The relationship between aggression, empathy skills and serum oxytocin levels in male children and adolescents with attention deficit and hyperactivity disorder

Esra Demirci[a], Sevgi Ozmen[a], Eser Kilic[b] and Didem B. Oztop[a]

Although attention deficit and hyperactivity disorder (ADHD) are recognized as neurodevelopmental disorders characterized by impairment in executive functions, impairments in social functioning are often accompanied by ADHD. Oxytocin (OT) has been investigated in a number of psychiatric disorders owing to its effects on social interactions. The aim of this study was to determine the relationship between aggression, empathy and OT levels in children with ADHD. Forty male patients with ADHD, ranging in age from 7 to 18 years, and 40 healthy age-matched and sex-matched individuals were included in this study. The patients and healthy controls filled in the Buss–Perry Aggression Questionnaire and Bryant's Empathy Index for Children and Adolescents; the Reading the Mind in the Eyes test was then completed. Blood samples were collected for OT at the beginning of the study. Lower serum OT levels were observed in patients with ADHD compared with the healthy controls. Moreover, there was a negative correlation between serum OT level and aggression scores and a positive correlation between the serum OT level and empathy scores in patients with ADHD. We conclude that OT may play a role in aggression and empathy skills, affecting the social life of those with ADHD. ***Behavioural Pharmacology*** **27:681–688**

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Departments of [a]Child and Adolescent Psychiatry and [b]Biochemistry, Erciyes University School of Medicine, Kayseri, Turkey

Correspondence to Esra Demirci, MD, Department of Child and Adolescent Psychiatry, Erciyes University School of Medicine, Kayseri 38039, Turkey
E-mail: esra_z_d_r@hotmail.com

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Introduction

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder associated with significant impairment in developmental, cognitive, emotional and academic domains. As a result of deficiencies in almost all domains of life, it manifests itself in the form of failure at school and defective personal relations. Problematic behaviours observed in ADHD have been associated with aggressiveness and low empathy skills (Hastings *et al.*, 2000). Deficiencies in problem-solving skills may lead to aggressiveness and behavioural disorders among children and adolescents diagnosed with ADHD. The hyperactive/impulsive and the combined subtypes showed increased rates of aggression, anger and emotional outbursts (Bagwell *et al.*, 2001). Furthermore, owing to prefrontal cortex functional disorder, children with ADHD have reduced emotional and cognitive empathy skills while they experience difficulties in interpreting social clues (Braaten and Rosen, 2000). Deficiencies in empathy may play an important role in the impairments in social cognition and peer relationships in children with ADHD, especially in children with a hyperactive component (Maoz *et al.*, 2014).

However, it has been suggested that within social skill deficiencies in children and adolescents with ADHD, there are endophenotypes related to socialization/temperament, face recognition, emotional expression recognition and empathy (Hattori *et al.*, 2006). It was reported that difficulty in the recognition of emotional facial expressions in ADHD causes impairments in peer relations (Pelc *et al.*, 2006). In addition, as core symptoms of ADHD, the presence of attention and impulsivity problems could cause difficulty in emotion recognition in patients with ADHD (American Psychiatric Association, 2000). Thus, the 'psychosocial dimension', in addition to clinical parameters, is increasingly important in multidimensional monitoring of the disorder (Wehmeier *et al.*, 2010).

Oxytocin (OT) has been the subject of a number of research studies in certain psychiatric disorders. The therapeutic potential of OT in enhancing prosocial behaviour and socioemotional processing has also been examined. It has been shown that OT administration reduced amygdala activity during fear-induced visual stimulation response (Kirsch *et al.*, 2005), also anxiety levels have been associated with increased aggressive behaviours in some animal models (Bosch and Neumann, 2012). It was reported that men with conduct disorder (CD) had higher OT reactive autoantibody levels compared with men without CD (Fetissov *et al.*, 2006). Furthermore, previous human studies have examined the acute effects of OT on experimentally induced

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aggression. Campbell and Hausmann (2013) found that OT moderated reactive aggression in women with high-state anxiety, but not in those with low-state anxiety. Alcorn *et al.* (2015a) investigated the effect of an intranasal placebo, and 12, 24 and 48 IU of OT in six adult men with antisocial personality disorder and substance use disorder. No clear effects on aggressive behaviour were observed as a function of OT dose.

There is an association between OT-induced changes in performance on the Reading the Mind in the Eyes Test (RMET) and emotional empathy. Emotional empathy, but not cognitive empathy, is supported by OT (Hurlemann *et al.*, 2010; Shamay-Tsoory, 2011). Individuals low in emotional empathy showed greater improvement after OT administration compared with those receiving a placebo (Radke and de Bruijn, 2015). Domes *et al.* (2007) and Feeser *et al.* (2015) observed that OT enhances interpretation of subtle social-affective cues from the eye region, measured by the RMET. Despite this, there is limited information on the relationship between aggressiveness, empathy, emotion recognition and OT levels in humans.

Considering the issues in the communication and social mutuality domains, it has been suggested that ADHD shares similar characteristics with pervasive developmental disorder (Hattori *et al.*, 2006). Various studies have suggested that OT reduces aggressiveness, and enhances social relations and interactions in autism (Kuehn, 2011; Hirotaka *et al.*, 2012). Intranasal OT, when administered to male patients with autism, enhanced the ability to recognize other individuals' emotions (Guastella *et al.*, 2010). Another study suggested that the signs of ADHD and OCD that are observed in autism spectrum disorder are related to OT dysregulation (Dalton *et al.*, 2005). Despite this, there are a limited number of studies evaluating the association the between ADHD and OT. In one of these studies, ADHD patients (10.4 ± 1.9 years) diagnosed using *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. (DSM-IV) differed from healthy control (HC) and autistic children by significantly decreased plasma OT concentrations (Taurines *et al.*, 2014). Four of these children with ADHD also had a comorbid mood or anxiety disorder diagnosis, and five had an oppositional defiant disorder (ODD) or CD. In addition, Park *et al.* (2010) linked specific OT receptor polymorphisms to lower social cognition in children with ADHD. In that study, which included 450 children aged 4–16 years, 211 children (46.9%) had comorbid ODD and 69 children (15.3%) fulfilled the criteria for comorbid CD.

In light of the above information, it has been suggested that OT serum levels are lower in patients with ADHD and that intranasal OT treatment may affect social cognition, empathy and aggression in children with ADHD. We could not obtain information on OT levels in the subtypes of ADHD, but we hypothesized that OT levels may be lower in the hyperactive/impulsive and combined subtypes because of high aggression and the hyperactive component causing empathy deficits, as well as the presence of attention and impulsivity problems that could cause difficulty in emotion recognition.

Because of the ethically and methodologically limited means of investigating central OT in humans, in the present study, peripheral neuropeptide concentrations were measured as a potential surrogate for dysregulation of the central OT system. It has been reported that peripheral OT is a global biomarker of central OT system activity (Neumann; 2007; Knobloch *et al.*, 2012). Nevertheless, no studies have as yet specifically investigated the correlation between serum OT levels and aggressiveness and empathy skills in patients with ADHD who manifest behavioural disorder while suffering limitations in personal relations. In the present study, we aimed to determine the relationship between serum OT levels and aggression and empathy in ADHD and subtypes and, if a correlation could be shown, to contribute towards the existing knowledge on the pathogenesis ADHD with a view to the development of novel treatment modalities.

Methods

Participants

This study included 83 male children and adolescents aged 7–18 years, with newly diagnosed ADHD, who had previously not used any drug therapy for ADHD. They were examined at Erciyes University, Faculty of Medicine, Department of Child and Adolescent Psychiatry, between November 2012 and April 2013. The participants were diagnosed with ADHD by two child and adolescent psychiatrists according to the DSM-IV-TR diagnostic criteria and the short form of the Conners Parent Rating Scale (35.38 ± 14.75). The patient group was designed on the basis of the information that ADHD is more prevalent in males compared with females (American Psychiatric Association, 2000). Furthermore, it was also aimed to eliminate the intersex differences in the effect of oestrogen on OT levels (Zak and Fakhar, 2006).

Patients and controls were selected after performing physical, psychiatric and neurologic examinations, routine biochemical tests, complete blood counts, cortisol levels and thyroid function tests. All participants were subjected to the Schedule for Affective Disorders and Schizophrenia for School Age Children – Present and Life time Version (K-SADS-PL) to rule out other psychiatric disorders and the Wechsler Intelligence Scale for Children. Eight patients with ADHD who had IQ scores lower than 85, 16 patients with comorbid ODD/CD, three of patients with ADHD who had abnormal cortisol levels and thyroid function tests, four children and adolescents with a history of neurological, metabolic, endocrinological diseases or hormone usage, three children

and adolescents with a history of substance use or addiction other than smoking (13 patients with comorbid ODD/CD also had a history of substance use or addiction) and three patients with neurological conditions such as epilepsy or who had suffered head trauma that could result in organic brain disorder were excluded. Six children were also excluded because of incomplete empathy–aggression questionnaires and RMET. Finally, 40 male children and adolescents remained in the study group. For classification of subtypes of ADHD, we used the short form Conners Parent Rating Scale (cut-off scores for inattentive subtype ≥ 5 hyperactive/impulsive subtype ≥ 7) (Dereboy *et al.*, 2007) and K-SADS-PL. The ADHD subtypes of the participants were as follows: combined (40%), inattentive (32.5%) and hyperactive/impulsive (27.5%).

The control group included 40 healthy sex-matched and age-matched (mean age:10.88 ± 1.45 years) children and adolescents evaluated with the K-SADS-PL and Wechsler Intelligence Scale for Children who had no intellectual disability ($IQ > 85$), psychiatric or chronic disorders, and volunteered to participate in the study.

This study was approved by the Ethics Committee of Erciyes University Medical School (2012/673-Project number: TTU-2013-4260). The objectives and procedures of the study were explained to the participants and their parents, and written informed consents were obtained from both the participants and their parents.

Method

The Buss–Perry Aggression Questionnaire (Buss and Waren, 2002) and the Spanish version of the Bryant Empathy Scale for Children and Adolescents (Del Barrio *et al.*, 2004) were administered to the patient and control groups in the study. Trait aggression was measured by the total score of the Buss–Perry Aggression Questionnaires and scores were calculated for the subscales physical aggression (items 1–9), verbal aggression (items 10–14), anger (items 15–21) and hostility (items 22–29). In this study, we used total scores for assessing trait aggression (Cronbach's α 0.83). The Spanish version of Bryant Empathy Scale for Children and Adolescents is a self-report questionnaire that assesses emotional empathy (Cronbach's α 0.73).

During the interview, the patient and the control group were subjected to the child and adolescent RMET to evaluate their emotional facial expression recognition and empathic response skills. The RMET has been developed as a subtle measure of emotion recognition. This test is made up of photos of actors' eyes and requires the participant to identify the emotion that the actor is portraying (Baron-Cohen *et al.*, 2001).

After the end of a 25 min rest period, to measure basal OT levels, fasting blood samples were collected between 08 : 00 and 09 : 00 before breakfast at the beginning of the study by standard phlebotomy in prechilled EDTA tubes. The samples were immediately stored on ice and centrifuged at 4°C for 15 min at 1000 rpm. Blood serum was separated and samples were frozen overnight at -20°C and then stored indefinitely at -80°C until analysis. A standardized and validated radioimmunoassay was performed according to the protocol of Turan *et al.* (2013).

Biochemical analysis

Serum samples were evaluated at the Biochemistry Research Laboratory of Erciyes University Medical School using the ELISA test device (Sunrise Basic Tecan; Tecan Austria GmbH, Salzburg, Austria).

Serum OT levels were assayed using ELISA (CUSABIO Human Oxytocin ELISA Kit, Maryland, USA) (assay range: 6–400 μIU/ml, sensitivity: < 14 μIU/ml). Three samples of known concentrations were tested in 20 assays to assess the intra-assay precision (precision within an assay): the coefficient of variation was less than 15%. Three samples of known concentration were tested 20 times on one plate to assess the interassay precision (precision between assays): the coefficient of variation was less than 15%. The optical density values obtained were converted into serum concentration values according to the formula calculated from linear regression analysis.

Statistical analysis

The data were analysed using the IBM SPSS Statistics 21.0 (IBM North America, New York, USA) and SigmaStat 3.5 (Systat Software Inc., North, Central and South America, USA) statistical software packages. The variables were expressed as number (n), percentage (%), mean and SD. The normality of data distribution was tested using the Shapiro–Wilk test. Variables that were not normally distributed were compared using the Mann–Whitney–U or Kruskal–Wallis tests. Comparisons across multiple groups were carried out using Dunn's test. The categorical variables were analysed using the exact χ^2-test. Correlational analyses between variables were carried out using Pearson correlation analysis on normally distributed data, or Spearman's correlation analysis for empathy scores that were non-normally distributed. We used partial correlation to test associations between empathy and aggression and between empathy and RMET, controlling for age and severity of ADHD. Statistical significance was set at P value less than 0.05.

Results

Aggression and empathy in ADHD compared with HCs

Compared with the HCs, the patients with ADHD had a significantly higher mean Buss–Perry Aggression Scale score ($P < 0.001$) (Table 1) and a significantly lower mean Bryant Empathy Scale score ($P < 0.001$) (Table 1).

There was a negative correlation between Bryant Empathy Scale and Buss–Perry Aggression Scale scores

Table 1 Comparison of test scores and serum levels of oxytocin with ADHD and control groups

	ADHD (mean ± 1 SD)	Control (mean ± 1 SD)	
Buss–Perry Aggression Questionnaire	74.25 ± 5.04	50.48 ± 7.11	$t = 7.694$, $P < 0.001$
Bryant's Empathy Index for Children and Adolescents	11.7 ± 1.89	16.13 ± 1.22	$Z = 7.559$, $P < 0.001$
Reading the Mind in the Eyes for Children	17.4 ± 2.3	23.57 ± 1.33	$t = 6.141$, $P < 0.001$
Reading the Mind in the Eyes for Adolescent	23.93 ± 2.25	29.2 ± 2.1	$t = 4.261$, $P < 0.001$
Serum oxytocin levels (μIU/ml)	37.62 ± 9	52.5 ± 18.1	$t = 4.384$, $P < 0.001$

ADHD, attention deficit and hyperactivity disorder.

in patients with ADHD ($r = -0.83$, $P < 0.001$). This relationship remained significant when controlling for age and severity of ADHD ($r = -0.34$, $P = 0.002$).

The patients with ADHD provided significantly fewer correct answers on both the child and adolescent RMET than the HCs ($P < 0.001$) (Table 1). The ADHD subtypes did not differ significantly with respect to the number of correct answers on the child and adolescent RMET ($P = 0.064$, $P = 0.07$). Adolescents with ADHD showed a positive correlation between Bryant Empathy Scale score and the number of correct answers on the RMET ($r = 0.34$, $P < 0.05$). This relationship remained significant when controlling for age and severity of ADHD ($r = -0.45$ $P < 0.05$).

Among the ADHD subtypes, the inattentive subtype ($n = 13$) had a lower Buss–Perry Aggression Scale score compared with the combined ($n = 16$) and hyperactive/impulsive subtypes ($n = 11$), whereas the hyperactive/impulsive subtype had a higher Buss–Perry Aggression Scale score compared with the combined subtype ($P = 0.001$) (Table 2). The hyperactive/impulsive subtype had a lower Bryant Empathy Scale score than the inattentive subtype ($P = 0.002$) (Table 2).

OT in ADHD compared with HCs

The patients with ADHD had a significantly lower serum OT level compared with the HCs ($P < 0.001$) (Table 1). Among the ADHD subtypes, the inattentive subtype had a significantly higher serum OT level than the hyperactive/impulsive subtype ($P < 0.025$) (Table 2).

Relationship between aggression, empathy and OT in ADHD

Unlike in the HCs, in the patients with ADHD, we found a negative correlation between the serum OT level and the Buss–Perry Aggression scale score ($r = -0.38$, $P < 0.02$) and a positive correlation between the serum OT level and the Bryant Empathy Scale score ($r = 0.67$, $P < 0.001$) (Table 3).

There was a positive correlation between the number of correct answers in the child RMET ($n = 25$) and serum OT level in both patients with ADHD and HCs. However, only adolescents with ADHD ($n = 15$) showed a positive correlation between the serum OT level and the number of correct answers in the RMET ($r = 0.69$, $P < 0.001$) (Table 3).

Discussion

OT and ADHD

To our knowledge, this is the first study to investigate the serum OT levels of ADHD patients without comorbidity and in subtypes of ADHD. Nevertheless, there is evidence in the literature that peripheral OT levels were found to be lower in ADHD.

Park *et al.* (2010) linked a specific OT receptor polymorphism to low social cognition in children with ADHD. In another study on ADHD, plasma OT levels were reported to be lower in boys with ADHD compared with HCs, and it was suggested that the decreased levels could result from difficulties in emotion regulation and recognition of emotion observed in ADHD (Taurines *et al.*, 2014). In that study, four children with ADHD also had comorbid mood or anxiety disorder and five patients had an ODD/CD. Another recent study observed

Table 2 Comparison of test scores and serum levels of oxytocin in subtypes of ADHD

ADHD subtypes	Serum oxytocin levels (μIU/ml) (mean ± 1 SD)	Bryant's Empathy Index for Children and Adolescents (mean ± 1 SD)	Buss–Perry Aggression Questionnaire (mean ± 1 SD)
Inattentive	41 ± 8.8	13.09 ± 0.94	69.27 ± 3.06***
Hyperactive/impulsive	33.1 ± 8.2*	10.62 ± 1.80*	78.85 ± 4.01**
Combined	38.8 ± 8.7	11.63 ± 1.92	73.94 ± 3.23
Compared with Dunn test	$\chi^2 = 7.547$, $d.f. = 2$ $P = 0.023$	$\chi^2 = 11.987$, $d.f. = 2$ $P = 0.002$	$\chi^2 = 22.600$, $d.f. = 2$ $P = 0.001$

ADHD, attention deficit and hyperactivity disorder.
*Lower than the inattentive subtype ($P < 0.05$).
**Higher than the combined subtype ($P < 0.05$).
***Lower than the combined and hyperactive/impulsive subtype ($P < 0.05$).

Table 3 Correlation between test scores and serum levels of oxytocin with ADHD and control groups

	ADHD serum oxytocin levels (μIU/ml)	Control serum oxytocin levels (μIU/ml)
Buss–Perry Aggression Questionnaire		
r	−0.391*	−0.114
P	0.013	0.482
Bryant's Empathy Index for Children and Adolescents		
r	0.668**	0.300
P	**< 0.001**	0.146
Reading the Mind in the Eyes for Children		
r	0.595*	0.756**
P	0.002	< 0.001
Adolescent		
r	0.691**	0.180
P	**< 0.001**	0.529

ADHD, attention deficit and hyperactivity disorder.
**0.01 level; significant correlation.
*0.05 level; significant correlation.
Bold values represent a significance level $P < 0.05$.

decreased levels of serum OT in 36 paediatric patients 6–15 years old with ADHD diagnosed with DSM-IV (Sasaki *et al.*, 2015). That study included only 23 drug-naive children and four children had comorbidity.

Our study showed that the serum OT level was significantly lower in male patients with ADHD than in the HCs, consistent with the literature. However, ours is the only study to determine serum OT levels in male patients with ADHD without comorbidity and also in subtypes of ADHD. This was important because it is known that disorders such as autism, and mood or anxiety disorder could affect OT levels independent from ADHD (Turan *et al.*, 2013). Among the ADHD subtypes, the inattentive subtype had a significantly higher serum OT level than the hyperactive/impulsive subtype. It was reported that OT gene knockout mice showed deficits in other behaviours, such as decreased social investigation and increased aggression (Insel *et al.*, 1999). Reduced OT levels in the hyperactive/impulsive subtype may cause high aggression and lower empathy in boys and this could be one reason why the hyperactive/impulsive subtype is more common in boys than girls.

In addition, dopamine (DA) is the main neurotransmitter suggested to have an association with ADHD. Altered DA levels elicit hyperactivity, attention deficit, dyskinesia, tics and selfmutilation (Carter *et al.*, 2001). It has been suggested that altered DA levels result from gene variations related to DA carriers and DA receptors (Arnsten and Castellanos, 2003; Barkley, 2006). Recent animal studies have suggested that DA receptors regulate hypothalamic OT-producing cells. Hypothalamic nuclei rich in OT are innervated by dopamine fibres and regulated by DA through D2-like dopaminergic receptors (Succu *et al.*, 2007). The OT level in ADHD may be impaired by variations in the genes related to the DA receptor, which play a role in the aetiology of ADHD and its subtypes, as well as by dysregulated DA receptors and deficits in DA level. Furthermore, in support of this hypothesis, it was shown that serum levels of OT in drug-naive ADHD patients were significantly lower than in those medicated with methylphenidate (Maoz *et al.*, 2014; Sasaki *et al.*, 2015). However, more studies, including molecular genetic studies, are needed to confirm this hypothesis.

Relationship between OT, aggression, empathy and recognition of emotional expression in ADHD

The target regions of the centrally projecting neuropeptidergic OT neurons are mainly involved in the modulation of social behaviours, emotions and stress coping (Lukas and Neumann, 2013). However, there is no study in the literature comparing serum OT levels with HCs and assessing its association with aggression, empathy and face recognition in patients with ADHD. In our study, there was a negative correlation between the Buss–Perry Aggression Scale score and serum OT level in children with ADHD, and positive correlations between serum OT level and the Bryant Empathy Scale score and the number of correct answers in the RMET.

There is evidence in the literature that OXTR SNPs rs6770632 and rs1042778 are associated with persistent and pervasive aggressive behaviours in females and males (Malik *et al.*, 2012). OT moderated reactive aggression in women with high-state anxiety (Alcorn *et al.*, 2015b). However, there is no study comparing serum OT level between ADHD patients and HCs and assessing its association with aggression in ADHD.

Moreover, OT causes enhanced emotional recognition and increased empathy (Bartz *et al.*, 2010). It has been reported that OT has potential as a treatment to improve the recognition of emotion in faces, allowing individuals to improve their insight into the intentions, desires and mental states of others (Shahrestani *et al.*, 2013). It was found that individuals with lower emotional empathy showed greater improvement after OT administration compared with a placebo (Radke and de Bruijn, 2015). Also, OT enhances interpretation of subtle social-affective cues from the eye region, measured by the RMET (Feeser *et al.*, 2015). However, a review of the relevant literature did not yield any studies relating serum OT level to ADHD and empathy skills; only one study reported a relationship between specific OT receptor polymorphisms and lower social cognition in ADHD children (Park *et al.*, 2010). Williams *et al.* (2008) found emotion recognition deficits in boys (age range 8–17) with unmedicated ADHD, but noted a significant improvement in the recognition of both these emotions with methylphenidate. In another study, stimulants improved empathic functions in male children with a mean age of 12.0 years as assessed by the Bryant Index of Empathy for Children and Adolescents (Maoz *et al.*, 2014). In that study, it was shown that serum levels of OT in drug-naive ADHD patients were significantly

lower than those in ADHD patients medicated with methylphenidate. The results of our study lead us to conclude that lower OT may cause higher aggression, lower empathy and emotional recognition deficits in ADHD, whereas methylphenidate may have potential as a treatment to regulate OT levels.

Differences in aggression, empathy and recognition of emotional expression in ADHD patients versus HCs

Adolescents showing aggressive behaviour are subject to mis-socialization and self-control problems (Van der Oord *et al.*, 2005) and aggressive children experience difficulties in recognizing facial expressions, whereas there is a significant correlation among correct RMET answers and the empathy rate, which represent social skills (Voracek and Dressler, 2006). It is known that children with ADHD show a high rate of social problems, and reduced social competence was found to be highly associated with the disorder (Lee *et al.*, 2012). In one study with borderline personality disorder and ADHD patients, both patient groups showed higher scores on self-reported impulsivity, anger and aggression compared with HCs (Ende *et al.*, 2015). Children with ADHD show less empathy than male children without ADHD (Braaten and Rosen, 2000; Marton *et al.*, 2009). Patients in the hyperactive/impulsive subtype had an increased rate of aggression, anger and emotional outbursts (Bagwell *et al.*, 2001) and lower empathy (Pelc *et al.*, 2006). Consistent with some previous studies, we found that patients with ADHD, compared with controls, had significantly higher aggression and lower empathy scores. Children with the hyperactive/impulsive subtype had a significantly lower Bryant Empathy Scale score and a higher Buss–Perry Aggression Score compared with those with the other subtypes. Our study also showed a lower level of empathy skill in male children with ADHD, which may cause higher levels of aggression.

Various studies have reported that children and adolescents with ADHD have difficulties with facial emotion recognition tasks (Boakes *et al.*, 2008; Sinzig *et al.*, 2008). Children with the hyperactive/impulsive ADHD subtype, in particular, make more mistakes in emotional facial expression recognition than controls; they particularly experience problems in recognizing facial expressions representing anger and sadness (Pelc *et al.*, 2006). A recent study, in contrast, reported that there was no difference among the subtypes with respect to recognition of emotions (Schwenck *et al.*, 2011). However, in no study was the relation between aggressiveness, empathy skills and face recognition investigated in patients with ADHD who manifest behavioural disorder while suffering limitations in personal relations.

In our study, the ADHD group provided fewer correct answers on the RMET. We found a negative correlation between scores on the Bryant Empathy Scale and correct answers in the RMET. We also could not find any significant difference among different ADHD subtypes with respect to correct and incorrect RMET answers.

The above data suggest that male children with ADHD experience difficulties in recognizing emotional facial expressions, but perform increasingly well as their empathy skills are improved and aggression levels are reduced.

Conclusion

This study suggests that decreased levels of OT may play a role in the pathophysiology of patients with ADHD and especially, the hyperactive/impulsive subtype. Furthermore, the results indicate that in ADHD, OT may play a role in social limitations, aggression and empathy skills, which affect the disease symptoms, and social functions such as emotion recognition, which affect social relations. However, further research is needed in this area to confirm this hypothesis. Thus, further studies on social communication and OT levels in children and adolescents with ADHD will not only contribute towards our understanding of the aetiopathogenesis of ADHD but also provide additional information that is necessary to discover novel therapies.

Limitations

The main limitation of this study is its small sample size. We did not assess the effects of medical treatment on the serum levels of OT. Serum OT might be a biomarker of central OT system activity. Providing evidence for coordinated release, numerous physiological stimuli trigger both central and peripheral OT release, including birth, suckling, sexual activity and various forms of stress (Neumann, 2007; Knobloch *et al.*, 2012). It was reported that plasma OT level is an important determinant of OT concentration in cerebrospinal fluid in children and that there is a positive correlation between plasma and cerebrospinal fluid OT levels (Carson *et al.*, 2014), although the results of this study need to be interpreted with caution because serum levels of OT might not reflect central release (Neumann and Landgraf, 2012).

Further limitations include the use of self-report measures of aggression and empathy scale, lack of consideration of certain factors such as puberty, increased osmotic pressure, haemorrhage, and nutrition and the fact that endocrinological and metabolic disease history was based on information received from the family.

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Conflicts of interest

There are no conflicts of interest.

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