

Mixed support for a causal link between single dose intranasal oxytocin and spiritual experiences: opposing effects depending on individual proclivities for absorption

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Abstract

Intranasal oxytocin (OT) has previously been found to increase spirituality, an effect moderated by OT-related genotypes. This pre-registered study sought to conceptually replicate and extend those findings. Using a single dose of intranasal OT vs placebo (PL), we investigated experimental treatment effects, and moderation by OT-related genotypes on spirituality, mystical experiences, and the sensed presence of a sentient being. A more exploratory aim was to test for interactions between treatment and the personality disposition absorption on these spirituality-related outcomes. A priming plus sensory deprivation procedure that has facilitated spiritual experiences in previous studies was used. The sample ($N = 116$) contained both sexes and was drawn from a relatively secular context. Results failed to conceptually replicate both the main effects of treatment and the treatment by genotype interactions on spirituality. Similarly, there were no such effects on mystical experiences or sensed presence. However, the data suggested an interaction between treatment and absorption. Relative to PL, OT seemed to enhance spiritual experiences in participants scoring low in absorption and dampen spirituality in participants scoring high in absorption.

Key words: oxytocin; spirituality; absorption; genotypes; replication

Introduction

In this sensory deprivation experiment, we examined the joint roles of a single dose of intranasal oxytocin (OT), OT-receptor genotypes and the personality disposition absorption on spirituality-related outcomes. Interestingly, recent experimental

research has indicated that OT may play a causal role in spirituality and that the effects of OT on spirituality are moderated, as expected, by genes critical for OT signaling such as oxytocin receptor (OXTR) and CD38 (Van Cappellen *et al.*, 2016). However, the role of the personality disposition absorption has not been addressed in this context. Absorption signifies

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a proclivity to have one's attentional system fully absorbed by stimuli currently under mental processing and is an important personality marker of suggestibility in general and hypnotizability in particular (e.g. Tellegen and Atkinson, 1974; Nadon et al., 1991). Not coincidentally, absorption has been described as the 'grand mediator' of spiritual experiences such as mysticism (Hood et al., 2009; Granqvist et al., 2012). In addition, a link between OT and absorption has been suggested in findings indicating that intranasally administered OT facilitates hypnotizability in individuals who had previously reported low hypnotizability (Bryant et al., 2012). Thus, absorption might conceivably qualify the effects of OT on spirituality-related outcomes.

OT and spiritual experiences

OT is a pituitary gland peptide hormone and neurotransmitter with a wide range of physiological effects. Initially considered a hormone of lactation and supporting the work of labor, it has, over the past decades, been extensively probed for its psychological effects, especially in the context of attachment and bonding (e.g. Buchheim et al., 2009). OT is triggered by projections from the hypothalamus where it is synthesized and is then secreted by the pituitary gland into the bloodstream (Gimpl and Fahrenholz, 2001). OT is also released by magnocellular neurons whose axonal projections affect the amygdala, hippocampus, striatum, nucleus accumbens and brainstem (Knobloch et al., 2012; Chini et al., 2017). Although OT is produced by both men and women, OT levels tend to be higher in women as OT is modulated by estrogen in the central nervous system and by other steroid hormones (Meyer-Lindenberg et al., 2011; Bos et al., 2012). OT and similar neuropeptides can be intranasally administered and reach the cerebrospinal fluid (Born et al., 2002; Beard et al., 2018; Lee et al., 2018); it is likely that they readily cross the blood-brain barrier via this route (Bos et al., 2012; Beard et al., 2018, but see Guastella and MacLeod, 2012). OT has also been suggested to play a key role in various socio-emotional abilities (for reviews, see Bartz et al., 2011; Van IJzendoorn and Bakermans-Kranenburg, 2012).

Spirituality is often understood as a panhuman proclivity for self-transcendence, where the self is experienced as fundamentally related or interconnected with the divine, with nature, with the world itself, with other living beings or simply with deeper (and usually hidden) layers of the self (Hill and Pargament, 2008). This proclivity has been extensively explored in human history, including experiments with plants, psychedelic drugs and rites. Further, previous research indicates that many people conceptualize the transcendent 'object' of spirituality in anthropomorphic terms as a person-like entity (e.g. God), who may also function as a non-corporeal attachment figure, providing a 'sensed presence' and yielding felt security for the individual (Granqvist and Kirkpatrick, 2013, 2016; Gruneau-Brulin et al., *in press*).

OT may influence particularly the relational components of spirituality, but the link between spirituality and OT is not yet well understood. Kelsch et al. (2013) assayed plasma oxytocin levels in human immunodeficiency virus (HIV) positive individuals, some of whom had reported spiritual transformations. In that sample, higher endogenous OT levels were associated with higher spirituality (but not with self-reported religiosity). OT levels were two times higher in individuals who had described spiritually transformative experiences relative to those who had not. However, plasma levels of OT may have been affected by antiretroviral medications, and the sample was not

representative of the population as a whole, making population inferences somewhat ambiguous. To address these limitations, Holbrook et al. (2015) examined endogenous OT levels through saliva samples in a non-clinical population of American Christians. Consistent with Kelsch et al. (2013), they found a positive relation between self-reported spirituality and endogenous oxytocin levels. This correlation held true even after controlling for variables like church attendance, positive mood, gender, and relationship status.

As noted, a causal role of exogenous OT on spirituality has also been indicated, corroborating the conclusions drawn in previous correlational studies (Kelsch et al., 2013; Holbrook et al., 2015). Van Cappellen et al. (2016) studied 83 midlife male participants, randomly assigned to receive a single dose of intranasal OT or placebo (PL) and completed the Spiritual Transcendence Scale (STS). Their results showed that OT led to an increase in participants' self-reported trait spirituality and then also facilitated their experience of positive emotions during a guided meditation task. Importantly, however, the significant effects of OT on spirituality were obtained only following statistical control of participant religious affiliation. Thus, OT did not have any statistically significant 'raw' (or unadjusted) effect on spirituality in that study (see Quintana and Williams, 2018; see also Supplementary Material in Van Cappellen et al., 2016 for detailed analyses). Nonetheless, given these demonstrated links between both endogenous and exogenous OT on the one hand and spirituality on the other, and given the relational features of spirituality, it may be hypothesized that OT promotes trait spirituality and perhaps also the occurrence of spiritual experiences and the sensed presence of a sentient being.

Spirituality and OT genotypes

The oxytocin receptor gene (OXTR) and the CD38 gene (CD38) are two of the genes implicated in OT signaling (Jin et al., 2007; Lee et al., 2009; Meyer-Lindenberg et al., 2011; Westberg and Walum, 2014). Previous research has shown that the OXTR rs53576 polymorphism is related to autism, depression, and stress reactivity, as well as to prosocial and bonding behaviors and social cognition (see Meyer-Lindenberg et al., 2011; Westberg and Walum, 2014; Li et al., 2015 for a review). Specifically, the heterogeneous effects of intranasal OT across individuals (e.g. Bartz et al., 2011; Olf et al., 2013) may depend on the OXTR rs53576, as it regulates the role of OT on social and affiliative behaviors (Feng et al., 2015; but see Bakermans-Kranenburg and van IJzendoorn, 2014). In line with this reasoning, Van Cappellen et al. (2016) genotyped participants for the OXTR rs53576 polymorphism and reported that the effects of exogenous OT on spiritual transcendence was marginally moderated by the OXTR rs53576.

Another gene that could potentially influence the administration of OT is the CD38 gene that regulates the release of OT and is therefore involved in OT signaling (Jin et al., 2007). There are two polymorphisms in the CD38 gene that are relevant for social behaviors (rs6449182 and rs3796863) (Munesue et al., 2010; Algoe and Way, 2014; Feldman et al., 2016). CD38 rs6449182 has mainly been associated with positive emotions (Algoe and Way, 2014; Van Cappellen et al., 2016), while there is evidence that CD38 rs3796863 is involved in parental behaviors such as touch and gaze (Feldman et al., 2012). Van Cappellen et al. (2016) consequently genotyped participants for these two polymorphisms of the CD38 gene as well and reported that the facilitative role

of OT on spirituality was moderated also by variations on the CD38 gene.

Mystical experiences and absorption

Beyond trait spirituality, highly spiritual people may be likely to have mystical experiences. Mystical experiences are characterized by a profound sense of unity, with perceptual objects or a sensed presence like God or by a sense of unity with internal experiences, for example, a 'pure being' without perceptual content (Hood et al., 2009; Granqvist et al., 2012). Mystical experiences do not always yield religious interpretations, as previous studies have shown that religiousness is not a pre-requisite for the occurrence of mystical experiences, but religious believers are more likely to assign a religious interpretation to their experiences (Granqvist and Larsson, 2006).

Absorption, often used as a proxy for suggestibility, is considered an altered state of consciousness (Granqvist et al., 2005) where attention is fully immersed in specific mental processes—one is literally absorbed in/by the task (Granqvist et al., 2012). As noted, absorption is intimately tied to mystical experiences. Not only are mystical experiences typically intense states of absorption in and of themselves, but such experiences are also strongly associated with absorption as a personality disposition (e.g. Spanos and Moretti, 1988; Granqvist et al., 2012). This is presumably in part because people high in absorption are highly suggestible and, in addition, prone to experiencing altered states of consciousness. Consequently, in suggestive settings, such as subtle spiritual priming coupled with sensory deprivation, absorption as a personality disposition has been found to predict mystical and sensed presence experiences (Granqvist et al., 2005; van Elk, 2014).

Conceptual replication and extension of Van Cappellen et al. (2016)

Since experimental research regarding the effects of intranasal OT has shown mixed results and inconsistencies (e.g. Walum et al., 2016), like much pioneering research, the findings reported by Van Cappellen et al. (2016) call for replication. The neurobiological mechanisms underlying spiritual experiences are still incompletely understood; therefore, the present study has been designed to conceptually replicate Van Cappellen et al.'s (2016) study. Replication is a justifiably important task in science in general, and perhaps psychological science in particular (Open Science Collaboration, 2015). In line with Van Cappellen et al.'s (2016) study, the present study combines a neurobiological manipulation with genetics to determine the effects of intranasal OT on spirituality. We do so using comparable OT vs PL procedures and conditions, similar genetic polymorphism analyses (CD38 rs6449182 being the exception, but see Supplementary Material) and an identical spirituality outcome variable.

The Van Cappellen et al. (2016) study had four specific characteristics or limitations that the present study was designed to complement or overcome. The majority of the studies conducted so far on intranasal effects of OT have included only male participants since there is evidence that OT affects men and women differently (Feng et al., 2015). In line with this reasoning, Van Cappellen et al.'s (2016) study included only male participants, thus restricting the generalizability of their findings to men alone. In contrast, our study includes roughly equal numbers of men and women. As it is also hypothesized that estrogen

and other steroid hormones may influence endogenous levels of OT (e.g. Bos et al., 2012), we resorted to controlling hormonal differences by exclusively testing women in the luteal phase of the menstrual cycle and those without consumption of oral contraceptives.

Second, Van Cappellen et al.'s (2016) study was conducted in the USA, with American participants. Importantly, religiosity and spirituality are more culturally normative in the USA than in other parts of the Western world, such as Sweden, where the present study was conducted (e.g. Gruneau-Brulin et al., *in press*; Norris and Inglehart, 2011). Thus, it remains an open question whether OT facilitates spirituality in more secular cultural contexts.

Third, Van Cappellen et al. (2016) did not design their experiment to cause or study spiritual experiences *per se*, that is, as occurring *in vivo* in the laboratory. Instead, the spirituality scale that they used, the STS was designed to tap spirituality as a dispositional personality trait (Piedmont, 1999). In contrast, using a priming plus sensory deprivation procedure that has previously been found reliable in triggering spiritual experiences (see Hood and Morris, 1981; Granqvist et al., 2005; Andersen et al., 2014; van Elk, 2014), our experimental procedure was designed to facilitate spiritual experiences *in vivo*, enabling us to directly study the role of OT in spiritual experience.

Lastly, although Van Cappellen et al. (2016) included measures of dispositional emotionality and mindfulness as control variables, they did not study whether other key dispositional individual differences contributed to the spirituality outcomes over and above, or in concert with, OT. This is in spite of the well-attested importance of, for example, suggestible personality traits like absorption (e.g. Granqvist et al., 2005; Hood et al., 2009).

The present study

In this study, we attempted to conceptually replicate and extend the findings of Van Cappellen et al. (2016). The primary aim was to examine whether a single dose of intranasal OT facilitates spirituality and whether a facilitative effect of OT extends to mystical experiences and the sensed presence of a sentient being as studied *in vivo* in a sensory deprivation context. A further aim was to determine whether OXTR polymorphism (rs53576) and CD38 gene polymorphisms (rs6449182 and rs3796863) moderate the effects of OT on spirituality, as in Van Cappellen et al. (2016) and/or on the other outcome variables. Our final aim was to test whether individual differences in absorption interact with OT in predicting spirituality, mystical experiences and the sensed presence of a sentient being.

We hypothesized that intranasal OT, relative to PL, would cause increased spirituality, and we examined whether such an effect would extend to mystical experiences and the sensed presence of a sentient being. We also hypothesized that the main effect of intranasal OT on spirituality would be moderated by OT-related genetic polymorphisms, and we asked whether genetic moderation would apply to the other outcome variables as well.

Finally, we explored whether sex, religiosity and the personality disposition absorption would interact with the effects of intranasal OT on the outcomes: sex, because Van Cappellen et al.'s (2016) study only included men; religiosity, because their data suggested that religious affiliation may be an important third variable; and absorption for reasons discussed above. For absorption, competing possibilities were suggested by previous research and theorizing. On the one hand, as previous research has found OT to cause increased hypnotizability (cf. absorption)

among participants who had previously scored low in hypnotizability (Bryant et al., 2012), it could be that OT facilitates spiritual experiences especially strongly among low absorbers. On the other hand, as absorption is often used as a proxy for suggestibility (e.g. Granqvist et al., 2005; van Elk, 2014), it could be that OT has a particularly facilitative role on spiritual experiences among high absorbers (i.e. highly suggestible participants).

The main hypotheses as well as the experimental design and questionnaires used in the present study were pre-registered on Open Science Framework (see <https://osf.io/52v8e/>).

Method

Participants and procedure

In total, 116 volunteers participated in the current study and received movie vouchers or gift cards in exchange for their participation. Participants were recruited during late spring and summer; specifically, the study was conducted between April and August 2017. Participants were randomly selected from a larger sample of 600 participants from which additional hypotheses not related to this study were tested (e.g. Cortes et al., 2017). The participants had also stated in a previous informed consent form (Cortes et al., 2017) that they were interested in participating in other studies. We specifically recruited individuals from this larger sample because genotyped data were already available for them (see Henningson et al., 2015; Karlsson et al., 2016; Hovey et al., 2017, for more details). For the present study, we did not take into account ethnicity and we included both Caucasian and non-Caucasian participants (see Barzan et al., 2013; Hovey et al., 2017, for how allele frequencies may differ between these ethnic groups).

The participants of the present study were recruited through mail outs or by phone contact. All participants were right-handed, fluent in Swedish and reported being in good health with no previous or current substance abuse or psychiatric medication. Among the exclusion criteria were pregnancy (as confirmed by pregnancy test), breastfeeding, intake of oral contraceptives (however, 12 women taking oral contraceptives were included; see results section) or drugs affecting the immunological system, known allergies to the preservatives in the nasal sprays, excessive smoking and caffeine drinking as well as claustrophobia and fear of dark places. Written consent was obtained from all participants prior to data collection, and the study was approved by the Stockholm Area Regional Ethical Review Board. The study was also approved by the Swedish Medical Products Agency (Läkemedelsverket; EudraCT: 2016-004826-40).

The sample included 57 men (age range = 22–34, $M = 27.11$, $s.d. = 3.24$ years) and 59 women (age range = 22–32, $M = 26.51$, $s.d. = 2.94$ years). Regarding religious affiliation, participants reported being Lutheran (18.97%), other Christian (5.17%; different denominations i.e. Catholic or Orthodox), Muslim (7.76%) and other (3.45%); 63% reported no religious affiliation. However, in Sweden, religious affiliation is not a good indicator of religiousness or active religious participation. Indeed, a majority of the general Swedish population are members of the Swedish (formerly state) church, and yet Sweden is among the most secular countries (e.g. Thurfjell, 2015).

Participants were instructed to stay well-hydrated before their visit but to abstain from smoking, caffeine, alcohol, and use of recreational drugs on the day of testing, and from food, exercise or engagement in sexual activity 2 h before drug

administration. Since estrogen is highly involved in the follicular phase of the menstrual cycle, and there is evidence that OT is moderated by estrogen (see Bos et al., 2012), female participants were instructed that their participation should happen either on the late ovulation phase or during the subsequent luteal phase of the menstrual cycle (i.e. 15–26 days from the first day of bleeding). In this double-blind, PL-controlled study design, participants self-administered via a nasal spray 24 international units (IUs) (three puffs per nostril) of either OT (Syntocinon, CD Pharma, Sweden) or PL (saline), ~30–40 min before entering the sensory deprivation room. Random assignment placed approximately half the participants into the OT ($n = 59$, 29 women) or the PL ($n = 57$, 30 women) groups. Before administering the nasal spray, participants were asked to smell a scented pen emitting a strong synthetic odor that resembled fish. The pen was used to numb the participants' sense of taste and smell in order to minimize the chance of guessing the treatment condition that they would receive. After smelling the pen, participants self-administered the nasal spray under the experimenter's supervision and following the recommendations for standardized single dose administration of intranasal OT proposed by Guastella et al. (2013).

Immediately after the spray administration, participants completed questionnaires on a computer to measure demographic items and variables of interest such as absorption (Tellegen and Atkinson, 1974), religiosity (Granqvist, 1998) as well as current affect (Positive and Negative Affect Scale, PANAS; Watson et al., 1988) and sleepiness in the present moment (Karolinska Sleepiness Scale; Åkerstedt and Gillberg, 1990; mood and sleepiness were answered before and after the sensory deprivation session). Besides assessment *per se*, some of these questionnaires (especially absorption and religiosity) were used to prime participants for spiritual states (cf. Granqvist et al., 2005; Granqvist and Larsson, 2006).

Approximately 30–40 min after spray administration, participants were blindfolded and then led into the sensory deprivation room (a special laboratory that is completely dark and sound proof) where they would spend 30 min sitting in a comfortable chair. Although there was no specific task in the sensory deprivation room, the participants were aware that they would report their experiences in the room once the time period had expired. Participants were explicitly instructed not to fall asleep and not to do anything in particular while being in the sensory deprivation room. Following the sensory deprivation session, participants completed additional pen and paper questionnaires assessing spirituality and mystical experiences.

Measures

Absorption. We assessed absorption with the Tellegen Absorption Scale (TAOS; Tellegen and Atkinson, 1974) that is a 34-item measure originally constructed to predict susceptibility to hypnotic induction. Absorption is defined as the tendency to have one's attentional system fully absorbed, reflecting an altered state of consciousness. Participants responded using a 6-point Likert scale (1 = 'strongly disagree' to 6 = 'strongly agree'). Sample items include 'Sometimes I feel as if my mind could envelop the whole world' and 'Sometimes I "step outside" my usual self and experience an entirely different state of mind'. The reliability and validity of the TAOS are well established (see Granqvist et al., 2005), and the internal consistency was found to be high also in the present study ($\alpha = 0.93$).

Religiosity. Six items related to involvement in traditional organized religion (Granqvist, 1998) were used as a measure of religiosity. Sample items include 'I pray to God on a regular basis' and participants responded using a Likert-type scale (1 = 'strongly disagree' to 6 = 'strongly agree'). Reliability for these items was high ($\alpha = 0.94$). This scale was included to enable statistical control of participants' base levels of religiosity. This was similar to Van Cappellen et al. (2016) who used religious affiliation as a covariate. Notably, although religious affiliation might function as a religiosity proxy in an American context, it is (as already noted) not a feasible proxy in the Swedish context.

Spirituality. Spirituality was measured by the STS (Piedmont, 1999). Spirituality refers to the personal proclivity to turn toward a larger perspective of reality than one's personal life. This encompasses the tendency to see a connection between oneself, other people and nature, transcending life and death (Piedmont, 1999). The STS consists of 24 items and the response alternatives were coded on a Likert-type scale from 1 = 'strongly disagree' to 5 = 'strongly agree'. Sample items include 'All life is interconnected' and 'It is important to me to give back to my community'. The STS comprises three subscales: connectedness, universality and prayer fulfillment. Van Cappellen et al. (2016) did not include the subscale prayer fulfillment because it is highly related to religious behaviors and attitudes. To be consistent with Van Cappellen et al. (2016), we also excluded this dimension from the study, and the internal consistency of the remaining scales was high ($\alpha = .90$).

Mystical experiences. We assessed mystical experiences through a widely used measure of mystical experiences, the Mystical experience scale (M-scale; Hood, 1975). The M-scale consists of 30 items scored on a 6-point Likert scale (1 = 'strongly disagree' to 6 = 'strongly agree'). Sample items include 'I had an experience of being absorbed into something larger than myself' and 'I had an experience in which everything seemed to disappear from my mind until I was conscious only of a void'. The original scale assesses mysticism during a lifetime, but, for this study, we adapted the scale to measure mystical experiences as they may have occurred in the sensory deprivation session (see Granqvist et al., 2005, for more details). Reliability for this scale was also high ($\alpha = 0.92$).

Sensed presence. An item from the Exit scale (Persinger et al., 2000), together with two items that we created, were used as a measure of sensed presence. These three items all focus on a sensation of felt presence of a sentient being. The items were 'I felt the presence of someone or something', 'I felt the presence of another being' and 'I experienced that someone else was there'. The three items were scored in a Likert-type scale (0 = 'never' to 2 = 'frequently'). The internal consistency for the sensed presence dimension was high ($\alpha = 0.83$).

DNA extraction and genotyping

DNA was extracted from saliva samples using OraGene DNA self-collection kit (DNA Genotek, Inc., Ottawa, ON, Canada). In total, three single-nucleotide polymorphisms (SNPs) in two different genes (OXTR rs53576 and CD38 rs6449182 and rs3796863) were genotyped with KASPar[®], a competitive allele-specific polymerase chain reaction SNP genotyping system using

FRET quencher cassette oligos (<http://www.lgcgenomics.com>). The genotyping success rate was > 95%. The SNPs were chosen based on the study by Van Cappellen et al. (2016). All SNPs had a minor allele frequency (MAF) of > 5%. In line with Van Cappellen et al. (2016), both CD38 gene rs3796863 and OXTR rs53576 were coded in a dominant way, for example, the rs3796863 included AA/AC = 0, CC = 1 and the rs53576 was coded as GG = 0, GA/AA = 1. However, we could not code the other polymorphism of the CD38 gene, the rs6449182, in a co-dominant way [as done by Van Cappellen et al., (2016)]. Here, the GG allele included a single participant in the OT and a single participant in the PL condition. Consequently, the CD38 gene rs6449182 was coded as follows: CC = 0 and CG/GG = 1 (but see Supplementary Material for co-dominant analyses). The distribution of the genotypes according to the treatment condition is shown in the Supplementary Material, Table S1.

Data analyses

Analyses were performed with SPSS v. 25 (IBM, Chicago, IL.), and although an alpha level of 0.05 was used for all analyses, we report exact *P*-values. The study comprised two treatment conditions (OT, PL) that were dummy coded as follows: PL = 0, OT = 1. Consistent with Van Cappellen et al. (2016), analyses of variance (ANOVAs) were conducted to test the main effects of treatment condition on the spirituality-related outcomes (i.e. trait spirituality, mystical experiences and sensed presence). Additionally, we performed covariate analyses (ANCOVA) in which we controlled for religiosity and sex as possible confounding variables.

We also performed the Bayesian independent samples *t*-tests (see Wagenmakers et al., 2017, for details) to verify the results of the ANOVAs using the free online statistical program JASP (v. 0.9; JASP Team, 2018). Advantages of Bayesian data analysis are, among others, that it provides the opportunity to quantify evidence in favor of the null hypothesis (H_0) as compared to the alternative hypothesis of an effect being present (H_1) and that prior beliefs about an effect are taken into account (Wagenmakers et al., 2017). For this analysis, we chose a prior that attributes the same probability to H_0 and H_1 being true by assuming a Cauchy prior distribution using the default settings in JASP that center the distribution on zero and manually entered a scale parameter of 0.5 in accordance with Quintana and Williams' (2018) Bayesian reanalysis of Van Cappellen et al.'s data. The results of Bayesian independent samples *t*-test are reported as Bayes factor and 95% credible interval (CI), which describe how strongly the observed data supports one hypothesis over the other, and the 95% confidence that the true value lies within a certain range, respectively. For an interpretation of the Bayes factors, we consulted the classification by Lee and Wagenmakers (2014), which is incorporated into JASP.

In the next step, two-way (factorial) ANOVAs were adopted to examine the effects of treatment condition, genotype and their interactions on the outcomes. Also here, we verified our results by applying Bayesian statistics. We performed separate Bayesian two-way ANOVAs for treatment, genotype and their interaction (for each of the genotypes) on each of the outcome measures (see Supplementary Material for details). Finally, hierarchical and logistic regression analyses were performed to test for interactions between treatment condition and sex, religiosity and absorption on the outcome variables, with explained variance (R^2) as the effect size estimate. We employed regression analyses here to retain all variance on the continuous absorption predictor.

Table 1. Means (M), standard deviations (s.d.), 95% CI of mean differences, effect sizes and P on the dependent variables by treatment condition

Variables	Treatment		Mean difference, 95% CI	F	P	d	η_p^2
	PL, M (s.d.)	OT, M (s.d.)					
Spirituality	2.93 (0.77)	2.99 (0.89)	[−0.37, 0.24]	0.19	0.67	0.08	0.002
Interconnectedness	3.19 (0.73)	3.32 (0.71)	[−0.40, 0.13]	1.05	0.31	0.19	0.01
Meaning/purpose	2.75 (0.94)	2.77 (1.15)	[−0.41, 0.37]	0.01	0.93	0.02	0.00
Mystical experiences	2.22 (0.79)	2.07 (0.63)	[−0.11, 0.42]	1.35	0.25	−0.22	0.01
Sensed presence	0.29 (0.42)	0.32 (0.44)	[−0.18, 0.13]	0.09	0.77	0.06	0.001

Note. One male participant had incomplete data on mystical experiences and was removed from the analyses on this particular scale ($n = 115$) but was included on the remaining scales ($N = 116$).

Results

Preliminary analyses

We initially conducted analyses to examine if participants in the treatment conditions differed on absorption and on our control measures: positive and negative affect, sleepiness (both measures were completed before and after being in the sensory deprivation room) and on a single-item asking if participants had actually slept in the sensory deprivation room. Table S2 shows that the OT and the PL groups were well balanced with regard to absorption, positive and negative affect, sleepiness or sleeping in the sensory deprivation room. Also, the two treatment groups were well balanced with respect to numbers of young women on oral contraceptives (OT: 20%, PL: 21%) compared to those not on oral contraceptives (OT: 80%, PL: 79%). We therefore decided to include women using oral contraceptives in the analyses.

Participants were instructed to indicate at the end of the experimental session whether they believed they received OT, PL or if they were not at all aware. We found no support for an association between treatment and guessed treatment. Of the 80 individuals who guessed OT or PL, 39 participants guessed correctly (compared to the 40 participants expected by chance).

Intranasal OT main effects on spirituality-related outcomes

Table 1 shows means, s.d. and 95% confidence intervals for the difference between treatment conditions on the relevant outcome measures, as well as effect sizes and P-values. Correlations among the dependent variables are detailed in the Supplementary Material, Table S3. Main effects of treatment were not significant on any of the dependent variables (spirituality, mysticism or sensed presence), and the effect sizes were in all cases negligible ($d < 0.22$).

To better understand these non-significant results, we performed Bayesian independent samples t-tests for the treatment condition on all three dependent variables. In the following, the Bayes factor in favor of the H_0 is reported (BF_{01}). In all three cases, there was more evidence in favor of H_0 as compared to H_1 , which supports our frequentist results. For spirituality, we found a Bayes factor of $BF_{01} = 3.48$, meaning that there is 3.48 times more evidence for the null-model relative to H_1 , which can be cautiously interpreted as moderate in size. The median for the posterior distribution was -0.06 and the 95% CI spans from -0.40 to 0.27 . For mystical experiences, we found a Bayes factor of $BF_{01} = 2.14$ ($Mdn = 0.18$; 95% CI, -0.15 to 0.53). Bayes factors below three are generally regarded as anecdotal evidence (Lee and Wagenmakers, 2014). For sensed presence, we found a moderate Bayes factor of $BF_{01} = 3.60$ ($Mdn = -0.05$; 95% CI, -0.40 to 0.28). Graphical illustrations of the Bayes factors

and prior and posterior distributions as well as the Bayes factor robustness checks are provided as Supplementary Material (Figures S1 and S2).

Additionally, to be consistent with Van Cappellen et al. (2016), we computed two scores for spirituality, grouping items according to the interconnectedness and meaning and purpose. There was no main effect of treatment on interconnectedness items nor on meaning and purpose items (Table 1). The results on spirituality were similar also after controlling for religiosity and sex, $F(1, 112) = 0.22$, $P = 0.64$ (Table S4, Supplementary Material). Similarly, this pattern of non-significant results extended to mystical experiences, $F(1, 111) = 1.19$, $P = 0.28$, and sensed presence, $F(1, 112) = 0.08$, $P = 0.78$, after controlling for both religiosity and sex (Table S4). Thus, neither religiosity nor sex accounts for our non-significant results of the treatment on spirituality, mysticism and sensed presence. For the interested reader, we report analyses including only men in the Supplementary Material. The non-significant result patterns held also for men only ($n = 57$).

Intranasal OT and genotype effects on spirituality-related outcomes

Separate two-way ANOVAs were conducted to test the effects of OT, genotype and their interactions on the dependent variables. Briefly, results revealed no significant effects on any of the dependent variables, see Table S5. More specifically, regarding the CD38 rs3796863 polymorphism, there were no main or interaction effects on spirituality ($P_s > 0.46$), mysticism ($P_s > 0.22$), or sensed presence ($P_s > 0.40$). Similarly, for the CD38 rs6449182 polymorphism, we observed no main or interaction effects on spirituality ($P_s > 0.62$), mysticism ($P_s > 0.09$), or sensed presence ($P_s > 0.12$). Finally, there were no main or interaction effects of the OXTR rs53576 polymorphism on spirituality ($P_s > 0.35$), mysticism ($P_s > 0.15$) or sensed presence ($P_s > 0.69$). The results did not change after controlling for religiosity and sex (all $P_s \geq 0.10$).

The results from the Bayesian two-way ANOVAs further support these findings; there was more evidence for the null model than for any alternative model (see Supplementary Material, Tables S6, S7 and S8). Thus, positive effects of treatment, genotype or treatment \times genotype interactions seem unlikely given the data.

Intranasal OT and absorption effects on spirituality-related outcomes

To examine whether absorption disposition interacts with intranasal OT on the spirituality-related outcomes, we performed hierarchical regression analyses on each outcome variable, entering the main effects of dummy-coded treatment,

Table 2. Hierarchical multiple regressions analyses for variables predicting spirituality, mystical experiences and sensed presence

Variables	Model 1			Model 2		
	B	SE B	β	B	SE B	β
Spirituality						
Treatment	0.04	0.16	0.02	0.05	0.15	0.03
Sex	-0.17	0.16	-0.11	-0.18	0.15	-0.11
Absorption	0.14	0.10	0.14	0.35	0.13	0.34**
Treatment \times absorption				-0.48	0.19	-0.31**
R ²			0.04			0.09
R ² change			0.04			0.05
F for change in R ²			1.43			6.44**
Mystical experiences						
Treatment	-0.17	0.13	-0.12	-0.16	0.13	-0.11
Sex	-0.25	0.13	-0.17	-0.26	0.13	-0.18*
Absorption	0.09	0.08	0.10	0.28	0.11	0.32**
Treatment \times absorption				-0.44	0.16	-0.33**
R ²			0.06			0.12
R ² change			0.06			0.06
F for change in R ²			2.34			7.38**
Sensed presence						
Treatment	0.01	0.08	0.01	0.01	0.08	0.01
Sex	-0.01	0.08	-0.01	-0.01	0.08	-0.01
Absorption	0.08	0.05	0.15	0.16	0.07	0.30*
Treatment \times absorption				-0.18	0.10	-0.23
R ²			0.02	0.05		
R ² change			0.02			0.03
F for change in R ²			0.87			3.43

Note. Absorption was centered at its mean. Bold type indicates values that were significant predictors, * $P < 0.05$. ** $P < 0.01$.

absorption (centered) and dummy-coded sex in the first model, and then in addition the treatment \times absorption interaction in the second model (Table 2).

The variables in the first model (main effects of treatment, absorption and sex) did not significantly predict spirituality, $F(3, 112) = 1.43, P = 0.24$. However, the second model, containing the treatment by absorption interaction, did significantly predict spirituality, $F(4, 111) = 2.74, P = 0.03$, and this second model explained an additional 5% of the variance in spirituality. As shown in Figure 1A, OT, relative to PL, was associated with higher spirituality scores among low-absorption scorers but lower spirituality scores among high-absorption scorers. Differential OT effects across levels of absorption thus cancelled out any main effect of OT.

Similarly, regarding mystical experiences, the first model in the regression was not significant, $F(3, 111) = 2.34, P = 0.08$, but the second model was significant, $F(4, 110) = 3.70, P = 0.007$. The treatment by absorption interaction entered in model 2 explained an additional 6% of the variance (Table 2). As shown in Figure 1B, OT again had differential effects on the outcome depending on levels of absorption. For mystical experiences, however, such experiences were rated lower in the OT (relative to PL) condition among high-absorption scorers, but mystical experience ratings were virtually identical across conditions among low-absorption scorers.

Although sensed presence was positively skewed, we decided to perform a hierarchical regression with the continuous sensed presence scores as the outcome in order to maintain symmetry in the analytic approach across analyses (but see Supplementary Material, Table S9, for results from a complementary logistic regression on a dichotomous sensed presence variable). Regarding the hierarchical regression on continuously scored sensed presence, none of the models were significant, model 1,

$F(3, 112) = 0.87, P = 0.46$, and model 2, $F(4, 111) = 1.53, P = 0.20$ (notably, though, model 2 of the logistic regression was significant, $\chi^2(1) = 4.20, P = 0.04$. Nagelkerke's $R^2 = 6.1\%$). However, absorption was significantly related to sensed presence in model 2 (see Table 2). Although the treatment \times absorption interaction was not significant in the first (unlike the second) regression, for consistency of presentation, we show the interaction pattern in Figure 1C. Like for spirituality, OT relative to PL was associated with more sensed presence experiences among low-absorption scorers but less sensed presence experiences among high-absorption scorers.

Finally, we made the corresponding analyses for treatment by sex and treatment by religiosity interactions. These analyses did not suggest any moderating effects of these variables, see the Supplementary Material, Table S10.

All data and analyses in SPSS and JASP can be found at OSF (<https://osf.io/52v8e/>).

Discussion

In this randomized, double-blind, PL-controlled experiment, we sought to conceptually replicate and extend the findings of Van Cappellen et al. (2016) indicating that intranasal OT causes increased spirituality among American males, as moderated by OT-related genotypes. We did so using a better powered study (given the effect sizes of Van Cappellen et al., 2016) and a priming plus sensory deprivation procedure that has previously been found capable of evoking spiritual experiences (Granqvist et al., 2005; van Elk, 2014). Moreover, we used a sample containing both sexes and drawn from a relatively secular cultural context (Sweden). In addition to trait spirituality, we studied whether the presumed experimental effects would extend to *in vivo* mystical experiences and the sensed presence of a

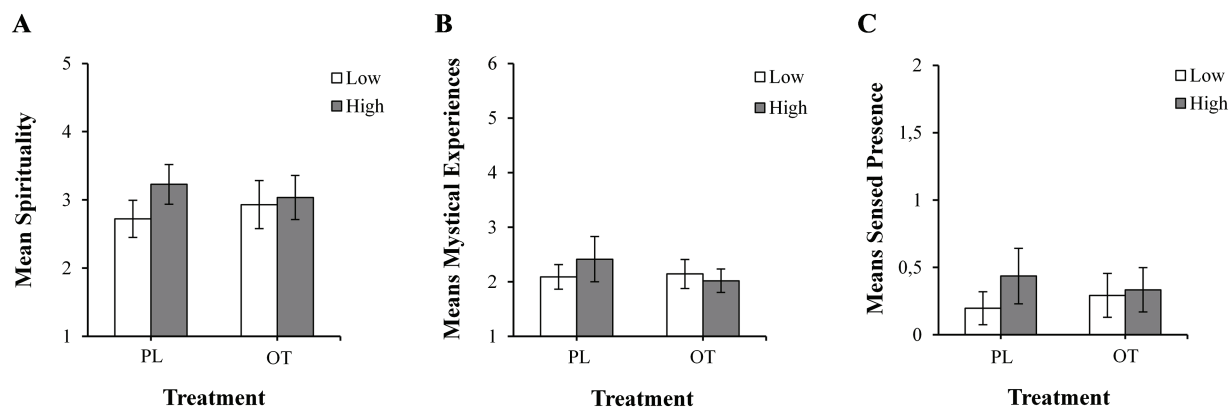


Fig. 1. Mean ratings for (A) spirituality, (B) mystical experiences and (C) sensed presence as a function of treatment and absorption groups. Error bars denote 95% CI. Note. The median was used to split into low- and high-absorption scorers.

sentient being. Finally, we asked whether a personality disposition (absorption) indicative of suggestibility would interact with the treatment (OT vs PL) on these spiritual outcomes.

Despite including a larger sample size, we failed to replicate both the main effects of treatment (OT vs PL) and the treatment by genotype interaction effects on trait spirituality that were reported by Van Cappellen *et al.* (2016). Similarly, there were no main effects of treatment or treatment by genotype interaction effects on *in vivo* mystical experiences or the sensed presence of a sentient being. Importantly, these results were not explained by the fact that both men and women were included in the present study, whereas only men were included in Van Cappellen *et al.* (2016). Additional Bayesian analyses of our data suggest that it is considerably more plausible that treatment and treatment by genotype interactions do not have an effect on spirituality-related outcomes than that they have such an effect (even though it has to be noted that the evidence in the case of *in vivo* mystical experiences is more of a trend). Thus, the present study is not merely a failed replication but provides evidence for the absence of treatment main effects and treatment by genotype interaction effects, relative to the alternative hypothesis.

Nevertheless, the study's sample size displays a limitation to the interpretability of our results, as the detection of small effects (especially when including several predictors) requires larger samples and the data could simply be insensitive to small effect sizes. Thus, the main results as well as the exploratory analyses have to be interpreted with a caution, even though our sample was larger than in Van Cappellen *et al.*'s (2016) study and larger than the average OT studies. However, we still believe that the results hold as they are consistent throughout three different spirituality-related outcomes and could consistently be confirmed by applying Bayesian methods illustrating more evidence in favor of the null hypothesis than for main and interaction effects of OT and the OT-related genotypes. Also, it should be noted that Van Cappellen *et al.* (2016) did not find a significant treatment effect in their study without controlling for religious affiliation, which makes the present study, one could argue contrarily, a successful replication of the previous result, with a larger sample. We note that the sample size was not optimal for genetic analyses and we are therefore cautious with these interpretations; however, we would have considered it more negligent not to include OT by genotype interactions into our study given the research on genetic influences on OT signaling.

On a more positive note, however, in our exploratory analyses, we found that the personality disposition absorption

and treatment displayed an interesting interaction pattern. Specifically, the observed pattern suggested that OT facilitated spirituality and the sensed presence of a sentient being among low-absorption scorers but had equally notable dampening effects on the spirituality-related outcomes among high-absorption scorers.

Though we observed neither main effects of OT nor any treatment by genotype interactions, this should not be confused with overall non-significant effects for OT (see also Quintana, 2018), as our treatment by absorption interactions suggest otherwise. Note that an average effect close to zero is consistent with at least two causal interpretations: the true *average causal effect* is close to zero because all *single-unit causal effects* are zero or negligible-to-small in effect size, or the true average causal effect is close to zero because non-negligible single unit causal effects cancel each other out. Although the exact treatment by absorption interaction patterns that we observed were not hypothesized in the pre-registration process—because previous research and theorizing suggested the possibility of competing interaction patterns (e.g. Bryant *et al.*, 2012; Granqvist *et al.*, 2005; van Elk, 2014)—we considered exploratory questions pertaining to the role of absorption.

As suggested by the graphical illustration of the interactions (Figure 1), OT, relative to PL, facilitated spiritual outcomes (at least trait spirituality and sensed presence) among participants low in absorption, perhaps because of a suggestibility-enhancing effect of OT for such participants. In other words, OT may promote spirituality among people who are not 'naturally' spiritually inclined so that even they may, at least temporarily, gain a sense of self-transcendence and connection to a sensed presence. This interpretation is in line with and further extends findings reported by Bryant *et al.* (2012) that indicate that OT facilitates hypnotic susceptibility in individuals previously low in hypnotic susceptibility. Importantly, these findings are also in line with results presented in the Supplementary Material of Van Cappellen *et al.*'s (2016) study, indicating that the strongest effects of OT on spirituality were observed among participants with no religious affiliation.

Of equal interest, and much more surprising, however, was that the interaction in our study is consistent with a dampening effect of OT (again relative to PL) on spirituality among participants high in absorption (Figure 1). High-absorption individuals who are habitually prone to enter altered states of mind appear, perhaps seemingly paradoxically, to become less inclined to do so from intranasal OT. We suggest as one possible explanation that OT may have a stabilizing effect on the minds of

high-absorption scorers, akin to the calming effects of low doses of the central stimulant medication observed especially on hyperactive individuals (Arnsten, 2006). Alternatively, while high-absorption scorers do not need OT because they are already prone to spirituality and sensed presence experiences, low-absorption scorers seemingly depend upon this additional factor (OT) to enable such experiences. Needless to say, these conjectures should be tested in future research, and our observed interaction pattern as a whole should of course be subjected to replication attempts.

Given the surprising pattern involving lower spiritual experiences among high-absorption scorers in the OT than the PL group, which was not anticipated in our pre-registered hypothesis, it is of course plausible that our interaction patterns were just chance findings. However, consistent with the notion that OT may enhance spirituality primarily among individuals who, in general, are less prone to having spiritual experiences (Van Cappellen et al., 2016, see Supplementary Material) we did not dismiss them as such at this stage. Furthermore, research on OT effects in behavioral sciences suggests that interindividual trait differences as well as contextual factors play an underestimated role in explaining OT effects (for reviews, see e.g. Bartz et al., 2011; Olff et al., 2013). Seen in this light, absorption is a plausible moderator for OT effects on spirituality-related outcomes, even if the specific mechanisms need to be scrutinized in further research.

It is not clear why we failed to replicate the findings reported by Van Cappellen et al. (2016). Although by no means unusual with failed replications in experimental psychology (Open Science Collaboration, 2015), let alone of experimental OT effects (e.g. Walum et al., 2016), the Van Cappellen et al. (2016) study had a comparatively strong study design, with a reasonable sample size, double-blind experimental protocol, relevant genotype moderators and evidence of mediation. Three possible reasons for our failed replication are especially noteworthy and should be considered in future replication and extension studies. First, although Van Cappellen et al. (2016) had a good justification for controlling religious affiliation (i.e. a potential confounder for spirituality), it is again worth noting that their significant effects of OT on spirituality were obtained only by following statistical control of participant religious affiliation. In other words, their crude unadjusted effects of OT on spirituality were not statistically significant although the point estimate was still positive (see also Quintana and Williams, 2018). This alone might indicate that there is no robust, 'true' main effect of intranasal OT on spirituality and that the significant effect observed following control of religious affiliation was a mere chance finding; indeed, we failed to conceptually replicate it.

Second, it is worth noting that our study was conducted in a relatively secular country, where neither religiosity nor spirituality is culturally normative (Gruneau-Brulin et al., *in press*; Norris and Inglehart, 2011). This is unlike the Van Cappellen et al. (2016) study, which was conducted in the USA, where religiosity and spirituality are more culturally normative than in Sweden, although we note that this may vary in different communities and across regions. Consequently perhaps, the mean scores on the trait spirituality outcome in Van Cappellen et al. (2016; 4.71 in the PL condition) were much higher than in the present study (2.93 in the PL condition), amounting to a huge effect size difference ($d = 2.31$). It is not inconceivable that OT-facilitated experiences of self-transcendence and a sense of connection may lend themselves to religious/spiritual terminology and interpretations among most Americans, whereas this may not be the case among most Swedes

(cf. Granqvist and Moström, 2014; Gruneau-Brulin et al., *in press*). In other words, OT could have well facilitated a sense of connection in our study, just as in Van Cappellen et al. (2016), but the spirituality-related outcome measures of the present study may have been unable to do that effect justice because of cultural matters relating to secularism. However, without denying this possibility, it cannot account for the treatment by absorption interactions observed on our spirituality-related outcomes. Nonetheless, future replication attempts should be undertaken across both relatively religious/spiritual and secular cultural contexts to help clarify these matters. Notably, contextual differences associated with culture may be key behind failed replications of research on culturally entrenched matters such as spirituality and religion (e.g. Gruneau-Brulin et al., *in press*).

Third, one could object that our priming plus sensory deprivation procedure could have played a role in our failed replication. On the one hand, priming plus sensory deprivation could have somehow interfered with the spirituality-promoting effects of OT. However, we deem this to be unlikely, as priming with religious topics followed by a sensory deprivation situation should most likely enable or even boost an effect of OT on spirituality instead of diminishing it. As noted, there is strong evidence for the effectiveness of priming plus sensory deprivation procedures in eliciting spiritual experiences (see Hood and Morris, 1981; Granqvist et al., 2005; Andersen et al., 2014; van Elk, 2014). This is presumably because priming serves to plant ideas in the mind which sensory deprivation then—by turning attention inwards to internal states while preventing disconfirmatory sensory evidence (Deikman, 1966)—may bring to fruition. Also, despite the possibility of context-dependent effects of OT (see e.g. Bartz et al., 2011), it seems highly implausible that positive OT effects on spirituality would only come into play in the absence of religious priming and sensory deprivation. On the other hand, it is still possible that the procedure was insufficient to produce mystical experiences and sensed presence *in vivo*. Future research could profitably add and evaluate more powerful induction components, such as explicit instructions of what to expect in order to enhance expectations (e.g. Andersen et al., 2014), suggestive technological tools (e.g. Granqvist et al., 2005; Andersen et al., 2014; van Elk, 2014), additional religious/spiritual primes (e.g. baroque organs, the smell of incense) and manipulation of motivational parameters (e.g. activation of the attachment system; Birgegard and Granqvist, 2004). Again, however, insufficient suggestive power cannot be the sole explanation for our failed replication, given the largely consistent treatment by absorption interaction effects observed and the credible track record of facilitating mystical and sensed presence experiences via priming plus sensory deprivation (e.g. Granqvist et al., 2005; Hood and Morris, 1981).

In closing, we have failed to conceptually replicate Van Cappellen et al.'s (2016) findings indicating that intranasal OT causes a general increase in trait spirituality, as moderated by OT-related genotypes. Our data suggests that there is likely no main-effect of OT, nor interactions with OT-relevant genotypes, on spirituality-related outcomes, even in interaction with OT-related genotypes. However, our exploratory analyses suggest that OT may have differential effects on spirituality-related outcomes depending on people's proclivities for absorption. Specifically, OT could facilitate spirituality-related outcomes among individuals who are not characteristically prone to suggestion or to enter altered states of consciousness, but to dampen spirituality among individuals who are characteristically prone to suggestion and to enter altered states of consciousness.

Supplementary data

Supplementary data are available at SCAN online.

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