Is there a publication bias in behavioral intranasal oxytocin research on humans? Opening the file drawer of one lab

Running title: "Possible file drawer problem in behavioral OT research"

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Abstract

The neurohormone oxytocin (OT) has been one the most studied peptides in behavioral sciences over the past two decades. Primarily known for its crucial role in labor and lactation, a rapidly growing literature suggests that intranasal OT (IN-OT) may also play a role in humans' emotional and social lives. However, the lack of a convincing theoretical framework explaining IN-OT's effects that would also allow to predict which moderators exert their effects and when, has raised healthy skepticism regarding the robustness of human behavioral IN-OT research. The poor knowledge of OT's exact pharmacokinetic properties, crucial statistical and methodological issues and the absence of direct replication efforts may have lead to a publication bias in IN-OT literature with many unpublished studies with null results lying in laboratories' drawers. Is there a file drawer problem in IN-OT research? If this is the case, it may also be the case in our laboratory. This paper aims to answer that question, document the extent of the problem and discuss its implications for OT research. Through eight studies (including 13 dependent variables overall, assessed through 25 different paradigms) performed in our lab between 2009 and 2014 on 453 subjects, results were too often not those expected. Only five publications emerged from our studies and only one of these reported a null-finding. After realizing that our publication portfolio has become less and less representative of our actual findings and because the non-publication of our data might contribute to generating a publication bias in IN-OT research, we decided to get these studies out of our drawer and encourage other laboratories to do the same.

Keywords: Intranasal Oxytocin, file drawer, lab report

Introduction

Behavioral scientists have been investigating the psychosocial effects of the neuropeptide oxytocin (OT) in humans for over two decades, making it one of the most studied hormones in the social sciences. A rapidly growing literature suggests that OT - that has a well-established physiological role in labor and lactation - may also play a role in humans' emotional and social lives.

During the past two decades, preliminary findings have suggested that intranasal OT (IN-OT) administration increases trust toward strangers (1, 2), promotes self-confidence (3, 4), improves recognition of familiar faces (5), enhances emotional recognition (6) and facilitates mind reading (7). Other studies proposed that IN-OT also fosters sharing of emotions with others (8), makes people more sensitive to others' feelings (9), promotes altruism (10), enhances perceived trustworthiness and attractiveness and facilitates parent-infant (11) and romantic (12) attachments. These findings helped to build OT's reputation as the prosocial hormone *par excellence*, and the popular press has largely reinforced this reputation.

Nevertheless, several findings have tempered this idealistic view of IN-OT. For example, it has been proposed that IN-OT might also promote anti-social behavior such as aggression (13), ethnocentrism (14) and gloating (15). These findings questioned the mainstream theory of IN-OT as an affiliative/prosocial hormone (16), and motivated the proposal of several new hypotheses. Two of them in particular have been studied in depth: the first postulates that IN-OT increases the salience of social cues (16); the second conjectures that IN-OT increases social approach behaviors, whether good or bad (17). Studies to date have not clearly favored one theory over the others. Some findings have been consistent with one (or more) of these theories, but others do not sit easily with either (18).

Another proposition that has emerged from the behavioral IN-OT literature is that IN-OT's influences are strongly moderated by environmental context and personal characteristics.

A recent review (19) has concluded that the majority of IN-OT studies do not yield a main IN-OT treatment effects. To account for their findings, the authors proposed that IN-OT's effect might occur only under certain circumstances or only in as a function of specific personality traits - reflecting the plausible complexity of the interaction between IN-OT, environment and genotype. The lack of a convincing theoretical framework that allows to predict which moderators exert their effects and when, has raised healthy skepticism regarding the robustness of human behavioral IN-OT research (20, 21).

One source of skepticism is that the vast IN-OT research enterprise has relied on the pharmacokinetic properties of arginine vasopressin (AVP) administration - a peptide that is structurally similar, yet not identical to OT (22-24). IN-OT pharmacokinetics are not fully understood and the only study conducted to date (with a very small sample size) found that IN-OT does not yield elevated cerebrospinal fluid (CSF) OT levels 45 minutes after administration (the time window following administration at which most behavioral tasks took place) (25). Moreover, it is uncertain whether the standard doses used in OT research (between 24 and 40 IU) can deliver sufficient quantities of OT to the brain in order to produce significant changes in individuals, especially as OT is avidly degraded in brain tissue (24). Future studies investigating the penetration of IN-OT into brain and its pharmacokinetic properties in human are crucially needed.

A second source of skepticism concerns statistics. A recent meta-analysis of published studies involving IN-OT in humans (21) demonstrated that most studies are dramatically underpowered [1] and report overestimated effects. The meta-analysts estimated (using information on power, pre-study odds and the alpha level) that the false discovery rate in the IN-OT literature is over 80%.

[1]Walum and colleagues' results indicate that the average study investigating intranasal OT in healthy subjects has a statistical power of 16%.

A third source of skepticism is a striking absence of efforts towards direct replication. As far as we know, almost none of the findings in the literature underwent direct replication attempts, despite the obvious importance of such efforts (26). Moreover, the seminal, highly cited study associating IN-OT with trust (1), that inspired much of the subsequent research, failed several times to replicate (20). Our lab has also failed to replicate a promising initial finding relating IN-OT with increased trust in a non monetary behavioral task (see (2) for the original study, see (27) for the failed replication). Furthermore, a recent study failed to replicate seminal findings associating IN-OT with mind-reading (see (7) for the original study, see (28) for the failed replication).

Finally, the methodological challenges accompanying behavioral OT research are not unique to the use of IN-OT administration: the literature using peripheral OT measurements also relies on OT assay methods that are considered by many researchers as bio-analytically invalid (29-31).

In the light of these concerns and after failing to replicate our own IN-OT trust-enhancing effect (2), we put forward four, non mutually exclusive, hypotheses regarding the true association between IN-OT and social behavior (27):

(A) The effects reported in the literature reflect the true state of the world, and failed replications are due to underpowered studies or methodological errors/differences.

(B) The effects found in the literature are indicative of an effect of IN-OT in humans, but the true effect of IN-OT on human behavior is much smaller than the impression given by published studies. Replications and highly powered studies would therefore allow to adjust the real effect size.

(C) The effects found in the literature are type I errors that reflect a publication bias of positive results (32), which is possible as we generally accept 5% rate of type I error.

(D) The effects of IN-OT do not truly exist but are artificially created (e.g., by extensive degree of researcher freedom (33), study misconduct).

If either of the two last hypotheses is true, there should exist many unpublished studies with null results lying in laboratories' drawers (32).

Is there a file drawer problem in IN-OT research? If this is the case, it may also be the case in our laboratory. This paper aims to answer that question, document the extent of the problem, and discuss its implications for IN-OT research. We present eight studies (including 13 dependent variables overall, assessed through 25 different paradigms) that were performed in our lab from 2009 until 2014 on a total of 453 subjects. All our studies relied on theoretical and experimental accounts of IN-OT's role in social behavior that had been published to date. As we will demonstrate below, the results were too often not those expected. Only four studies (most often a part of them) of the eight were submitted for publication, yielding five articles (2, 8, 27, 34, 35). Of these five article, only one (27) reports a null-finding. We submitted several studies yielding null-findings to different journals (from general interest in psychology to specialized in biological psychology and in psychoenodcrinolgy) but they were rejected time and time again[2]. After realizing that our publication portfolio has become less and less representative of our actual findings, and because the non-publication of our null-findings might contribute to generating a publication bias in IN-OT research, we decided to get these studies out of our drawer, hoping that other laboratories will do the same.

[2] We submitted four articles that were rejected at least once (IN-OT and conformity to peer pressure, submitted once and rejected after review; IN-OT and mimetic desire, submitted twice and rejected twice after review; IN-OT and compassion, submitted twice and rejected twice after review; failed replication of IN-OT effect on trust, submitted twice, rejected once after review and then accepted in another journal).

To avoid an overly pessimistic view by only presenting the null results obtained, we instead present a complete overview of the research performed in our lab since we started studying IN-OT in 2009. This will allow readers to form their own opinion about the findings and allow us to meta-analyze the cumulative effects.

Methods and results

Methods

We will present eight studies assessing 13 dependent variables (emotional, cognitive, behavioral or physiological) through 25 different paradigms, performed in our lab over the past seven years, in chronological order. The methodological details of our studies are summarized in Table 1, and a full description of the studies including each behavioral task appears in Appendix 1. In each study, the tasks were conducted in a fixed order determined by the importance we attributed to each paradigm: the most important target variable was tested in the first task in order to eliminate the potential of spillover effects from other tasks[3]. All studies met the guidelines for ethical conduct of research and were conducted in accordance with the Declaration of Helsinki. The Biomedical ethics committee of the Université catholique de Louvain approved the protocols. Exclusion criteria included medical or psychiatric condition, substance dependence and female gender (except for the Study 8 on jealousy which involved couples and focused on female reactions). The number of subjects varied between 12 and 95[4] (see Table 1, column 4). All studies followed a between-subject design (except for Study 3 on sleep) and were either single or double blind (see Table 1, column 7). The dose of IN-OT (Syntocinon spray, between 24 and 40 IU in order to get

[3] The use of more than one task is common practice because of the imperative to maximize the knowledge gained from each subject undergoing pharmacological treatment
[4] Based on the standard found in IN-OT literature

through the dosing spectrum found in IN-OT literature) and the provider varied across studies (see Table 1, column 6). The placebo was always a saline solution administered in a bottle similar to IN-OT one. Each spray bottle was numbered and covered with sticky paper that covered the product label. The timing of the tasks was set according to the current norms in behavioral IN-OT research. Thus, the first task took place at the earliest approximately 35 minutes after IN-OT administration (usually 45 minutes), and when there were several tasks in the same study, the last task ended no later than 85 minutes after IN-OT administration (see Table 1, columns 3 and 8). Generally, the subjects performed the experiment alone unless the presence of a confederate was required (Table 1, column 9). Across all studies, there were no differences between the treatments groups (OT vs. PL) with respect to all baseline measures (all *p*s > .05) that were focused on self-reported questionnaires regarding the dependent variables relevant to each study, (specified for each study in Appendix 1). All studies also involved a personality questionnaire and collected demographic information.

Table 1: Presentation of the studies, including methodology and results

Study	Dependant Variable	Paradigm & time following product administration	Number of participants	Sex of the participants	Dose & Product	Administration type and design	Time between administration and testing	Testing type	OT Main effect	Interaction effect
Study 1: Oxytocin, trust and social sharing of the emotions (2009)	Trust (monetary)	Trust game 45 minutes after product administration	60 (30 OT & 30 PL)	Male	32 IU Syntocinon Spray, Novartis, Basel Switzerland	Single Blind Between-subject design	45 minutes	Participant alone	N.S.[1] Cohen's *d* =0.13 OT possibly increases trust [95% CI: -0.38;0.64]*	Condition x Partner reliability: OT only increases trust for reliable partners
	Social Sharing of the Emotions	Self reported willingness to share emotions 55 minutes after product administration							N.S. Cohen's *d* = 0.19 OT possibly increases the willingness to share emotions [95% CI: -0.33;0.70]*	Condition x Content of the sharing (Facts vs. Emotions): OT only increases willingness to share emotions
	Trust (non monetary)	Envelope Task 65 minutes after product administration							Significant Cohen's *d* = 2.09 OT increases trust [95% CI: 0.80;3.38]	No
Study 2: Oxytocin	Empathy	Reading the Mind in the Eyes test	60 (30 OT & 30 PL)	Male	32 IU Syntocinon	Single Blind Between-	45 minutes	Participant alone	N.S. Cohen's *d* = 0.26	Condition x Level of Alexithymia:

and empathy (2009)		45 minutes after product administration			Spray, Novartis, Basel Switzerland	subject design			OT possibly increases mind reading [95% CI: -0.26;0.78]*	OT only increases empathy for participants with a high level of alexithymia
	Compassion	Explicit measurement of Compassion after something bad happens to someone in a story . 55 minutes after product administration							N.S. Cohen's *d* = -0.39 OT possibly decreases compassion [95% CI: -0.91;0.14]*	No
	Empathy	Self reported empathic feeling and tendency to help someone who is first presented as a victim and then as a culprit in scenarios 65 minutes after product administration							N.S. Sympathy: Cohen's *d* = -0.42 OT possibly decreases sympathy [95% CI: -0.93;0.10]* Help: Cohen's *d* = -0.19 OT possibly decreases helping behaviors [95% CI: -0.70;0.32]*	No
Study 3:	Sleep latency	Multiple Sleep Latency test	12	Male	32 IU	Single Blind	45 minutes	Participant alone	N.S. Cohen's *d* =	No

Oxytocin and sleep (2011)		45 minutes after product administration			Syntocinon Spray, Novartis, Basel Switzerland	Within-subject design			-0.14 OT possibly decreases sleep latency [95% CI: -0.94;0.66]*	
	Sleep duration								N.S.Cohen's *d* = 0.27 OT possibly increases sleep duration [95% CI: -0.48;1]*	No
	Proportion of REM sleep								N.S.Cohen's *d* = 0.68 OT possibly increases REM sleep proportion [95% CI: -0.14;1.48]*	No
	Psychomotor vigilance	Psychomotor Vigilance Task							N.S.Cohen's *d* = -0.41 OT possibly decreases psychomotor vigilance [95% CI: -1.20;0.04]*	No
Study 4: Oxytocin, pain and sensitivity to baby's cry (2011)	Pain threshold	Cold Pressure test 45 minutes after product administration	60 (30 OT & 30 PL)	Male	32IU Syntocinon Spray, Novartis, Basel Switzerland	Double Blind Between-subjects design	45 minutes	Participants alone	N.S. Cohen's *d* = -0.28 OT possibly decreases pain threshold [95% CI: -0.78;0.23]*	No

	Pain tolerance								N.S. Cohen's *d* = 0.16 OT possibly increases pain tolerance [95% CI: -0.35;0.66]*	No
	Willingness to endure Pain								N.S. Cohen's *d* = 0,32 OT possibly increases willingness to endure pain [95% CI: -0.20;0.82]*	No
	Perceived pain intensity								N.S. Cohen's *d* = 0.19 OT possibly increases perceived pain intensity [95% CI: -0.32;0.70]*	No
	Sensitivity to a baby's cry	Self reported annoyance from baby's cry sound tracks 55 minutes after product administration							N.S. Cohen's *d* = 0.24 OT possibly increases sensitivity to baby's cry [95% CI: -0.27;0.75]*	No

Study 5: The dark side of Oxytocin: guilt, conformism and compliance to antisocial behaviors (2012)	Compliance to anti-social behaviors	Anti-social peer pressure 35 minutes after product administration	61 (31 OT & 30 PL)	Male	40IU Syntocinon Spray, Novartis, Basel Switzerland	Double Blind Between-subject design	35 minutes	With 2 confederates	N.S. Cohen's *d* = 0.47 OT possibly increases compliance to peer's anti-social requests [95% CI: -0.05;0.98]*	No
	General conformism	Numeric estimation task 45 minutes after product administration						Alone	N.S.Cohen's *d* = -0.47 OT possibly decreases conformism [95% CI: -0.99;0.04]*	No
	Behavioral measure of guilt after guilt induction	Effective splitting of money with partner or charity to make amend 75 minutes after product administration						Alone	N.S. Cohen's *d* = 0.33 OT possibly increases guilt [95% CI: -0.18;0.83]*	No
	Guilt after guilt induction	Self-reported questionnaire 85 minutes after product administration						With 1 confederate	N.S. Cohen's *d* = 0.41 OT possibly increases guilt [95% CI: -0.10;0.92]*	No
Study 6:	Mimetic Desire	Neutral painting	95 (48 OT & 47 PL)	Male	32 IU	Double Blind	45 minutes	Alone	N.S. Cohen's *d* =	No

Oxytocin, Mimetic Desire, Visual perspective taking and Trust (2012)		evaluation task (looked at vs looked away) 45 minutes after product administration			Syntocinon Spray, Fuerte Farma, Funchal, portugal	Between-subject design			0.19 OT possibly increases mimetic desire [95% CI: -0.22;0.60]*	
	Self vs. Others' Visual perspective taking	Visual Perspective Taking task (accuracy) 55 minutes after product administration							N.S. Cohen's *d* = -0.17 OT possibly decreases visual perspective accuracy [95% CI: -0.57;0.23]*	No
		Visual Perspective Taking task (reaction time) 55 minutes after product administration							N.S. Cohen's *d* = 0.01 OT does not influence visual perspective reaction time [95% CI: -0.39;0,41]*	No
	Trust (non-monetary)	Envelope Task 65 minutes after product administration							N.S. Cohen's *d* = -0.10 OT possibly decreases trust [95% CI: -0.50;0.30]*	No
Study 7: Oxytocin,	Vicarious experience of another's	Explicit measure of compassion:	61 (32OT & 29 PL)	Male	32IU Syntocinon	Double Blind Between-	45 minutes	Alone	N.S. Cohen's *d* = 0.10	No

Compassion and Trust (2013)	distress	self reported evaluation 45 minutes after product administration			Spray, Defiante Farmaceutica, Funchal, portugal	subject design			OT possibly increases compassion [95% CI: -0.40;0.60]*	
		Implicit measure of compassion: neutral painting evaluation 45 minutes after product administration							N.S. 0.031 [95% CI: -0.47;0.53]*	No
	Trust (non-monetary)	Envelope Task 60 minutes after product administration							N.S. Cohen's *d* = -0.15 OT possibly decreases trust [95% CI: -0.65;0.36]*	No No No No
	Behavioral compassion	Number of gazes towards a suffering target 65 minutes after product administration							N.S. Cohen's *d* = -0.12 OT possibly decreases compassion [95% CI: -0.62;039]*	No
		Duration of gaze towards a suffering target 65 minutes after product administration							N.S. Cohen's *d* = 0.03 [95% CI: -0.48;0.53]*	

		Number of interaction with a suffering target 65 minutes after product administration							N.S. Cohen's *d* = 0.07 [95% CI: -0.44;0.57]*	
		Number of interaction with a suffering target 65 minutes after product administration							N.S. Cohen's *d* = -0.09 [95% CI: -0.59;0.41]*	
Study 8: Oxytocin and jealousy in woman (2014)	Jealousy	Self-reported mood (PANAS) 75 minutes after product administration	44 (22OT & 22 PL)	Female	24IU Syntocinon Spray, Defiante Farmaceutica, Funchal, portugal	Double Blind Between-subject design	45 minutes	With life partner & 1 female confederate	N.S. Positive affects: Cohen's *d* = 0.13 OT possibly increases positive affects [95% CI: -0.58;0.83]* Negative affects: Cohen's *d* = -0.07 [95% CI: -0.66;0.52]*	No
		Behavioral jealousy: the mime game 80 minutes after product							N.S. Cohen's *d* = -0.35 OT possibly decreases jealousy	No

		administration							[95% CI: -0.94;0.25]*	
		Implicit cognitive measure: word completion 85 minutes after product administration							N.S.Cohen's *d* = -0.52 OT possibly decreases jealousy [95% CI: -1.12;0.08]*	No
		Implicit cognitive measure: positive vs. negative valence words recall 90 minutes after product administration							N.S. Cohen's *d* = -0.03 [95% CI: -0.62;0.56]*	No

[1] Even if our original findings reported in Psychological Science were significant, we have been told afterward that the analysis recommended by our statistician was not controlling for the fact that observations coming from the same subject are dependent. When we perform a repeated measures ANOVA with the partner (computer vs. reliable human partner vs. unreliable human partner) as within-subjects variables and with condition (OT vs. PL) as between-subjects factor, we do not find a significant effect of OT ($F(2,57) = 1.24$, $p = .294$). Therefore our published results seem to be erroneous. The only significant effect of OT we have found was with the computer as partner ($F(1,58) = 4.61$, $p = 0.04$)

* Confidence interval includes zero

Results

The last two columns of the Table 1 summarize the main and interaction effects of IN-OT treatment on target behaviors. We found a statistically significant main IN-OT effect for only one of 25 tasks, and a significant interaction effect including the treatment condition (OT vs. PL) for only five out of 25 tasks across our 8 studies and 13 dependent variables (see full results and statistical details in Appendix 1). Table 1 (column 10) reports the effect sizes for each variable. Only 13 out of 25 task points estimating effect size reach the lower bound on a small affect size (Cohen's $d > 0.2$). Among those, one task reaches the lower bound of a moderate effect size (Cohen's $d > 0.5$); another reaches the lower bound of a large effect size (Cohen's $d > 0.8$) but this result has to be interpreted carefully as we have failed to replicate it twice (27). Furthermore, only one task rules out the zero effect size with a 95% confidence interval, but once again the results of this particular study did not replicate well (27).

In order to determine the extent of IN-OT's influence on human behavior in our studies, we meta-analyzed[5] the effects of IN-OT on cognitive, emotional or behavioral variables (excluding the studies of OT's effects on physiological processes, namely sleep and pain). The aggregated effect size was not reliably different from zero (Cohen's d = 0.003 [95% CI: -0.10;0.10]). We further aggregated IN-OT's effects on variables assessing behaviors, affect or cognition in isolation (see Table 2), and could not reliably reject the null hypothesis for either ($d_{behaviors}$= 0.09 [95% CI = -0.07;0.25]; $d_{affects}$ = -0.003 [95% CI = -0.20;0.24]; $d_{cognitions}$ = 0.1, [95% CI = -0.32;0.13]). Finally, aggregating our effect sizes in reference to the three major behavioral OT theories (i.e., OT as a hormone of affiliation (16); OT as a hormone of social salience (15) and OT as a hormone of social approach (17), see Table 2), did not yield any effects that were reliably different from zero ($d_{prosocial}$ = -0.04 [95%

[5] We computed the cumulative effect sizes using the "Comprehensive Meta-Analysis" software (36).

CI = -0.13;0.06]; $d_{\text{social saliance}}$ = -0.01 [95% CI = -0.11;0.10]; $d_{\text{social approach}}$ = -0.002 [95% CI = -0.11;0.11]).

Table 2 : Computed effect sizes for main variables and theories

Variable	Cohen's *d*	95% Confidence interval	Size of the effect according to Cohen's norms
Trust (in Studies 1, 6 & 7)	0.04	-0.22 ; 0.30	Null effect size
Compassion (in Studies 2 & 7)	-0.05	-0.21 ; 0.14	Null effect size
Empathy (in Study 2)	- 0.12	-0.42 ; 0.18	Null to small negative effect size
Conformism (in Study 5)	-0.003	-0.36 ; 0.36	Null effect size
Jealousy (in Study 8)	-0.12	-0.39 ; 0.14	Null to small negative effect size
Affects: feeling of sympathy (Study 2), feeling of compassion (Studies 2 & 7), feeling of guilt (Study 5) & mimetic desire (Study 6)	With jealousy[6] = - 0.02	-0.19 ; 0.14	Null effect size
	Without jealousy = - 0.003	-0.20 ; 0.24	
Behaviors: trust (Studies 1, 6 & 7), compassion (Study 7), guilt (Study 5) & antisocial conformism (Study 5)	With jealousy = 0.06	-0.10 ; 0.22	Null effect size
	Without jealousy = 0.09	-0.07 ; 0.25	
Cognition: RMEt (Study 2), conformism (Study 5) & visual perspective taking (Study 6)	-0.10	-0.32 ; 0.13	Null to small negative effect size
Theory	Cohen's *d*	95% Confidence interval	Size of the effect according to Cohen's norms
Prosocial theory (all variables excepted antisocial conformism (Study 5))	-0.04	-0.13 ; 0.06	Null effect size
Social salience theory (all variables excepted social sharing of the emotions (Study 1))	-0.01	-0.11 ; 0.10	Null effect size
Social Approach theory (all variables excepted RMEt (Study 2) and visual perspective taking (Study 6))	-0.002	-0.11 ; 0.11	Null effect size

[6] As OT could either promotes or decreases jealousy regarding the adopted theoretical approach, we thought important to present both results

Discussion

We reviewed eight studies testing the influence of IN-OT on human cognition and behavior, assessing 13 dependent variables through 25 different paradigms performed in our lab since 2009. We found a statistically significant main effect of IN-OT for only one out of 25 tasks and a significant interaction effect including the treatment condition (OT vs. PL) for only 5 out of 25 tasks. All of our hypotheses were derived from the three major behavioral IN-OT theories (i.e., OT as a hormone of affiliation (16); OT as a hormone of social salience (15) and OT as a hormone of social approach (17)).

This large proportion of "unexpected" null-findings (92% for IN-OT's main effect) raises concerns about the validity of what we know about the influence of IN-OT on human behaviors and cognition. As reported in the meta-analytic section, the aggregated effects are not reliably different from zero, regardless of how they have been pooled (by dependent variables, by theories or altogether). Our initial enthusiasm on IN-OT findings has slowly faded away over the years and the studies have turned us from "believers" into "skeptics". This led us to raise several questions.

If the published literature on IN-OT's behavioral effects does not reflect the true state of the world, how has the vast behavioral IN-OT literature accumulated? We reiterate here two possible accounts. First, the significant findings might be a consequence of a Type I error (the commonly accepted p-value to reach significance level allows a 5 % of false positive). If this is the case, much unpublished data must be lying in the drawers of laboratories studying IN-OT.

Second, the significant effect of IN-OT may be the result of methodological, measurement or statistical artifacts. As this has been demonstrated for peripheral OT measurements (29), it should not be excluded here, although the artifacts would be different. We see four potential sources of generating artifacts in IN-OT research: 1) small sample

between subject-designs that might not be internally valid, 2) single blind designs 3) IN-OT pharmacokinetics and dosage and 4) statistical methods.

The massive use of between-subject designs of relatively small samples (about 30 participants per cell) carries the risk of attributing effects to IN-OT that are in fact generated by baseline group differences in various unobservable factors (e.g., personality)[7].

The use of single blind studies, where the subject is blind to the treatment condition but the experimenter is not, introduces the risk that the experimenter might unconsciously influence the subjects (37).

The dosage of IN-OT and typical timing of tasks following IN-OT administration is based on three assumptions that to our knowledge have not been directly or reliably (i.e. through several replications) tested: that IN-OT crosses the brain-blood barrier following administration, that 24-40 IU is a sufficient dose to produce behavioral changes, and that IN-OT pharmacokinetics mimics that of vasopressin (24).

Recent findings have demonstrated that IN-OT increases OT concentration in CSF in both human (25) and animal (38, 39). Furthermore, it has recently been demonstrated that IN-OT modulates amygdala responses in monkeys in a manner equivalent to humans (40). Taken together, those results suggest that IN-OT reaches, directly or indirectly (41), the central nervous system and would so produces observable affective, behavioral or cognitive modifications. However, if IN-OT produces a significant elevation of OT concentration in the CSF after 30 minutes in animals, this significant elevation takes place 75 minutes after IN-OT in human, which is not consistent with the literature where most tasks start 40-45 minutes after IN-OT. Furthermore, in a recent research, Quintana and colleagues (42) suggest that the IN-OT doses commonly used (24 – 40 IU) may not be the most adequate as their results show

[7] Note that within-subject designs also suffer from limitations such as reduced statistical power (e.g.: see Uri Simonsohn's post http://datacolada.org/2015/06/22/39-power-naps-when-do-within-subject-comparisons-help-vs-hurt-yes-hurt-power/)

that IN-OT effect on emotional recognition appears with an administration of 8 IU but not with 24 IU. Facing these challenges, further studies would be needed in order to strengthen our knowledge about IN-OT pharmacokinetic properties. Even if IN-OT reaches the brain, we cannot assure that the three assumptions on which IN-OT's literature is based are reliable.

Finally, the use of too small samples (21) and the vast amount of candidate factors that could potentially moderate IN-OT's behavioral effects (19, 20) might inflate the false discovery rate unless direct replication efforts and correction for multiple hypotheses are applied.

Two alternative hypotheses can also explain the seemingly puzzling results described in this paper.

First, our studies, like most published studies on IN-OT, might be underpowered (21). Thus, the fact that effects of IN-OT observed in our studies are non-significant does not mean that they are point estimates of a zero effect. For example, some of our studies do not rule out a small effect size (Cohen's d = 0.2)[8]. In order to detect such effects, or even a moderate effect, a sample size between 120 (Study 9, jealousy assessment through the word completion task, Cohen's d = 0.518) and 468 (Study 2, empathy assessment through the RMEt, Cohen's d = 0.260) participants would be required to reliably detect an IN-OT effect with 80% of power. Such sample sizes are much greater than the norm in both the IN-OT field and our lab. Therefore, several of our findings could potentially have turned significant in well-powered experiments. Yet, as shown in Table 1, their significance would not always have been in the expected direction.

A second proposition is that IN-OT effects do exist, but that they are strongly moderated by various factors, making them appear large in some circumstances but not others. Through the literature, more and more findings suggest that IN-OT influences behaviors by

[8] We have excluded the highest effect size found, in Study 1 - non monetary trust assessment, as it has been questioned by Lane et al.(27)..

interacting with several moderators (for a review see (19)). Arguably, our findings do not rule out the possibility that the effects of IN-OT are moderated by various factors – a proposition that will be difficult to rule out, given the infinitely large set of factors that could potentially moderate IN-OT's behavioral influences (genes, personality or environmental factors). Unfortunately, as far as we know, candidate moderators do not seem to replicate from one study to another[9] and appear most often to represent post-hoc data fits rather than a-priori hypotheses[10]. Indeed, one can be sure to find a "significant" interaction in any data set, simply by conducting many statistical tests, even in the absence of a true signal in the data, unless the test level alpha is corrected for multiple hypothesis testing (43, 44).

We can either believe that these interactions are statistical artifacts (see above) or believe that they are real. If we believe that they are real, it means that there is no such "general effect of IN-OT on behavior" but that IN-OT effects are always context dependent (for a review see (19)). In the studies reported in this article, the relevant potential moderators have been taken into account and only provided five interaction effects. Yet, it is possible that less obvious moderators, or moderators that we did not measure, would have provided more significant effects.

As we write these lines, we do not know which of the four hypotheses is true; IN-OT might not influence human behaviors at all or may influence it only under specific circumstances. In any case, falsifiable theories must emerge in order to progress in our understanding of IN-OT's behavioral influences, as no current theory seems to yield robust behavioral predictions - and almost every behavioral effect can be explained by one of the

[9] For example, in their failed replication of IN-OT's influence on the RMEt, Radke and de Bruijn (28) did not find any moderating effect of items' difficulty as demonstrated by Domes and colleagues (7).

[10] And we do not make exception to the rule: it is because we could not replicate IN-OT effect on the RMET that we looked for personality moderators and found a significant interaction with alexithymia (34)

theories ex-post. Along this line, although the value of replications cannot be over-estimated for increasing the reliability of scientific findings (26, 45), replication attempts are almost absent in IN-OT research, and the only attempts made to replicate high profile publications did not yield the expected effects (e.g.: trust game investment (46); non-monetary trust (27); empathy through the RMEt (28)).

To our view, nothing can be taken for granted with IN-OT and some non-replicable findings might have biased the development of existing theories. Hopefully, incorporating null findings and failed replications into the theoretical process would allow to draw lines between robust, replicable IN-OT effects and facilitate the development of falsifiable theories. It is therefore crucial that non-significant findings and failed replications are published[11]. Every piece of evidence, even experiments that did not yield "significant" effects, should be taken into account and weighted according to its evidential value.

In the present case, only 5 articles (2, 8, 27, 34, 35) have been published across the 13 dependent variables we have assessed, producing a publication rate of 38.5%. If our lab is a representative sample of IN-OT research, then for 626 search results found in Scopus by entering "oxytocin" and "human" as research keys (and limiting the outputs to "Psychology"), approximately 1000 potential studies have remained in labs' drawers. Unraveling these 1000 data sets is extremely important for understanding whether IN-OT exerts reliable effects on humans and under which circumstances.

We believe that a systematic shift in the IN-OT publication process is essential in order to reveal the true state of the world. Pre-registration of ex-ante hypotheses, replication attempts of the findings before their submission and submission of null results and failed replication for publication, especially when the studies are well-powered to detect the original findings, should be encouraged. Review processes should insist on fully reporting all of the of

[11] http://psychfiledrawer.org

the candidate moderators that were measured and tested and encourage publication of well-conducted studies, whatever their results (47). Many labs do report their work transparently. But as far as the editorial process does not sufficiently promote non-significant results and failed replications, it is difficult to obtain a complete overview of IN-OT research field. One way to improve the standards is by institutionalization[12]: as suggested by Leng and Ludwig (24): journals could oblige researchers to preregister trials, declare hypotheses and primary outcomes in advance, specify statistical methods to be applied and fully disclose the data, including tasks that did not yield results and assessed moderators that did not moderate the findings. This would help to drastically decrease reporting bias (i.e., picking significant results from a battery of tests and only reporting these). Moreover, authors could easily test the robustness of their findings by adjusting the alpha level to the number of tests that were performed (e.g. if the subjects were asked to perform three tasks, the level of significance would be 0.05/3 = 0.016, instead of 0.05).

These considerations must be taken into account if we want to dispose of a solid theoretical background for interpreting and understanding the complex effects of IN-OT and to warrant all the efforts and resources invested in IN-OT research.

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[12] As it is encourage by, notably, the American Psychological Association (http://www.apa.org/research/responsible/publication/index.aspx), the Association for Psychological Science (http://www.psychologicalscience.org/index.php/news/releases/psychological-science-sets-new-standards-for-research-reporting.html) and the NHI (http://grants.nih.gov/grants/policy/data_sharing/data_sharing_faqs.htm#900)

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APPENDIX 1

In this Appendix, all the studies are precisely presented. For each study, we present the dependent variables under investigation, the hypothesis we put forward, the methods we have used and the results.

Study 1: Oxytocin, trust and social sharing of emotions (2009)

Based on Kosfeld et al. (1) seminal work, our first study aimed to assess if OT enhances trust regardless of the perceived reliability of one's partner. Based on the trust game paradigm (2), we hypothesized that OT will only increase trust toward a stranger if he seems reliable (for further information, see (3)).

Because all studies on trust so far (e.g.(1, 4)) resorted to monetary paradigm, one could not rule out the possibility that the effect of OT on trust was conflated with an effect of OT on generosity (especially as other scholars reported that OT increased generosity (5)). Therefore, we assessed in a second task OT's influence on trust when confidential information (rather than money) was at stake. If OT indeed increases trusting behaviors, it should have increased trust that one's privacy would not be violated (which is unrelated to generosity; For further information, see (6)).

Finally, in a third task we assessed the potential influence of OT on Social Sharing of Emotions (SSE). As sharing emotions with a stranger requires trust toward this individual, and as it has been suggested that OT increase trusting behavior, we hypothesized that OT would increase the willingness to share emotions - especially with strangers (For further information, see (7)).

Participants

Sixty healthy young adult males (age= 21.2 years; *SD* = 2.4) took part in the study and were randomly assigned to receive either intranasal placebo (PL; n = 30) or OT (n=30; 32 IU Syntocinon Spray – 4 puffs in each nostril – Novartis, Basel, Switzerland).

Procedure

After providing written informed consent, participants completed demographic, risk taking (8), self-esteem (9), kindness (10), agreeableness (11), emotional disposition (12), and psychological disorders (13) questionnaires, in order to ensure that both groups were equal regarding individual differences relevant to the study. The following tasks were then administered in a fixed order.

OT and trust: the monetary paradigm (trust game)

Participants took part in the "trust game"[13](2). In one part of the game, participants were told that they would play 10 rounds with a computer partner that would randomly determine the back transfer; in another part, participants were told that they would play online with real people. We gave participants a brief description of their partner before each round. These descriptions, based on a pretest, were manipulated to induce high or low trust. Each participant played 10 rounds with 10 different partners (5 trustworthy and 5 untrustworthy). No back-transfers information was given during the game and the target presentation order was randomized. We measured the level of trust by the sum of money that a participant had transferred (the trust game is based on the assumption that the more you transfer, the more you trust your partner).

Results

After removing one outlier, we performed a 2 (group: OT or placebo) x 3 (partner type: computer, reliable human, unreliable human) mixed-model analysis on investment, with

[13] In the «Trust game », each participant assumed the role of investor and could transfer money to a "trustee," in whose hands the funds would triple. The trustee would then transfer all, some or none of the money, back to the investor. The amount of money transferred by the participant to the trustee in considered as an indicator of his level of trust.

partner type as a within-subjects factor. Analyses yielded a main effect of partner type, F (2, 1051) = 65.44, $p \leq .001$; participants made smaller investments with unreliable partners than with computer, $t(58) = 7.47$, $p \leq .001$, or reliable partners, $t(58) = 5.38$, $p \leq .001$. There was also a main effect of group, $F(1, 1051) = 5.76$, $p < .018$, with the OT group making larger investment than the placebo group. Crucially, group interacted with partner type ($F(2, 1051) = 3.29$, $p = .038$) such that OT completely lost its trust-enhancing effect when the partner was untrustworthy. These results supported our hypothesis and were published in Psychological Science in 2010 (3). However, we have been told afterward that the analysis recommended by our statistician was not controlling for the fact that observations coming from the same subject are dependent. When we perform a repeated measures ANOVA with the partner (computer vs. reliable human partner vs. unreliable human partner) as within-subjects variables and with condition (OT vs. PL) as between-subjects factor, we do not find a significant effect of OT ($F(2,57) = 1.24$, $p = .294$). Therefore, the inaccurate statistical method firstly used has led us to report erroneous results in our article (3).

OT and SSE

After the trust game (1 hour after product administration), participants were asked to recall a past negative experience that *still currently affects them* and rate its emotional intensity on a 10-pont Likert scale[14]. Participants were then asked to describe the event (fact and emotions) on a sheet of paper and were told that their anonymous description might be subject to a computerized content analysis. Participants were also asked to rate their current negative emotional intensity on a 10-point Likert scale. Finally, participants had to indicate on four five-point Likert scales whether they would agree to share the related facts and the

[14] Previous studies (14) showed that unextinguished emotional experiences elicit an ongoing need to be shared)

related emotions with either a same-sex or an opposite-sex person. Two judges manually analyzed the narratives and reached a 100% inter-rater agreement.

Results

Both groups were comparable with respect to the emotional intensity of the recalled event either at the time or now. We performed a repeated measures ANOVA to test whether OT affects inclination to engage in a SSE, with context (fact vs. emotions) as a within-subject factor and condition (OT vs. PL) as a between-subjects factor. We found no main effect of treatment group ($F(1,57) = .51$; $p > .05$) and a significant effect of the type of content ($F(1,57) = 23.82$; $p < .001$), suggesting that participants were generally more inclined to share facts than emotions. We also found a significant content x group effect, $F(1,57) = 4.55$; $p < .05$, revealing that OT group subjects were more inclined to share their emotions. These results supported our hypothesis and were published in the International Journal of Psychology in 2013 (7).

OT and trust: the non-monetary paradigm (the envelope task)

Before substance administration, participants were invited to complete an intimate questionnaire about their sexual fantasies and practices (e.g.: anal sex, exhibitionism, sado-masochism…) to ensure a type of content that one would not divulge to a stranger. Participants were told that the questionnaire would be analyzed via an optical character recognition device, were given an envelope for their completed questionnaire and were instructed not to seal it yet. At the end of the session, participants were asked to complete a similar questionnaire and return both to the experimenter. The experimenter assured participants that he would not look at their answer. However, they were free to seal the envelope, and to even add sticky tape (that was provided). The degree of envelope's opening

(opened, sealed or sealed plus taped) was considered as participants' degree of trust toward the experimenter.

Results

No differences were found between groups regarding sexual practices or fantasies neither before (p>.25) nor after product administration (p>.20), which suggest that OT does not decrease people inhibition. However, the ordinal regression performed on the degree of envelope's opening suggested that OT substantially increased trust (-2 Log -Likelihood = 11.57, p < .001). These results supported our hypothesis and were published in Biological Psychology in 2010 (6).

Study 2: Oxytocin and empathy (2009)

Empathy may be defined as the subjective experience of similarity between the feelings expressed by self and others without loosing sight of whose feelings belong to whom (15).

. It is thought to be the prerequisite of the emergence of prosocial behaviors like altruism and generosity (16). As it has been suggested that OT enhances the ability to infer emotions from a target's eyes region (17) and increases generosity (5), we hypothesized that OT would increase empathy and compassion. In the vein of our first study about OT and trust, we also wanted to determine the boundaries of this effect: would OT increase empathy and compassion regardless of the target, or is the effect moderated by the target's responsibility in his misfortune?

Participants

Sixty healthy young adult males (*M*age= 21.1 years; *SD* = 2.1) took part in the study and were randomly assigned to receive either intranasal placebo (PL; n = 30) or OT (n=30; 32 IU Syntocinon Spray – 4 puffs in each nostril – Novartis, Basel, Switzerland).

Procedure

After providing written informed consent, participants were invited to complete demographic, empathy (18), alexithymia (19), the big-five factors of personality (20), and emotional disposition (12) questionnaires, in order to ensure that both groups were equal regarding individual differences relevant to the study. The following tasks were then administered in a fixed order.

OT and empathy: "Reading the Mind in the Eyes test (RMEt)

The RMEt (21) is a validated test that has been used successfully to assess the ability to recognize complex emotions based on the target's eye region. Previous studies suggested that RMET is sensitive to OT administration among healthy subjects (22). The RMET consists of 36 photographs (18 males) of eyes expressing a complex mental state. Each photograph is presented individually with four mental states (a target and three foils) displayed around the face. For each item, participants decide which mental state best describes what the person in the photograph is feeling (by clicking on the mental state with the mouse). The distractors have roughly the same emotional valence as the target word. In the current study, participants had unlimited time to respond, but were asked to respond as fast as possible. A first item was used as an example the reminding 36 experimental items appeared successively. Global performance (percentage of correct answers) was calculated (for further information, see (23)). This task aimed to replicate Domes et al. (22) effect of OT on the RMEt before going further in the investigation of the effect of OT on empathy and compassion.

Results

We performed a univariate General Linear Model with the RMEt score as dependent variable and the condition (OT vs. PL) as fixed factor and found no differences between the groups ($F(1,55) = 0.629$, $p > .05$) questioning the original, well-cited finding. We then looked

for post-hoc interaction effects with baseline individual differences (testing interaction effect with each variable in turn) and observed a similar interaction pattern (e.g., greater effect of OT on mind reading for less socially competent individuals), that was significant for alexithymia. The interaction emerged in a hierarchical regression analysis with the RMET score as the dependent variable, OT vs. PL condition, alexithymia, and condition x alexithymia interaction as independent variables. Results revealed an interaction between the condition (OT vs. PL) and alexithymia scores, F (1,53) = 4,56, $p < .05$, suggesting that OT only increased RMEt performance for less efficient individuals (high alexithymia score). The results were published in Biological Psychology in 2011 (23).

OT and measurement of compassion

We aimed to examine OT effect on compassion and the possible moderating role of the nature of the misfortune that the target had experienced. We presented each participant with twelve stories about individuals who suffered physical losses – either as a consequence of bad luck, risky behavior, risky behavior with predictable consequences or misdeed. For measuring compassion, participants indicated (4-point Likert scale) how compassionate they felt for the individual in the story. We also asked the participants to rate how responsible the targets were for what had happened.

Results

We performed a repeated measures ANOVA with compassion score for each categories (bad luck vs. risky behavior vs. risky behaviors with predictable consequences vs. misdeed) as within subject variables and condition (OT vs. PL) as between subjects variable. We found a strong main effect of category, providing a robust manipulation check: participants showed the greatest compassion for people whose misfortune was due to bad luck, less compassion for people whose misfortune was due risky behavior, even less compassion for people whose misfortune was due risky behaviors with predictable negative consequences

and no compassion at all for people whose misfortune was due to a misdeed. However, there was no effect of group, indicating OT did not enhance compassion (there was a trend in the opposite direction, though the effect was not significant (F (1,59) = 2.141, p > .05). There was no interaction between group and category (F (1,59) = 0.57, p > .05) either. These results have remained unpublished.

OT and empathy: the inflexible judge task

We aimed to examine OT's effect on empathy and the possible modulating role of the information available about the target. Participants listened to two stories in which an individual was both a victim and a culprit in a complex situation. We split the stories into 4 parts: 1) a neutral introduction; 2) the presentation of the individual as a victim; 3) the presentation of the individual as a culprit; and 4) the crime he committed. At the end of each part, participant evaluated (6-point Likert scale) to which extent they felt sympathy for the individual and how much they wanted to help him.

Results

We performed multivariate General Linear Models with sympathy scores and willingness to help scores[15] as dependent variables, and condition (OT vs. PL) as fixed factor. We found a strong main effect of time for both sympathy and willingness to help in both stories, providing a robust manipulation check: empathy and willingness to help the target increased from the first part of the story (general presentation of the protagonists) to the second part (presentation of the target as a victim), then strongly decreased from the second part to the third part (where the target is presented as a culprit) and continued to decrease in the fourth part where the target commits a crime. Unexpectedly, we found no differences between OT and PL groups, neither for sympathy (F(1,59) = 2.796, p > .05) nor for

[15] We pooled the scores obtained in the two stories for sympathy and helping behavior, respectively.

willingness to help ($F(1,59) = .802$, $p > .05$) and no interaction between group and story part either. These results have remained unpublished.

Study 3: Oxytocin and sleep (2011)

In the early nineties, Uvnas-Moberg et al. (24) investigated the link between OT and sleep in rats. They showed that low doses of OT led to a decrease of locomotor activity and that higher doses led to clear signs of sedation. As a study by Heinrichs and colleagues suggested that OT may also have anxiolytic proprieties in humans (25), we hypothesized that OT administration may influence sleep in human by decreasing sleepiness latency, thereby potentially lengthening sleep duration.

Participants

Twelve healthy young adult males (between 20 and 35 year old) took part in the within-subject design study and were randomly assigned to receive either intranasal placebo (PL; n = 6) or OT (n= 6; 32 IU Syntocinon Spray – 4 puffs in each nostril – Novartis, Basel, Switzerland) before the first testing session. Two weeks later, participants who received PL received OT, and vice versa. Except for the product administered, testing sessions were identical. We asked participants to have a regular wake-sleep cycle during the two weeks preceeding each testing sessions, complete a sleep diary and wear an actimeter during these weeks to ensure this was the case. No participant had to be excluded based on these measures.

Procedure

After providing written informed consent, participants completed anxiety and depression (26), self perceived sleepiness (27), fatigue severity (28), and positive and negative affects (29) questionnaires, in order to ensure that both groups were equal regarding individual differences relevant to the study. Each experimental session were split into 4 similar parts in the following fixed order.

First, participants completed the *Fatigue & Somnolence Visual Analogue Scale (VAS-F,S) (30),* a self reported evaluation of the current fatigue and somnolence state of the individual and the *Psychomotor Vigilance Task (PVT)* (31), which assess current attention and vigilance.

Next, participants received the product (OT vs. PL). During the 45 minutes delay, electrodes were placed for conducting electroencephalogram, electrooculogram and electromyogram measurements.

Finally, participants took part in a Multiple Sleep Latency Test (MSLT, 4 trials per session, separated by 2 hours) (32). In the MSLT, participants have to sleep for 20 minutes and their sleep latency, sleep duration and the proportion of REM sleep is measured.[16]

Results

For each dependent variable (fatigue, psychomotor vigilance, sleep latency, sleep duration, REM sleep proportion), we performed a mixed linear model with the score at each trial (6 PVT in total, 8 MSLT in total over the two sessions) as the dependent variable, the condition (OT session vs. PL session) as fixed factor, and the participants as random factor.

The analyses showed no main effect of the product on either sleep latency ($F(1,94) = .27$, $p > .05$), sleep duration ($F(1,93) = 2.82$, $p = .097$) or REM sleep proportion ($F(1,93) = 2.53$, $p = .115$). No significant effect of the product on psychomotor vigilance was found ($F(1 ;70) = 3,09$; $p = 0,083$). These results have remained unpublished

Study 4: Oxytocin, pain and sensitivity to baby's cry (2011)

[16] Even if the first REM episode occurs about 70 minutes after falling asleep (33), some subjects may present a REM EEG and occulomotor pattern a way farster. The REM sleep can actually occur pretty rapidly in some individuals according to the MD (sleep specialist) who co-supervised this study. Furthermore, the MSLT has specialy been built for this puporse (see 32)

Many studies in rodents have demonstrated the antinociceptive effect of OT (e.g. (34, 35)). In humans, it has been suggested that OT to decrease pain in some specific clinical population (e.g.(36)). Based on these early findings, we hypothesized that OT would increase pain threshold, pain tolerance, willingness to endure pain and by decreasing perceived pain intensity in neurotypical humans.

In this study, we also assessed whether OT would attenuate the psychological discomfort produced by babies' cry, based on a previous study suggesting that OT promotes women's functional reactivity to infants' cry by decreasing neural activitation brain regions associated with anxiety and negative affect and enhancing activity in regions linked with empathy (37).

Participants

Sixty healthy young adult males (*M*age= 21.35 years; *SD* = 2.15) took part in the study and were randomly assigned to receive either intranasal placebo (PL; n = 30) or OT (n=30; 32 IU Syntocinon Spray – 4 puffs in each nostril – Novartis, Basel, Switzerland).

Procedure

After providing written informed consent, participants were invited to complete demographic, alexithymia (19), social desirability (38), the big-five factor of personality (39), fear of pain (40) and emotional disposition (12) questionnaires, in order to ensure that both groups were equal regarding individual differences relevant to the study. The following tasks were then administered in a fixed order.

OT and pain

Before product administration, participants took part in a baseline measure of pain through a Cold Pressure Test (CPT) (for a review, see (41)). In this paradigm participants have to put their non-dominant hand in a cold (4°) bucket of water. This disposal activates the nociceptive system and allows to measure several variables: the pain threshold (time between

hand immersion and reported feeling of pain), pain tolerance (time between immersion and withdrawal of the hand from the water), willingness to endure pain (time difference between pain threshold and pain tolerance) and perceived pain intensity.

We repeated this procedure 45 minutes after product administration.

Results

We performed repeated measures ANOVA on each dependent variable with Time (pretest vs. posttest) as within-subject factor and Condition (OT vs. PL) as between-subject factor.

OT enhanced neither *pain threshold* compared to baseline (F (1,58) = 1.18, $p > .05$), nor pain tolerance (F (1,58) = 1.55, $p > .05$), or willingness to endure pain (F (1,58) = 2.23, $p > .05$). It did not decrease perceived pain intensity either (F (1,58) = .55, $p > .05$). These results have remained unpublished.

OT and tolerance to baby's cry

After the second CPT, participants took part in a tolerance to babies and infants' cries test. For this assessment, they listened to 24 sound tracks (20s each) of babies or infants cry and rated their annoyance (10-point Likert scale, 1 = not annoying at all, 10 = extremely annoying).

Results

The one-way ANOVA conducted on mean annoyance ratings showed no differences between the two groups (F (1,58) = 1.17, $p > .05$). OT did not modulate sensitivity toward baby or infant's cry. These results have remained unpublished.

Study 5: The dark side of Oxytocin: guilt, conformism and compliance to antisocial behaviors (2012)

While the positive social consequences of oxytocin (OT) attracted a great deal of attention, the potential for negative social consequences of OT administration was much less studied. At the time we conducted the study (2012) almost all OT studies had tested its effect on socially desirable outcomes and only two investigated its effect on less desirable outcomes. These studies showed that OT actually increased - rather than decreased - envy, gloating and ethnocentrism (42, 43). These findings emphasized that OT might, in some contexts, produce undesirable behavioral effects.

We hypothesized that if oxytocin enhances affiliation (44), it should not only facilitate the emergence of prosocial emotions, thoughts and behaviors that contribute to initiate (e.g. trust), maintain (e.g. positive communication) or reinforce (e.g. empathy) social bounds, but also the emergence of undesirable consequences that ensue from such increased affiliation (e.g.:. conformism, guilt). The first part of the study focused on conformism and compliance to peer pressure. To ensure his affiliation to a group, one needs to conform to the group norms (45); it is therefore possible that OT increases conformism, which can be problematic when the group norms are antisocial. In this study, we examined whether OT increases conformism and whether it ironically increases responses to antisocial peer pressure.

The second part of the study focused on guilt, testing whether OT increased guilt feelings and repair behaviors (behaviors aimed at repairing the harm caused).

Participants

Sixty-one healthy young adult males (*M*age= 23.16 years; *SD* = 2.87) took part in the study and were randomly assigned to receive either intranasal placebo (PL; n = 30) or OT (n=31; 40 IU Syntocinon Spray – 5 puffs in each nostril – Novartis, Basel, Switzerland).

Procedure

After providing written informed consent, participants completed demographic, alexithymia (19), mood (29), the big-five factor of personality (39), social desirability (38)

and psychological disorders (13) questionnaires in order to ensure that both groups were equal regarding individual differences relevant to the study. The following tasks were then administered in a fixed order.

Creation of affiliation bond

Each experimental session involved one naïve participant and two confederates (one male and one female, both took part in all session. The male confederate was the one who took part in the guilt assessment). The naïve participant and a first confederate were together with the experimenter and asked to complete control measures together. The confederate then asked the naïve participant two predefined questions in order to create a social connection. They were then administered the product at the same time in order to create a form of complicity.

Framed to feel guilty: The setting of the guilt paradigm (part 1)

To measure guilt, we had to first induce this feeling to the participants. Because the procedure aimed to create guilt is long (the instructions are complicated and the task itself is long), it started shortly after substance administration. The feeling of guilt can only emerge at the end of the game, approximately 75 minutes after product administration. After product administration, the naïve participant and the confederate were left together in a waiting room. After 4 minutes alone (during which the confederate asked the naïve participant two standardized questions, in order to maintain the connection), the experimenter gave to the two an instruction sheet for a card game - explaining that each player would play 6 trials in a row (the first player plays the 6 first trials and the second player plays the 6 next ones). In each trial, 2 cards, faces up, appeared on the computer screen. On one card appeared the number “1” written, on the second appeared the number “0”. Participants had to memorize which card was where and then the cards would turn over (faces down) and mixed. Participants were asked to find the card with the “1” on. If they succeeded, their partner would receive 1€. Thus, the

participant's performance did not affect their income but only their partner's. After each trial, a feedback would appear. After reading the instruction, the experimenter re-explained the rules verbally to make sure that participants understood the task. He then invited questions and the confederate always asked a question aiming to emphasize that one played for his partner. Then, a factice lottery designated the confederate as the first player.

OT and conformism to antisocial behaviors

The participant and the confederate were escorted to the waiting room, where the second confederate was introduced as a participant of another study. Shortly afterwards, the antisocial peer pressure procedure, adapted from (46) was initiated. In brief, a second experimenter presented as a friend of the main experimenter asked the participants to select a set of questions for participants in an upcoming study, whose gains would directly depend on their performance. This second experimenter handed the participant and confederates a sheet with 45 questions about movies: 15 easy, 15 medium, and 15 difficult (the items have been validated in (46)). These questions appeared in counterbalanced order and their level of difficulty was indicated in bold font. After the experimenter had left the room, the two confederates urged (in order to produce the peer-pressure the participant to select the hardest questions, rather than creating a fair and balanced set of questions. Then, the two confederates and the naïve participants immersed themselves in the response sheet to independently select their questions. Finally, the second experimenter returned and participants handed their sheets back to her. The number of difficult questions selected by the naïve participants served as a measure of compliance to antisocial peer pressure.

Results

Two participants (one in each group) deviating from more than 5SD from the chosen items' difficulty mean were excluded, leaving 59 participants for this analysis. We performed univariate General Linear Model with conformity to antisocial behaviors score as dependent

variable and condition (OT vs. PL) as fixed factor. We did not find a significant effect ($F(1,58) = 3.315$, $p = .078$), whereby participants in the OT condition did not chose significantly more difficult questions than participants in the PL condition, suggesting that OT does not alter conformism to antisocial behaviors. We tried to publish these results in three different journals, without success.

OT and general conformism

The players were then separated to two different rooms (both participants went to the experiment room and the first confederate just left). Participants were then placed in front of a computer screen and took part in a numeric estimation task (47). For each trial (n=16), a number of letters "A" (between 148 and 1156) appeared on screen and participants had to estimate this number. Each trial lasted only 4 seconds, in order to prevent participants from counting. Between trials, participants had time to write down their estimates. Participants were told that for half of the trials, they would see the estimates provided by the three individuals who took the task before them and that they were free to choose whether to use these estimates when making their own judgments. In 4 trials, the software provided overrated estimations and in the other 4 trials it provided underrated estimations (20%, 25% and 30% over / under the correct number, respectively). As explained by Van Cappellen and colleagues (47), conformity was estimated by calculating the differences between the numeric value provided by the participant and those allegedly provided by each of the three other. To control for variations in sizes, each of these three difference scores were divided by the corresponding estimate provided by the other (bogus) participant and the absolute value of these proportional difference scores were then computed. Finally, the latter scores were averaged across the eight screens to come up with a single deviation score, such that lower values of this deviation score thus reflected higher conformity.

Results

Two participants (one in each group) deviating from more than 3SD from the mean were excluded, leaving 59 participants for this analysis. We performed a univariate General Linear Model with conformity score as dependent variable and condition (OT vs. PL) as fixed factor. We did not find a significant effect of the group ($F(1,58) = 3.302$, $p = .074$). These results have remained unpublished.

Framed to feel guilty: the guilt paradigm (part 2)

At the end of the conformity task, the participants took part in the card game in order to induce guilt. Participants watched first the confederate "performance" (managed by the computer), who scored a 6 on 6 (very beneficial for the participants who thereby won 6 EUR). Then, the participants played their 6 trials and, regardless of their performance (which cannot be easily monitored by the subject because the cards are very rapidly mixed), the computer showed them 4 negative feedbacks (only 2 success trials choices out 6, very unfavorable for their partner who made only 2 EUR). This task is known to make participants guilty (48).

OT and behavioral measure of guilt

At the end of the card game, the participants received 12 tickets worthing 1€ each as a bonus for their participation. However, participants could choose, for each ticket, whether they keep it, give it to their partner or to donate it to charity (in order to avoid confound with generosity). Three sealed boxes were in the room (one for each condition), and after the experimenter had left the room participants could put the amount of tickets they assigned to each condition in a corresponding box. In order to avoid social desirability bias, the participants were told that they would receive their potential bonus (amount of tickets they have decided to keep for themselves) from another experimenter (who is not informed that they have made lost money to their partner during the card game). The behavioral measurement of guilt relied on their propensity to make amend to the partner they thought

they had disadvantaged during the card game. For this purpose, we have calculated the following ratio:

Amount of ticket given to the partner/(Amount of ticket given to the charity + Amount of ticket kept)

Results

We performed a univariate General Linear Model with behavioral measures of guilt as dependent variables, and condition (OT vs. PL) as fixed factor. There were no differences between groups on the behavioral measure of guilt ($F(1,59) = 1.103$, $p > .05$). These results have remained unpublished.

OT and self reported guilt

At the end of the experiment, participants completed a 12 items questionnaire where they rated (7-point Likert scale) how they felt during the game. One of the items assessed guilt.

We performed a univariate General Linear Model with self-reported guilt as dependent variables, and condition (OT vs. PL) as fixed factor. There were no differences between groups on self-reported feeling of guilt ($F(1,59) = 1.103$, $p > .05$)nor on the behavioral measure of guilt. These results have remained unpublished.

Study 6: Oxytocin, Mimetic Desire, Visual perspective taking and Trust (2012)

Bayliss et al. (49) have shown that people evaluate stimuli gazed by another person more positively. This refers to what we call mimetic desire. It has been demonstrated the social rather than purely attentional nature of this effect. For example mimetic desire is modulated by the facial expression (50) and the trustworthiness of the gazing person (51). As OT increases perceived trustworthiness of strangers (52) and makes the social clues more salient (42), a collaborators of ours thought that this hormone might play a role in this

mimetic desire effect. She hypothesized that OT would magnify mimetic desire comparing to a control group.

We also though that OT, as a social hormone that increases the salience of social clues (42), would the visual perspective taking. Finally, in this study, we also replicated the non-monetary trust paradigm (Envelope task). At the beginning, we wanted to use this paradigm as a manipulation check given the huge effect size we found in the original study.

Participants

Ninety-five healthy young adult males (*M*age= 22.53 years; *SD* = 2.89) took part in the study and were randomly assigned to receive either intranasal placebo (PL; n = 47) or OT (n=48; 32 IU Syntocinon Spray – 4 puffs in each nostril – Novartis, Basel, Switzerland).

Procedure

After providing written informed consent, participants were invited to complete demographic, alexithymia (19), mood (29), the big-five factor of personality (39), social desirability (38), empathy (18), self-monitoring (53) and psychological disorders (13) questionnaires, in order to ensure that both groups were equal regarding individual differences relevant to the study. The following tasks were then administered in a fixed order.

OT and mimetic desire

Participants were informed that they would see a 3D person on the screen, turning his attention towards or away from paintings. They were instructed to watch what happened on the screen during 5 minutes. As in Treinen et al. (51), movie clips created from Oosterhof and Todorov's face database (54) were used as stimuli. Participants were exposed to a single male, neutral (no emotional expression) gazing face associated with 4 pre-tested neutral art painting. More precisely, a fixation cross was presented. Then, a face with direct gaze (looking toward the participant) appeared on the left or right side of the screen. After 1 second, one of the paintings appeared on the other side and the face either turned his attention towards it or away

from it for 2 seconds. Then the painting disappeared and the face turned back to a direct gaze position. The face turned his attention towards two art paintings and away from the other two. The associations were presented 8 times. After exposure, participants indicated how much they liked each painting on a 9-point Likert scale.

Results

Four multivariate outliers (>2.5 SD) were excluded from analysis (2 in each groups). We performed a repeated measures ANOVA on paintings evaluations, with attention orientation (towards vs. away) as within-subject factor and condition (OT vs. PL) as between subject factor. No main effect of the condition was found ($F(1,90) = .690$, $p > .05$) indicating that we did not find a general mimetic desire effect. However, the interaction predicted by our collaborator was significant ($F(1,90) = 4.7$, $p < .03$). In the OT condition, paintings looked at were rated more positively than paintings looked away from. In PL condition, no significant difference emerged. So in this study, the mimetic desire effect only emerged in the OT condition. Our collaborator submitted this paper for publication twice, without success. She decided not to resubmit this paper when we discovered that we could not replicate our effects on trust for the second time (see Study 7) and started to doubt about OT effects.

OT and visual perspective taking

Participants were informed that they would see on their computer screen an individual in the center of a room. This individual would look either to the left wall or to the right wall. On both walls there would be a number of red dots (from 0 to 3). Participants have to answer if the number of dots is similar to information they received just before and according to the point of view they are asked to take. More precisely, a fixation cross was presented. Then a number appeared on the screen followed by the picture of the room with the individual and the red dots on the walls. Then the picture disappeared was replaced by the instruction for the point of view they have to adopt (self vs. other). Finally participants indicated if the presented

number was similar to the amount of dots presented at the beginning (pressing key “1”) or not (pressing key “3”). Fifty-two trials were randomly presented, 26 for each condition (self vs other). The accuracy and response time were recorded.

Results

We performed a repeated measures ANOVA on accuracy scores, with visual perspective condition (self vs. other) as within-subject factor, and condition (OT vs PL) as between subject factor. There was no main effect of condition ($F(1,94) = 1.46$, $p > .05$) and no significant interaction effect ($F(1,94) = .55$, $p > .05$). We also have controlled for the empathy level (either IRI total score or IRI subscales specific scores), which did not modified our results. A second repeated measures ANOVA was performed on reaction times, with visual perspective condition (self vs. other) as within-subject factor, and condition (OT vs. PL) as between subject factor. There was no main effect of condition ($F(1,94) = .004$, $p > .1$) and no significant interaction ($F(1,94) = .007$, $p > .1$). These results have remained unpublished.

OT and non-monetary trust

Here, we used a modified version of the paradigm we presented in Study 1. Indeed, even if procedure was the same, we replaced the sexual openness questionnaire by a questionnaire where participants have to evaluate experimenters’ competences. They were told that their evaluation and comment about the experimenter’s competences would be transmitted to the experimenters’ supervisors. Their feedback put together with all the participants’ feedbacks will help the experimenter’s supervisors to make constructive comments that will help me to improve the experimenter’s skills. Here again, the experimenters assured participants that they would not look at their answers. However, they were free to seal the envelope, and to even add sticky tape (which were provided). The degree

of envelope's opening (opened, sealed or sealed plus taped) was considered as participants' degree of trust toward the experimenter.

Results

We performed a one-way ANOVA with the degree of openness of the envelope as dependent variable and the condition (OT vs. PL) as between-subject factor. Surprisingly no differences were found ($F(1,93) = .229$, $p > .05$) suggesting that OT did not enhance trust toward the experimenter. We published this failed replication together with the second failed replication of the envelope effect (Study 7) in PLoS ONE (55).

Study 7: Oxytocin, Compassion and Trust (2013)

Compassion may be defined as the vicarious experience of another's distress, leading to a helping behavior (56). It is thus a prosocial feeling associated to a prosocial behavior. It is a cornerstone of cooperative relations with non-kin (57). It reinforces group cohesiveness, which is essential to species survival. Nevertheless compassion is shaped by contextual cues and occurs when the potential costs underweight the potential benefits (56). As OT has been described as a prosocial hormone that notably promotes altruistic behaviors (58) and reinforces group cohesion (43), we hypothesized that OT should also promote compassion both from a cognitive or a behavioral point of view, and even more in context in which it is not costly. In the context of all the non significant findings we had accumulated so far, the choice of compassion was not random. Compassion is the only variable that OT must influence whichever the theory of OT adopted (OT as the hormone of affiliation which enhances prosocial feelings and behaviours (44), OT as the hormone of social salience, leading to prosocial or antisocial effects depending of what is salient (42); OT as the hormone of social approach, which enhances social approach behaviors and inhibits social withdrawal behaviors (59)). All these theories lead to the same prediction: OT should increase

compassion because 1) compassion is a prosocial behavior; 2) OT should have made the "suffering one" more salient and 3) compassion involves a social approach behavior.

In addition to the compassion tasks and given the results we obtained in study 6, we also included for second time our non-monetary trust paradigm in order to clarify the effect of OT on trust regarding confidential information.

Participants

Sixty-one healthy young adult males (*M*age= 21.28 years; *SD* = 2.46) took part in the study and were randomly assigned to receive either intranasal placebo (PL; n = 29) or OT (n=32; 32 IU Syntocinon Spray – 4 puffs in each nostril – Fuerte Farmaceutica, Funchal, Portugal).

Procedure

After providing written informed consent, participants were invited to complete demographic, mood (29), personality (39), social desirability (38), empathy (18), emotional disposition (12) and psychological disorders (12, 13) questionnaires, in order to ensure that both groups were equal regarding individual differences relevant to the study. The following tasks were then administered in fixed order.

OT and explicit/implicit measures of emotional compassion

Participants were invited to take part in a computerized task measuring their ability to experience vicariously another's emotional state. Participants were staged with a virtual friend in 40 randomly presented scenarios. Those were split into eight "participant only scenarios" (nothing happened to the virtual friend but something happened to the participants), 16 "virtual friend onlyscenarios" (nothing happened to the participants but something happened to the virtual friend) and 16 "participant and virtual friend contrasted scenarios" (something happened to both but the valence of each one experience is reversed). Every script conditions were equally split in a positive version and in a negative version (either something good

happens, either something bad happens). At the end of each scenario, participants were asked to rate their own emotional state by answering the following question: "Now I feel…" on a 7-point Likert scale (1 = I feel very sad → 7 = I feel very happy). This was the explicit measure of emotional compassion. Right after each explicit measurement of compassion, participants were also asked to rate attractiveness of neutral images on a 7-point Likert scale (1 = this picture is very ugly → 7 = this picture is beautiful). This was the implicit measure of emotional compassion. It has indeed been shown that mood biases the evaluation of neutral items. When individuals are in a bad mood, they under evaluate the attractiveness of neutral items. When they are in a good mood, they tend to over evaluate the attractiveness of neutral items (60).

The aim of this task was double. First it assessed if OT has a general influence on the vicarious experience of another distress, which is proper to compassion. And, secondly it assessed if OT has an influence on the vicarious experience of another feeling, regardless of the valence of the emotion lived by someone else.

Results

We performed two repeated measures ANOVA on mood scores and evaluation scores, respectively, with scenario type (participant only - positive vs. participant only - negative vs. friend only - positive vs. friend only - negative vs. contrasted positive vs. contrasted negative) as within-subject factor and condition (OT vs. PL) as between-subject factor. No differences between groups were found, neither for mood ($F(1,60) = 1.166$, $p > .05$), nor for evaluations ($F(1,60) = .162$, $p > .05$). We tried to publish these null results several times, without success.

OT and non-monetary trust

Here, we used exact same paradigm as described in Study 1.

Results

We performed one-way ANOVA with the degree of openness of the envelopes as dependent variable and the condition (OT vs. PL) as factor. Surprisingly no differences between groups were found ($F(1,60) = .295$, $p > .05$) suggesting that OT did not enhance trust toward the experimenter. This confirmed the results we obtained in Study 6. As mentioned above, we published this failed replication together with the first failed replication of the envelope effect (Study 6) in PLoS ONE (55).

OT and behavioral measurement of compassion

Because the previous task relied on fictitious scenarios, we also included a real scenario in this study. In this part of the experiment, participants were asked to fill a distractor questionnaire when the experimenter suddenly received an email reporting a very bad news: he started to sigh, to moan, to swear and to have tears in the eyes. This lasted for 5 minutes. Two hidden webcam filmed participants' reactions, which permitted us to count the number of gaze toward the sufferer, the number of interaction with him and the duration of both gazes and interactions. Half of the participants were placed in a "low-cost" condition (the visual pathway between participants and the experimenter was clear) and the second half in a "high-cost" condition (the visual pathway was obstructed, forcing the participants to move if they wanted to see or to interact with the experimenter).

Results

We performed a multivariate General Linear Model with the amount of gazes, the duration of the gazes, the amount of interactions and duration of interactions as dependent variables and with condition (OT vs. PL) and cost (high vs. low) as fixed factors, according to the cost for the participants. No differences between groups were found (Gazes: $F(1,60) = .123$; Duration of the gazes: $F(1,60) = .06$; Interactions: $F(1,60) = 168$; Duration of the interactions: $F(1,60) = .065$; all *ps* $> .05$). No interaction effect with the cost was found either. We tried to publish these null results several times, without success.

Study 8: Oxytocin and jealousy in woman (2014)

This study was run a month after Study 7 (before the results were analyzed) and we chose jealousy as dependent variable for the same reason as in study 7: Whichever the theory of OT adopted (OT as the hormone of affiliation (44), OT as the hormone of social salience (42) or OT as the hormone of social approach (59)), OT should influence jealousy. The difference with Study 7 is that, here, the various theories predict influences of *opposite* directions, which we saw as an aid to decide between theories.

Jealousy involves three persons et emerges when X is afraid of loosing his *relationship* with a person Y because of a rival Z (61). It is close but different from envy, which involves only two persons and emerges when X lacks of *something* that Z has (Smith & Kim, 2007). In short words, jealousy involves the fear of loosing what we have to the benefit of someone else, when envy involves the desire of obtaining something we don't have and that someone else has.

Because OT is supposed to foster secure attachment (62) and because people with secure attachment are the least jealous (63), the affiliation theory of OT predicts that OT would decrease romantic jealousy. By contrast, the two other theories would predict increased jealousy after OT administration. According to the social salience theory, OT would make people more jealous just as it makes people more envious (42): because it will make the rival more salient. According to the social approach theory, OT would magnify all approach-related emotions, whether good or bad. As romantic jealousy is associated with approach motivation(64), it should be increased by OT.

Participants

Forty-four couples (Female : *M*age= 21.48 years; *SD* = 2.2 ; Male : *M*age= 22.38 years; *SD* = 3.03; Relationship duration (in month): *M*=25.68; *SD* = 21.15 , range 3-84) took

part in the study. Females were randomly assigned to receive either intranasal placebo (PL; n = 22) or OT (n=22; 24 IU Syntocinon Spray – 3 puffs in each nostril – Fuerte Farmaceutica, Funchal, Portugal).

Procedure

After providing written informed consent, male participants were invited to complete a demographic questionnaire about their relationship. They were also asked to complete a jealousy questionnaire (65) and a relationship questionnaire (66) by adopting their partner's point of view (in order to avoid to disclose our study goal to the female participants), in order to ensure that both groups were equal regarding individual differences relevant to the study. Female participants were asked to complete a mood questionnaire (29) in order to compare their basal mood with their mood after the jealousy induction. After the jealousy induction, the following tasks were administered in fixed order.

Jealousy induction

For this study, we needed to induce jealousy. Because the jealousy-inducing procedures existing in the literature relied all on fictitious scenarios or memory of past jealousy experienced, we created the following paradigm. The naïve female participant, her life partner (who would become the confederate of the experimenter) and a female confederate took place in a general knowledge quiz. In order to explain the presence of the female confederate, the quiz was presented as a task assessing cognitive differences between single women vs. women engaged in a romantic relationship. The quiz opposed the two females and was split in two parts. The first part was about general culture (e.g.., covering many different topics from art to science, nature, sport etc). The second part was a specialized quiz whose topic was chosen among a list by the male partner. He was secretly instructed to choose a topic which he is interested in, but not his girlfriend. Of course, our female confederate had memorized all the answers, although she voluntary made mistakes from time

to time to increase plausibility. Then the male partner was asked to play the questioner role and the female participant competed again with our confederate. The reason why we asked him to choose a topic that disadvantages his girlfriend was to induce the feeling of relational insecurity that is necessary for the emergence of jealousy. In order to trigger jealousy per se, we also (secretly) aksed him to congratulate our confederate twice during the game with very flattering comment implying that he is impressed to meet a girl who shares and knows so much about this subject. After the quiz, the female participant, her partner and our confederate took part in a Cyberball game (67). Only the female participant played for real. As jealousy is magnified in a social rejection context (64), the game was programmed to put her in ostracism situation.

OT and explicit measure of mood

After jealousy induction, participants were asked to complete the mood questionnaire again (PANAS, (29)). This aimed to see if a mood variation in negative affects and in jealousy in particular occurred comparing to pretest assessment and to see if OT modulate this variation, and how.

Results

We performed a repeated measures ANOVAs with Time (pretest score vs. posttest score) as within-subject factor and condition (OT vs. PL) as between subject factor either for the positive affect than for the negative affect. No differences between groups were found (Positive Affects: $F(1,43) = 1.353$; Negative Affects: $F(1,43) = .200$, all ps $> .05$) .

OT and behavioral measure of jealousy

Here the participant, her partner and our confederate were brought together in the same room again. The experimenter asked the participants to choose five mimes in a list of 20. They were told that the confederate would mimic their choices to their life partner. This list contained 10 rewarding mimes (to take a shower, being a model…) and 10 disvaluing mimes

(imitating a monkey, being sick…). Jealousy was assessed by participants' propensity to choose either rewarding or disvaluing items. Indeed, by choosing a larger amount of disvaluing items, participants expressed their need for revenge after having lived strong jealous experience.

Results

We performed a one-way ANOVA with the amount of target words as dependent variable and condition (OT vs. PL) as factor. We did not obtain a significant result ($F(1,43) = 2.847$; $p = .098$) suggesting that OT would not increase or decrease jealousy. These results have remained unpublished.

OT and implicit cognitive measure: word completion task

In this task, participants were asked to complete orally (their answers were recorded) a phoneme read by the experimenter in order to make a word As it has been demonstrated that after being exposed to violent lyrics people are more tend to produce words linked with aggressiveness (68), we considered that if participants lived a strong jealousy experience they would produce more words associated to semantic fields linked with jealousy. Those semantic fields were: jealousy, betrayal, deception, attention and danger. High interrater agreement was found to spot words falling within these categories (reported as target words). The hypothesis here is that if OT modulates jealousy, the numbers of target words would be different comparing to the placebo group.

Results

We performed a one-way ANOVA with the amount of target words as dependent variable and condition (OT vs. PL) as factor. We did not obtain a significant result ($F(1,43) = 2.847$; $p = .098$) suggesting that OT would not alter jealousy as the amount of target word is equivalent between conditions. These results have remained unpublished.

OT and implicit cognitive measure: positive vs. negative words recall

Participants were firstly asked to assign a positive or a negative valence to words appearing on their computer screen. This first part of the task aimed to implicitly prime positive (related to attractiveness or not) vs. negative female qualifiers. A filler task was then performed (write down as many countries they know for 2 minutes). Finally, participants were asked to write down a maximum of words they can recall from the first task. The aim of this implicit recall task is to see if a memory bias occurred during the words recall. Our hypothesis was that if OT modulates jealousy, words related to the positive-attractive category would be better recalled in the OT compared to the PL group.

Results

We performed a multivariate General Linear Model with the amounts of positive words recalled, positive and attractive words recalled and negative words recalled as dependent variables and condition (OT vs. PL) as fixed factor. We found no differences at all between the groups (Positive words: $F(1,43) = .000$; Positive and attractive words: $F(1,53) = .088$); Negative words: $F(1,53) = .239$; all ps $> .05$).

These results have remained unpublished.

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