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Intranasal oxytocin enhances positive self-attribution in healthy men

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ABSTRACT

Objective: A growing body of studies consistently demonstrates that social responsiveness toward others is influenced by the neurohormone oxytocin. However, the potential role of oxytocin for self-perception remains relatively unexplored. Thus, we investigated whether oxytocin administration influences the self-attribution of positive and negative adjectives at the early, effortful stage of self-related information processing.
Methods: Sixty healthy male participants received either 24 I.U. oxytocin or a placebo in a randomized double-blind study before completing a sorting task, in which they were instructed to co-classify, as fast as possible, positive and negative adjectives into either self or non-self categories.
Results: Oxytocin-treated participants reported stronger positive attitudes toward themselves compared to placebo.
Conclusions: The present findings demonstrate that oxytocin administration influences the early stage of self-related information processing and suggests that the oxytocinergic system might be involved in psychopathological conditions characterized by a negative representation of self.

Introduction

In everyday life, one's availability to engage in social interactions, to trust others, and to understand others' emotions is deeply related to the affective perception of the self. A positive attitude toward self is central for the development of securely attached relationships in adulthood. By contrast, negative self-view and insecure attachment style are more likely associated with a diminished understanding of and responsiveness toward others' needs [1].

That the construction of perception of self and other are interrelated during development is supported by extensive research evidence [2]. However, whether the perception of self and the perception of others share the same brain mechanisms remains unclear.

A growing body of neurobiological studies consistently demonstrates that the perception of and responsiveness toward others is modulated by evolutionarily ancient neurohormones. In particular, the neurohormone oxytocin influences several domains of complex social behavior and social cognition in humans [3]. Specifically, increased availability of oxytocin following intranasal administration increases the perception of others as supportive during stress [3,4] and as pleasant [5,6]. In addition, intranasal oxytocin administration modulates trust in unfamiliar persons [7,8], leads to embracing of altruistic choices [9], and promotes the recollection of feelings associated with attachment security in healthy individuals [10], although these effects seem context- and person-dependent [11].

Open questions remain about the specificity of oxytocin effects and whether a highly relevant neuropeptide in daily interactions with the "other" might also be fundamental for the perception of self. Several studies offer support for a possible involvement of oxytocin in influencing self-view. For example, oxytocin administration facilitates self-attribution of positive socially-relevant personality traits on personality scales [12], self-referential cognition during an autobiographical memory task [13], and the perception of being more other-focused (i.e., kind, warm, caring) than self-focused [14]. In addition, oxytocin administration moderates the negative mental appraisal of one's own performance in individuals with high levels of anxious traits [15]. Oxytocin's effects on prosocial choices might be associated with an increase of self-confidence [16]. Most of the above-mentioned findings regarding oxytocin's effects on self-view rely on self-report outcome measures. However, the perception of self and others occurs before highly cognitively mediated self-appraisal [17].

Whether oxytocin-mediated self-attribution of positive traits emerges at the early, effortful stage of information processing is unknown. Thus, the present study aims to investigate whether administration of oxytocin might boost the positive view about self at an early stage of processing of stimuli. Indeed, oxytocin does induce behavioral effects on automatic, introspectively inaccessible processes [18,19]. Thus, we investigated the effects of a single dose of intranasal oxytocin on self-view using the single-category implicit association test (SC-IAT, [17]). Like other implicit measures, this test is designed to assess relatively automatic associations by asking a participant to

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react quickly and spontaneously and limiting highly cognitively mediated introspection. Although self-view and other-view are difficult to separate and study independently, we acknowledge that several measures, such as the SC-IAT, might be suitable to stress self-related responses while reducing the possible effects of self-other comparisons [17]. In fact, the main difference between the SC-IAT and the classic implicit-association test (IAT, [20]) is that in the classic IAT procedure the subjects are asked to perform self versus other comparisons, whereas in the SC-IAT the self-responses are stressed by excluding explicit social comparisons. Thus, the participants are induced to focus on self and reduce automatic comparisons with others.

Methods and materials

Participants

Sixty healthy men, aged 20–30 (M = 23.7; SD = 2.8) years, were recruited from the University of Freiburg, Germany, by distributed brochures and flyers. The participants were randomly assigned to either the oxytocin (n = 30) or placebo (n = 30) group in a randomized, double-blind, between-subjects design. Twenty-five additional participants were involved for the selection of the stimuli. Self-reported history of psychiatric illness, substance abuse, and neurological disorder were the exclusion criteria. All participants were native German speakers, non-psychology students, and had normal or corrected-to-normal vision.

To control for possible baseline differences between groups with respect to psychological characteristics and self-related view, one week prior to the test (as in previous studies, [21,22]), all participants completed a set of validated questionnaires: the Adult Attachment Scale (AAS, [23]), the Autism Spectrum Quotient (AQ, [24]), the Freiburg Personality Inventory-Openness scale (FPI, [25]), the Interpersonal Reactivity Index (IRI, [26]), the State-Trait Anxiety Inventory—Trait Anxiety (STAI, [27]), and the State-Trait Anger Expression Inventory (STAXI-T, [28]). As additional control for baseline group differences, the participants completed a test of verbal intelligence (Wortschatztest, WST, [29]). Furthermore, the participants completed the 12-item Multidimensional Mood Questionnaire (MDBF, [30]) prior to substance administration. As additional control for substance-induced mood changes, the participants also completed the MDBF after the testing session.

The participants abstained from smoking, exercise, and alcohol during the 24 h before the testing; they also refrained from consumption of food and drink (except water) for 2 h prior to the test. On the testing day, each participant self-administrated a single dose of either oxytocin (24 I.U. in 6 puffs of Syntocinon-Spray, Novartis, Basel, Switzerland) or placebo (containing all the ingredients except for the neuropeptide) intranasally. After substance administration and prior to the SC-IAT test, the participants completed an independent evaluation test of physical size of other male individuals from pictures displayed on the computer screen for a separated study. Because all participants evaluated the same stimuli, we assume that this previous test had, if any, similar effects on the results reported in our study. Thus, after about 60 min from substance administration, they completed the SC-IAT test. Finally, all participants addressed two additional dichotomous questions to detect possible side effects and made a guess as to the substance received.

The Institutional Review Board (IRB) of the University of Freiburg in Germany provided ethical approval, and all participants signed written informed consent.

SC-IAT procedure

The idea behind the SC-IAT is that individuals with a positive self-view are faster to associate automatically oneself with positive rather than with negative adjectives. Following a validated protocol [17], the stimuli used for the SC-IAT were composed of a list of positive (i.e., active, strong, optimistic, imaginative, warm-hearted) and negative (i.e., inactive, weak, pessimistic, unimaginative, cold-hearted) adjectives mixed with self-referent words (i.e., I, mine, my, and me). As a personalized selection of the stimuli has no negative impact on the psychometric properties of the SC-IAT [31], we have selected the stimulus words considered relevant for our sample population. Specifically, the list of adjectives was selected by asking an additional 25 male German students to rate 50 pairs of adjectives used by previous studies on implicit association tests (good, excellent, wonderful, great, dreadful, awful, bad, terrible) mixed with adjectives from several personality scales on a 10-point "pleasantness" Likert scale. The five pairs of adjectives falling at the extreme points (i.e., 1–2 and 9–10) of the Likert scale were selected for use in this study.

The participants were seated in front of a computer monitor at a distance of approximately 30 cm. They were instructed to sort, as quickly and as accurately as possible, the stimuli presented one after another on the center of the screen as belonging to the categories displayed on the corners of the screen. The categories displayed at the top left or right of the screen changed during the test. During the first stage of the test, the categories were "self + positive" versus "negative". During the second stage of the test, the categories were "positive" versus "self + negative". In the case of an incorrect response, a red cross appeared at the center of the screen, and the word stimulus remained on the screen until the correct key was pressed.

The SC-IAT consisted of seven blocks. The test blocks (four and seven) were both preceded by practice blocks. In the practice blocks, participants were trained to use the keyboard key "E" to sort self-referent words in the target category "self" (block 1), the keys "E" and "I" to sort positive and negative adjectives, respectively (block 2), and both keys for the combined sorting of self-referent words + positive words versus negative words (block 3). Test block 4 was identical to practice block 3. In the following block, the key assignment was reversed and participants were instructed to sort self-referent words + negative adjectives versus positive adjectives. After a practice block for the new assignment (block 6), participants completed the last combined test block (block 7). Each practice block comprised 20 trials, while each test block comprised 65 trials.

Data analysis

The strength of the perceived association between the self and positive vs. negative adjectives was measured using the improved algorithm to calculate the D600-score [20]. Specifically, the D600 is calculated excluding the trials greater than 10,000 ms and subjects with 10% of trials below the 400 millisecond range. In addition, the reaction time for error trials is replaced with the mean response latency for that block increased with a penalty of 600 ms [20]. All participants responded within the 1700 millisecond range. After excluding participants with more than 10% of trials below the 400 millisecond range, our final sample consisted of 28 oxytocin- and 29 placebo-treated participants.

A positive SC-IAT score indicates that subjects have a positive self-view [17]. They are, in fact, relatively faster in associating self with positive words than with negative words. The comparison between the oxytocin and placebo substance groups with respect to their SC-IAT score and psychological measures was performed using an independent sample *t*-test.

To detect possible substance-induced mood changes, the MDBF scores were analyzed using a repeated measures ANOVA with substance (oxytocin versus placebo) treated as a between-subjects factor and time (before the substance administration and after the task) as a within-subjects factor.

To explore whether oxytocin selectively influenced one of the two test blocks, an additional analysis on the values for the reaction time and the number of errors during the two test blocks was performed using a mixed ANOVA, with substance (oxytocin versus placebo) treated as a between-subjects factor and the test block (self + positive versus self + negative) as a within-subjects factor. Since the two test blocks were presented in a fixed order to assess the effects of a time-

dependent change in participants' responses during the test, each test block was split into two sub-blocks. A repeated measures ANOVA with the sub-blocks as within-subjects factors indicated that there were no differences between the first and last halves of each series of stimuli within each block (all $p > 0.1$). Thus, this factor was not considered further. The $\chi 2$ test was used to detect the possible relationship between a participant's belief regarding the substance group allocation and the actual substance allocation.

Results

The oxytocin substance group had a higher SC-IAT score (i.e., positive self-view) than the placebo substance group (D-600 SC-IAT score, mean ± SE: oxytocin group: 0.44 ± 0.07; placebo group: 0.22 ± 0.04, $t(55) = 2.5$, $p = 0.017$, d = 0.67). As revealed by ANOVA analysis on the two test blocks for the two substance groups, the oxytocin-treated participants were faster than the placebo-treated participants in associating self with positive words, but no differences between substance groups were observed during the self-attribution of negative adjectives (substance: $F(1,55) = 0.006$, $p = 0.9$, $\eta_p^2 = 0.0001$; block: $F(1,55) = 104.3$, $p < 0.0001$, $\eta_p^2 = 0.65$; substance group x block: $F(1,55) = 4$, $p = 0.048$, $\eta_p^2 = 0.07$, M ± SE self + positive words: oxytocin: 673 ± 16; placebo: 713 ± 25; M ± SE self + negative words: oxytocin: 893 ± 39; placebo: 859 ± 33). No difference between groups was found with respect to the number of errors (main effect of substance: $F(1,55) = 0.5$, $p = 0.47$, $\eta_p^2 = 0.01$ and substance x block interaction: $F(1,55) = 1.1$, $p = 0.3$, $\eta_p^2 = 0.02$). Both groups made more errors on the self + negative word block than on the self + positive word block (block: $F(1,55) = 172$, $p < 0.0001$, $\eta_p^2 = 0.75$). The SC-IAT scores and the mean reaction times for the test blocks are presented in Fig. 1.

No differences between the oxytocin- and placebo-treated groups were found on any of the psychological self-reported measures that were considered (all $p > 0.05$, Table 1).

In addition, the two groups did not differ in baseline measures or after substance administration on alertness (substance: $F(1,55) = 0.1$, $p = 0.7$, $\eta_p^2 = 0.002$; substance x session: $F(1,55) = 0.001$, $p = 0.1$, $\eta_p^2 = 0.0002$; M ± SE; baseline, oxytocin: 14.3 ± 0.6 placebo: 14.4 ± 0.6; after substance administration, oxytocin: 12.2 ± 0.7 placebo: 12 ± 0.5), calmness (substance: $F(1,55) = 3.6$, $p = 0.06$, $\eta_p^2 = 0.06$; substance x session: $F(1,55) = 0.2$, $p = 0.9$, $\eta_p^2 = 0.0003$; M ± SE baseline, oxytocin: 16.7 ± 0.5 placebo: 15.7 ± 0.4; after substance administration, oxytocin: 16.8 ± 0.5 placebo: 15.6 ± 0.3), or mood (substance: $F(1,55) = 3.7$, $p = 0.06$, $\eta_p^2 = 0.06$; substance x session: $F(1,55) = 0.13$, $p = 0.7$, $\eta_p^2 = 0.002$; M ± SE baseline, oxytocin: 17.4 ± 0 .4 placebo: 16 ± 0.5; after substance administration, oxytocin: 16.7 ± 0.5 placebo: 15.6 ± 0.4). Furthermore, no differences between groups were found in the beliefs regarding substance allocation ($\chi 2 = 1.4$, df = 1, $p = 0.052$; 11 oxytocin-treated participants and 16 placebo-treated participants believed they received oxytocin). No side effects related to substance administration were reported.

Table 1
Mean and SD of participants' psychological characteristics.

	Placebo (n = 29)		Oxytocin (n = 28)		Statistics		
	M	SD	M	SD	t(55)	p	d
AAS-A	10.6	4.4	10.7	5.1	0.1	0.9	0.03
AAS-C	19.8	4.3	20.0	4.6	0.1	0.9	0.03
AAS-D	20.4	3.8	20.2	4.5	0.1	0.9	0.03
AQ	16.8	6.7	15.8	6.5	0.5	0.6	0.14
FPI	8.5	1.9	7.7	2.4	1.3	0.2	0.35
IRI	56.5	8.7	52.7	10.6	1.5	0.1	0.39
STAI-T	38.8	9	36.9	9.3	0.8	0.4	0.21
STAXI-T	19.3	5.3	18.5	4.1	0.7	0.5	0.18
WST	34.5	3.1	33.5	4.6	0.9	0.3	0.3

AAS-A, Adult attachment Scale — Anxious; AAS-C, Adult Attachment Scale — Close; AAS-D, Adult Attachment Scale — Depend; AQ, Autism Quotient; FPI, Freiburg Personality Inventory — Openness Scale; IRI, Interpersonal Reactivity Index; STAI-T, State Trait Anxiety Inventory — Trait Anxiety; STAXI-T, State-Trait-Anger Expression/Regulation Inventory; WST, Wortschatz-Test, verbal IQ test.

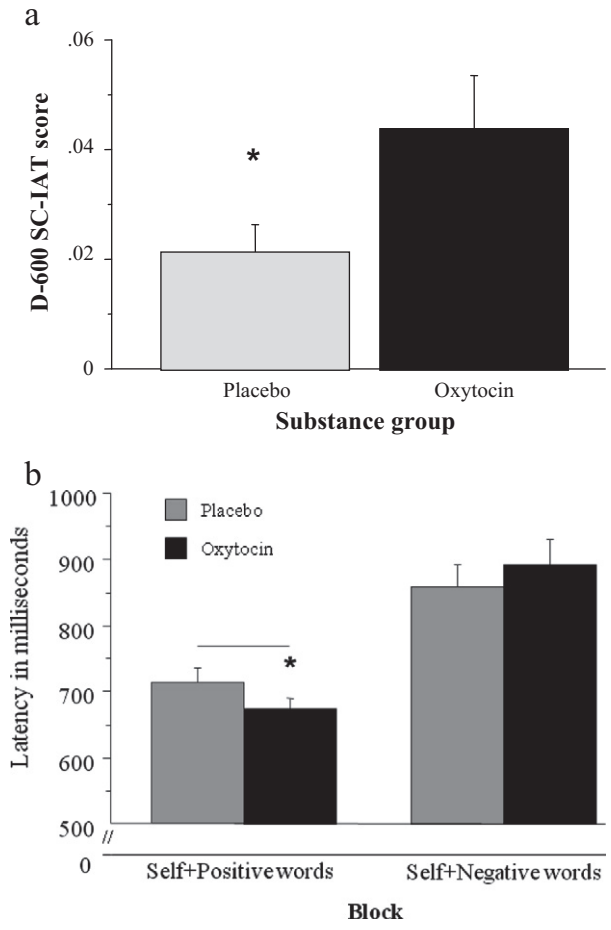

Fig. 1. a) Mean ± SE of D-600 SC-IAT in the placebo and the oxytocin groups; b) Mean ± SE of latency in milliseconds during the SC-IAT by the two substance groups. *$p < 0.05$, after post-hoc analysis.

Discussion

Our findings demonstrate that the oxytocinergic system is involved in the processing of self-related stimuli and that increased oxytocin levels boost the degree to which one perceives oneself in a positive view. Notably, positive self-perception is enhanced at a cognitive level preceding explicit self-reflection and introspection.

Consistent with previous studies showing that oxytocin enhances attention (i.e., seeking and approach/selection) toward positive stimuli [19], we found that oxytocin selectively shortened the latency to associate positive adjectives with self without influencing the self-attribution of negative adjectives.

From an evolutionary perspective, it is worth considering that the oxytocinergic system plays a key role in parent–infant interactions and pair bonding. Across mammalian species, efficacious parental care relies on personal confidence and strength (e.g., "strong", "active"), and the main goal of a vulnerable infant is to reach the feeling of safety and comfort by relying on others perceived as sensitive and strong [32]. In addition, independent studies indicate a positive association between positive attachment security and positive self-view, prosocial attitude, and tolerance of others' distress [1].

The effect of oxytocin on the block self-positive is particularly intriguing considering the increasing interest in the therapeutic potential of oxytocin for several psychopathological disorders characterized by negative self-appraisal [3,33], though the extent to and the conditions under which oxytocin modulates self-view remain unclear. For example, whether the fast association between self and positive adjectives following oxytocin administration is due to a boost of positive, personal self-view or to an enhanced positive perception of self-in-relation-to others, that is, a "social self" deserves further investigation.

Of note, recent neuroimaging studies have reported an overlap between brain areas involved in the processing of reward and self-related stimuli [34], as well as between areas activated during the processing of reward and other-specific stimuli [35]. Thus, considering that the oxytocinergic and the dopaminergic systems have interconnections in the mesolimbinc areas involved in reward-processing [3], it is

plausible that the brain chemistries underlying the perception of rewarding values of others and surrounding resources might also be involved in the affective evaluation of self. Studies specifically focused on these interconnections would offer great insights regarding the possible role of the oxytocinergic system in anxious individuals, who are typically focused on negative self-evaluation and self-blaming behaviors [36], and in persons with borderline personality disorder, in which self-loathing feelings and affective instability toward self and others are dominant [37]. Interestingly, though the oxytocin-treated participants had a higher SC-IAT score than the placebo-treated participants, no self-reported mood differences emerged between groups in baseline measures and after substance administration. Therefore, it is possible that oxytocin alters the subtle self-perception without necessarily reaching awareness levels.

Of note, while in the present study we used the traditional SC-IAT procedure with the blocks presented in a fixed order, future studies using a counter-balanced block presentation order are warranted to exclude the possible learning and un-learning effects of oxytocin. At present, the effects on the self + positive block seems unlikely to be driven by a time-dependent performance or learning effects, as suggested by the preliminary exploratory comparison of sub-blocks within each block and the comparison of errors in the two test blocks.

Based on the present findings, it is reasonable to speculate that oxytocin mitigates stress responses under challenging social circumstances [4] and enhances social skills during social conflicts [38] not only by supporting the feelings that others are pleasant and trustworthy [5] and distinct from self [6], but also by fueling a positive self-view in healthy individuals.

Oxytocin-mediated self-confidence might be at the basis of specific social affiliative choices, such as the preference of dominant, physically strong persons as possible allies [39] or potentially risky investments [7,8]. Indeed, oxytocin modulates amygdala reactivity [22] without impairing the ability to recognize potentially threatening social stimuli [21,40]. Of note, individuals with a positive view about self prefer upward instead of downward social comparison under stressful circumstances. That is, they are prompt to affiliate and compare themselves with potentially stronger others without fear of being "overpowered" by them, whereas the other represents a resource for a valuable self [41].

In sum, our findings indicate that increased brain oxytocin levels are involved in subtle subconscious fluctuations of self-view and related self-attribution of positive traits. The present findings stand out not only because they addresses basic research questions on the implications of ancient neuropeptides on basic mechanisms subserving social cognition and self-perception, but also for the possible clinical implications for psychopathological conditions characterized by a negative representation of self.

Conflict of interest statement

There is no conflict of interest.

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