



A double-edged hormone: The moderating role of personality and attachment on oxytocin's treatment facilitation effect

Dana Tzur Bitan^{a,b,*}, Ariella Grossman-Giron^{a,b,1}, Omer Sedoff^{a,b}, Sigal Zilcha-Mano^c, Uri Nitzan^{b,d}, Hagai Maoz^{b,d}

^a Department of Psychology, Ariel University, Israel

^b Shalvata Mental Health Center, affiliated with the Sackler School of Medicine, Tel Aviv University, Israel

^c Department of Psychology, University of Haifa, Haifa, Israel

^d Sackler School of Medicine, Tel Aviv University, Israel

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ABSTRACT

Background: Studies exploring the potential augmenting effect of oxytocin for patients with mental disorders have thus far reported mixed effects. However, oxytocin's effect may differ across patients with different interpersonal characteristics. This study aimed to examine the moderating role of attachment and personality traits on the effect of oxytocin administration on the therapeutic working alliance and symptomatic change, among hospitalized patients with severe mental illness.

Methods: Patients (N = 87) were randomly assigned to receive oxytocin or placebo, as an add-on to psychotherapy for a period of four weeks, in two inpatient units. Therapeutic alliance and symptomatic change were measured weekly, and personality and attachment were assessed at pre- and post-intervention.

Results: Oxytocin administration was significantly associated with improvement of depression (B=2.12, SE=0.82, t = 2.56, p = .012), and suicidal ideation (B=0.03, SE=0.01, t = 2.44, p = .016) for patients low in openness and extraversion, respectively. Nonetheless, oxytocin administration was also significantly associated with a deterioration in the working alliance for patients high in extraversion (B=-0.11, SE=0.04, t = -2.73, p = .007), low in neuroticism (B=0.08, SE=0.03, t = 2.01, p = .047) and low in agreeableness (B=-0.11, SE=0.04, t = 2.76, p = .007).

Conclusions: Oxytocin may act as a double-edged sword when it comes to its effect on treatment process and outcome. Future studies should focus on routes to characterize patients who might benefit the most from such augmentation.

Clinical trial registration: Pre-registration in clinicaltrials.com: NCT03566069; Israel Ministry of Health: MOH_2017-12-05_002003.

1. Introduction

Oxytocin (OT), a nine-amino acid neuropeptide synthesized in the hypothalamus and released into peripheral circulation by the pituitary gland, has been previously suggested as a potential facilitator of psychotherapeutic interventions. As early as 2010 it was argued that OT may affect the therapeutic process through its ability to modulate trust and sense of safety, which seem crucial for effective therapeutic processes to take place (Olf et al., 2010). Indeed, many studies have been conducted thus far to explore the potential augmenting effect of OT

across many clinical populations. Nonetheless, results have thus far been elusive, with some studies reporting no facilitating effect (Clarici et al., 2015; Buchanan et al., 2021), some an adverse negative effect (Acheson et al., 2015; MacDonald et al., 2013), and some a positive effect (Flanagan et al., 2018; Stauffer et al., 2020). These findings have led to the suggestion that the effects of OT are constrained by context and individual features (Bartz et al., 2011), thus leading to the need to further explore under which conditions OT's effects may be optimal.

One of the compelling theoretical formulations to account for the large variability in findings pertaining to OT's therapeutic effect is the

* Correspondence to: Department of Psychology, Ariel University, Ariel 40700, Israel.

E-mail address: danatz@ariel.ac.il (D. Tzur Bitan).

¹ Mutual contribution

social salience hypothesis. In 2016, Shamay-Tsoory and Abu Akel suggested that OT administration might amplify the salience of approach or threat signals, which in turn might facilitate a differential emotional response, depending on the social context (Shamay-Tsoory and Abu-Akel, 2016). Thus, OT might increase antisocial effects such as aggression and envy under threatening circumstances, and social affiliation in secure situations. Studies in the field of cognitive psychology have provided some evidence for increased attentional processes following OT administration, such as increased visual fixation toward communicative areas of the face, for instance the eye region (Guastella et al., 2013), and improved capacity to read subtle non-verbal cues from eye regions (Domes et al., 2007). Thus, there is some evidence to suggest that the variance in response to OT may be modulated by external cues which provide information about the context.

Studies conducted among healthy participants suggest that OT's effects may be modulated not only by external cues but also by internal constructs and representations. Studies demonstrate that OT improves empathic accuracy only among less socially capable individuals (Bartz et al., 2010). Similarly, Human et al. (2016) found that OT administration led to greater prosocial tendencies only among healthy participants who were low in extraversion. These findings suggest that patients with less adaptive personality characteristics, such as those low on extraversion, openness or agreeableness, may benefit more from OT administration. Furthermore, Wang et al. (Wang et al., 2020) found that OT administration increased gaze to the eye region in a differential manner across individuals with different attachment patterns, such that individuals with high attachment anxiety displayed more eye gaze following OT administration. Similarly, Bernaerts et al. (2017) reported that OT-induced changes were most pronounced among healthy young adults with a less secure attachment toward their peers, thus suggesting that OT administration may be most beneficial to patients with less secure attachment patterns. Taken together, these findings suggest that OT effects may be modulated by internal representations such as personality and early attachment pattern, leading to a selective beneficial response to OT administration only among individuals with less socially-adapted internal representations (Shamay-Tsoory and Abu-Akel, 2016).

In a recent randomized controlled trial (RCT) conducted by Grossman-Giron et al. the effect of OT administration on therapeutic process and outcome was assessed among 87 patients undergoing psychiatric hospitalization. Patients in this study received intranasal OT or placebo twice a day, for four weeks of psychiatric hospitalization. The authors found a significant effect of oxytocin administration on symptomatic change, as evaluated by the Hopkins Symptom Checklist (HSCL-11) (Lutz et al., 2006), indicating a symptomatic improvement in the OT but not the placebo group. Furthermore, they found a trend of improved working alliance only in the placebo group but not in the OT group. Thus, one of the potential explanations to account for the improved outcomes and no improvement in the therapeutic alliance following OT administration, is that the effects of OT are moderated by potential internal representations such as attachment and personality patterns.

To the best of our knowledge, studies assessing the moderating role of personality traits and attachment patterns in response to OT administration have thus far focused on healthy participants. Furthermore, no study has previously examined the moderating role of attachment and personality in the effects of OT administration on psychotherapy process and outcome. In this study we aimed to bridge this gap, by conducting a secondary analysis to the RCT conducted by Grossman-Giron et al. exploring moderators of OT's effects. Following the literature review, we hypothesized that: (a) Baseline attachment patterns would moderate the effects of OT administration, such that individuals high in avoidance and anxiety attachment would demonstrate larger improvements in therapeutic outcome and process, and (b) Baseline personality traits would moderate the effects of OT administration, such that individuals with less socially-adapted personality characteristics - those low in extraversion, openness, agreeableness and consciousness, and high in

neuroticism - would show the largest gains.

2. Methods and materials

2.1. Participants

An elaborative description of the research design and procedures, the study population, and baseline characteristics of the study participants can be found in Grossman-Giron et al. Patients were recruited for the study from the inpatient adult psychiatric wards at the Shalvata Mental Health Center (MHC). Inclusion criteria included adults aged 18 and above, with a diagnosis of a psychiatric disorder of any kind. A total of 125 patients were assessed for eligibility, of whom 38 were not enrolled due to various reasons. The remaining patients ($N = 87$) were recruited and randomized to the study groups, with 23 patients dropping out of the study or the treatment (following discharge) before completing full four weeks. No significant differences between dropouts and completers were found in age, sex, or type of diagnoses, and study groups did not significantly differ in frequency of dropouts. Patients were a mean age of 36.44 ($SD = 16.26$), and most of them were females (71.3%). In the OT group, 73% were females, whereas in the placebo group 70% were females, with no statistically significant differences in sex between the groups. Patients' diagnoses were affective disorders (55.2%), anxiety disorders (17.2%), and other diagnoses (27%). The average number of previous hospitalizations was 4.33 ($SD = 4.86$). Patients were eligible to participate in the study if they were 18 years of age or older, diagnosed with a psychiatric disorder of any kind, and hospitalized with an expected hospitalization of at least four weeks. Patients who were pregnant, received electroconvulsive therapy (ECT), had substance abuse, psychosis, autism spectrum disorder, or mental retardation spectrum disorder comorbidity, or exhibited immediate suicidal risk, were not eligible to participate in the study.

2.2. Procedure

Ethical approval of the study protocol was obtained through the institutional review board of the Shalvata MHC (reference number: 0023-17-SHA). The study was pre-registered in clinicaltrials.com (reference number: NCT03566069) and in the Israel Ministry of Health (reference number: MOH_2017-12-05_002003). After signing informed consent forms, patients meeting inclusion criteria completed all the study measures and thereafter were randomized and double-blindly allocated to receive OT or placebo. The intervention period lasted for four weeks, during which patients received either OT or placebo, twice a day (at 08:00 a.m. and at 5:00 p.m.). Oxytocin and placebo were administered by the nursing staff, which was blind to the group allocation and study objectives. Compliance monitoring was performed by the nurses staff. Safety monitoring was performed by a senior psychiatrist, and also by weekly administration of a side effect questionnaire. Treatment as usual in the psychiatric ward included two to three sessions of psychotherapy per week, case management, and medication management meetings. Psychotherapy orientation was primarily psychodynamic. The working alliance and level of distress were evaluated after each psychotherapy session, whereas side effects and an extended assessment of distress were evaluated every week. Attachment, personality, depression, and anxiety were assessed at baseline and after four weeks of intervention. Oxytocin was administered intranasally twice a day using a spray containing 16IU, sorbitol, benzyl, alcohol, glycerol, and distilled water. Placebo administration included sorbitol, benzyl, alcohol, and glycerol. Dosage and method of delivery were determined by standard guidelines (Guastella et al., 2013).

2.3. Instruments

2.3.1. Outcome measures

Anxiety was assessed using the State-Trait Anxiety Inventory (STAI)

(Spielberger et al., 1983), a widely used self-report questionnaire aimed at evaluating the current state (STAI-ST) of anxiety as well as general anxiety proneness (STAI-TR) (Rossi and Pourtois, 2012). In the current sample, Cronbach's alpha were $\alpha = .93$ for the STAI-ST and $\alpha = .92$ for the STAI-TR, indicating high internal reliability. The Hamilton Rating Scale for Depression (HRSD) (Hamilton, 1960) was used to assess depression severity, and produced alpha coefficient of .78, indicating acceptable internal consistency. The Scale for Suicidal Ideation (SSI) (Beck et al., 1979) is a self-report inventory for evaluating current suicidal severity in terms of attitudes, behaviors, and plans to commit suicide. The scale was utilized to assess suicidal ideation and produced high internal reliability of .95. The Outcome Questionnaire-45 (OQ-45) (Lambert, 2012), a 45-item self-report instrument used for evaluating symptomatic distress, interpersonal relationships, and social role performance, was used to assess treatment outcomes. In the current sample, the scale demonstrated high internal reliability ($\alpha = .93$). The Hopkins Symptom Checklist –short form (HSCL-11) (Lutz et al., 2006) is a brief self-report tool for assessing symptomatic distress, found to be suitable for detecting changes in symptom severity during the course of therapy (Lutz et al., 2009). The alpha coefficient of the current sample indicated high internal reliability ($\alpha = .92$).

2.4. Process measure

The Session Alliance Inventory (SAI) (Falkenström et al., 2015) was used to assess patient-therapist working alliance through three components: agreement on treatment goals, agreement on therapeutic tasks, and positive patient-therapist emotional bond. The scale demonstrated high internal reliability in the current sample ($\alpha = .93$).

2.5. Moderation measures

Attachment patterns were assessed via the Experiences in Close Relationships scale (ECR) (Brennan et al., 1998), a self-report instrument aimed at evaluating anxious and avoidant attachment in adults. High scores in a dimension reflect anxious or avoidant attachment, and low scores in both dimensions reflect secure attachment. In the current sample, the scale demonstrated high internal consistency for the attachment anxiety dimension ($\alpha = .89$) as well as for the attachment avoidance dimension ($\alpha = .91$). The Big Five Inventory (BFI) (John et al., 1991) was used to assess personality traits based on five personality dimensions: neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness. Cronbach's alpha scores indicated good reliability across the five dimensions (neuroticism $\alpha = .81$; extraversion $\alpha = .80$; openness to experience $\alpha = .80$; agreeableness $\alpha = .82$; and conscientiousness $\alpha = .76$).

2.6. Statistical analyses

Sample size was a-priori calculated and determined (Grossman-Giron et al.). Individual growth curves for each patient, and for each of the study measures, was calculated using multilevel modeling (MLM). Intraclass correlations (ICCs) assessing the amount of variance explained by therapists indicated effects which were too small to be estimated (Grossman-Giron et al); therefore, all models followed a two-level structure, where measurements (Level 1) were nested within patients (Level 2). Slopes were then considered as the outcome variable in all subsequent moderation analyses, which were performed using Hayes' (Hayes, 2022) PROCESS macro version 4.0, with 10,000 bootstrap resampling. Group (OT versus placebo) served as the predictor, while attachment and personality baseline values were entered as moderators. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) v.25 (IBM Corp. Armonk, NY, USA) and R Version 4.1.0 package 'nlme' (Pinheiro et al., 2016).

3. Results

Results of the moderation analyses are presented in Table 1. Several interaction effects were found for the moderating effects of personality patterns on the effects of OT administration. Neither avoidant nor anxious attachment moderated the effect of OT administration on any of the process and outcome measures.

For the moderating effects of extraversion, a significant interaction effect was found for suicidal ideation ($B=0.03$, $SE=0.01$, $t = 2.44$, $p = .016$). Simple slope analyses for significant interaction effects are elaborated in Table 2. As can be seen, there was a nonsignificant trend of association between OT and a decrease in suicidal ideation (SSI) when extraversion was low ($B=-0.03$, $SE=0.01$, $t = -1.76$, $p = .082$). However, when extraversion was high, this trend was reversed, and indicated a non-significant increase in suicidal ideation among high extraversion patients ($B=0.02$, $SE=0.01$, $t = 1.71$, $p = .089$).

An additional interactive effect of personality and OT was found for the subscale of openness to experience and its effect on depressive symptoms ($B=2.12$, $SE=0.82$, $t = 2.56$, $p = .012$). Specifically, when openness was low, OT administration was associated with a decrease in depression symptoms ($B=-3.53$, $SE=1.02$, $t = -3.44$, $p < .001$). This effect remained significant although somewhat reduced in medium levels of openness ($B=-1.66$, $SE=0.71$, $t = -2.32$, $p = .022$); nonetheless, it became non-significant when openness to experiences was high ($B=0.19$, $SE=1.01$, $t = 0.19$, $p = .847$).

Extraversion, neuroticism, and agreeableness all showed significant interactive effects with OT on the working alliance (SAI). For extraversion ($B=-0.11$, $SE=0.04$, $t = -2.73$, $p = .007$), simple slope analyses indicated that when extraversion was high, OT administration was associated with a significant decrease in the working alliance ($B=-0.16$, $SE=0.05$, $t = -3.14$, $p = .002$), but not when extraversion was low ($B=0.03$, $SE=0.05$, $t = 0.75$, $p = .451$). Similarly, neuroticism significantly moderated the effect of OT administration on the working alliance ($B=0.08$, $SE=0.03$, $t = 2.01$, $p = .047$), such that in low levels of neuroticism, OT administration was significantly associated with a decrease in the working alliance ($B=-0.13$, $SE=0.05$, $t = -2.64$, $p = .009$), but not when neuroticism was high ($B=0.01$, $SE=0.05$, $t = 0.22$, $p = .821$). A similar significant effect was observed for agreeableness ($B=0.11$, $SE=0.04$, $t = 2.76$, $p = .007$), with OT being significantly associated with a decrease in the working alliance when agreeableness was low ($B=-0.17$, $SE=0.05$, $t = -3.26$, $p = .001$), but not when agreeableness was high ($B=0.03$, $SE=0.05$, $t = 0.66$, $p = .509$). Fig. 1 presents a graphical illustration of the significant interaction effects.

4. Discussion

This study was aimed to explore whether personality and attachment patterns moderate the effects of OT administration on therapeutic process and outcome among psychiatric inpatients. The results indicated that personality traits modulated the effect of OT administration. Specifically, when extraversion and openness to experience were low, OT administration was associated with improvement in suicidal ideation and depression, respectively. Low extraversion was also associated with higher symptomatic improvement following OT administration across several anxiety and depression scales as compared to high extraversion; nonetheless, the interaction only reached the level of a trend (p values of .08–.09, see Table S3). These findings support the results reported by Human et al. (2016) which demonstrated a selective pro-social effect of OT administration among healthy individuals with low extraversion. The finding that indicated improvement in depressive symptoms among individuals low in openness to experience suggests that decreased flexibility and willingness to engage in novel experiences (McAdams, 1992), which is also associated with social deficits (Kemp et al., 2020), may lead to a beneficial response to OT administration. Such interspersed also resonates with the idea that OT's effects are more beneficial to individuals with reduced social capabilities (Shamay-Tsoory and

Table 1
Interaction effects of attachment and personality patterns with OT administration on therapy process and outcome.

Structure	Moderator	Parameters	Outcome measures						Process measures
			Anxiety		Depression		Distress		Working alliance
			STAI-ST	STAI-TR	HRSD	SSI	OQ-45	HSCL	SAI
Attachment patterns	Anxious Attachment	B (SE)	-1.35 (0.81)	-0.46 (0.45)	-0.32 (0.55)	-0.01 (0.00)	-0.60 (1.01)	-0.01 (0.03)	0.01 (0.02)
		t	-1.66	-1.01	-0.57	-1.85	-0.59	-0.45	0.47
		p	0.098	0.311	0.564	0.067	0.554	0.651	0.634
	Avoidant Attachment	B (SE)	-0.09 (0.76)	-0.12 (0.43)	-0.22 (0.53)	0.00 (0.00)	-0.30 (0.97)	-0.00 (0.03)	-0.04 (0.02)
		t	-0.11	-0.29	-0.42	0.84	-0.31	-0.22	-1.64
		p	0.905	0.770	0.668	0.401	0.755	0.820	0.104
Personality	Extraversion	B (SE)	2.11 (1.22)	1.17 (0.67)	1.45 (0.83)	0.03 (0.01)	2.49 (1.45)	0.05 (0.05)	-0.11 (0.04)
		t	1.72	1.73	1.75	2.44	1.71	1.02	-2.73
		p	0.088	0.085	0.083	0.016 *	0.090	0.310	0.007 * *
	Neuroticism	B (SE)	-0.31 (1.18)	-0.63 (0.65)	0.28 (0.80)	-0.01 (0.01)	-1.75 (1.41)	-0.01 (0.04)	0.08 (0.03)
		t	-0.26	-0.97	0.35	-1.25	-1.23	-0.37	2.01
		p	0.791	0.334	0.724	0.213	0.218	0.705	0.047 *
	Agreeableness	B (SE)	-0.06 (1.20)	0.10 (0.67)	-0.24 (0.82)	-0.02 (0.01)	-0.30 (1.46)	-0.04 (0.04)	0.11 (0.04)
		t	-0.05	0.15	-0.29	-1.75	-0.20	-0.95	2.76
		p	0.960	0.875	0.767	0.082	0.835	0.340	0.007 * *
	Conscientiousness	B (SE)	-0.40 (1.35)	0.17 (0.75)	-0.24 (0.92)	-0.01 (0.01)	-0.46 (1.63)	-0.07 (0.05)	0.00 (0.04)
		t	-0.29	0.22	-0.26	-0.73	-0.28	-1.38	0.01
		p	0.765	0.821	0.791	0.467	0.778	0.170	0.989
	Openness	B (SE)	2.28 (1.24)	0.37 (0.70)	2.12 (0.82)	0.02 (0.01)	-0.41 (1.52)	0.01 (0.05)	0.00 (0.04)
		t	1.83	0.53	2.56	1.80	-0.27	0.26	0.04
		p	0.069	0.596	0.012 *	0.074	0.785	0.792	0.965

Notes. STAI-ST: The State-Trait Anxiety Inventory, state anxiety; STAI-TR: The State-Trait Anxiety Inventory, trait anxiety; OQ-45: The Outcome Questionnaire-45; HSCL-11: The Hopkins Symptom Checklist-short form scale; HRSD: The Hamilton Rating Scale of Depression; SSI: The Scale for Suicidal Ideation; SAI: The Session Alliance Inventory. Bold represents significant findings. * <.05, ** <.01, *** <.001.

Table 2
Simple slope analysis of significant interaction effects.

Moderator	Process/outcome measure	Parameter	Low moderator	Medium moderator	High moderator
Extraversion	SSI	B (SE)	-0.03 (0.01)	-0.00 (0.01)	0.02 (0.01)
		t	-1.76	-0.06	1.71
		p	0.082	0.952	0.089
	SAI	B (SE)	0.03 (0.05)	-0.06 (0.03)	-0.16 (0.05)
		t	0.75	-1.68	-3.14
		p	0.451	0.096	0.002 * *
Neuroticism	SAI	B (SE)	-0.13 (0.05)	-0.06 (0.03)	0.01 (0.05)
		t	-2.64	-1.73	0.22
		p	0.009 * *	0.086	0.821
Agreeableness	SAI	B (SE)	-0.17 (0.05)	-0.06 (0.03)	0.03 (0.05)
		t	-3.26	-1.86	0.66
		p	0.001 * *	0.065	0.509
Openness	HRSD	B (SE)	-3.53 (1.02)	-1.66 (0.71)	0.19 (1.01)
		t	-3.44	-2.32	0.19
		p	< .001 * *	0.022 *	0.847

Notes. SSI: The Scale for Suicidal Ideation; SAI: The Session Alliance Inventory; HRSD: The Hamilton Rating Scale of Depression. Bold represents significant findings. * <.05, ** <.01, *** <.001.

Abu-Akel, 2016).

Although OT's administration was found to have a beneficial effect on therapeutic outcome, the results also highlight the potential harmful effects of OT primarily on therapeutic process. Specifically, when extraversion was high, and neuroticism and agreeableness were low, OT administration was associated with a deterioration in the working alliance. Other studies assessing the effect of OT in therapeutic settings have also reported a negative effect of OT on the working alliance. For example, Acheson et al. (2015) administered OT prior to a brief single-session exposure treatment for arachnophobia and found that the OT group trended toward lower ratings of therapeutic alliance compared to the placebo group. Grossman-Giron et al demonstrated a similar effect of no improvement in alliance following OT administration, as compared to controls. One potential explanation to account for the opposing effect of OT administration among individuals high in extraversion and low in neuroticism is rested in OT's effects on social value representation in the amygdala. Liu et al. (2019) used model-based fMRI to examine the neural representation of social values in prosocial and individualistic participants following OT and placebo

administration, and found that OT selectively amplified the neural representation of social values in the amygdala in more individualistic but not in prosocial individuals. Therefore, it is possible that OT administration to individuals with high affiliative tendencies either results in non-activation, or alternatively increases social engagement beyond an optimal level, resulting in negative outcomes for relationships and wellbeing (Human et al., 2016). Taken together, these findings suggest that OT administration is not "one size fits all" and that its negative effects on therapeutic process may counter-balance its positive effects on therapeutic outcome.

Contrary to our initial hypotheses, anxious and avoidant attachment patterns did not moderate the effect of OT administration on any of the process or outcome measures. Studies assessing the moderating effect of attachment patterns are relatively scarce due to the limitations of sample size; however, those that have been conducted tended to show differential patterns of moderation. For example, Bernaerts et al. (2017) found a stronger effect of OT in individuals with less secure attachment, but Rockliff et al. (2011) found that participants with lower attachment security gained less from imagery intervention under OT administration

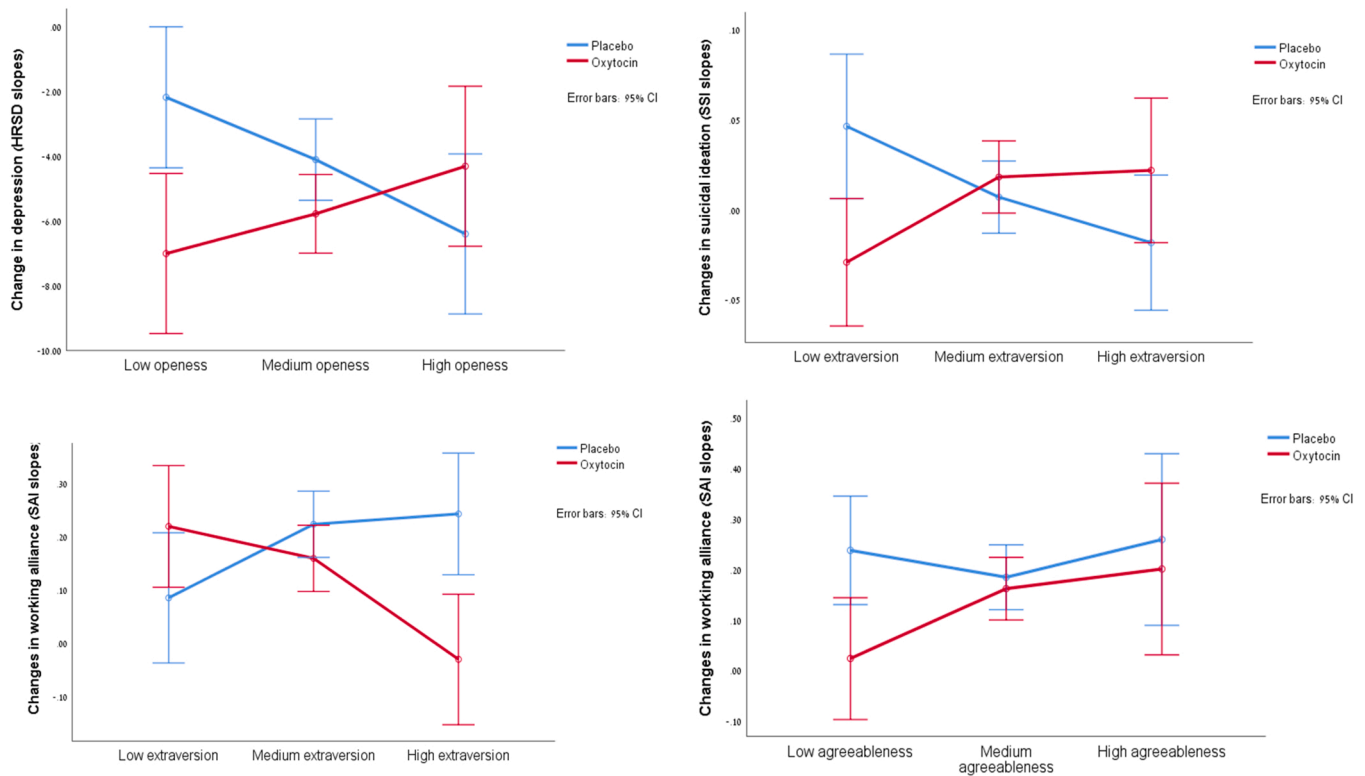


Fig. 1. Significant interaction effects of oxytocin administration and personality traits on therapy process and outcome.

than did securely attached individuals. Although the results of the current study fail to provide clear evidence to reconcile these findings, a review of the simple effects indicates that the optimal response to OT administration is for individuals with medium to high anxious and avoidant attachment, which suggests that individuals with insecure attachment benefit more from OT administration than do secure patients. Specifically, among the individuals with insecure patterns of attachment, a significant improvement was found primarily in depressive and anxiety symptoms, with no significant effect for individuals with secure (low anxiety and avoidance) attachment (see [Tables S1 and S2](#) of the [supplementary materials](#)).

The pattern of findings observed in the moderation analyses suggest that OT can act as a double-edged sword, by improving therapeutic outcome for individuals with specific personality traits and worsening therapeutic process for others. Collectively, the results suggest that individuals low in extraversion and openness, high in agreeableness and neuroticism, and with insecure attachment patterns at baseline may benefit the most from OT administration, and with minimal adverse effects to the alliance. Additional studies are needed to further explore routes to personalize the administration of OT as an add-on to psychotherapeutic interventions. Additional studies are needed to assess whether compliance to the treatment administration may act as additional predictive factor of outcome. Future studies should also explore potential sex, personality and OT administration interaction effects, as well as routes to optimize OT administration using machine learning approaches.

The results reported in this study have significant clinical and empirical implications. To the best of our knowledge, the current study is the first to explore the moderating effects of personality and attachment patterns on OT and psychotherapy process and outcome associations. The relatively large sample size compared to previous studies assessing OT administration, and the exploration of a clinical population undergoing psychotherapy in inpatient settings, contributes to the ecological validity of the study and allows for a direct assessment of its clinical implications. Clinically, the results of this study might suggest

that a thorough screening of patients' personality and attachment patterns prior to therapy combined with OT administration might increase the likelihood of a favorable outcome. Furthermore, they can set the stage to consider personalized administration of OT for severely distressed patients undergoing psychotherapy, dependent on their baseline individual characteristics. Future studies should examine whether personally adapted dosages of OT, fitted to individuals' OT baseline levels, may also enhance outcomes for individuals with personality patterns found to predict less favorable outcomes in our study. Empirically, the observed differential effects of OT administration across individuals with different attachment and personality traits may account for the large variability observed thus far in the literature and suggest that future studies should account for these patterns when assessing the effect of OT administration in clinical populations.

Several limitations should be noted. As previous studies have suggested high rates of comorbidity, overlapping therapeutic mechanisms, and shared deficits in patients with severe mental illness ([Elliott et al., 2018](#)), the RCT which formed the basis for the current analysis included inpatients with different psychiatric diagnoses. Additional studies are needed to assess whether the observed effects can be replicated in clinical populations from distinct diagnostic groups. Therapist factors were not evaluated in this study and could also contribute to OT's effect on therapy process and outcome. Finally, patients in this sample were receiving relatively large dosages of psychiatric medications (3.64 types of medication on average, $SD=1.90$) ([Grossman-Giron et al.](#)). Although this state of affairs is part of the ecological setting of psychiatric hospitalizations, an interactive effect of the medications with the OT cannot be ruled out. Notwithstanding these limitations, the current study highlights the importance of interpersonal characteristics in the evaluation of OT as an add-on to psychotherapy and sets the stage for advancing research and clinical practice through patient-tailored approaches.

Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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Author Statements

none.

Competing interests

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.psyneuen.2023.106074](https://doi.org/10.1016/j.psyneuen.2023.106074).

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