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Oxytocin in Postnatally Depressed Mothers: Its influence on Mood and Expressed Emotion

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Abstract

Background: Postnatal depression is common and negatively affects the mother–baby relationship; oxytocin has been found to have positive effects on parenting behavior. We hypothesize that intranasal administration of oxytocin to mothers with depression will influence their parenting related expressed emotion, creating a better basis for sensitive parenting.

Methods: Twenty-five depressed mothers with infants under one year participated in a randomized, double blinded, placebo controlled within subject clinical trial in 2011. Mothers attended an out-patient perinatal psychiatry setting in NSW, Australia. They received 24IU of oxytocin alternating with placebo approximately one week apart in random order, prior to completing outcome measures. The outcome measures were the Five Minute Speech Sample, the Self-Assessment Manikin and the Controlled Oral Word Association Test.

Results: In the oxytocin condition mothers with postnatal depression were sadder ($p = .01$), more often initially described their babies as
difficult ($p = .038$) but reported that the quality of their relationship with their infant was greater ($p = .036$).

**Conclusion:** Oxytocin did not make depressed mothers happier but their perception of the relationship with their baby improved. Treatment with intranasal oxytocin might show some unwanted side-effects in depressed individuals.

**Keywords:** Oxytocin, postnatal depression, Expressed Emotion, mood, Self-Assessment Manikin, Randomised Controlled Trial
Introduction

Postnatal depression (PND) is a common mental health problem. A meta-analysis of fifty-nine studies (including 12,810 women) found the prevalence of maternal depression in the early postnatal period to be thirteen percent [1]. Depression during the postnatal period has effects upon the mother, the infant, and the broader family. The disorder affects the mother’s mood, thought processes [115] and ability to parent [116]. Children whose mothers experienced chronic depression had various negative outcomes by the beginning of primary school [116]. The current study explores the effects of oxytocin administration on parenting related mood, cognition, and expressed emotion in mothers with a diagnosis of PND.

The processes involved in the ability to parent are complex. One recent area of interest is the oxytocinergic system. Oxytocin (OT) is a hormone and neurotransmitter produced centrally in the paraventricular (PVN) and supra optic nuclei. It functions in the physiological processes of parturition [9], aids social affiliation
processes [11], and is involved in parenting behaviors [12]. Animal studies have shown that maternal behavior such as licking and grooming of pups can be induced or inhibited by central administration of OT or an OT antagonist respectively [117, 118]. In a non-clinical sample plasma OT levels taken during pregnancy and early postpartum were found to be stable and predict maternal bonding behaviors[119]. In addition, maternal OT levels increased after affectionate contact with the infant [120], and this effect was enhanced if the mother had a secure attachment classification [121].

Given the above, understanding associations between OT and depression generally, and PND specifically, is important for potential clinical benefits. Human post mortem studies have documented anatomical and physiological differences in the brains of those previously depressed compared to controls. In previously depressed individuals an increase in the number, size [16] and mRNA concentration [17] of OT neurons in the PVN was found. It is not known whether these differences are a result of depressed mood, or conversely, cause depressive symptoms. However, in living participants, lower plasma OT levels were found to be related to
depressive symptomatology [18]. With regard to PND, in women at risk for developing PND lower plasma OT levels in mid-gestation have been found to be predictive of PND symptoms [19].

Understanding the role of OT in parenting is in its infancy [12]. Initial findings include a significant association between OT levels and the quality of community mothers’ interactions with their infants [12]. Studies with intranasal OT administration have added to the body of knowledge, though most of them focused upon non-parents, for whom OT administration has been reported to result in changes in brain function. Exposed to infant cry sounds, brain areas involved in empathy are more activated whilst those related to fear and aversion are attenuated after OT administration [122]. Conversely, during exposure to infant laughter OT reduces activity in brain areas related to emotional arousal whilst enhancing reward areas [123]. Other studies, not using infant cues, have found that OT administration enhances altruism [124], increases duration of gaze to eyes [125] and promotes the ability to interpret social cues [126]; all processes likely to be helpful when parenting an infant. A study
specific to parental behavior found that community fathers were more responsive to their toddlers after administration of OT [15].

In the current study we tested the effects of intranasal OT administration on maternal expressed emotion, mood, and cognitive processes in a double-blind randomized within-subject design with postnatally depressed mothers of 3-12 month old infants. Expressed Emotion (EE) is a construct originally used to establish rates of criticism and emotional over-involvement in relatives of adults with a diagnosis of schizophrenia [127]. Relapse rates are higher if the patient has a relative who either criticizes more frequently or is too emotionally involved (high EE) [127, 128]. In previous research EE was measured using a long semi-structured interview [129]. A shorter version, the Five Minute Speech Sample (FMSS), has been validated and is now widely used [130]. In addition to scoring criticism and emotional over-involvement it also takes into account the quality of the initial statement and the reported quality of the relationship. Studying different age groups, including adolescents [131], and diagnoses other than schizophrenia, such as mood disorders [129], has documented the relevance of EE for a variety of
psychiatric disorders. EE in parents of young children was associated with children’s disorganised attachment [132]. In mothers with depressed mood, EE has been found to be higher than in controls [133], and is one factor linked to the intergenerational transmission of depression [134]. To our knowledge no published work has tested the effect of OT administration upon EE. We predict that oxytocin administration will lead to less critical, less over-involved EE, more positive initial statements and greater quality of relationship reported, creating a better basis for sensitive parenting in depressed mothers of infants.

In terms of the effect of intranasal OT administration on emotional experience and mood, it is difficult to compare published results given varying methodologies used. Some studies not specific to parenting found that intranasal OT either did not improve anxiety levels or even increased negativity in response to social situations [23, 135]. Conversely, OT reduced anxiety levels but only if participants coped poorly [136]. OT administration has been found to produce no effect on mood in both a community sample [22] and a clinical sample of participants with anxiety [24]. Given that OT appears to
have either no effect or amplifies mood experience [23], we predict that OT will not improve PND mothers’ current mood.

The effect of OT on cognition has been studied both in the peripartum period and in non-parents. Studies reported either no effect, or a negative effect, of either plasma level or administration of OT upon various cognitive processes [137-139]. These studies used different tests of multiple aspects of cognition including visual memory, retention, recall and alertness. OT had a negative effect on recall [137, 138] but no effect could be established when numerous cognitive tests were performed [139]. To our knowledge, no study has explored the effect of OT upon verbal fluency.

The Controlled Oral Word Association Test (COWAT) is a measure of verbal fluency based on inhibitory control [140]. It requires the participant to attend to one task, filtering out extraneous stimuli and suppressing impulses to utter incorrect answers. Debatably, these executive skills are useful for parenting in a demanding setting [141]. No association between plasma oxytocin levels and various cognitive tasks was found in a non-parent sample with a diagnosis of depression [142]. However, participants with
severe depression produce lower scores than controls, and their scores improve if treatment is successful in ameliorating their depressive symptoms [143]. As we expect no effect of OT on current mood, we also expect no effect upon verbal fluency in this depressed cohort.

Finally, given that clinical populations with a diagnosis of PND have experienced increased rates of childhood abuse compared to community samples [144], we examined childhood abuse as a moderator of the effects of OT. Several experiments showed that the effects of OT are moderated by the type of parenting a participant experienced in childhood. Participants with a background of harsh and rejecting parenting seem less affected by intranasal OT administration than their peers with happier childhood experiences. For example, participants (community, non-parents) who had not experienced harsh discipline when they were children used less excessive handgrip force in response to an infant cry in the OT condition. There was no effect of OT on handgrip force if the participant had experienced harsh parenting [145]. In another experiment OT effects on processing facial expression, measured by electroencephalography, were also moderated by past parenting,
specifically maternal love withdrawal. Those participants who had not experienced high rates of love withdrawal were found to have heightened processing of happy and disgusted facial expressions after OT administration, whereas similar effects were absent in the group that had experienced more than average levels of love-withdrawal from the parents [146]. In yet another study individuals with a diagnosis of Borderline Personality Disorder with histories of abuse, became less trustful compared to controls who showed the expected increase in trust after administration of OT [104]. These findings point to the importance of including childhood experiences as a moderator of OT administration effects in clinical populations with an increased prevalence of adverse childhood experience.

In a within-subject study of mothers with a diagnosis of postnatal depression we expected that OT administration would be associated with less criticism about the infant, improved reported quality of relationship with the infant, a more positive initial statement, and less emotional over-involvement during the Five Minute Speech Sample but no improvement to current mood or cognitive performance.
Method

Procedure

Twenty five mothers (mean age 28.24 years, $SD = 5.93$, range 19-38) participated in the randomized double-blind, placebo-controlled, within-subject design. All participants received once intranasal oxytocin and once placebo on two visits with an intervening period of one week. Stenlake Compounding Chemist (Bondi, Australia) produced both the oxytocin and placebo, which contained all components except oxytocin. Sprays were bottled in identical containers for double blind purposes. Roughly half the participants ($n = 13$) received oxytocin during the first visit. Randomisation was conducted using block design and participants were stratified according to whether they were prescribed anti-depressant medication or not. The master file was held by Stenlake pharmacy until completion of the trial. The study protocol was approved by the Hunter New England Human Research Ethics Committee. All mothers gave written informed consent before their
participation. This informed consent included participation of their infant. The participants were recruited from various health agencies, and all had a diagnosis of postnatal depression made by the referring agency. Infants participating in the study were aged between 3 and 12 months (mean age 6.22 months, $SD = 2.44$).

The day before initial attendance, each participant was telephoned and completed the Edinburgh Post Natal Depression Scale (EPNDS) [99] to establish that symptoms were current, with a cutoff score of 12. On arrival a single dose of 24 IU oxytocin or placebo nasal spray was administered (One spray of 12IU per nostril). It has been shown that after intranasal oxytocin administration salivary levels of oxytocin remain elevated for more than two hours[147], which covered the duration of the visits. Forty-five minutes later participants were video-taped whilst interacting with their infants (results reported separately). During the waiting time between intranasal spray and the interaction session on the first visit, the mothers provided written demographic and pregnancy/delivery related information. They also completed a self-report questionnaire to establish occurrence of child abuse and neglect during their past
(Conflict Tactic Scales: Parent-Child Version [148]). During the final part of the interaction session the mothers completed the Self-Assessment Manikin [149], which measures current mood. At the conclusion of the interaction session the Five Minute Speech Sample was administered. This is an audio taped interview designed to elicit mothers’ attitudes towards their baby and the relationship that they share. Finally participating mothers completed the Controlled Oral Word Association Test, a test of verbal fluency [150].

Participants underwent both the oxytocin and the placebo condition with an interval of one week in a balanced within-subject design. Both sessions took place within a clinical setting for families with young children (the Parent and Infant Mental Health Service, Wallsend, NSW, Australia).

Participants

Gestational age of the infants ranged from 26 - 41 weeks (mean 38.32, SD 3.35). Term babies, as defined by a gestational age between thirty-eight and forty weeks, comprised sixty-four percent (n
= 16) of the sample. Seventy-six percent \((n = 19)\) of participants had delivered their babies vaginally, as opposed to by Caesarian Section. Birth weights of the infants ranged from 0.90 kg to 4.74 kg (mean 3.26, \(SD\ 0.90\)). Fifty-six percent \((n = 14)\) of the infants were female. Forty percent \((n = 10)\) of the infants were breast-fed.

Seventy-two percent \((n = 18)\) of participants were either married or in a de-facto relationship; the remaining mothers were single. In terms of income, sixteen percent were well off, earning more than AUD$100,000 per annum as a household. Thirty-two percent \((n = 8)\) of participants lived well under the poverty line, with access to less than AUD$20,000 per year. Twenty-eight percent \((n = 7)\) of participants only completed the four years of high schooling legally required in Australia. Fifty-six percent \((n = 14)\) of participants completed six years of high-school, but did not continue further study. Twenty-four percent of participants \((n = 6)\) had completed a university degree. Two participants \((8\%)\) identified as Aboriginal or of Torres Strait Islander descent.

Sixty percent \((n = 15)\) of participants reported that they were receiving treatment for their postnatal depression \((n = 6\) received both...
medication and counseling; \( n = 6 \) received medication alone and \( n = 3 \) received counseling alone). Of those participants prescribed antidepressant medication, the duration of administration ranged from one week to four years (mean 9.77 months, \( SD \ 15.48 \)). Sixty percent \( (n = 15) \) were prescribed medication for another condition (apart from PND; \( n = 2 \) antipsychotic; \( n = 4 \) oral contraceptive pill; others include antibiotics, anti-epileptic, \( H_2 \) blocker, thyroid replacement.

Measures

*Maternal Depression*

The presence of recent depressive symptoms in the mothers was measured using the Edinburgh Post Natal Depression Scale (EPNDS) [99]. Mothers were asked to fill out a questionnaire indicating their level of affective symptoms during the previous week on a 4-point scale. Internal consistency (Cronbach’s alpha) was .62. A score of 12 or higher was required for inclusion into our study. Coding occurred using the directions as established by Cox et al. Participants in our study presented on their first visit with scores ranging from 12 to 29 (mean 16.96, \( SD \ 3.41 \)). Data inspection revealed a single
outlier, which was winsorized by replacing the outlying score with a score just above the next highest value (with \( z < .29 \)) [151].

**Childhood Abuse**

Self-reported rates of child abuse in our sample was collected using the Conflict Tactic Scales: Parent Child Version [152] which have often been used to establish rates of child abuse [152]. Participants were required to indicate the frequency of occurrence of a parental strategy in the year that they turned thirteen. An example of a prompt is “My mother threw or knocked me down”; separate items are used for both parents. We used the scale for physical aggression. In our sample, internal consistency (Cronbach’s alpha) for physical abuse was .84.

**Current mood**

Mothers completed the Self-Assessment Manikin [149] to rate their current mood. This 3 item, non-verbal, pictorial assessment tool was designed to measure the affective domains of pleasure, arousal and dominance in response to a variety of contexts. It can be used to
measure current mood, as opposed to depression scales which ask a participant to report on mood symptoms over the past week or more. The measure has been validated across adult age groups [153]. Both community participants [154-156] and clinical samples including those with depression [157-160], have been studied. Each domain is examined using five cartoon like drawings depicting a continuum of affective states on three scales: ‘Happy to Sad’, ‘Calm to Agitated’ and ‘Controlled to In-control’. For these analyses we were interested in the two items most closely aligned to depression, the Happy to Sad scale and the Calm to Agitated scale. The manikin was scored from 1 - 9 with higher scores assigned to ‘positive’ aspects of the continuum (happy, calm).

Expressed Emotion

The concept of ‘expressed emotion’ (EE), refers to criticism and emotional over-involvement. The Five Minute Speech Sample [130] is a tool developed to assess high EE in a brief fashion. Participants were audio-taped whilst responding to the following verbal request: “I’d like to hear your thoughts about [baby’s name] in your own
words and without my interrupting you with any questions or comments. When I ask you to begin, I’d like you to speak for 5 minutes, telling me what kind of a baby [infant’s name] is and how the two of you get along together. After you have begun to speak, I prefer not to answer any questions. Are there any questions you would like to ask me before we begin?” The audiotape was subsequently coded by two independent coders and interrater reliability was established by double coding 20% of randomly chosen tapes (mean intraclass correlation = .86 (single measure, absolute agreement), range .84 - .89). The following categories were coded: quality of initial statement, number of criticisms uttered, quality of relationship and number of comments classified as emotional over-involvement [130].

Capacity to attend to a cognitive task
To test the mothers’ ability to focus on one task, suppressing other input, the participants completed the Controlled Oral Word Association Test (COWAT) [150]. This is a test of executive cognitions, specifically verbal fluency. Participants were asked to
utter as many words as possible within one minute timed aliquots, from prompted categories. They were asked for words beginning with three separate letters, ‘F’, ‘A’, and ‘S’; then asked to retrieve as many animals that they could think of. The test was audiotaped for subsequent collation of totals per category. Internal consistencies (standardized scores, Cronbach’s alpha) for the first and second visits were .79 and .76, respectively.

Results

A multivariate repeated measures analysis of variance was performed on the four subscales of the Five Minute Speech Sample (FMSS) and the two Self-Assessment Manikin (SAM) mood items as dependent variables with condition (oxytocin or placebo) as a within-subject factor. Results showed an overall effect of oxytocin administration on expressed emotion and mood, $F(6, 18) = 2.76, p = .04, \eta^2 = .48$. Initially results for expressed emotion will be presented, followed by those for mood.
Univariate analyses showed significant effects for Quality of Relationship, $F(1, 23) = 4.99, p = .036, \eta^2 = .18,$ and for Quality of Initial Statement, $F(1, 23) = 4.83, p = .038, \eta^2 = .17.$ Effects for Emotional Over-Involvement, $F(1, 23) = 0.48, p = .50, \eta^2 = .02,$ and for number of Criticisms uttered, $F(1, 23) = .06, p = .82, \eta^2 = .00$ were not significant. In the oxytocin condition depressed mothers were more likely to describe their baby as difficult in some way but reported a more positive relationship with their infant. Adding depression as a covariate did not yield a significant effect for depression ($p = .85$), showing that the effect of oxytocin was independent of level of depression at intake. Adding physical abuse as a covariate, and as a potential moderator, did not change results either ($p = .56$ for covariate; $p = .97$ as moderator). The effect of oxytocin upon aspects of expressed emotion was independent of and not moderated by depressed mothers having been physically abused during childhood.

Univariate analyses showed significant effects for the Happy to Sad item, $F(1, 23) = 7.39, p = .01, \eta^2 = .24;$ but effects for the Agitated to Calm scale were not significant, $F(1, 23) = 2.86, p = .11,$
$\eta^2 = .11$. In the oxytocin condition mothers with a diagnosis of postnatal depression scored lower, that is sadder than in the placebo condition. Adding depression as a covariate and physical abuse as a covariate or as a moderator did not change the results. The effect of oxytocin on reported mood was independent of both depression at intake and whether the mothers had been physically abused during their childhood. The effect was also not moderated by the experience of severe physical abuse.

Univariate analyses showed no significant effect of oxytocin on performance on the verbal fluency task, $p = .38$. Adding abuse and depression at intake as covariates revealed no significant results ($p = .57$ and $p = .87$, respectively).
Discussion

This is the first experiment to test the effects of OT administration on parenting related mood, cognition and expressed emotion in a clinical population with PND. We found that in the OT condition mothers with PND commence their description of their baby more negatively; the same mothers rate the quality of their relationship with their babies as more positive. In addition, after OT
administration, mothers with PND rate current mood as poorer. There was no effect of OT upon cognitive ability as tested by the COWAT.

OT was associated with lower current mood in this depressed sample. In previous studies oxytocin has been shown to increase the salience of a mood state [104, 123, 135], for better or for worse. In postnatally depressed mothers feelings of low mood might always be present in the background, and become more salient after the oxytocin inhalation. This magnifying effect of oxytocin on mood might be more pronounced when participants had been involved in a rather stressful and exhausting situation. In our case participants completed the self-report mood scale moments after being videoed interacting with their baby, a potentially stressful scrutiny. Our finding suggests that the use of OT in populations with depression might not always be positive and should be considered carefully if implemented in a therapeutic context.

We expected that in the OT condition participants would be more positive in their initial description of their baby, as well as more positive about their relationship to the baby in general. Only the latter prediction was borne out by our data. The instruction that participants
were given immediately prior to the commencement of the interview to measure expressed emotion may help us understand the findings. Mothers were asked to ‘describe what kind of baby ‘x’ is and how the two of you get along’. In the OT condition two distinct differences occurred. On the one hand participants’ first descriptor of their baby tended to be negative, such as ‘he is a poor sleeper’ but then more often this was followed up by examples of how closely connected they are in their relationship. An explanation of this seeming discordant response pattern may be that the OT condition enhances trust in the interviewer. OT has been found to enhance trust [124]. Thus the participant may feel more able to be honest about difficult aspects of her baby, but more primed to simultaneously reflect on the value the relationship holds for her. Given all participants were experiencing depressed mood, the presence of both an acknowledgement of how difficult their baby can be, but how connected the two of them feel is particularly poignant.

We predicted that childhood abuse would act as a covariate or moderator of our findings. The results did not support this prediction.
A larger study with more statistical power or using alternate method
of collecting abuse data, such as child welfare records, may or may not lead to different results. The inclusion of a wider range of normal to clinical participants with varying childhood experiences might also lead to greater power to find the expected interaction between childhood experiences and oxytocin effects. In our sample only clinically diagnosed cases of postnatally depressed mothers were included which might have led to restriction of range in parenting experiences. Replication in a larger study would add to the reliability of our results.

The findings of this study prompt important questions. Are changes in expressed emotion sustainable, perhaps by the regular therapeutic use of intranasal OT? If EE changes persist, does this lead to enhanced infant outcomes? Future research should also establish if OT generally leads to lower mood in depressed populations which would imply a cautionary note on potentially unwanted side-effects of OT in therapeutic contexts with depressed patients. It should also be examined whether the inferred increased trust in the interviewer indeed can be substantiated and whether this effect generalizes to enhanced trust in therapists that could promote
the alliance between patient and therapist and aid future therapeutic interventions.

Conclusion

Mothers with a diagnosis of postnatal depression after administration of oxytocin, report poorer current mood, state that their baby is more difficult but rate the quality of the relationship with their baby as higher, compared to the placebo condition.