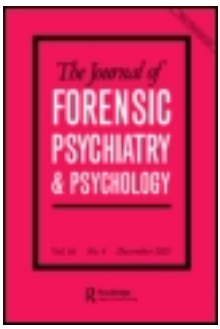

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Psychopathic characteristics are related to high basal urinary oxytocin levels in male forensic patients

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Psychopathic characteristics are related to high basal urinary oxytocin levels in male forensic patients

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Background: Cerebral levels of oxytocin, elevated by intranasal administration, can increase trust, empathy and altruism, and decrease fear. We hypothesised that low levels of these characteristics (found in some personality-disordered forensic patients), would be associated with reduced oxytocin levels. *Aims*: To assess whether patients, with psychopathic characteristics associated with selfishness, callousness and the remorseless use of others, plus a chronically unstable, antisocial and socially deviant lifestyle, would show depressed levels of oxytocin. *Method*: Basal urinary oxytocin levels (an indicator of cerebral oxytocin) were assessed in 47 forensic psychiatric patients. Levels were compared with those in 21 non-patient controls, and correlated with psychopathic characteristics. *Results*: Oxytocin levels were markedly elevated in the patient sample compared to controls. Levels were also strongly correlated with traits associated with a socially deviant lifestyle. *Conclusions*: The results point to oxytocin playing a role in antisocial, as well as prosocial behaviours.

Keywords: oxytocin; psychopathy; antisocial behaviours

Introduction

The role of oxytocin in human social behaviour has been studied where levels in the brain have been shown to increase following pleasant, social tactile contact (Light, Grewen, & Amico, 2005). Conversely, oxytocin release is attenuated in children who suffered severe early neglect (Fries, Ziegler, Kurain, Jacoris, & Pollack, 2005). Levels can be boosted by intranasal administration, which can lead to increases in trust (Kosfeld, Heinrichs, Zak, Fischbacher, & Fehr, 2005), empathy (Hurlemann et al., 2010) and altruism (Barraza, McCullough, Ahmadi, & Zak, 2011), and decreases in fear (Kirsch et al., 2005). These potent effects on promoting affiliative behaviours, and positive emotions, lead to the prediction that individuals with psychopathic traits will evidence

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depressed cerebral oxytocin levels. The clinical concept of psychopathy entails persistent behavioural deviancy, plus emotional/interpersonal detachment (Patrick, Fowles, & Krueger, 2009). Psychopathy can be assessed using the Psychopathy Checklist Revised (PCL-R) (Hare, 2003), with scores of 26 marking the European cut-off for a diagnosis (Cooke, 1998).

Psychopaths are thought to be responsible for roughly half of all crimes committed (http://www.mentalhealth.com/dis/p20-pe04.html). Statistical analysis of the PCL-R has shown that it measures four facets of the disorder (Hare, 2003): *Facet 1* relates to an arrogant and deceitful interpersonal style; *Facet 2* refers to deficient affective experience; *Facet 3* measures impulsive/irresponsible behaviours; and *Facet 4* measures aspects of antisocial behaviour. The combined traits of Facets 1 and 2 (Factor 1 scores) are generally regarded as the core personality traits of psychopathy (i.e. selfish, callous and the remorseless use of others). Facets 3 and 4 (Factor 2) refer to the deviant behaviours side of psychopathy (i.e. measures a chronically unstable, antisocial, socially deviant lifestyle). It was predicted that psychopathy scores would be related to depressed levels of basal urinal oxytocin, especially Facet 1 + Facet 2 (Factor 1) scores since this refers more directly to the emotional/interpersonal detachment side of psychopathy.

Method

Participants

A total of 68 males (mean age 42.31 ± 10.96 years), 47 forensic psychiatric patients and 21 staff members of the Van der Hoeven secure forensic hospital in Utrecht, the Netherlands, participated in the study. The mean age of the participants was 41.21 years (SD = 11.64) for the patients and 44.95 years (SD = 9.23) for the controls, with no significant difference between the two groups. All controls and 78% of the patients were educated to a level beyond elementary school, consisting of some sort of vocational training, or higher-level education. The majority of the patients used some form of psychiatric medication: 43% used antidepressants (36% serotonergic antidepressants); 64% used (predominantly low doses of) antipsychotic medication (13% classic and 51% atypical antipsychotics); and 26% used androgen deprivation therapy medication. Apart from salbutamol (for asthma), none of the controls used any form of medication. Psychiatric disorders and type of offence in the patient sample are shown in Table 1. None of the participants in the control sample were diagnosed with any form of psychiatric disorder.

Procedure

The study protocol was approved by the ethics committees of the University of Birmingham and the University of Amsterdam. All subjects gave written, informed consent before participation. There were no exclusion criteria for par-

Table 1. Psychiatric disorders and type of offence in the patient sample.

	Frequency	Percentage
Disorder		
Psychotic disorder	10	21
Autistic spectrum disorder	9	19
Mood disorders	8	17
Personality disorders	41	87
Cluster A	0	0
Cluster B	24	51
Cluster C	4	8
Not otherwise specified	11	23
Cluster A + B	2	4
Borderline intellectual functioning	6	13
Type of offence		
Violent	23	49
Sexual	16	34
Mixed	8	17

ticipation, but all psychiatric and medication details were carefully registered to enable evaluation of their influence on basal urinary oxytocin levels (see Table 2).

Regular drug checks made it unlikely that any of the participants used any non-prescribed drugs during (at least) the six-week period prior to the collection of the samples. (A detailed description of the urine checks, specific drugs tests and results for all participants etc. can be provided on request).

Urine samples were taken from the first void of the day on four successive occasions. The average time expired between urinating and freezing at −80 °C was 61 min (± 35 min). All samples were defrosted once to enable pooling of the samples for each participant before being refrozen and stored until analysis. Oxytocin levels were determined by an ELISA using a procedure that has been previously validated for human urine (Gray, Parkin, & Samms-Vaughan, 2007). Creatinine levels were also measured in each sample to enable the neuropeptide level to be expressed as pg oxytocin per mg creatinine and thus correct for variation in the water content of the urine. The urinary levels taken were assumed to reflect cerebral levels. This assumption is based on a number of lines of experimental evidence. First, oxytocin has been shown to be excreted into the urine from the blood in humans (Amico, Ulbrecht, & Robinson, 1987). Second, numerous studies have shown an association between increases in peripheral oxytocin due to contact such as touch in humans (Feldman, Gordon, Schneiderman, Weisman, & Zagoory-Sharon, 2010). Third, Feldman et al. (2012) have shown that there is a link to genetic markers of oxytocin and peripheral levels. Thus in humans, individuals homozygous for the CD38 rs379863 CC risk allele had lower plasma oxytocin compared with carriers of the A allele and less touch contact with their infants.

Table 2. Distribution of the use of specific types of medication among patients with different basal urinary oxytocin levels.

	Patient oxytocin levels			
	Normal ($n = 32$)		High ($n = 15$)	
Type of medication	*N*	%	*N*	%
Androgen deprivation therapy	9	28	3	20
Antipsychotics	21	66	9	60
First generation	5	16	1	7
Second generation	15	47	7	47
First and second generations	1	3	1	7
Antidepressants	12	37	8	53
Serotonergic	10	31	7	47
Selective serotonin re-uptake inhibitors	3	9	2	13

Note: No significant differences were found.

Patients' psychopathic traits were rated by two trained professionals using the Dutch translation of the PCL-R (Vertommen, Verheul, de Ruiter, & Hildebrand, 2002) and a consensus score obtained. Participants also completed the Childhood Trauma Questionnaire-Short Form (Bernstein & Fink, 1998), the Liebowitz Social Anxiety Scale (Liebowitz, 1987) and the Experience in Close Relationships Revised (Fraley, Waller, & Brennan, 2000) to measure psychological characteristics.

Results

Comparisons of samples

Mean basal urinary oxytocin levels (oxytocin pg/mg creatinine) were found to be 276% higher in the patient ($M = 15.97$, SD = 22.35) compared to controls ($M = 5.78$, SD = 2.38). See Figure 1 for comparisons of the patient and control samples on basal urinary oxytocin levels. While, mean basal urinary oxytocin levels (oxytocin pg/mg creatinine) were 261% higher in the patients with a diagnosis of psychopathy ($M = 27.53$, SD = 30.66) than in the patients without a diagnosis of psychopathy ($M = 10.55$, SD = 10.55).

Basal urinary oxytocin levels for controls were normally distributed whereas those in the patient sample showed extreme variance. To enable cross-group comparisons, basal urinary oxytocin levels were divided into: *low levels* (< 1.02 oxytocin pg/mg creatinine); *normal levels* (1.02–10.54 oxytocin pg/mg creatinine); and *high levels* (> 10.54 oxytocin pg/mg creatinine), based on the mean of the control group ± two standard deviations. Only two subjects (both patients) had low levels of basal urinary oxytocin levels. Chi-square analyses showed that the patient group contained significantly more subjects with high basal urinary oxytocin levels (33%) than the control group (0%) Pearson χ^2 (1,

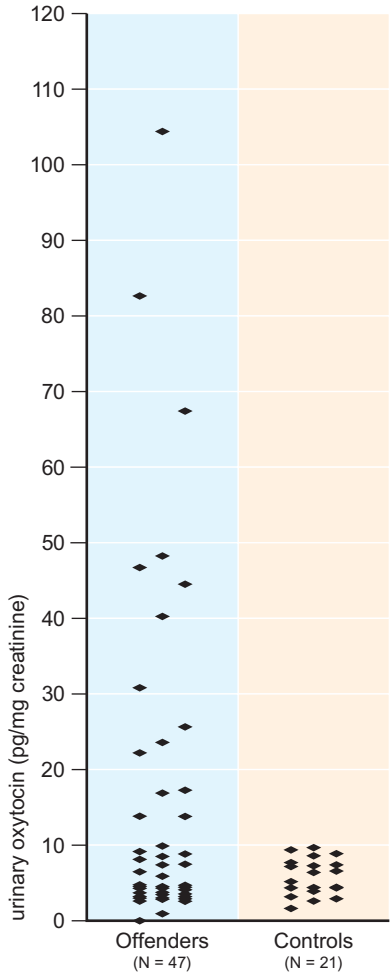

Figure 1. Comparisons of the patient and control samples on basal urinary oxytocin levels.

$N = 66) = 9.06$, $p = .003$, Cramer's $V = .37$. The patient group diagnosed with psychopathy contained significantly more subjects with high basal urinary oxytocin levels (53%) than the patient group not diagnosed with psychopathy (23%) Pearson χ^2 (1, $N = 45) = 4.05$, $p = .044$, Cramer's $V = .30$.

Analysis of the relationship between oxytocin and psychopathy scores

Psychopathy scores were associated with basal urinary oxytocin levels. Spearman correlational analysis showed that basal urinary oxytocin levels in the patient samples were significantly positively related with PCL-R scores

($\rho = .39$, $p < .01$ two-tailed, $N = 47$). Partial correlations showed that basal urinary oxytocin levels were unrelated to PCL-R Factor 1 scores when controlled for Factor 2. By contrast, basal urinary oxytocin levels showed a large and significant, positive correlation with PCL-R Factor 2 ($\rho = .51$, $p < .0001$ one-tailed, $n = 47$) when controlled for Factor 1. Partial correlations showed that basal urinary oxytocin levels were unrelated to PCL-R Facet 1, Facet 2 and Facet 3 scores when controlled for the other facets. By contrast, basal urinary oxytocin levels showed a significant, positive correlation with PCL-R Facet 4 scores ($\rho = .29$, $p < .05$ one-tailed, $n = 47$) when controlled for the other facets. Additional analyses showed that two of the five individual items of Facet 4 items had a significant and strongly positive correlation with basal urinary oxytocin levels: item 12 (early behavioural problems) ($\rho = .58$, $p < .0001$ one-tailed, $n = 47$) and item 18 (juvenile delinquency) ($\rho = .40$, $p < .01$ one-tailed, $n = 47$).

Additional analyses

To control for the heterogeneity of the sample in this field study, all registered variables were tested for their possible confounding influence on the results. A series of non-parametric statistical tests (Mann Whitney *U* Tests) were used to test whether the basal urinary oxytocin levels within the patient group were related to medication. No significant differences were found for basal urinary oxytocin levels between patients with and without antidepressants, antipsychotic or antiandrogenic medication. Particular attention was paid to medication that could increase 5HT levels as this could potentially heighten basal urinary oxytocin levels. It should be noted that of the 15 patients who had a PCL-R score of 26 or higher, only two were taking selective serotonin uptake inhibitors (SSRIs). A series of non-parametric statistical tests were also used to test whether the basal urinary oxytocin levels within the patient group were related to any other additional factors including: mental health problems (diagnoses of major mental disorder, substance abuse disorder or intellectual disability); self-reported childhood trauma (assessed by the Childhood Trauma Questionnaire-Short Form (Bernstein & Fink, 1998), including emotional neglect, physical neglect, emotional abuse, physical abuse and sexual abuse); specific self-reported attachment style (healthy, fearful, preoccupied or avoidant/dismissive); and relationship status (single or in a relationship). No significant differences were found. Furthermore, in the patient group, no relationship was found between oxytocin level and total IQ score for the 39 patients for whom IQ data were available.

Discussion

The current finding that not low, but *high* basal urinary oxytocin levels are associated with the antisocial behavioural aspect of psychopathy, is the opposite of what would be predicted based on this literature (Barraza et al.,

2011; Hurlemann et al., 2010; Kosfeld et al., 2005). Any effects of the observed elevated baseline levels of oxytocin on behaviour will be mediated via an action at the oxytocin receptors. Several polymorphisms of the oxytocin receptor gene, which have been identified, have been linked with a series of psychological factors including empathy problems and emotional dysregulation (Bradley et al., 2011; Rodrigues, Saslow, Garcia, John, & Keltner, 2009), although none have as yet been associated with offending behaviour. Medications aimed at manipulating oxytocin function have been suggested as tentative targets for a range of conditions (Striepens, Kendrick, Maier, & Hurlemann, 2011). However, the current findings show that increasing oxytocin levels may not be the solution to combating antisocial/criminal behaviour in serious patients. Indeed, increasing oxytocin levels may even be contra-indicated in some cases.

The current results may also reflect the capacity for oxytocin to attenuate stress responses (Heinrichs, Baumgartner, Kirschbaum, & Ehlert, 2003; Quirin, Kuhl, & Duesing, 2011). High levels of the neuropeptide are associated with increased parasympathetic neuromodulation, leading to reductions in blood pressure and heart rate during stress (Gutkowska & Jankowski, 2012), while intranasal oxytocin has been reported to reduce fear and stress responses (Kirsch et al., 2005). The patients in the current study were far more likely to have been traumatised in childhood, than controls, and these traumatic experiences might consequently be expected to lead to increased oxytocin release which would suppress the release of the stress hormone, cortisol (Pierrehumbert, Halfon, Ansermet, & Popovic, 2010). Indeed, a blunted cortisol responsivity to stress has been found in antisocial children and adolescents (Van Goozen, Matthys, Cohen-Kettenis, Buitelaar, & van Engeland, 2000) and a low cortisol level at age 10–12 years has been found to predict aggression at age 15–17 years (Shoal, Giancola, & Kirillova, 2003). High oxytocin and low cortisol levels would be expected to extinguish the stress-and-fear reactions that ordinarily promote social adjustment/adaption and the ability to learn from punishment and mistakes. This model is in keeping with Patrick's (Patrick et al., 2009) triarchic conceptualisation of the development of psychopathy, which theorises that difficult children (with early behavioural problems) who are raised by unable and abusive parents (inducing childhood trauma) develop a coercive interactional style and hostility towards others, while striving for immediate gratification of their own needs.

Limitations of the study

The elevated basal urinary oxytocin levels, found in a substantial subgroup of patients, could potentially have been influenced by drugs taken by the patients. 3,4-methylenedioxy-N-methylamphetamine (ecstasy) is known to stimulate oxytocin containing neurons in rats (Hunt, McGregor, & Callaghan, 2011) and increase oxytocin concentrations and prosocial feelings in humans (Dumont

et al., 2009). It should be noted, however, that the extremely strict drug-screening policy, with regular urine checks, employed by the forensic hospital makes it extremely unlikely that any of the participants will have taken an illicit substance prior to or during the experimental period. Furthermore, only two of the patients with PCL-R scores in the psychopathic range were taking SSRIs. It is extremely unlikely, therefore, that the elevated levels of oxytocin in the patients and their substantial correlation with psychopathy scores reflect the action of drugs that boost 5HT levels. Several of the patients were taking neuroleptics. However, neuroleptics are not thought to affect oxytocin concentrations (Glovinsky, Kalogeras, Kirch, Suddath, & Wyatt, 1994). Nor the observed oxytocin levels relate to the presence or absence of major mental disorders, intellectual disability or IQ.

Conflict of interest

There were no conflicts of interest from any of the authors involved in the study.

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