correlation with median reaction time of the emotion surprise ( $P = 0.026$ ) (Fig. 1) and the emotion disgust ( $P = 0.054$ ) (Fig. 2). This means that those with predominately hyperactive impulsive ADHD subtype were more rapid while detecting surprise and disgust emotions.

There was no significant correlation between subtypes of ADHD (according Conner's parent rating scale-revised (L)) and correct detection of different emotions (Table 4).

There was significant negative correlation between age of onset of ADHD and total false alarms (errors) of the emotion anger ( $P = 0.048$ ) (Fig. 3), there was significant

**Table 2** Comparison of the mean salivary oxytocin level between subtypes of ADHD

Oxytocin level (pg/ml)	Predominantly inattentive type		Predominantly hyperactive type		Combined type		P value
	Mean	SD	Mean	SD	Mean	SD	
	22.397	7.693	27.816	3.148	23.446	9.599	0.279

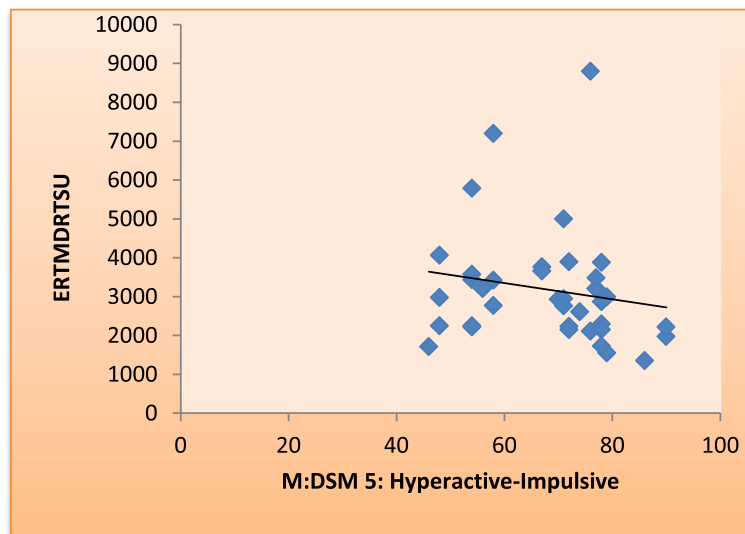
**Table 3** Comparison of the mean scores of total hits (correct response) and total false alarm (error in detection) of each emotion separately between different subtypes of ADHD

Items of ERT	Predominantly inattentive type		Predominantly hyperactive type		Combined type		P value
	Mean	SD	Mean	SD	Mean	SD	
ERTTH	18.07	4.026	16.67	5.317	17.00	4.497	0.513
ERTTHH	5.53	1.922	4.67	1.211	5.53	2.038	0.306
ERTTHS	3.07	2.052	2.17	1.722	4.26	1.968	0.060
ERTTHF	1.67	1.291	3.00	2.366	1.00	1.491	0.035
ERTTHA	2.13	1.642	3.00	0.894	1.26	1.368	0.030
ERTTHSU	4.20	2.145	2.33	2.503	3.68	2.335	0.224
ERTTHD	1.47	1.642	1.50	1.517	1.26	1.727	0.778
ERTTFAH	4.73	3.900	4.50	3.017	5.16	3.804	0.974
ERTTFAS	6.40	4.222	6.83	3.656	8.58	4.718	0.340
ERTTFAF	5.20	3.668	6.50	6.473	3.21	3.853	0.169
ERTTFAA	3.87	2.615	5.83	4.021	3.37	2.813	0.421
ERTTFASU	6.27	5.021	4.00	2.530	6.74	5.98	0.685
ERTTFAD	3.47	2.722	3.67	3.386	3.47	4.623	0.784

*ERTTH* ERT total hits, *ERTTFAH* ERT total false alarm happiness, *ERTTHH* ERT total hits happiness, *ERTTFAS* ERT total false alarm sadness, *ERTTHS* ERT total hits sadness, *ERTTFAF* ERT total false alarm fear, *ERTTHF* ERT total hits fear, *ERTTFAA* ERT total false alarm anger, *ERTTHA* ERT total hits anger, *ERTTFASU* ERT total false alarm surprise, *ERTTHSU* ERT total hits surprise, *ERTTFAD* ERT total false alarm disgust, *ERTTHD* ERT total hits disgust

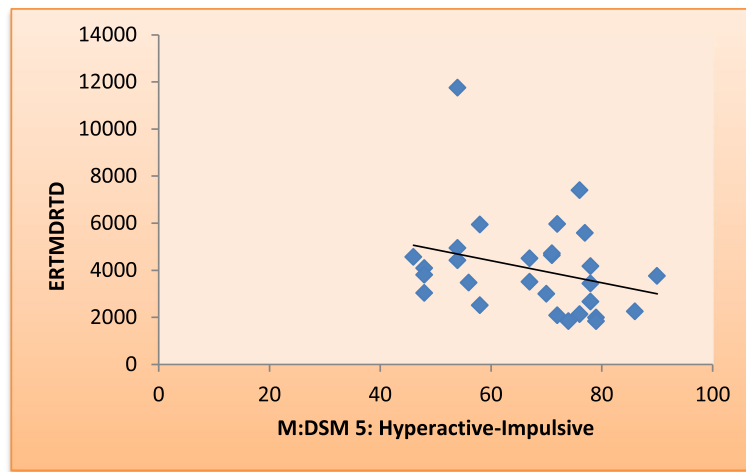
positive correlation between age of onset of ADHD and total false alarms (errors) of the emotion surprise ( $P = 0.04$ ) (Fig. 4), but there were no significant correlations between age of onset of ADHD and total false alarm (errors) of the emotions (happiness, sadness, anger, and disgust). This means that the younger the age of onset of ADHD the more errors in anger recognition but less error in surprise recognition.

Only total hits of the emotion happiness showed significant positive correlation with salivary oxytocin level ( $P = 0.03$ ). However, there was significant negative correlation between salivary oxytocin level and total hits of the emotions fear ( $P = 0.059$ ). This means that the correct detection of happiness was associated with increased oxytocin level but the correct detection of fear was inversely related to oxytocin level (Table 5).



**ERTMDRTSU:** ERT median reaction time Surprise

**Fig. 1** Scatter chart showing negative correlation between ERTMDRTSU and ADHD hyperactive impulsive subtype



ERTMDRTD: ERT median reaction time Disgust

Fig. 2 Scatter chart showing negative correlation between ERTMDRTD and ADHD hyperactive impulsive subtype

However, there was no significant correlation between salivary oxytocin level and total hits (correct responses of the emotions (sadness, anger, surprise, disgust) or with false alarms (errors) of the six emotions) (Table 5).

**Discussion**

In this study, the age of the study group was selected from 6 to 12 years old. This was guided by studies in literature which studied behavioral problems and cognition in ADHD [22, 23].

This study showed that only 30% of cases had family history of ADHD. This is inconsistent with studies in many different countries, in which high heritability rates for ADHD was shown to be around 71–90% [24–26]. This can be explained by small sample size. Also, it is not an epidemiological study. It is worth noting that not all of the risk for ADHD is genetic, and estimates of heritability also include an element of gene environment

**Table 4** Correlation between subtypes of ADHD according Conner’s parent rating scale- revised (L) and items of ERT (total hits and total hits of each emotion separately)

ERT	L		M		N	
	R	P value	R	P value	R	P value
ERTTH	0.095	0.561	−0.007	0.966	0.044	0.785
ERTTHH	0.165	0.309	0.228	0.156	0.258	0.108
ERTTHS	0.123	0.450	−0.043	0.792	0.121	0.458
ERTTHF	−0.193	0.234	−0.094	0.565	−0.224	0.164
ERTTHA	−0.239	0.138	−0.184	0.255	−0.288	0.072
ERTTHSU	0.202	0.212	0.087	0.594	0.139	0.391
ERTTHD	−0.078	0.634	−0.036	0.824	−0.090	0.580

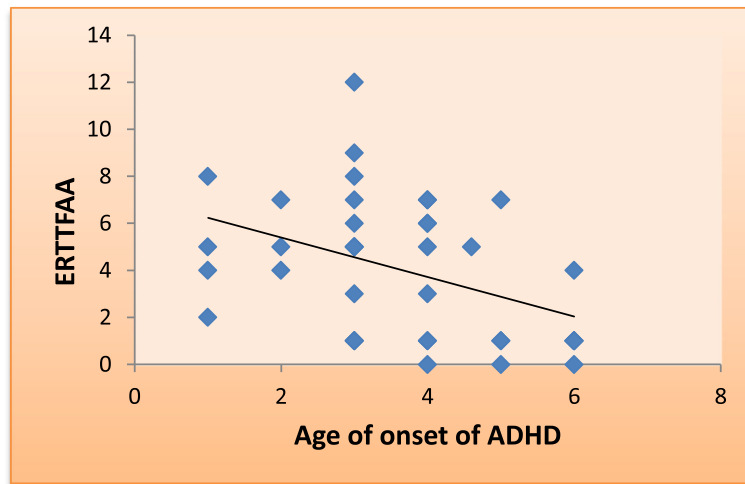
ERTTH ERT total hits, ERTTHH ERT total hits happiness, ERTTHS ERT total hits sadness, ERTTHF ERT total hits fear, ERTTHA ERT total hits anger, ERTTHSU ERT total hits surprise, ERTTHD ERT total hits disgust, L DSM-IV: inattentive, M DSM-IV: hyperactive-impulsive, N DSM-IV: total

interaction. It is estimated that between 10 to 40% of the variance associated with ADHD is accounted for environmental factors [27]

This study showed that 37.5% (N = 15) showed predominantly inattentive presentation (ADHD-PI) and 47.5 % (N = 19) showed combined presentation (ADHD-CT). This is in line with clinic samples prevalence but not with results in community prevalence. In clinic samples, ADHD-CT is approximately one and one half times more prevalent than ADHD-PI. Although predominantly inattentive type (ADHD-PI) appears to be more prevalent in the general population, children diagnosed with ADHD-CT are more likely to be referred for treatment probably reflecting the greater amount of disruptive behavior associated with the ADHD-CT symptoms [28].

This study showed that there was no significant difference between oxytocin levels in different ADHD subtypes (Table 2). This is inconsistent with Insel, [29] who found that among the ADHD subtypes, the ADHD-PI subtype had a significantly higher serum OT level than the ADHD-HI subtype. Demirci et al., [22] also supported this and explained that reduced OT levels in the ADHD-HI subtype may cause high aggression and lower empathy in boys. This inconsistency may be explained by using salivary samples which may not reflect CNS OT levels and also, could be explained by small sample size.

There was significant difference between ADHD subtypes as regard the total number of correct responses (times the subject correctly selected the emotion anger and fear), where subjects with predominately hyperactive impulsive ADHD subtype (ADHD-HI) were the better performers, and subjects with combined presentation (ADHD-CT) were the worst (Table 3). This is in line with a study conducted by Kemp and Korkman, [30] who assessed emotion recognition using NEPSY-II and



ERTTFAA: ERT total false alarm Anger

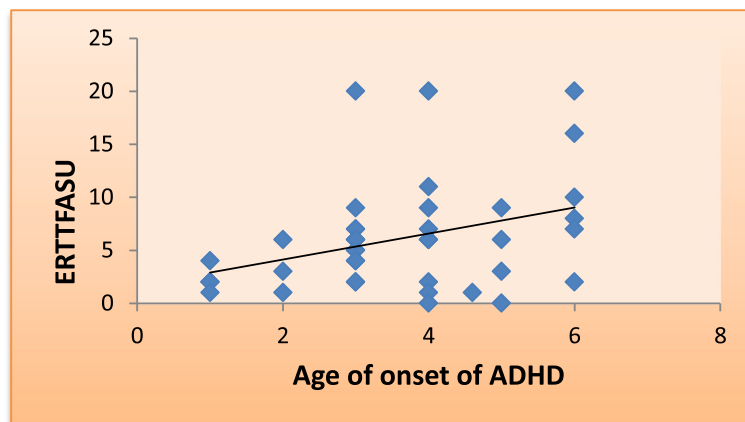
**Fig. 3** Scatter chart showing negative correlation between age of onset of ADHD and ERTTFAA

found that ADHD-CT performed significantly lower in affect recognition subtest. Also, consistent with meta-analysis study conducted by Bora and Pantelis, [31] who concluded that the most robust facial emotion recognition deficits were evident in anger and fear, yet they did not study them among different ADHD subtypes.

However, this is inconsistent with Yuill and Lyon, [32] who showed that impaired emotional processing in children with ADHD is unrelated to general cognitive limitations, such as impulsivity and inattentiveness, which affect the subtypes of ADHD [33]. Also, this is inconsistent with the findings of Pelc et al., [34] who found that children with the ADHD-HI subtype, in particular, make more mistakes in recognition of emotional facial expression; they particularly experience problems in recognizing facial

expressions representing anger and sadness. Also, inconsistent with reports of Schwenck et al., [35] who concluded that there was no difference among the ADHD subtypes with respect to recognition of emotions. This inconsistency may be explained by different methodologies in studies which were used to detect social cognitive domains. Tasks for the assessment of social cognition varied and included affective adult and child faces, timed or non-timed presentations, cross-matching tasks, matching faces to emotional stories and matching emotions to eyes, different social backgrounds, and socioeconomic status. Also, different age group among researches may be operative.

Hyperactive impulsive ADHD subtype was associated with rapid speed in detection of the emotions (surprise, disgust) (Figs. 1, 2 respectively). This finding is closely



ERTTFASU: ERT total false alarm Surprise

**Fig. 4** Scatter chart showing positive correlation between age of onset of ADHD and ERTTFASU

**Table 5** Correlation between salivary oxytocin level and items of ERT (total hits, total hits and false alarm for each emotion separately)

ERT	Oxytocin level	
	<i>R</i>	<i>P</i> value
ERTTH	-0.153	0.176
ERTTHH	0.232	0.038
ERTTHS	-0.144	0.201
ERTTHF	-0.188	0.059
ERTTHA	0.073	0.521
ERTTHSU	-0.041	0.718
ERTTHD	-0.052	0.649
ERTTFAH	-0.073	0.521
ERTTFAS	0.166	0.141
ERTTFAF	0.055	0.631
ERTTFAA	0.129	0.255
ERTTFASU	0.104	0.359
ERTTFAD	-0.064	0.574

*ERTTH* ERT total hits, *ERTTFAH* ERT total false alarm happiness, *ERTTHH* ERT total hits happiness, *ERTTFAS* ERT total false alarm sadness, *ERTTHS* ERT total hits sadness, *ERTTFAF* ERT total false alarm fear, *ERTTHF* ERT total hits fear, *ERTTFAA* ERT total false alarm anger, *ERTTHA* ERT total hits anger, *ERTTFASU* ERT total false alarm surprise, *ERTTHSU* ERT total hits surprise, *ERTTHD* ERT total hits Disgust, *ERTTFAD* ERT total false alarm disgust

related to findings of a study that examined visual and auditory emotion recognition in a wide scale of children and adolescents with ADHD which was conducted by Waddington et al., [36]. The latter study showed that speed of visual and auditory emotion recognition was positively correlated with hyperactivity and inattention on Conner's parent rating scale, and speed of auditory emotion recognition positively correlated with inattention on the Conner's teacher rating scale; however, the latter study did not specify each emotion separately. A study conducted by Tehrani-Doost et al., [37] found that the time spent in recognizing happy faces was higher in the ADHD group; however, the relation between the time needed to detect the emotion and different ADHD was not studied in this research. However, these study results are expected as patients with ADHD hyperactive impulsive subtype are characterized by being reluctant in doing effort and usually make rapid and impulsive decisions. This inconsistency may be due to the different methodologies and different assessment settings.

There was no correlation between subtypes of ADHD and the total number of correct responses of emotions (happiness, sadness, fear, anger, surprise, and disgust) (Table 4). These findings were inconsistent with that of the study conducted by Tehrani-Doost et al., [37] which showed that inattention associated with a considerable effect on detection of both angry and sad targets, also found significant negative association of hyperactivity-

impulsivity with anger detection. Another study showed that hyperactivity measures were positively correlated with the recognition of disgust and inversely correlated with the recognition of fear [4]. This inconsistency may be due to small sample size and using only one task for assessment of social cognition (emotion recognition) in which only one social cognitive domain was assessed.

In this study, the earlier onset was associated with more errors in anger detection (Fig. 3) yet less errors in surprise detection (Fig. 4). A meta-analysis conducted by Bora and Pantelis, [31] showed that social cognitive deficits in emotion recognition and theory of mind (ToM) were very subtle and non-significant respectively in adults with ADHD. There is some evidence that aspects of social cognition like affect perception deficits are present in younger but not older patients with ADHD. In an early study by Shapiro et al., [38], the author concluded that this finding reflects a developmental improvement in allocation of attention resources or the implementation of compensatory strategies to cope with the emotion perception deficit; this was also supported by Guyer et al., [39] who did not yield significant affect recognition deficits in patients aged 12 or older. This is inconsistent with Waddington et al., [36] who found that older patients with ADHD unexpectedly showed poorer emotion recognition than children with ADHD.

This study showed that there was significant positive correlation between salivary OT levels and total hits (correct responses) of the emotion happiness; also, there was significant negative correlation between salivary OT levels and total hits fear (correct responses) (Table 5). In a study conducted by Feeser et al., [40], the administration of intranasal OT improved recognition of avoidance-related facial expressions of emotions (fear, sadness, and disgust) but had no effect on approach-related expressions of emotion (happy, angry, and surprise). In other studies, OT improves only specific emotions such as facial expressions of happiness [41], fear [42], or anger [43], which may conclude the possible relation between OT level and emotion recognition.

Examination of different age groups, males, females, and interventional studies in a large sample may be helpful in accurate assessment of this relation and its role in improvement of ADHD deficits.

This study was based on sample size calculation so results constitute statistical power. Including only boys to reduce the impact of estrogen on social cognition and OT level lessened confounding factors. Using a well-validated tool to measure social cognition which is used to assess multiple dimensions of affect recognition including reaction time, correct responses, incorrect responses, and assessment of secondary emotions, such as surprise, and positive emotions, such as happiness, also, it was interesting for the participants being iPad application.

The use of cross-sectional studies can prevent drawing conclusions about causal relationships. Reliance on only

semi-structured clinical interview without using standardized structured diagnostic tool may affect diagnosis; also, comorbid conditions may be missed; this can affect our results as many other psychiatric conditions can affect social cognition and OT level. Using salivary OT rather than cerebrospinal fluid (CSF) might not have completely reflected OT action in the CNS because the relationship between peripheral and central levels of OT is unclear.

## Conclusion

This study concluded that oxytocin may play a role in social cognitive deficits and also supported the possible difference between ADHD subtypes in affect recognition as those with combined subtype may affect anger and fear recognition. Further studies are needed to find the possible effect of social cognitive deficits in ADHD presentations and impairments. Investigational studies are needed to find the possible therapeutic role of oxytocin in ADHD.

## Abbreviations

ADHD: Attention deficit hyperactive disorder; ADHD-CT: ADHD combined type; ADHD-HI: ADHD hyperactive type; ADHD-PI: ADHD predominantly inattentive; CANTAB: Cambridge Neuropsychological Test Automated Battery

## Acknowledgements

The authors thank Cambridge Neuropsychological Test Automated Battery for the help with the emotion recognition task.

## Authors' contributions

MD analyzed and interpreted the patient data regarding the clinical data and psychometric tools and was a major contributor in writing the manuscript. MA performed the clinical pathology examination of the salivary samples. All authors read and approved the final manuscript.

## Funding

This study did not receive any fund.

## Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

## Ethics approval and consent to participate

This study was approved by the Ethics Committee of Faculty of Medicine, Fayoum University. Child assents and parents' consent were obtained from both the participants and their parents. The number of approval is not applicable.

## Consent for publication

Not applicable.

## Competing interests

The authors declare that they have no competing interests.

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Received: 8 January 2020 Accepted: 14 February 2020

Published online: 31 March 2020

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