

Oxytocin enhances creativity specifically in approach-motivated individuals

Chen Yang^{1,2,3}, Zhaoyang Guo^{1,2,3}, Liang Cheng^{1,2,3,*}

¹Key Laboratory of Adolescent Cyberpsychology and Behavior (CCNU), Ministry of Education, Wuhan 430079, China

²Key Laboratory of Human Development and Mental Health of Hubei Province, Wuhan 430079, China

³School of Psychology, Central China Normal University, Wuhan 430079, China

*Corresponding author. School of Psychology, Central China Normal University, 382 Xiongzhu Street, Wuhan, Hubei 430079, China. E-mail: chengl@ccnu.edu.cn

Abstract

Oxytocin (OT), a neuropeptide pivotal in social and reproductive behaviors, has recently gained attention for its potential impact on cognitive processes relevant to creativity. Yet, the direct intricate interplay between OT and creativity, particularly in the context of individual differences in motivational orientations, remains poorly understood. Here, we investigated the effects of intranasal OT on creative thinking in individuals characterized by varying levels of approach and avoidance motivations. The initial study, involving participants with high approach or avoidance motivation, employed the Alternative Uses Task to assess creativity under OT administration. Subsequently, the second study induced different motivational states through a recall task, aiming to validate and extend observed effects. Results revealed a significant enhancement of creativity in individuals with approach motivation following OT administration, while no parallel effect was discerned in those with avoidance motivation. Aligning with behavioral findings, functional connectivity and graph theory analyses of neural data illuminated the coordinated effects of OT on creativity-related neural networks. These outcomes collectively suggest that OT exerts a dissociable influence on creativity contingent upon an individual's motivational tendencies, providing insights into the intricate relationship between OT and human creative behavior.

Keywords: oxytocin; creativity; approach-avoidance motivation; prefrontal cortex; temporal lobe

Introduction

Human beings demonstrate an exceptional capacity for creative thought and innovation, a skill that empowers them to navigate dynamic circumstances and intricate social landscapes, contributing to their success amidst evolving social and technological dynamics (Newell and Simon 1972, Amabile 1996, De Dreu and Nijstad 2008). This capacity, defined by the generation of novel and potentially valuable ideas and solutions—commonly known as creativity—has been proposed as a pivotal driver of human evolution (Flinn et al. 2005), providing a distinct competitive advantage during critical periods of social progress and development (Mithen 1998).

Oxytocin (OT), a highly conserved nonapeptide, is released from the paraventricular nucleus of the hypothalamus via the posterior pituitary (Gimpl and Fahrenholz 2001). It plays a crucial role in interacting with emotion- and reward-associated brain regions, contributing to the down-regulation of stress and the up-regulation of reward processing circuitry (Skuse and Gallagher 2005, Carter et al. 2008, Donaldson and Young, 2008, Bartz et al. 2011). While extensive research across diverse species, including humans, underscores its significance as a central mediator

in pair-bond formation and pro-social approach behaviors (Insel and Fernald 2004, Donaldson and Young 2008), recent investigations have expanded our understanding of OT, implicating it in the modulation of cognitive processes relevant to creativity (De Dreu et al. 2015, Pfundmair et al. 2017).

Previous studies have explored the intricate connections between OT and traits associated with creativity, revealing positive correlations between OT-related genes and a spectrum of creativity-related traits, including imagination, cognitive flexibility, extraversion, and behavioral adaptability (Crespi and Summers 2014, De Dreu et al. 2014, Haram et al. 2014, Hovey et al. 2014, De Dreu et al. 2015). Moreover, elevated levels of plasma OT have consistently been linked to heightened scores in extraversion, openness, and novelty-seeking (Bell et al. 2006, Andari et al. 2014, De Dreu et al. 2015). These findings collectively suggest a potential positive linkage between OT and creative thinking. However, direct linkages between OT and creative cognition have not been extensively reported. De Dreu et al. (2015) and Pfundmair et al. (2017) investigated the direct relationship between intranasal OT and behavioral performance in creative thinking tasks, revealing a consistent effect that OT augmented creative

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performance relative to a placebo (PL) control condition (De Dreu et al. 2015, Pfundmair et al. 2017). Achieving a more comprehensive understanding of how OT intricately modulates and regulates the execution of creativity remains an ongoing and dynamic subject of investigation.

Notably, prior research in the field of OT emphasizes the critical consideration of individual-specific differences when examining its impact on social cognition and behavior (Bartz et al. 2011, Wong et al. 2021). For example, OT has been found to augment altruistic behavior exclusively in participants who reported low levels of parental love-withdrawal during infancy (van Ijzendoorn et al. 2011). Additionally, it has been shown that OT enhances cooperation and trust and diminishes aversion to betrayal primarily in individuals with high attachment avoidance, but not in those with high attachment anxiety (De Dreu 2012). These observations highlight the notion that the effects of OT are modulated by individual-specific factors, emphasizing an interactive relationship between OT and various person-specific traits. Consequently, it is imperative to account for the influence of individual specificity when further investigating the intricate relationship between OT and creativity.

Approach-avoidance motivation, a key factor in individual cognitive differentiation, reflects the inclination of individuals to seek rewards while avoiding punishments in the face of stimuli encompassing both positive and negative elements (Elliot and Church 1997, Elliot 2006). This motivational orientation significantly shapes diverse cognitive processes, including attention, memory, and thinking (Friedman and Förster 2002, 2005b, Gable et al. 2016). Therefore, individuals with distinct approach-avoidance tendencies are likely to demonstrate varied cognitive processing styles and strategies. Specifically, those with an approach orientation, as opposed to avoidance, tend to exhibit heightened global processing, reduced attention to detail, and enhanced cognitive flexibility—factors that can potentially facilitate creative performance (Friedman and Förster 2001, 2005a, Förster et al. 2006). Given the substantial influences of motivational orientation on individual creativity, and OT's role in modulating motivation (De Dreu and Nijstad 2008, Donaldson and Young 2008, Carter 2014, Harari-Dahan and Bernstein 2014), our hypothesis suggested that OT may yield dissociable effects on creative thinking in individuals characterized by different approach-avoidance motivations. To empirically test this hypothesis, two randomized, double-blind studies were conducted. The first study recruited participants exhibiting high levels of approach or avoidance motivation and assessed the impact of intranasal OT on creativity using the Alternative Uses Task (AUT). Subsequently, the second study induced distinct motivational states (approach or avoidance) through a recall task to validate and extend the findings from the initial experiment.

Furthermore, recent research into the neural underpinnings of creativity has revealed its close association with brain networks, including the default mode network (DMN) and the executive control network (ECN) (Beatty et al. 2014, 2016). It is increasingly evident that creative thinking results from the synergy and interaction of multiple brain regions, rather than isolated activity in a single area (Beatty et al. 2017, Zhu et al. 2017). In light of this, the present study targeted specific regions of interest (ROIs) within these neural networks: the prefrontal cortex (a key component of the ECN), temporoparietal junction, and temporal lobe (critical regions of the DMN). To gain a comprehensive understanding of the neural dynamics underpinning creativity, we deployed two complementary analytical approaches: functional connectivity

analysis and graph theory-based network topology analysis. Functional connectivity analysis was used to explore the coordinated interactions and communication patterns among the selected ROIs, while graph theory analysis quantified the topological properties of the brain network, including local interconnectivity, global and local information transmission, and information integration capacities (Menon 2013, Sporns 2013). These two methodologies were complementary in providing a multifaceted view of the neural mechanisms involved in creativity. The metrics derived from functional connectivity analysis, such as connectivity strength, and those from graph theory analysis, like the clustering coefficient and small-world properties, together offer valuable insights into how OT may modulate the neural architecture that supports creative thinking processes. By examining these metrics, the present study aims to contribute crucial neural evidence for the effects of OT on creativity.

Materials and methods

Participants

To minimize potential confounding variables linked to endogenous estrogen, our study exclusively enrolled male participants. Sample size calculations, conducted using GPower (Faul et al. 2007), determined that Study 1 required a total of 34 participants with an α error probability of 0.05, power ($1 - \beta$ error probability) of 0.80, and an effect size (f) of 0.25. To account for potential dropouts and meet this requirement, we recruited 68 male college students (age: 18–22) from Central China Normal University. Before the study, participants completed the Behavioral Activation and Behavioral Inhibition System questionnaires (Carver and White 1994) to assess approach-avoidance motivation. Based on their scores, participants were categorized into either the approach or avoidance group (see [Supplementary material](#) for details). Consequently, our subsequent analyses included 31 participants (age: 20.1 ± 2.3) in the approach group (Ap) and 32 participants (age: 19.1 ± 1.6) in the avoidance group (Av) after accounting for two withdrawals and three outliers. Study 2 recruited a total of 66 male college students (age: 18–22) to meet the sample size requirement by GPower ($\alpha = 0.05$, $1 - \beta = 0.80$, and $f = 0.25$). After motivational induction, 28 participants (age: 20.3 ± 2.2) were assigned to the approach group and 33 (age: 20.9 ± 2.8) to the avoidance group (three withdrawals, two outliers; see [Supplementary material](#) for details). In Study 2, half of the participants were randomly selected for functional near-infrared spectroscopy (fNIRS) scanning, consisting of 16 participants in the approach group and 17 in the avoidance group (the subsample of participants selected for fNIRS measurements did not differ significantly from the remaining sample in terms of their creativity scores under PL condition, as shown in [Supplementary Table S1](#)).

All participants were right-handed, possessed normal or corrected-to-normal vision, had no history of psychiatric or neurological disorders or substance abuse, and were not taking prescription medications before or during the study. Participants refrained from smoking or consuming alcohol before the experiment. Before the formal experiment, all participants provided written informed consent, including detailed information about their rights, the experimental procedures, and the administration of intranasal OT. They were compensated following standard payment procedures. Ethical approval for all experimental protocols was obtained from the Ethics Institute Review Board of Central China Normal University (CCNU-IRB-202208 016b).

Alternative uses task materials

In our study, we utilized a modified version of the AUT, originally developed by Guilford (1967). The AUT is a well-established tool for assessing verbal divergent thinking, a crucial component of creative thinking (Runco and Acar 2012, Hao et al. 2014). Twenty commonly used items (e.g. umbrella, spoon, toothbrush) were selected and divided into two parts (Part A and B, 10 for each) as the materials for the AUT. Each part conducted AUT assessments within-subjects under both intranasal OT and PL conditions. Following the task, we evaluated participants' responses based on three dimensions: (I) novelty, the originality of ideas (5-point Likert scale); (II) fluency, the number of ideas; and (III) flexibility, categories of ideas (divided by fluency).

To establish the reliability and consistency of these AUT items for creativity assessment, a separate group of participants was recruited. They received only a PL treatment and were asked to generate original uses for these items. The responses were independently scored by two trained raters, demonstrating satisfactory inter-rater reliability (internal consistency coefficient, ICC=0.80 for novelty, 0.89 for flexibility). Importantly, our analysis revealed no significant differences in novelty, fluency, and flexibility between the two sets of items, confirming the equivalence of these two item sets [novelty: $t(18) = -0.53, P > .05$; fluency: $t(18) = 0.48, P > .05$; flexibility: $t(18) = 1.17, P > .05$].

Experimental procedure

The procedures for both studies followed a randomized, double-blind, PL-controlled within-subjects design. In Study 1, participants first provided informed consent and were then randomly administered either OT (24 IU, Defeng Pharmaceutical Co., China) or PL (with identical ingredients except for the peptide itself, mainly composed of saline and glycerol), under close supervision. After the initial administration, participants engaged in a 30-min practice and relaxation session. Following this, they were introduced to the formal AUT experiment (materials of Part A or B randomly). The AUT protocol included several phases: (i) resting phase: a 20-s period with closed eyes to establish a baseline, especially for the fNIRS scan; (ii) task commencement: this phase commenced with a 3-s blank screen, followed by a 7–14 second fixation point to signal the start of the task; (iii) thinking phase: in this 30-s phase, participants were instructed to generate as

many novel uses as possible for the given items without verbalizing them, with an emphasis on both quantity and novelty; (IV) reporting phase: subsequently, in the reporting phase, participants verbally articulated all the uses they had conceived (Fig. 1). For within-subjects comparison, participants returned at least 1 week later (to avoid drug interaction) for a second session. This time, they received the opposite treatments (PL or OT) and completed the AUT using the other Part (A or B) of the materials (no significant difference in AUT scores between the two parts, Supplementary Table S2). The order of treatments (PL-OT or OT-PL) and AUT materials (Part A-B or Part B-A) was systematically counterbalanced across participants.

In Study 2, an additional experimental induction was introduced to explore the moderating effect of approach-avoidance motivation on the relationship between OT and creativity. The procedures closely mirrored those of Study 1, utilizing the same AUT materials and treatments (Supplementary Table S2). After administration, participants were induced into either an approach or avoidance motivational state through a 5-min recall task. This recall task manipulated motivation types by prompting participants in the approach group to recall past experiences related to seeking or pursuing something, while participants in the avoidance group were asked to recall experiences involving avoidance behaviors. Before initiating the creativity thinking assessment, a verification step was introduced to confirm the effectiveness of the motivational induction (Fig. 1).

The performance on the AUT was evaluated based on novelty, fluency, and flexibility, using the same procedures as those applied in the pre-experiment. Novelty and flexibility scores were calculated as the mean value generated from two raters (for novelty: ICC=0.79 in Study 1 and 0.81 in Study 2; for flexibility: ICC=0.93 in Study 1 and 0.97 in Study 2) for each participant.

Control variables

To control for potential confounding effects of drug treatment on mood throughout the experiments, participants reported their emotions at the end of the AUT task. All participants rated their current levels of relaxation, happiness, anxiety (reverse-scored), fear (reverse-scored), and unhappiness (reverse-scored) on a 5-point Likert scale (1=not at all, 5=very much) (De Dreu and Nijstad 2008). Additionally, participants were briefly interviewed to determine whether they were aware of what they had received,

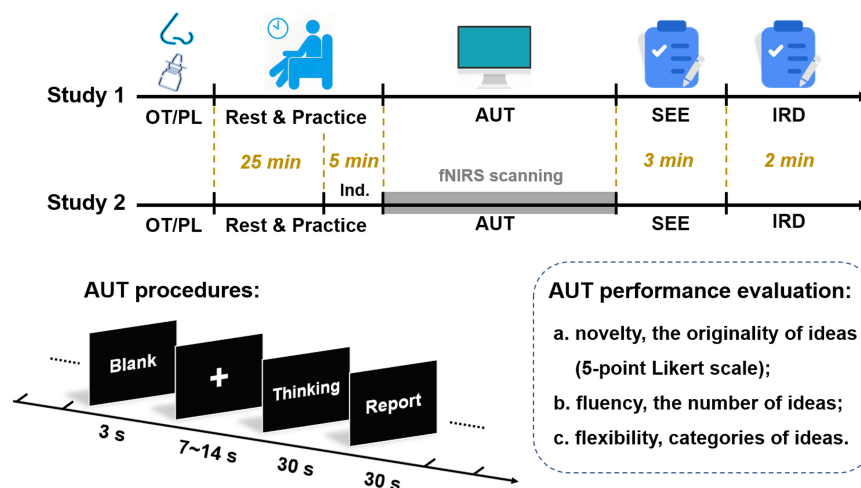


Figure 1. Experiment flow and the procedures of the alternative uses task (AUT). OT, oxytocin; PL, placebo; Ind., induction procedure; SEE, self-evaluation of emotions; IRD, identification of received drugs.

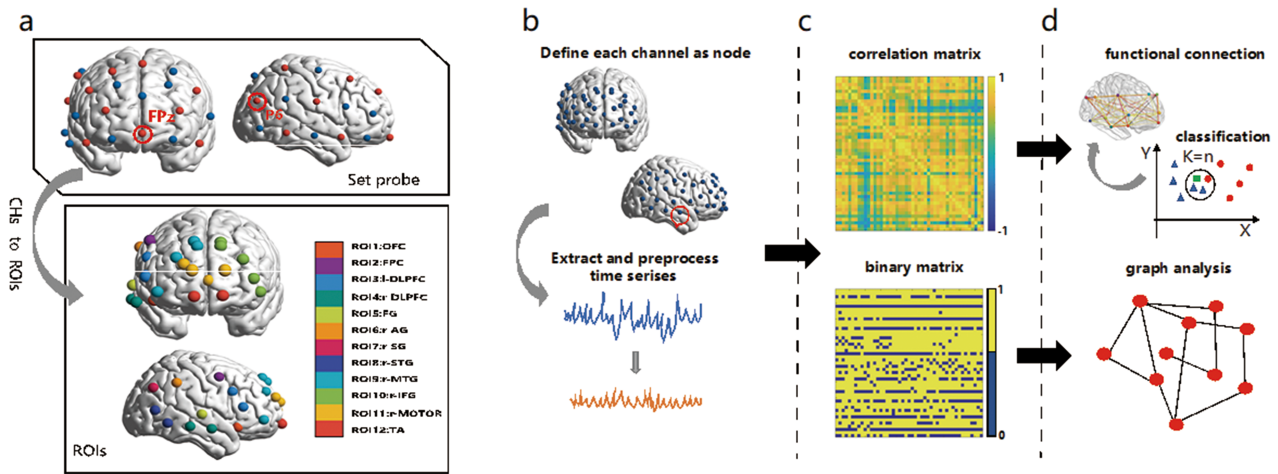


Figure 2. The optode probe sets and neural data analysis. (a) The optode probe sets were placed on the prefrontal cortex, temporo-parietal junction, and temporal regions of the brain. A total of 12 regions of interest (ROIs) were created based on shared source localizations according to the Montreal Neurological Institute coordinates of the CHs. (b–d) Diagrams show the procedures of functional connectivity and graph theory analysis.

Table 1. The ROI channels and their corresponding Brodmann area

Regions	Channels	Brodmann area
OFC	3,4	11
FPC	5,10,13,15	10
l-DLPFC	7,22,23,9,26	9,46
r-DLPFC	2,17,2,24	9,46
FG	28,29	37
r-AG	30	39
r-SG	33	40
r-STG	37	22
r-MTG	36,38	21
r-IFG	42,44	44,45
r-MOTOR	41	6
TA	47	38

l, left hemisphere; r, right hemisphere; OFC, orbitofrontal cortex; FPC, frontopolar cortex; DLPFC, dorsolateral prefrontal cortex; FG, fusiform gyrus; AG, angular gyrus; SG, supramarginal gyrus; STG, superior temporal gyrus; MTG, middle temporal gyrus; IFG, inferior frontal gyrus; MOTOR, pre-motor and supplementary motor cortex; TA, temporopolar area.

OT or PL, to verify double-blind manipulation and eliminate subjective biases.

fNIRS data acquisition and analysis

NIRScout (NIRx Medical Technologies, New York, USA) recorded changes in oxyhemoglobin (HbO) and deoxyhemoglobin (HbR) concentrations for each participant during the experimental task. Data were sampled at 4.17 Hz, capturing near-infrared light absorption at wavelengths of 785 and 830 nm. Participants wore one 3 × 4 probe array over the right temporal and parietal regions and one about 4 × 5 probe array over the bilateral prefrontal regions (Fig. 2a). These probe arrays were configured to create a total of 47 channels that encompassed the temporal lobe, temporo-parietal region, and prefrontal cortex according to the positioning criteria of the International 10-20 system. The precise locations of the optode and scalp landmarks were digitized using a 3D digitizer (NIRx Medical Technologies, New York, USA), which were registered to MNI space coordinates with a probability-based approach and used to define ROIs (Table 1).

The recorded NIR data underwent band-pass filtering to isolate relevant frequency bands, and a 5 SD thresholding step was applied to remove any discontinuities. Hemodynamic states were computed using the modified Beer-Lambert law (Cope and Delpy 1988), with the resting state serving as the baseline. Due to its heightened sensitivity to changes in cerebral blood flow (Liu et al. 2016), only HbO data were analyzed.

Functional connectivity analysis

Functional connectivity was assessed by calculating pairwise regional correlation coefficients using Pearson's correlation coefficient. This yielded a 12 × 12 correlation matrix of ROIs for each participant. Fisher's r-to-z transformation was applied to enhance normality. A two-way mixed analysis of variance (ANOVA) was conducted on region pairs, with motivation (approach or avoidance) as the between-participant factor and treatment (OT or PL) as the within-subjects factor. To further confirm the changes in functional connectivity by OT administration, a K-nearest neighbors (KNN) classifier was used to distinguish approach and avoidance groups based on changes in functional connectivity strength between OT and PL. Evaluation included three-fold cross-validation, receiver operating characteristic metrics, and confusion metrics. Permutation tests were performed to address potential errors arising from multiple comparisons (Fig. 2b–d). Permutation tests elegantly tackle the issue of multiple comparisons by generating new datasets through random shuffling, allowing for a comparison of the observed test statistic to a distribution under the null hypothesis, without relying on assumptions about the data's underlying distribution.

Graph theory analysis

Graph theory analysis was used to explore the topological properties of brain networks during creativity. An unweighted, undirected binary network, 1000 random networks, and a thresholding method with sparsity were implemented (Fig. 2c and d). Sparsity, defined as the ratio of existing edges to the maximum possible edges, was maintained at an equivalent level across all groups, enabling comparisons of topological organization. A sparsity (S) range of $0.3 \leq S \leq 0.5$ was selected with intervals of $\Delta S = 0.01$,

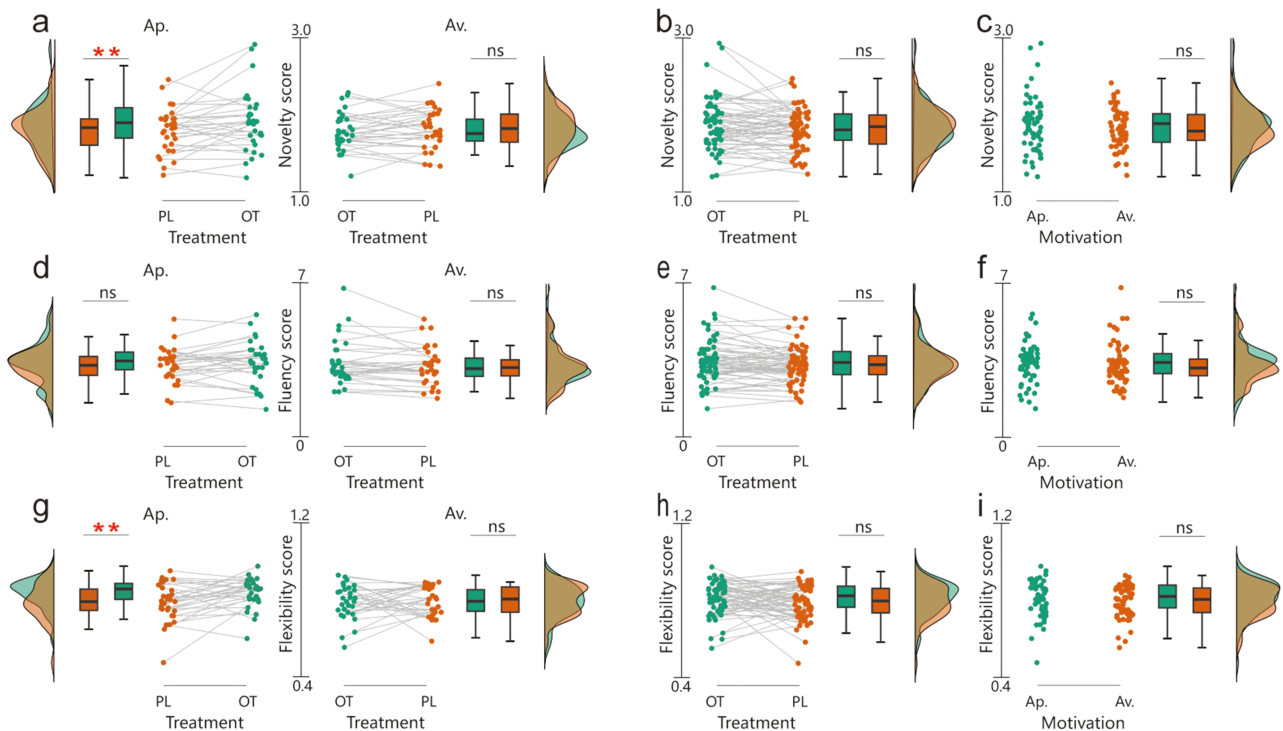


Figure 3. Creativity performance of individuals with approach- (Ap) or avoidance (Av)-motivation traits under oxytocin (OT) and placebo (PL) treatments. (a, d, g) Raincloud plots show the interactions between drug treatments (OT or PL) and motivation (Ap or Av) on AUT novelty, fluency and flexibility, respectively. (b, c, e, f, h and i) Main effect of drug treatments (b, e, h) and motivation (c, f, i) on AUT novelty, fluency and flexibility, respectively. **, $p < 0.01$.

ensuring the estimability of small-world properties while avoiding overly fragmented networks.

To characterize brain functional networks, five metrics of brain network connectivity were calculated: clustering coefficient (Cp), shortest path length (Lp), small-world properties (σ), global efficiency (Eg), and local efficiency (Eloc). These metrics quantified the capacities of the brain with local interconnectivity, information dissemination, and global and local information transmission capacities (Achard and Bullmore 2007, Bullmore and Sporns 2009, Menon 2013, Sporns 2013). Two-way mixed ANOVAs were conducted on all these metrics as well as the area under the receiver operating characteristic curve (AUC) to assess the effect of experimental treatment, with motivation (approach or avoidance) serving as the between-subject factor and treatment (OT or PL) as the within-subject factor. False discovery rate correction was applied to all P -values according to Benjamini and Hochberg (1995).

Data analysis

All statistical analyses were calculated using SPSS (Version 26.0). Descriptive characteristics of group variables were expressed as means and standard deviations. The significance of variables between groups was assessed using χ^2 test, Mann-Whitney U test, independent-sample/paired-sample t -tests, Spearman correlation analysis and ANOVA, with a simple effect test used when appropriate. Only P values less than .05 were considered significant.

Results

Behavioral results

Study 1

In Study 1, an initial assessment ensured participants were unable to accurately identify administered drugs (OT or PL) before

task commencement. The chi-squared tests revealed no significant differences in participants' accuracy to discern the specific drug (Ap: $\chi^2 = 0.12$, $P = .74$; Av: $\chi^2 = 0.17$, $P = .19$; excluding uncertain responses), ensuring the unbiased nature of subsequent creativity assessments.

To explore the influence of drug type (OT and PL) and motivation type (approach and avoidance) on novelty, fluency, and flexibility within the AUT, a two-factor mixed-design ANOVA was conducted. The analysis revealed no significant main effects for drug [$F(1, 61) = 2.17$, $P = .15$] or motivation [$F(1, 61) = 0.69$, $P = .41$] in terms of novelty (Fig. 3b and c). However, a notable drug-motivation interaction concerning novelty emerged [$F(1, 61) = 5.51$, $P = .02$]. Simple effect analysis disclosed that approach group participants exhibited significantly higher novelty scores with intranasal OT, compared to PL ($P = .009$), while avoidance group scores showed no significant differences ($P = .54$) (Fig. 3a).

For fluency, no significant main effects were observed for drug [$F(1, 61) = 3.60$, $P = .06$], motivation [$F(1, 61) = 0.02$, $P = .90$], or drug-motivation interaction [$F(1, 61) = 0.01$, $P = .92$] (Fig. 3d-f).

However, results revealed a significant interaction in flexibility between drug and motivation [$F(1, 61) = 5.70$, $P = .02$], with higher flexibility scores under OT condition compared with PL in the approach group ($P = .003$), not in the avoidance group ($P = .77$) (Fig. 3g). No significant main effects of drug or motivation on flexibility were found [drug: $F(1, 61) = 3.88$, $P = .06$; motivation: $F(1, 61) = 1.36$, $P = .25$; Fig. 3h and i]. Further analysis using the PROCESS macro (model 4) by Hayes (2013) indicated that flexibility mediated the relationship between OT and novelty ($B = 0.88$, $P = .08$ for flexibility-novelty correlation), with a 95% CI of [0.002, 0.128] (Table 2).

Additionally, ANOVA on emotional states showed no significant variations between OT or PL, irrespective of motivation types [drug: $F(1, 61) = 2.31$, $P = .13$; motivation: $F(1, 61) = 0.73$, $P = .40$;

Table 2. Results of the mediation model

Predictors	Study1				Study2			
	Flexibility		Novelty		Flexibility		Novelty	
	B	t	B	t	B	t	B	t
Drug	0.05	2.39*	0.07	0.79	0.04	2.03*	0.03	0.31
Flexibility			0.88	1.75#			1.80	3.44***
R ²	0.09		0.08		0.07		0.20	
F	5.70*		2.45#		4.10*		6.73***	
95% CI	[0.002, 0.128]				[0.005, 0.206]			

* $P < .05$.*** $P < .01$.# $P < .09$ (marginal significant). CI: confidence interval.**Table 3.** Examination of induced effectiveness of the recall task among different groups

Drug	Vocabularies in the recall task	Group			Statistical result*	
		Ap	Av	U	z	P
OT	Approach-related	2.71 (1.10)	1.03 (0.10)	128.0	-5.05	.000
	Avoidance-related	0.75 (0.82)	2.79 (1.43)	80.5	-5.30	.000
PL	Approach-related	3.25 (1.50)	1.06 (0.81)	78.0	-5.79	.000
	Avoidance-related	0.86 (0.83)	3.30 (1.58)	68.0	-5.94	.000

Data were shown as mean (SD).

*The Mann-Whitney U test.

interaction: $F(1, 61) = 0.66$, $P = .42$]. These findings suggest that OT's impact on creativity is not mediated through emotional modulation (Supplementary Table S3).

Study 2

In Study 2, the Mann-Whitney U test revealed significant differences in participants' motivational orientation after recall task. Approach group exhibited more approach-related words in their responses (OT: $U = 128.0$, $z = -5.05$, $P < .001$; PL: $U = 78.0$, $z = -5.79$, $P < .001$), while the avoidance group showed a greater use of avoidance-related words (OT: $U = 80.5$, $z = -5.30$, $P < .001$; PL: $U = 68.0$, $z = -5.94$, $P < .001$), irrespectively of PL or OT conditions (Table 3). Notably, no significant motivational orientation differences were observed before the recall task [$t(59) = 0.57$, $P = .57$]. These findings robustly confirmed the effectiveness of the priming manipulation.

The results of Study 2 mirrored those of Study 1, with no significant main effects for drug or motivation on novelty [drug: $F(1, 59) = 0.67$, $P = .42$; motivation: ($F(1, 59) = 0.36$, $P = .55$)] and flexibility [drug: $F(1, 59) = 2.84$, $P = .18$; motivation: ($F(1, 59) = 2.85$, $P = .10$)] scores; however, significant drug-motivation interactions for novelty [$F(1, 59) = 7.45$, $P = .01$] and flexibility [$F(1, 59) = 4.26$, $P = .04$] persisted (Fig. 4). Approach group had significantly higher novelty ($P = .02$) and flexibility ($P = .02$) scores after intranasal OT compared to PL, while avoidance group showed no significant differences (novelty: $P = .16$; flexibility: $P = .60$) (Fig. 4a and g). Hayes' PROCESS macro (model 4) also indicated the mediating role of flexibility in the relationship between OT and novelty (95% CI = [0.005, 0.206], $B = 1.80$, $P < .01$ for flexibility-novelty correlation, Table 2).

Regarding fluency, a significant main effect of motivation emerged [$F(1, 59) = 6.29$, $P = .02$], but no effect for drug [$F(1, 59) = 1.35$, $P = .25$] or drug-motivation interaction [$F(1, 59) = 0.10$, $P = .76$] was found (Fig. 4d-f).

Study 2 also revealed no significant differences in drug types guessing (Ap: $\chi^2 = 0.05$, $P = .82$; Av: $\chi^2 = 0.51$, $P = .47$) and emotional states among participants following OT and PL administration [drug: $F(1, 59) = 0.06$, $P = .81$; motivation: $F(1, 59) = 1.51$,

$P = .22$; interaction: $F(1, 59) = 0.52$, $P = .47$] (Supplementary Table S3).

fNIRS results

Functional connectivity results

Figure 5a-d illustrated the functional connectivity patterns in the OT and PL conditions for approach and avoidance groups. Analysis unveiled significant drug-motivation interactions for several ROI pairs [FG-rMTG: $F(1, 31) = 4.67$, $P = .04$; FG-rSTG: $F(1, 31) = 5.43$, $P = .04$; rSTG-rIFG: $F(1, 31) = 6.22$, $P = .03$] (Fig. 5a; shown by red asterisks). Simple effect analysis showed increased functional connectivity strength in the approach group under intranasal OT conditions (FG-rMTG, $P = .02$; FG-rSTG, $P = .07$; rSTG-rIFG, $P = .08$; Fig. 5e-f).

Classification results based on KNN demonstrated an average accuracy of 81.1%, sensitivity of 87.5%, specificity of 76.5%, and an average AUC of 0.81, confirming the distinguishability of approach and avoidance groups utilizing the changes of functional connectivity strength as features (Fig. 5i).

Correlation analysis in the approach group under OT administration revealed a robust positive association between the magnitude of functional connectivity and behavioral outcomes (z -transformation for data). This observation underscores a potential mediating mechanism through which these neural alterations contribute to shaping the observed behavioral differences (FG-rSTG vs. novelty: $r = 0.59$, $P = .016$; rSTG-rIFG vs. novelty: $r = 0.73$, $P = .001$). These findings strengthen the notion that functional connectivity patterns, modulated by OT, play a pivotal role in influencing creative behavioral responses.

Graph theory results

Figure 6b-f displayed the distribution of five global metrics from real brain networks (warm colors) and matched random networks (cool colors) within sparsity range of 0.3–0.5 which ensured connectivity among ROIs (Fig. 6a). The Cp and Eloc of real networks exceeded that of the matched random networks (Fig. 6b and c); meanwhile, the Lp and Eg remained similar (Fig. 6e and f). Both the approach and avoidance groups demonstrated small-world

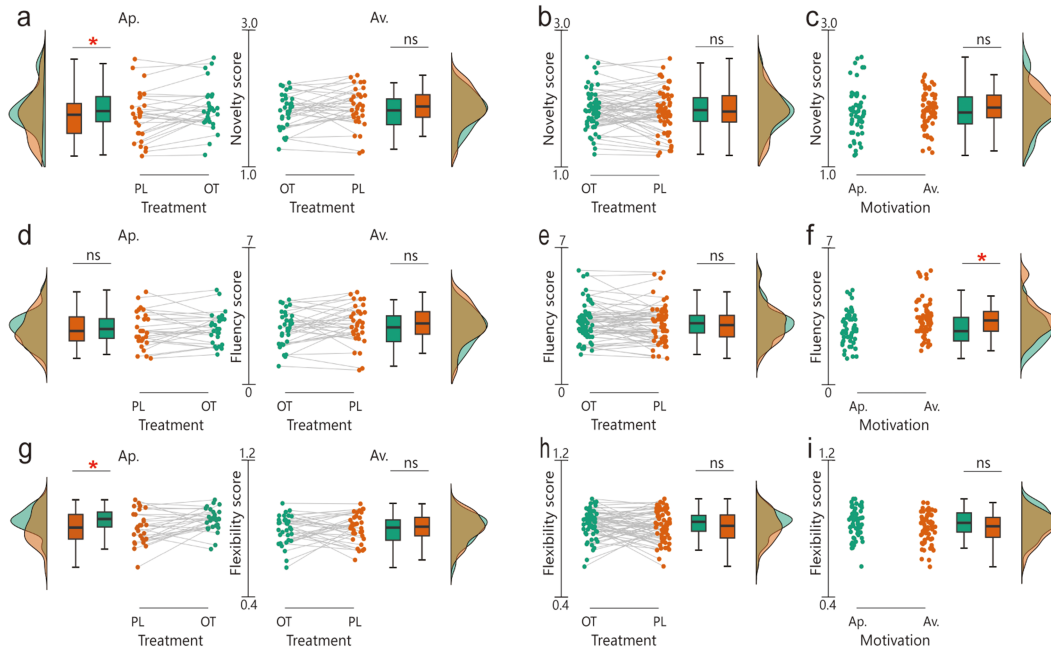


Figure 4. Creativity performance of individuals under induced states of Ap or Av motivation after OT and PL treatments. (a, d, g) Raincloud plots show the interactions between drug treatments (OT or PL) and motivation (Ap or Av) on AUT novelty, fluency and flexibility, respectively. (b, c, e, f, h and i) Main effect of drug treatments (b, e, h) and motivation (c, f, i) on AUT novelty, fluency and flexibility, respectively. *, $p < 0.05$.

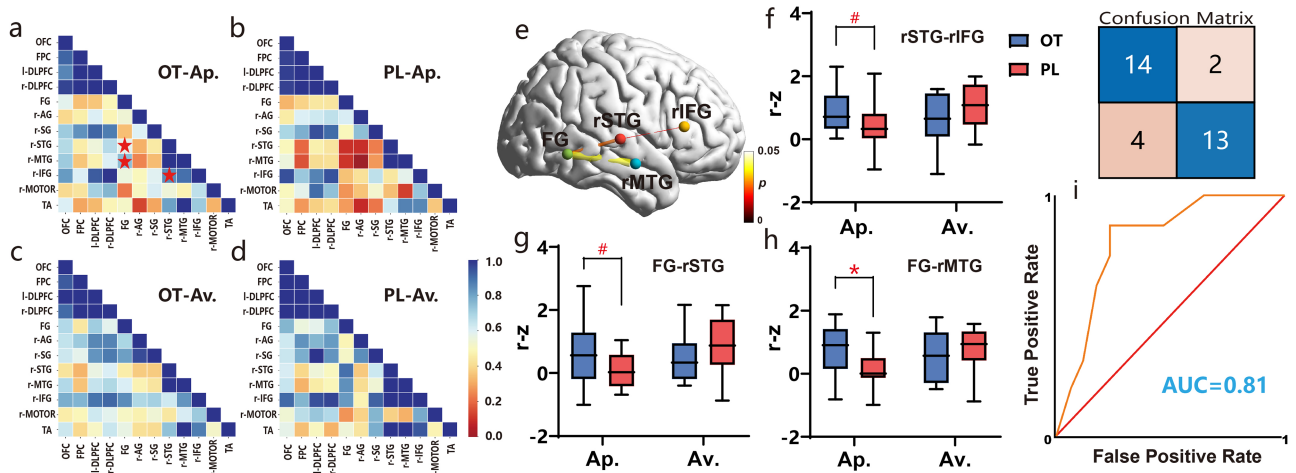


Figure 5. Functional connectivity results. (a–d) Correlation patterns between the ROIs of the Ap and Av groups under condition of OT and PL treatments. The bar of assorted colors represents the level of correlation coefficients between ROIs. Significant interactions of drug treatments and motivation on ROI pairs are marked with the red asterisks (corrected by permutation tests). (e–h) Functional connectivity between ROI pairs with significant interactions of drug treatments and motivation in graph (a). The significant levels of interaction effects are demonstrated by the thickness and color of the interregional connection lines in the brain diagram. The bar of assorted colors represents the p values. Simple effect analyses results (Bonferroni-corrected) are shown in graphs (f) (rSTG–rIFG), (g) (FG–rSTG), and (h) (FG–rMTG). *, $p < 0.05$; #, marginal significant ($p < 0.08$). (i) Classification results of distinguishing Ap and Av groups using changes in functional connectivity strength as features based on K-nearest neighbors (KNN). The matrix on the top of graph (i) is the confusion matrix of classification. The curve on the bottom is the receiver operating characteristic (ROC) curve for a 3-fold cross-validation.

values larger than one ($\sigma > 1$) under OT and PL conditions (Fig. 6d). All these findings indicated a typical feature of small-world topology.

In a two-factor ANOVA, significant drug-motivation interactions were unveiled in Lp and Eg across various sparsity levels (Fig. 6g and j; shown by red asterisks). At a sparsity of 0.36, for instance, OT significantly influenced the Lp ($P = .01$) and Eg ($P = .01$) in approach group while showing no effect in avoidance group [interaction: $F(1, 31) = 5.42$, $P = .03$ for Lp; $F(1, 31) = 5.35$,

$P = .03$ for Eg; Fig. 6h and k]. The AUCs in Eg and Lp across sparsity were larger ($P = .04$) or smaller ($P = .02$), respectively, under OT for approach group, not for avoidance group, further confirming these interactions [interaction: $F(1, 31) = 5.47$, $P = .07$ for Lp; $F(1, 31) = 5.32$, $P = .07$ for Eg; Fig. 6i and l].

Further exploration via correlation analysis between the graph theory metrics and behavioral outcomes revealed intriguing insights into their mediating effects on shaping behavioral differences (z-transformation for data). Notably, in the approach

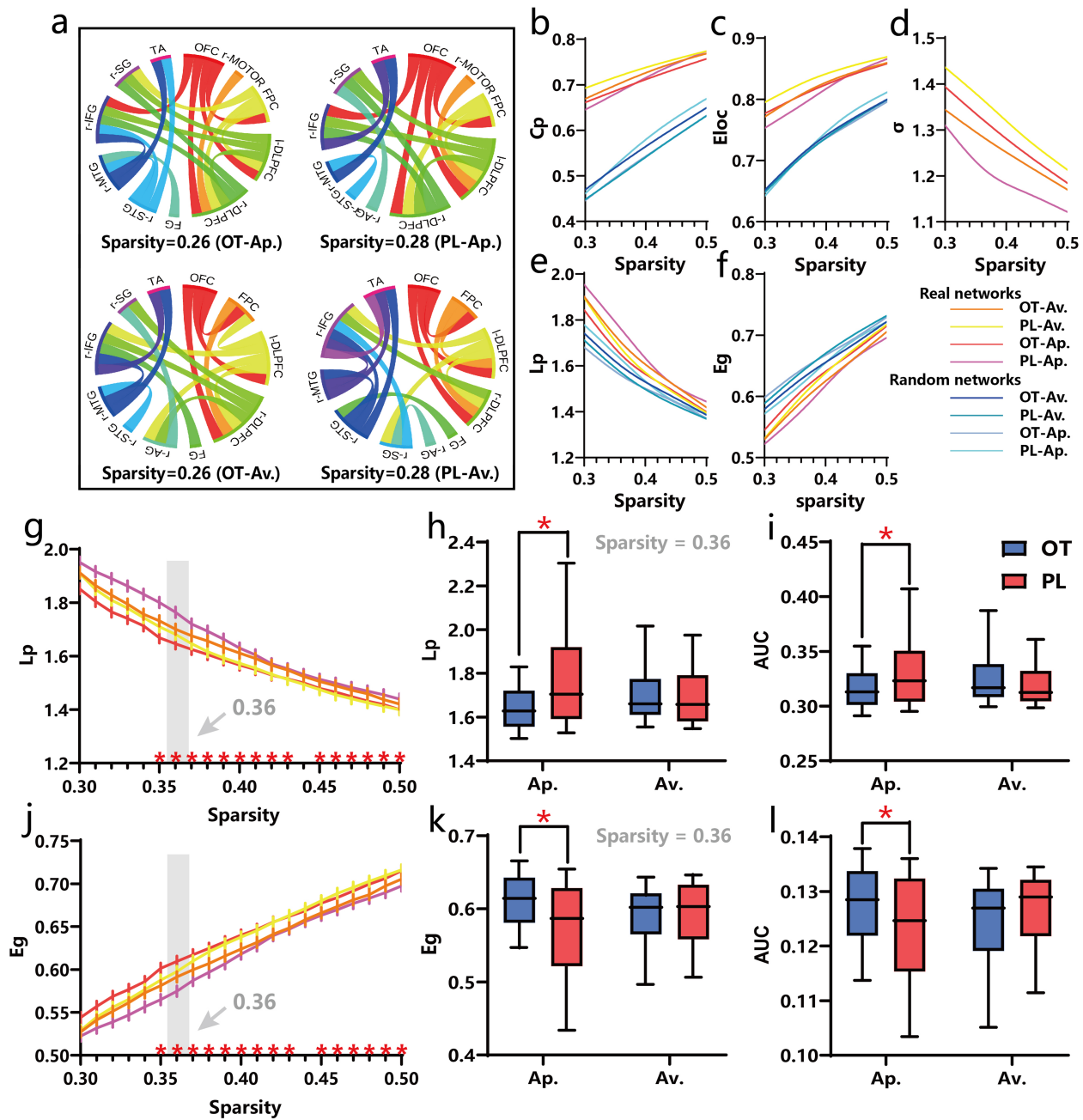


Figure 6. Graph theory analysis results. (a) Connections among the ROIs of the Ap and Av groups under OT and PL treatments at the minimum network sparsity that ensuring unconnected nodes ≤ 1 . (b–f) Distribution of the five metrics of brain network as a function of sparsity thresholds within range of 0.3–0.5. The real brain networks and matched random networks are indicated with cool and warm colors, respectively. (g, j) The comparison of the shortest path length (Lp) and global efficiency (Eg) among the four conditions cross different sparsity. Red asterisks indicate significant interaction at a certain sparsity (FDR corrected). (h, k) Simple effect analysis results of Lp values and Eg of the network at sparsity of 0.36 (shown by shadows and arrows in graphs (g) and (j)). *, $p < 0.05$ (Bonferroni-corrected). (i, l) The comparison of the area under the receiver operating characteristic curves (AUC) on the Lp values and Eg in graphs (g) and (j). *, $p < 0.05$ (Bonferroni-corrected).

group under OT administration, the Lp at a sparsity of 0.36 and its AUC exhibited significant negative correlations with novelty (Lp: $r = -0.66$, $P = .006$; AUC: $r = -0.70$, $P = .003$) and flexibility scores (Lp: $r = -0.63$, $P = .005$; AUC: $r = -0.68$, $P = .004$). Conversely, Eg at the same sparsity level and its AUC showed positive correlations with these behavioral outcomes (novelty: Lp: $r = 0.67$, $P = .006$; AUC: $r = 0.67$, $P = .005$; flexibility: Lp: $r = 0.63$, $P = .005$; AUC: $r = 0.65$, $P = .004$). These results highlight the intricate interplay between neural patterns modulated by OT and behavioral responses, reinforcing the importance of considering OT's role

in shaping brain network properties and subsequent creative behaviors.

Discussion

In the present investigation, we conducted a comprehensive exploration of the impact of OT on creativity in humans, specifically focusing on individuals motivated by either approach or avoidance tendencies. Contrary to the previously held belief that OT has uniformly positive relationship with individual creativity,

our findings unveil a nuanced effect contingent upon an individual's motivational orientation. Specifically, intranasal OT administration resulted in a significant elevation in creativity levels among individuals with approach-oriented motivation compared to a PL group. However, this enhancement was conspicuously absent among individuals exhibiting avoidance-oriented motivation. These findings underscore a dissociable effect of OT on creativity linked to individual motivational tendencies, a conclusion further supported by our additional experiments deliberately inducing approach-avoidance motivational states in subjects.

The behavioral effects were further validated through neurophysiological indicators. Following OT administration in the approach group, we observed a profound enhancement in dynamic interactions within the DMN and ECN—networks crucial for creativity (Beaty et al. 2016, Jiao et al. 2017). In contrast, avoidance-oriented individuals displayed no significant alterations in connectivity patterns. Specifically, the functional connectivity strengths of FG-rMTG, FG-rSTG, and rSTG-rIFG were notably augmented in the approach-motivated individuals subsequent to OT administration. As fundamental constituents of the DMN, the FG, MTG, and STG regions in the temporal lobe perform pivotal functions in conceptual information processing, encompassing the formation, retrieval, and integration of conceptual representations (Beaty et al. 2020). The enhancement of these connectivity patterns facilitated the formation of remote linkages between concepts, thereby positively contributing to the generation of novel perspectives and bolstering creativity. Moreover, the IFG within the ECN is responsible for selecting and executing remote associations during conceptual elaboration process (Cogdell-Brooke et al. 2020). The strengthened connection of rIFG-rSTG indicated that OT enabled approach-oriented individuals to bridge and integrate distant concepts, thus fostering the emergence of creative ideas.

Additionally, post-OT administration, the approach group exhibited an increase in global efficiency and a concurrent reduction in the shortest path length within their brain networks, while the avoidance group displayed no substantial alterations. These alterations effectively shortened information conduction pathways within networks, expedited transmission rates, and enhanced the efficiency of processing and integrating semantic concepts, which was conducive to the generation of creative thinking (Schilling 2005, Bullmore and Sporns 2012). Overall, these observations suggest that OT enhances the function and efficiency of creativity-related brain networks in the approach group, facilitating and promoting creative problem-solving (Mednick 1962, Schilling 2005, Jiao et al. 2017).

Our study results indicated that OT enhanced creative potential selectively for people with high approach orientation, in contrast to the findings of De Dreu et al. (2015), who reported a main effect of OT on creative potential. However, the authors also noted that some of the effects they observed appeared to be relatively weak. This weakness may be attributed to different individual characteristics constraining the effect of OT, or its inherent weakness requiring specific features and states for manifestation. Our results here emphasized the critical consideration of individual-specific differences when examining its impact on human behavior.

OT, as a neurotransmitter, targets emotion-related brain regions, including the amygdala, implying its potential role in regulating emotional functions (Ebner et al. 2005, Frijling et al. 2015, Kou et al. 2022). Previous research also suggests that OT may facilitate social cognition and functioning by reducing anxiety, particularly social anxiety (Taylor et al. 2006). This decrease in anxiety

is considered a possible underlying mechanism mediating apparently complex effects of OT (Schwarz 1990, Kumsta and Heinrichs 2013). However, in our study, we found no significant emotional differences following OT and PL administration, excluding the possibility that the improved creativity in the approach group was due to emotional modulation. This suggests that OT-induced changes in creativity are not primarily driven by anxiety modulation. The observed effect of OT on cognitive flexibility might suggest an alternative mechanism that OT promotes creativity by influencing individual cognitive styles and creative cognitive processes, with individual cognitive characteristics playing a pivotal role.

OT has been associated with heightened holistic processing, emphasizing a preference for global over detailed information. Moreover, it tends to diminish convergent thinking and analytical performance while fostering divergent thinking (De Dreu et al. 2015). These cognitive changes are likely conducive to more original ideation and creative problem-solving (Mehta and Zhu 2009, Fletcher and Benveniste 2022). However, an inconsistent result in the effects of OT on creativity was observed among different individuals. This raises the question: Why does the same OT functions result in divergent effects in different individuals? This inconsistency may stem from inherent differences in individuals' cognitive characteristics and strategies. Individuals with an avoidance orientation typically demonstrate a narrow attentional focus and an analytical thinking style, incongruent with the cognitive changes induced by OT (Friedman and Förster 2005b, De Dreu et al. 2011). This incongruence leads to a conflict in cognitive processing strategies for avoidance-motivated individuals, preventing the attainment of the necessary to elicit the desired effect and failing to promote original insight novelty in creative task performance. Conversely, these promotive effects of OT would reach its peak magnitude when the cognitive processing style induced by OT closely aligns with the cognitive characteristics typically observed in approach-oriented individuals, who exhibit a holistic, flexible processing style.

Another plausible explanation for the effects of OT on creativity is its influence on perceptual salience and processing of reward-related information. OT participates in the functioning of the dopamine (DA)-reward system, regulating the processing of reward-related cues (Skuse and Gallagher 2005, Lee et al. 2020, Chong et al. 2021). This may lead participants to focus more on rewards and achievements, adopting a more positive, adventurous, and unconstrained thinking style—an advantageous factor for creative behavior (Schwarz 1990, Zhang et al. 2020a). However, individuals' behavioral profiles across contexts reflect not only the gross features of situations themselves but also how individuals interpret those features. For avoidance-oriented individuals, motivated by negative goals such as evading failures and errors, heightened attention to task performance and reward means increase of perceived risk of failures, leading to a bias toward interpreting them negatively (Grajcevcic and Shala 2021). This negative bias potentially negates the creative-promoting effects of OT. Conversely, for approach-oriented individuals with positive goal orientation, increased attention to task reward could be beneficial (Zhang et al. 2020a). In support of this speculation, further experimentation utilizing magnetic resonance imaging techniques is required, as near-infrared spectroscopy is limited in its ability to probe deeper subcortical structures such as the nucleus accumbens, a crucial component of the DA system.

It is noteworthy that the dissociable effect of OT among individuals with different motivational orientations pertained predominantly to the flexibility aspect in creative performance, as

opposed to fluency. Additionally, flexibility could mediate the impacts of OT on enhancing the generation of original ideas in the task. These suggest that OT's impact on individual creativity primarily manifests in its capacity to promote cognitive flexibility and divergent thinking, rather than in the depth and persistence of cognitive processing. According to the dual-pathway model of creativity (De Dreu et al. 2008, Nijstad et al. 2010, Peterson and Pattie 2022), which posits creativity is fostered through dual channels of flexibility and perseverance, our study indicates that, in the present context, OT appears to primarily act through the "flexibility pathway" within the dual-channel model, resulting in increased individual creativity levels. Previous perspectives from a social aspect proposed pathways through which OT might influence creativity, such as collectivism or individualism (Pfundmair et al. 2017); our study indicated an impact pathway at a cognitive level, specifically regulating flexibility to promote creativity. Nevertheless, further empirical evidence is warranted to substantiate this conclusion and provide a more comprehensive understanding of the underlying functional mechanisms of the neuropeptide OT in human creativity.

In the future, additional research is imperative to address several unresolved questions regarding the effects of OT on human creativity. First, our study administered only a single dose of 24 IU OT to the subjects based on previous studies. However, creativity is a high-level cognitive function that may require different optimal dosages and frequencies of OT administration compared to those used in social-domain effects (Kapetaniou et al. 2021, Kou et al. 2022). Therefore, future research efforts should aim to determine the ideal dosage and frequency of OT administration to optimize its impact on creativity. Secondly, given the demonstrated gender-specific effects of OT in previous studies (Bakermans-Kranenburg and van Ijzendoorn 2013, Ma et al. 2016), it is necessary to investigate potential differences in the impact of OT on creativity between male and female participants in future research. Additionally, future investigations could delve into the roles of additional individual differences, beyond motivational orientation, in modulating the effects of OT, including exploring the potential for negative effects of OT under specific states or characteristics of individuals.

Furthermore, while our study utilized a widely recognized AUT scoring method (fluency, flexibility, and novelty) to assess divergent thinking, we acknowledge that the adoption of varied scoring methodologies (e.g. originality and usefulness) could lead to divergent outcomes (Vartanian et al. 2020). Thus, future research endeavors should delve deeper into the application of diverse scoring methodologies to gain a more nuanced understanding of the intricacies and variations within AUT imaging results. Moreover, although AUT effectively serves as a tool for assessing divergent thinking, creativity in cognition is a multifaceted construct that encompasses crucial aspects beyond divergent thinking, such as convergence and combination (Zhang et al. 2020b, Ward and Kolomyts 2010). To achieve a more holistic evaluation of creativity, future studies ought to consider incorporating a variety of methods and tools. Investigations into these matters could refine our understanding of the nuanced and differential effects of OT on human creative processes.

Supplementary data

Supplementary data is available at SCAN online.

Conflict of interest: The authors declared that there were no conflicts of interest with respect to the authorship or the publication of this article.

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Data availability

Data are available from the corresponding author upon request.

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