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Oxytocin and vasopressin modulate risk-taking ☆

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HIGHLIGHTS

- Oxytocin (OT) and arginine vasopressin (AVP) influence risk-taking.
- OT and AVP induce risk-aversiveness, but in different outcome probabilities.
- OT's influence on risk-taking is modulated by sex and social-stress.
- Findings extend the role of OT and AVP beyond social-context to risk-taking.

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ABSTRACT

The modulation of risk-taking is critical for adaptive and optimal behavior. This study examined how oxytocin (OT) and arginine vasopressin (AVP) influence risk-taking in function of three parameters: sex, risk-valence, and social context. Twenty-nine healthy adults (14 males) completed a risk-taking task, the Stunt task, both in a social-stress (evaluation by unfamiliar peers) and non-social context, in three separate drug treatment sessions. During each session, one of three drugs, OT, AVP, or placebo (PLC), was administered intra-nasally. OT and AVP relative to PLC reduced betting-rate (risk-averse effect). This risk-averse effect was further qualified: AVP reduced risk-taking in the positive risk-valence (high win-probability), and regardless of social context or sex. In contrast, OT reduced risk-taking in the negative risk-valence (low win-probability), and only in the social-stress context and men. The reduction in risk-taking might serve a role in defensive behavior. These findings extend the role of these neuromodulators to behaviors beyond the social realm. How the behavioral modulation of risk-taking maps onto the function of the neural targets of OT and AVP may be the next step in this line of research.

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1. Introduction

Risk-taking is a critical aspect of motivated behavior. It can be modulated by many factors, including the nature of the risk (e.g., risk-valence: positive vs. negative probabilistic outcome), social context (e.g., presence or absence of peer groups), and individual differences (e.g., trait anxiety, sex). In addition to these factors, we propose that neuromodulators, such as the neuropeptides oxytocin (OT) and arginine vasopressin (AVP), can significantly influence risk-taking proclivity. This hypothesis stems from the fact that OT and AVP potently affect fundamental behaviors, specifically in the social realm. Social stimuli are probably the most powerful reinforcers of behavior, and thus a potential role of these neuromodulators on motivated behaviors, particularly risk-taking behaviors, is conceivable and deserves to be considered. Here, we foray a new untouched area of research.

Thus, OT and AVP may affect risk-taking indirectly through their documented influence on social and affective processes [5,19], or perhaps directly. Studies have examined risk-taking in social exchange tasks that manipulate trust and cooperation (e.g., [7]). However, no studies have yet examined the potential impact of these neuropeptides on risk-taking behavior outside social economic exchange tasks. The present study aimed to directly investigate the impact of OT and AVP on risk-taking behavior. To this aim, we assessed the influence of intra-nasal administration of OT, AVP, and placebo (PLC) on the performance of a risk-taking task.

The monetary risk-taking task used in the current study is a novel task that was developed to provide a unique parametrization of risk level over a wide range of nine levels. It also presents favorable (greater likelihood of winning than losing) and unfavorable (greater likelihood of losing than winning) contexts, in which individuals select a safe (pass) or risky (bet) option. Recent work suggests that the behavioral

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influence of OT, and perhaps AVP as well, varies as a function of environmental factors. This has been documented in the context of a social vs. non-social environment (e.g., [7]), or in response to positive vs. negative social stimuli (e.g., [9]). In general, findings support stronger effects in a social vs. non-social situation, and towards positive vs. neutral/negative social stimuli. Here, we examine the effects of OT and AVP vs. PLC on risk-taking as a function of the risk-valence (positive vs. negative) and social context.

We address the social context by implementing the task in a social and a non-social situation. We selected a stress-related social situation (social stress by virtue of being judged by unfamiliar peers), because the administration of OT has been found to modulate neuroendocrine responses to external stressors [16]. Social stress, typically associated with anxiety, is expected to reduce risk-taking and promote risk-aversion as a protective response [14,21]. We expect OT to mitigate this effect. This prediction is based on work showing that OT can alleviate anxiety ([27,33]; see review, [22]), and, perhaps in turn, stimulates trust, cooperation and other affiliative behaviors [5,7,8]. As a result, OT would diminish the impact of social stress on risk-taking, and produce a relative decrease in risk-aversion. In contrast, AVP is thought to exacerbate anxiety [2,31], associated with defensive responses. Accordingly, AVP would be expected to enhance the impact of social-stress on risk-taking, and amplify risk-aversion.

Finally, we expect sex to be a powerful modulator of these effects, given the presence of sex differences in social responses and risk-taking. Very broadly, males tend to be more competitive and aggressive, as well as more risk-takers than females [4,6], suggesting that males may be more sensitive to the modulation of risk-taking by OT and AVP.

Based on this brief background, we hypothesize that, in general, OT will enhance risk-taking through favoring approach behavior, whereas AVP might reduce risk-taking through promoting defensive responses. We expect these effects to be modulated by risk-valence (positive vs. negative probability of winning) and social context (social-stress vs. non-social). Regarding risk-valence, the nature of its impact is difficult to predict without previous related work. Regarding social context, we could expect stronger effects in the social-stress vs. non-social context for both OT and AVP. Lastly, because of sex-differences in risk-taking and social behavior, the modulation of risk-taking is expected to be stronger in men than women.

2. Methods

2.1. Subjects

Thirty-two healthy adults were tested. Three subjects (2 men and 1 woman) were excluded because of unreliable performance (see below). The final sample included 14 men (age 21 to 35 years; mean = 26.67, SD = 4.68) and 15 women (age 20 to 38 years; mean = 27.43, SD = 4.59). Subjects were recruited through the intramural National Institutes of Health (NIH) volunteer system and general advertisements.

Participants were free of medical (determined by a clinical interview and physical exam) or psychiatric disorders (determined by the Structured Clinical Interview for DSM-IV; [11]) and were not taking any psychotropic medications, contraceptive hormones, or recreational drugs.

The protocol was approved by the National Institute of Mental Health Institutional Review Board. Written informed consent was obtained after the study was explained and all questions were answered. Participants were financially compensated.

2.2. Procedure

2.2.1. Study design

This study tested the effects of OT, AVP and PLC on risk-taking and its modulation by social context. A within-subjects, double-blind, placebo-controlled, randomized crossover design was adopted, in which a different drug treatment was administered on three separate days, at an average of five-week intervals. Women were tested during the same menstrual cycle phase (either in the follicular phase or during the luteal phase) across the three sessions to avoid intra-individual variability unrelated to the study manipulations.

Each session followed the same procedures. Subjects arrived in the morning. A state anxiety measure (State-Trait Anxiety Inventory, STAI; [30]) was collected twice, before and 50 min after drug administration. The task was initiated about 100 min after drug administration. For all sessions, during the drug treatment-to-task time interval, participants completed another independent study [15]. This independent study assessed the neuropeptides' effects on anxiety. It involved a measure of physiological anxiety via eye-blink startle responses during conditions of threat (potential for mild electrical shocks) or safety (absence of electrical shocks). To minimize carry-over effects, a 20 minute break was implemented and our experiment was conducted in a different part of the clinic by a different research assistant.

We used a novel risk-taking task to manipulate the risk-level and risk-valence of the trials, a feature that has not been systematically included in existing risk-taking tasks (see review, [26]). It was designed to probe risk-taking decisions over a wide range of risk levels, nine different probabilities of negative/positive outcome. In addition, this novel task readily evoked the notion of risk by featuring a stunt-like behavior (motorcyclist jumping over buses). This design was thought to promote more "gut-feeling" rather than explicit calculation of risks (e.g., monetary type decision-making) and to tap more strongly emotional/motivational processing than cognitive evaluative functions. The Stunt task was administered twice at a 15-minute interval. During this time interval, participants were distracted from the study by performing an independent, irrelevant, simple attention task (passive eye movement attention task). The two Stunt task administrations were conducted in a social-stress and a non-social context, and the order of these contexts was counter-balanced across subjects. At the end of each session, a questionnaire was administered to obtain information on participants' subjective experience regarding the risk-taking task and the social-stress/non-social contexts.

2.2.2. Drug administration

OT, AVP, and PLC were each administered intra-nasally in four doses over 2 min. Doses totaled 24 International Units (IU) (60 units/mL at .4 mL) for OT and 40 IU (100 units/mL at .4 mL) for AVP. Prior studies using similar drug administration (dosage and route) have found drug treatment effects on social information processing, such as facial emotion recognition [9,13,35]. Additionally, intra-nasal administration of OT in rats has been found to increase OT levels in the brain [23] and intra-nasal administration of AVP in humans has been found to increase AVP levels in cerebrospinal fluid (CSF) [3]. Subjects did not report side effects from drug administration. The order of drug administration was counter-balanced.

2.2.3. Stunt task

The Stunt task (see Fig. 1) featured a motorcyclist who was challenged to jump over a variable number of buses. The number of buses ranged from 1 to 9 (i.e., 9 different risk levels), which corresponded to the probability of success. Specifically, the probability of a successful jump was 10% for the 9-bus trial, 20% for the 8-bus trial, 30% for the 7-bus trial, and so on, down to 90% for the 1-bus trial. These probabilities were not divulged to participants. Trials of each risk level were presented 10 times, and all trial types were fully randomized across the task.

Each trial started with the presentation of the motorcyclist about to jump a certain number of buses (3000 ms) (see Fig. 1). Participants were asked to bet or pass by button press, indicating whether they believed the stunt motorcyclist would succeed or not, respectively. Next, the motorcyclist was shown jumping (1000 ms), followed by the

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