Oxytocin normalises the implicit processing of fearful faces in psychopathy: a randomised crossover study using fMRI

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Abstract

Adults with antisocial personality disorder with (ASPD + P) and without (ASPD-P) psychopathy commit the majority of violent crimes. Empathic processing abnormalities are particularly prominent in psychopathy, but effective pharmacological interventions have yet to be identified. Oxytocin modulates neural responses to fearful expressions in healthy populations. The current study investigates its effects in violent antisocial men. In a placebo-controlled, randomised crossover design, 34 violent offenders (19 ASPD + P; 15 ASPD-P) and 24 healthy non-offenders received 40 IU intranasal oxytocin or placebo and then completed an fMRI morphed faces task examining the implicit processing of fearful facial expressions. Increasing intensity of fearful facial expressions failed to appropriately modulate activity in the right anterior insula and bilateral midcingulate cortex in violent offenders with ASPD + P, compared to those with ASPD-P. Oxytocin abolished these group differences by enhancing fear-associated activity in key social brain areas in ASPD + P. This represents the first evidence of neurochemical modulation of the empathic processing of others' distress in psychopathy.

Main Text

Introduction

A small group of men engage in a life-course-persistent pattern of antisocial behaviour [1]. These men are disproportionally responsible for violent crimes [2], resulting in considerable personal and societal costs [3]. They meet diagnostic criteria for Conduct Disorder (CD) in childhood and Antisocial Personality Disorder (ASPD) in adulthood. However, there is significant heterogeneity within this group. Approximately one third of men with ASPD meet additional diagnostic criteria for psychopathy (ASPD + P) [4]. They exhibit callous-unemotional traits in childhood [5], begin offending at earlier ages, and engage in a broader range and greater density of offending behaviours [6], than those without psychopathy (ASPD-P). Importantly, they also respond less well to psychosocial treatment programmes [7].

Abnormalities in reinforcement-based decision making and emotional (particularly empathic) responsiveness may help to explain the behaviours of these violent offenders. Decision-making abnormalities are observed in antisocial men with and without psychopathy [8] when they undertake tasks in which they must learn which responses to make to gain a reward or to avoid punishment. There are differences in the neural response to unanticipated punishment between those with and without psychopathy [9]. Such impairments may underpin reduced reinforcement sensitivity, resulting in impulsivity, frustration-induced reactive aggression, and recidivism [10]. By contrast, deficits in different components of empathic processing appear to be relatively specific to antisocial men with psychopathy. Behaviourally, individuals with psychopathy demonstrate impaired emotion expression recognition, particularly for fear, when explicitly asked to emotionally 'label' static two-dimensional images of facial emotions [11]. Functional MRI work indicates reduced neural responses to empathy-inducing pictures of physically painful situations in individuals with psychopathy [12]. A reduced ability to recognise and

respond to another's fear, pain and distress may be related to the use of goal-directed instrumental aggression that is particularly prevalent in individuals with psychopathy because the individual is less concerned by the distress of others and less fearful of punishment [13].

However, a key aspect of empathic processing – neural responses to others' facial expressions of fear – has not been explored in violent antisocial offenders to date. In healthy subjects, partially separable neural systems are involved in the processing of specific emotions, with prominent roles for the amygdala, insula, and anterior and midcingulate cortex in processing fearful expressions [14–16]. Studies in antisocial youth suggest reduced amygdala activity to fearful faces in children with high levels of CU traits (the developmental precursor of ASPD + P) [17], but increased amygdala activity in those with low levels of CU traits (the developmental precursor of ASPD-P) [18], in comparison to normally developing children. However, only two preliminary investigations have been conducted to explore the implicit neural processing of fearful facial expressions in violent antisocial adults. In a small pilot study [19], men with ASPD + P (n = 6; compared to 19 healthy non-offenders) showed significantly reduced activation in the core face processing network to fearful facial expressions at 'low' and 'prototypical' intensities. In a larger study (n = 80) [20], men with ASPD + P (compared to men with ASPD-P) showed reduced activation in the core face processing network and associated emotional and motivational processing regions (OFC and vmPFC), but increased dorsal insula responses, when passively viewing dynamic facial expressions of fear. However, this study lacked a non-offender control group.

Furthermore, no study to our knowledge has investigated if group differences in brain activation can be modified by pharmacological agents. One potential agent is oxytocin, a neuropeptide central to the regulation of complex social behaviors. Oxytocin plays a key role in social functions such as emotion recognition [21], binding to receptors in social brain regions reported as functionally abnormal in ASPD (such as the amygdala and cingulate cortex [22]). In healthy individuals, oxytocin enhances the explicit emotional recognition of fearful faces [23] and significantly impacts on activity within fearful facial processing regions including the amygdala, insula and anterior cingulate cortex [24]. In antisocial adults, a small behavioural study [25] has suggested that a single dose of 24IU of intranasal oxytocin can improve fearful expression recognition, at least in the short term. However, no previous work has examined the neural basis of this potential effect.

Hence, we carried out the first double-blind, placebo controlled, randomised crossover study in male violent offenders with ASPD + P and ASPD-P and healthy non-offenders to explore the impact of oxytocin on brain functional differences when implicitly processing others' distress in the form of fearful facial expressions at varying intensities.

Results

Behavioural data

Across the whole sample, participants successfully performed the gender rating task (mean accuracy 96.7% (SD = 1.0), mean response latency= 938.8 milliseconds (SD=183.3)). For accuracy, there were no

significant effects of group (NO, ASPD-P, or ASPD+P; $\eta_P^2 = 0.071$, $F_{2,55} = 2.114$, $p = 0.13$), condition (placebo or oxytocin, $\eta_P^2 = 0.017$, $F_{1,42} = 0.553$, $p = 0.333$), or intensity of emotion (40%, 60%, 80%, or 100%; $\eta_P^2 = 0.33$, $F_{1,42} = 1.899$, $p = 0.174$). For response latency, there were no significant effects of group ($\eta_P^2 = 0.41$, $F_{1,42} = 1.174$, $p = 0.317$), condition (placebo or oxytocin, $\eta_P^2 = <0.001$, $F_{1,42} = 0.001$, $p = 0.981$), or intensity of emotion ($\eta_P^2 = 0.38$, $F_{1,42} = 2.17$, $p = 0.146$). No group-by-intensity interactions for accuracy or response latency were observed.

fMRI results

Parametric modulation of neural responses by fearful facial emotion intensity (across whole sample)

The main 3MVM analysis revealed significant activation of the right middle occipital gyrus, involving the primary visual cortex, extending into right fusiform gyrus; the left middle occipital gyrus, extending into left fusiform gyrus; and a separate region within left fusiform gyrus, associated with modulation by fearful expressions (further details in supplementary materials, S5).

Between and within group differences in responses to modulated fearful expressions

In the 3-Group MVM (ANOVA) ROI analyses for fearful expressions, there was an overall effect of group in right and left midcingulate cortex (see Table 2). Exploratory post-hoc between-group analyses revealed four key findings:

1. Violent offenders with ASPD+P showed reduced modulation of BOLD responding by fearful expression intensity within bilateral mid-cingulate and right anterior insula compared with the group of violent offenders with ASPD-P under placebo conditions. The right anterior insula finding did not survive correction for multiple comparisons (Figure 2A and 2B).
2. Violent offenders with ASPD+P showed significant increases in modulation by fearful expression intensity in bilateral mid-cingulate cortex and left anterior insula under the oxytocin relative to the placebo condition (Figure 3A and 3B).
3. There were thus no group differences between ASPD+P and ASPD-P in the oxytocin condition- that is, differences under placebo were abolished under oxytocin. This was supported by a statistically significant Group (ASPD-P, ASPD+P) by Condition (placebo, oxytocin) interaction effect in left midcingulate cortex (Supplementary Figures S3 and S4).
4. There were no significant main effects or between- or within- group effects findings in amygdala in either placebo or oxytocin condition.

Discussion

We investigated the neural basis of implicit fearful facial emotion processing in violent offenders with antisocial personality disorder with and without psychopathy, and the effect of intranasal oxytocin on brain functional differences. Offenders with antisocial personality disorder and psychopathy displayed

reduced modulation by fearful expression intensity in the anterior insula and midcingulate cortex (but not the amygdala) in comparison to offenders with antisocial personality disorder without psychopathy. Oxytocin abolished differences in fear-associated activity within left anterior insula and bilateral midcingulate cortex for the offenders with ASPD + P.

The identification of reduced anterior insula and midcingulate cortex reactivity to implicit processing of facial expressions of fear in ASPD + P relative to ASPD-P is broadly consistent with the previous literature [17–20]. The anterior insula is critical in representing the salience of stimuli [26]. In processing the fear of others, it contributes to the fine tuning of behavioural responses. It generates an integrated awareness of one's cognitive, affective and physical state that becomes re-represented in the anterior cingulate cortex in order to facilitate homeostatic autonomic and behavioural responses [27]. The midcingulate cortex is a key part of reactive fear circuitry, helping to inform rapid escape decisions from predators, which may be signaled by the fearful face of a con-specific [28]. It appears to coordinate emotional responses and motor actions according to learned values, particularly when a predatory threat is near [28]. Especially robust links have been demonstrated between activity in the anterior subdivision of the midcingulate cortex (aMCC) and the experience of more intense states of negative affect [28], including fear [29]. The posterior MCC (pMCC) may play a more specific role in threat appraisal and risk assessment by approaching the threat [30]. Our significant midcingulate cluster encompassed both aMCC and pMCC, suggesting that the impaired processing of fear in ASPD + P may be related to deficits in both responsivity to intensity and threat appraisal. Relative functional deficits in these key areas of the fear processing network in ASPD + P is in keeping with a model whereby impairment in the ability to recognize and integrate distress cues (such as fear in others) predisposes such individuals to especially pronounced aggressive behavior [13].

Our findings on the effect of oxytocin demonstrate for the first time that neural processing abnormalities in ASPD + P may be modified by neurochemical intervention. Oxytocin resulted in increased modulation by fearful expression intensity in ASPD + P in left anterior insula and bilateral midcingulate cortex. These effects resulted in the baseline differences between ASPD + P and ASPD-P in the implicit processing of others' fear being abolished. The enhancement of fear associated activity in these regions suggests that the fearful faces are accorded increased salience under the influence of oxytocin, with potential 'downstream' behavioral impacts [31, 32]. The observed short-term normalisation in the empathic processing of others' distress should prompt further investigation into the neurochemical modulation of the social cognitive abnormalities in this disorder which has such a profound personal and societal impact.

Our study had several limitations. The relatively small sample sizes in the ASPD groups meant that we may have been under-powered to detect further group differences: for example, the lack of significant findings in the amygdala in between- and within-group analyses, in both placebo and oxytocin conditions, was unexpected, given previous work showing amygdala activation by fearful faces using this task [17, 33]. This observation suggests caution is required in interpretation of both positive and negative findings in our study. Equally, while there were significant brain function differences between the antisocial

groups, neither violent antisocial group differed significantly from the non-offender group, although the pattern of parameter estimates in the midcingulate cortex (ASPD-P activity > NO activity > ASPD + P activity) were in the expected direction. While both ASPD groups had similar lifetime histories of substance misuse, there were some differences in substance misuse measured on the day of scanning (for example, more of the ASPD + P group had recently consumed cocaine than the ASPD-P group). However, such group differences were carefully controlled for in the imaging analyses, and the observed group differences at baseline and in response to oxytocin cannot be simply attributed to such differences. This study also had important strengths. Firstly, this is the first study in a group of subjects with ASPD to establish differences between antisocial groups in adulthood in the implicit processing of fearful facial expressions, a central aspect of empathic responding. Secondly, it is the first study to investigate the neural effects of oxytocin in this group, achieved using a randomized, placebo-controlled method. Further, diagnoses and PCL-R ratings were made by trained clinicians, with use of official criminal records to help classify participants.

In conclusion, we have demonstrated, for the first time, that the implicit processing of fearful facial emotion expressions significantly differs between violent antisocial male offenders with and without psychopathy. Oxytocin abolished these group differences by enhancing fear-associated activity in the anterior insula and mid cingulate cortex in the violent antisocial male offenders with psychopathy. This represents the first evidence of neurochemical modulation of the empathic processing of others' distress in psychopathy. Neurochemical modulation of core deficits in the condition could have profound implications for treatment of this complex disorder.

Declarations

Funding and disclosure

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Contributors

JT, DM, SW, and NB designed the study and acquired funding. AS, YP, MC, SW and RJB provided critical contributions to study design process and subsequent project co-ordination. JT obtained ethical approval. JT was the overall study administrator and coordinator and supervised the study from the outset, JG took on sharing these roles at midpoint in the study. JT and JG coordinated recruitment. Psychometric and diagnostic assessments were done by JT. JT did the behavioural outcome analysis. Using templates from the lab of JB, AS programmed the functional MRI experiment, JT and JG obtained the scans, JT and AS processed the images and analysed the scans. AS, JB, JT, DM and NB interpreted the findings. JT and NB wrote the first draft of the article and made revisions on subsequent drafts, addressing critical review comments contributed by AS, JG, YP, MC, RJB and DM. All authors disclose they had full access to data and accept responsibility for publication.

Methods

Participants and assessment

Between September 2017 and March 2020, we enrolled 58 men, aged 20 to 58 years, with an IQ greater than 70 as defined by the Wechsler Abbreviated Scale of Intelligence (WASI-II) [34]. Offenders with convictions for violent crimes (murder, rape, attempted murder, grievous and actual bodily harm) who met DSM-5 criteria for antisocial personality disorder (Structured Clinical Interview for DSM-5 Personality Disorders (SCID-5 PD; [35]) were recruited via the National Probation Service of England and Wales and local forensic personality disorder services. Healthy non-offenders were recruited from the general population using online adverts and fliers in job centres and local recreational centres. All participants completed diagnostic (SCID-5) and Psychopathy Checklist- Revised (PCL-R; [36]) interviews and authorised access to their criminal records. A cross-cultural validation study [37] of the PCL-R demonstrated that cut off scores for psychopathy in men vary between North America (30 out of a possible 40 points) and Europe (25 out of a possible 40 points). In line with previous research in UK samples [8,9], we used a score of 25 as the threshold for psychopathy in this English population. We calculated total, factor 1 and factor 2 PCL-R scores for all participants. Factor 1 scores are a total of facet 1 (interpersonal traits, such as pathological lying) plus facet 2 traits (affective traits, such as lack of empathy), while factor 2 scores are a total of facet 3 (antisocial lifestyle traits, such as impulsivity) plus facet 4 traits (overt antisocial behaviors, such as criminal versatility). Exclusion criteria were: history of major mental disorders (bipolar 1, bipolar 2, major depression or psychotic disorders) or self-reported neurological disorders, head injury resulting in loss of consciousness for 1 hour or longer, severe visual or hearing impairments, or contraindications to MRI.

After receiving a complete description of the study, all participants provided written consent. Ethical approval was obtained from the national UK research authority (National Health Service Health Research Authority Research and Ethics Committee, project number 15/LO/1083). All assessments were conducted by an experienced forensic psychiatrist (JT). Participants completed the reactive-proactive aggression questionnaire [38]. On the day of each MRI scan, participants provided a urine sample to assess for

substance misuse. Following psychometric assessments, only participants who attended for two MRI sessions were included in the analyses.

The three groups did not differ significantly except for years of education and PCL-R total and facet scores (Table 1). The offenders with antisocial personality disorder and psychopathy had significantly higher proactive, reactive and total aggression scores than those without psychopathy. The offenders with antisocial personality disorder and psychopathy also had a significantly higher rate of comorbid Cluster A personality disorder diagnosis compared to healthy non-offenders. Offender groups (with and without psychopathy) had a significantly higher rate of comorbid Cluster B personality disorder diagnosis compared to healthy non-offenders. Both offender groups also had a significantly higher rate of lifetime substance misuse disorders than healthy non-offenders, however the proportion of offenders with and without psychopathy with lifetime substance use disorders did not differ. Urinary drug screening on the day of scanning revealed some significant differences in active illicit substance misuse (see Supplementary Table S1), therefore this was included as a covariate in fMRI analysis.

Study Design and Procedures

In a double-blind, placebo controlled, randomised crossover design, participants self-administered, under instruction from the researcher, 40 IU of IN-OT (Syntocinon; Novartis, Basel, Switzerland) or placebo (identical composition to Syntocinon except for the omission of oxytocin). Participants began the morphed faces task within 25-30 minutes of administration. The oxytocin dose employed was the highest clinically applicable safe dose administered to human volunteers, in keeping with a protocol which demonstrated significant neural activation over a period of 25–78 minutes with this dose [39]. Further discussion about the dose and timing of intranasal oxytocin, and mechanism for delivery to the brain, is included in Supplementary Materials (S1).

At a second session (occurring between three and twenty-eight days later), participants completed the fMRI task again under the alternative treatment condition. Participants were instructed to avoid food, drinks (except water), and nicotine two hours before starting the experiment. Participants completed the Morphed Faces task (see Figure 1). During the task, participants were asked to indicate the sex of each face with a left-right button press using the index and middle finger of their right hand during a single run, which lasted 9 minutes 56 seconds. Full description of the Morphed Faces task, together with information on data quality control and motion parameters, is available in Supplementary Materials (S2).

General linear model analysis of behavioural data

For the Morphed Faces task, means were first calculated across the whole sample for both accuracy and reaction time in rating the gender of the faces displayed. To investigate the effect of oxytocin and its interaction with other variables, for both accuracy and response latency data, a three group (NO, ASPD-P, ASPD+P) by two condition (oxytocin, placebo) by four intensity (40%, 60%, 80%, 100% of fearful facial expression) repeated-measures analysis of variance was conducted. Post-hoc repeated-measures

analysis of variance was performed for ASPD-P vs ASPD+P. SPSS version 25.0 was used. A threshold for significance of $p < 0.05$ was set for all tests.

Primary outcome measure and MRI processing

Whole-brain blood oxygen level dependent (BOLD) fMRI data were acquired using a 3.0 Tesla General Electric Magnetic Resonance Scanner. The principle outcome measure was a regressor for modulation of neural activity (BOLD responsivity) by intensity of fearful expression. Specific MRI parameters, and full details of preprocessing and individual level analyses and data quality control are available in supplementary materials (S3 and S4).

MRI Data group analysis

Following preprocessing steps, modulated emotion data were entered into a 3 Group (NO, ASPD-P, ASPD+P) by 2 Condition (placebo, oxytocin) 3dMVM (ANOVA style computations) model. Within this framework, general linear tests were coded to assess differential effects of drug between the groups. Post hoc t-tests were conducted to decompose these interactions by examining between- and within- group effects. Correction for multiple comparisons was performed using a spatial clustering operation in AFNI's 3dClustSim utilising the autocorrelation function (-acf) with 10,000 Monte Carlo simulations for the whole-brain analysis. Spatial autocorrelation was estimated from residuals from the individual-level GLMs. The initial threshold was set at $p = 0.005$. As outlined above, bilateral amygdala, anterior insula and midcingulate cortex, were selected a priori for ROI analysis. Small-volume corrections, calculated using an anatomically defined mask (TTN27, a Talaraich atlas from AFNI), yielded thresholds of $k = 13$ for anterior/mid-cingulate cortex, $k = 8$ for anterior insula, and $k = 2$ for amygdala at an initial significance threshold of 0.005 (multiple comparison corrected $p<0.05$).

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Tables

	Group			*Group comparison*		*Post Hoc Tests (p values)*		
Demographic/ Clinical Characteristic	NO (n =24)	ASPD-P (n= 15)	ASPD+P (n= 19)	Statistic[a]	P value	Control vs ASPD-P	Control vs ASPD+P	ASPD-P vs ASPD+P
Age (years)	37.6 (10.3)	40.9 (9.6)	38.7 (9.1)	0.52	0.59	0.92	1.0	1.0
IQ	100.9 (12.6)	97.6 (16.7)	91.8 (11.3)	2.31	0.11	1.0	0.11	0.7
Duration of education (years)	13.9 (3.2)	10.8 (2.2)	10.0 (2.0)	13.07	<0.001**	0.002**	<0.001**	1.0
Age at first violent conviction	n/a	20.6 (6.2)	18.5 (5.5)	0.97	0.34	n/a		
Number of violent convictions	n/a	3.7 (3.1)	4.7 (2.9)	-0.87	0.39			
RPQ Reactive Aggression	6.0 (4.0)[$]	12.4 (4.8)[$]	17.2 (4.5)[$]	29.28	<0.001**	<0.001**	<0.001**	0.013*
RPQ Proactive Aggression	1.0 (1.3)[$]	7.8 (6.3)[$]	14.2 (6.2)[$]	33.71	<0.001**	0.003	<0.001**	0.016*
RPQ Total Aggression	6.7 (5.0)[$]	20.2 (10.8)[$]	31.4 (10.2)[$]	37.61	<0.001**	0.001	<0.001**	0.012*
PCL-R Facet 1 (Interpersonal)	0.75 (0.98)	2.02 (1.64)	4.42 (1.86)	32.25	<0.001**	0.038**	0.001**	0.001**
PCL-R Facet 2 (Affective)	0.75 (0.94)	3.13 (1.64)	5.42 (1.95)	50.40	<0.001**	0.001**	<0.001**	0.001**
PCL-R Facet 3 (Lifestyle)	1.16 (1.63)	5.46 (1.68)	7.52 (1.17)	99.15	<0.001**	<0.001**	<0.001**	0.001**
PCL-R Facet 4 (Antisocial)	0.91 (1.72)	6.33 (2.16)	8.63 (1.11)	117.96	<0.001**	<0.001**	<0.001**	<0.001**
PCL-R Total	2.70 (2.74)	18.41 (3.49)	28.84 (3.14)	391.56	<0.001**	<0.001**	<0.001**	<0.001**
Personality Disorder other than ASPD (%)								
Cluster A	0	6.7	31.5	12.97	0.005**	0.38	0.0045**	0.10
Cluster B	0	20	36.8	10.19	<0.006**	0.016*	0.0016**	0.46
Cluster C	0	13.3	5.2	3.34	0.19	0.57	0.33	0.44
Lifetime Substance Use Disorder (%)	8.3	33.3	21	3.83	0.15	0.047*	0.23	0.42

Table 1. Demographic and clinical characteristics

Group data are mean (SD) unless otherwise stated. NO= non-offenders. ASPD-P = violent offenders with antisocial personality disorder but not psychopathy. ASPD+P = violent offenders with antisocial personality disorder and psychopathy [a] = $F_{(2,55)}$ for continuous variables in 3-group analyses; Chi-squared/Fisher's exact test for categorical data; *= statistically significant at p <0.05 level; **= statistically significant at p <0.01 level. [$] Not all participants completed Reactive-Proactive Aggression (RPQ) questionnaire: N for NO= 21; ASPD-P= 12, ASPD+P = 15.

Region	BA	Voxels	X	Y	Z	Statistic*	p
Overall Group Effect							
R midcingulate gyrus	24	29	-13.5	+4.5	+32.5	9.464 (F)	0.0003
L midcingulate gyrus	23/24	28	+10.5	+10.5	+35.5	9.135 (F)	0.0003
ASPD+P < ASPD-P (placebo condition)							
L midcingulate gyrus	23/24	109	+7.5	+13.5	+35.5	3.95	0.0002
R midcingulate gyrus	24	92	-10.5	+4.5	+32.5	4.115	0.0001
R anterior insula**	13	6	-40.5	+4.5	+17.5	3.045	0.003
Effect of oxytocin in ASPD+P (oxytocin > placebo)							
R midcingulate gyrus	24	173	-10.5	-1.5	+26.5	4.033	0.0001
L midcingulate gyrus	24	119	+10.5	-10.5	+29.5	4.074	0.0001
L anterior insula	13	15	34.5	-4.5	+14.5	3.498	0.0009
Group (ASPD+P vs ASPD-P) x Condition (placebo vs oxytocin) interaction effect							
L midcingulate gyrus	23/24	16	+7.5	+13.5	+32.5	3.21	0.0022

Table 2. Significant BOLD responses to modulated fearful expressions (covaried for active substance misuse).

Hypothesised regions first, then ordered by cluster size. BA = Brodmann Area. t statistic unless otherwise stated. *Statistic refer to t-tests unless stated otherwise. Significance threshold set at p =< 0.005, all findings significant after cluster-wise correction for multiple comparisons except**.

Figures

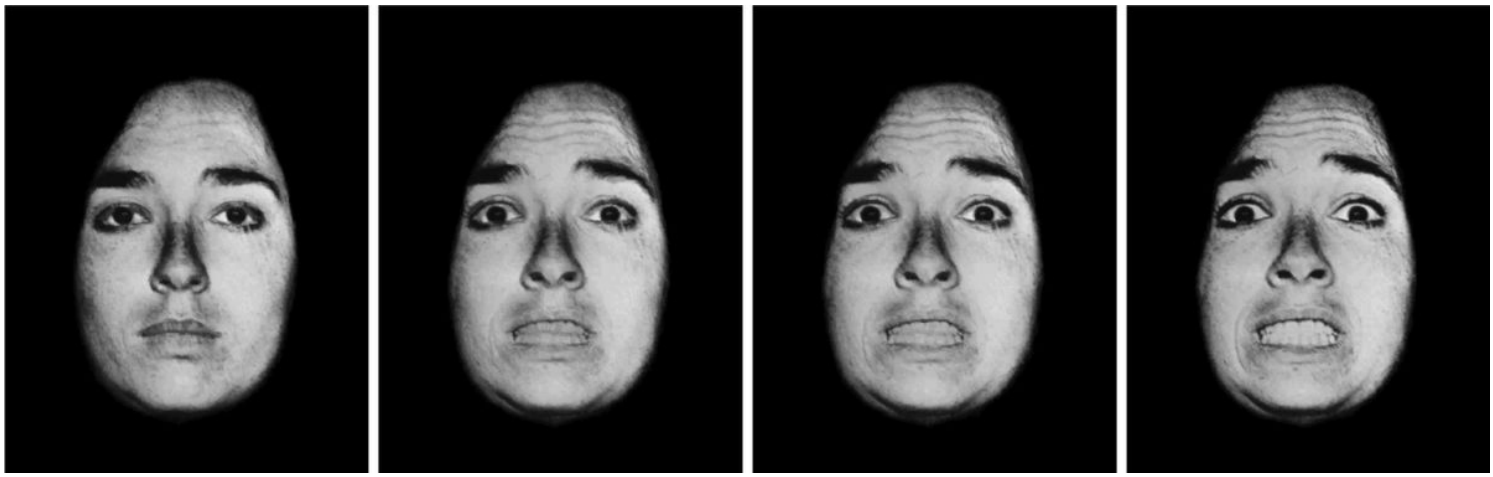
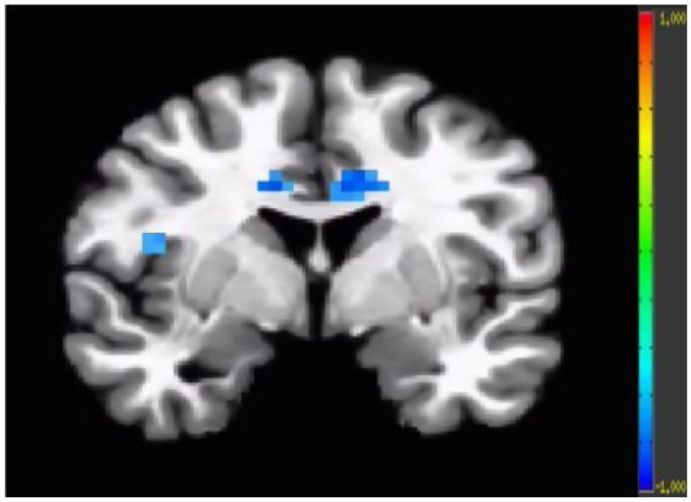
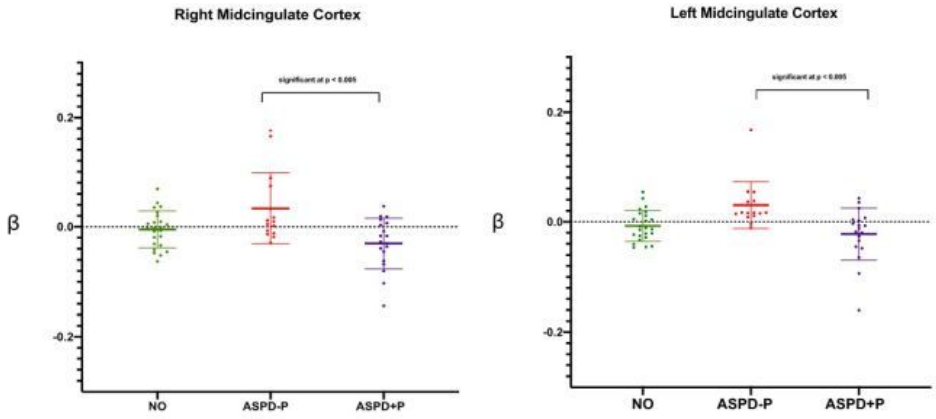


Figure 1

Facial expressions of fear at different intensities on the Morphed Faces Task (40%, 60%, 80%, 100%). Participants were presented with images of male and female faces expressing fearful expressions. All images were of Caucasian adults (50% female) drawn from well-validated images in the Pictures of Facial Affect Series [40]. To allow for analysis of parametric modulation, photos displaying each target emotion were morphed with a photo of the same face displaying a neutral expression in 4 different gradients (40%, 60%, 80%, 100% of the target emotion) to produce a total of 16 unique images (4 individuals (2 men, 2 women) x 4 intensities). Images were rapidly presented in a series of 50ms frames. Stimulus presentations were followed by a fixation point, which was on screen for a jittered duration of 1250-4250ms.



a

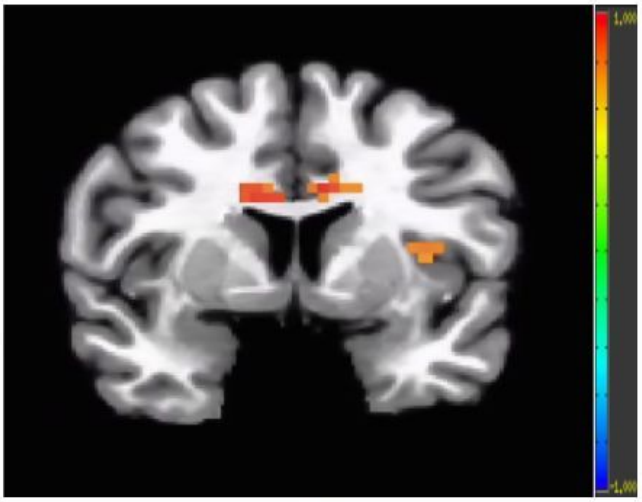


b

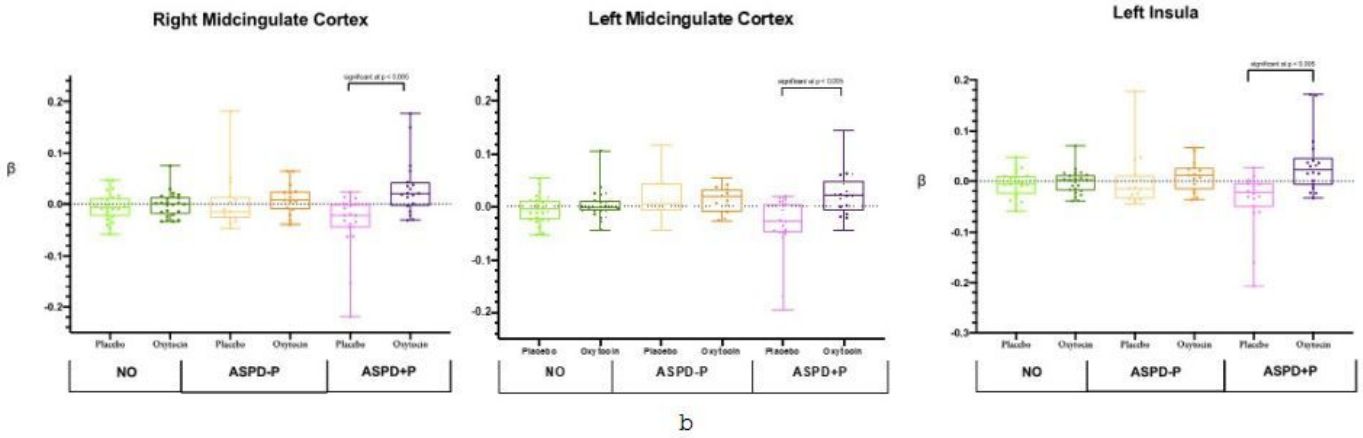
Figure 2

a. Reduced modulation by fearful intensity in bilateral midcingulate cortex and right anterior insula in violent offenders with (ASPD+P) compared to violent offenders but not psychopathy (ASPD-P), placebo condition. Color bar represents t statistic.

b. Individual beta values for fear processing (modulated fear regressor) in bilateral midcingulate cortex, placebo condition. Individual subjects' data plotted as dots. Means are indicated by horizontal bars. Error bars represent standard deviations. Findings in insula did not survive multiple comparison corrections. NO= non-offenders ASPD-P = violent offenders with antisocial personality disorder but not psychopathy. ASPD+P= violent offenders with antisocial personality disorder and psychopathy.



a



b

Figure 3

a. Increased modulation by fearful intensity in bilateral midcingulate cortex and left insula in oxytocin relative to placebo condition in violent offenders with ASPD+P. Color bar represents t statistic.

b. Individual beta values for fear processing (modulated fear regressor) for contrast oxytocin > placebo in bilateral midcingulate cortex and left insula in violent offenders with ASPD+P. Individual subjects' data plotted as dots. Means are indicated by horizontal bars. Error bars represent standard deviations.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- NMHSupplementaryMaterials.docx