

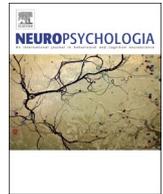
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# Transcutaneous vagus nerve stimulation (tVNS) enhances divergent thinking

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## ABSTRACT

Creativity is one of the most important cognitive skills in our complex and fast-changing world. Previous relative evidence showed that gamma-aminobutyric acid (GABA) is involved in divergent but not convergent thinking. In the current study, a placebo/sham-controlled, randomized between-group design was used to test a causal relation between vagus nerve and creativity. We employed transcutaneous vagus nerve stimulation (tVNS), a novel non-invasive brain stimulation technique to stimulate afferent fibers of the vagus nerve and speculated to increase GABA levels, in 80 healthy young volunteers. Creative performance was assessed in terms of divergent thinking (Alternate Uses Task) and convergent thinking tasks (Remote Associates Test, Creative Problem Solving Task, Idea Selection Task). Results demonstrate active tVNS, compared to sham stimulation, enhanced divergent thinking. Bayesian analysis reported the data to be inconclusive regarding a possible effect of tVNS on convergent thinking. Therefore, our findings corroborate the idea that the vagus nerve is causally involved in creative performance. Even though we did not directly measure GABA levels, our results suggest that GABA (likely to be increased in active tVNS condition) supports the ability to select among competing options in high selection demand (divergent thinking) but not in low selection demand (convergent thinking).

## 1. Introduction

“Creativity is just connecting things”, Steve Jobs, arguably one of the most creative minds of our time, once said (Wolf, 1996). From a scientific point of view, creativity is a complex concept, commonly defined as the ability to generate ideas, solutions, or products that are both novel and appropriate (e.g., (Amabile, 1996; Sternberg and Lubart, 1999)), and is not about connecting the obvious, but about making remote associations (Guilford, 1967; Mednick, 1962; Wallas, 1926). For example, when a person is asked to think of different uses for a brick, the first association may be to ‘build a house’ or to ‘break a window’. However, a more remote, out of the box, creative in that sense, association, may be to ‘crush the brick and use the pieces as sidewalk chalks’. The ability to generate novel ideas to open-ended problems (e.g., generate uses for a brick) is called divergent thinking. Creativity, however, also requires convergent thinking—the most creative ideas also have to be recognized and selected for implementation (Guilford, 1967; Ritter, 2012).

Creative thinking skills are inherent to normative cognitive functioning rather than an innate talent available to only a few (e.g., (Ward et al., 1999)). Importantly, various behavioral studies have shown that

creative thinking skills can be enhanced (e.g., (Baas et al., 2014; Colzato et al., 2012, 2013, 2015; de Bloom et al., 2014; Ritter and Mostart, 2016; Scott et al., 2004; Zabelina and Robinson, 2010)).

Recently, we suggested that transcutaneous vagus nerve stimulation (tVNS) may be used as a novel tool in healthy humans (van Leusden et al., 2015) probing the relationship between vagus nerve and cognitive-behavioral performance. In contrast to imaging techniques, which provide only correlational insight, tVNS allows to infer a causal relation between the stimulated vagus nerve and the related cognitive functions driven by them. tVNS activates the auricular branch of the vagal nerve which innervates the skin of the concha in the human ear (Peuker and Filler, 2002), causing a reliable transcutaneous electrical stimulation of the nerve fibers in this area. Indeed, active tVNS causes the propagation of the afferent signal from the vagus nerve to travel from peripheral nerves towards the brain stem and from there to intracranial subcortical and cortical structures (Shiozawa et al., 2014; Vonck et al., 2014). Scientific evidence demonstrates that tVNS indeed activates the vagus nerve: two imaging protocols in healthy humans have revealed that active tVNS, compared to sham, increased activation in the locus coeruleus and nucleus of the solitary tract, showing that tVNS is able to reliably stimulate vagal afferents to the brainstem (Dietrich et al., 2008;

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Frangos et al., 2015). Furthermore, a new study found that tVNS and invasive VNS engage the same neural pathways (Assenza et al., 2017). In healthy humans tVNS has been found to be a reliable technique to modulate vagal related functions such as emotion recognition (Colzato et al., 2017a, 2017b; Colzato et al., 2017b; Sellaro et al., in press), flow (Colzato et al., 2017a, 2017b), multitasking (Steenbergen et al., 2015), and explicit fear extinction learning (Burger et al., 2016).

The goal of the current study was to test if the vagus nerve is causally involved in the creative process in healthy individuals. Therefore, while being stimulated, participants performed validated creativity tasks tapping into divergent (Alternate Uses Task) and convergent thinking (Idea Selection Task; Remote Associates Test; Creative Problem Solving Task).

## 2. Methods

### 2.1. Participants

One hundred and four Leiden University undergraduate students were recruited to take part of this experiment. Participants were enrolled via an on-line recruiting system and were given either partial course credit or 10 euros for participating in a study on the effects of brain stimulation on creativity. Participants were enrolled via an on-line recruiting system and were given either partial course credit or 10 euros for participating in a study on the effects of brain stimulation on creativity. Once recruited, participants were randomly allocated to the placebo/sham or active tVNS group. All participants were screened individually using the Mini International Neuropsychiatric Interview (M.I.N.I.; (Sheehan et al., 1998)). The M.I.N.I. is a short, structured interview of about 15 min that screens for several psychiatric disorders and drug use, and is often used in clinical and pharmacological research (Colzato et al., 2014; Colzato et al., 2014, 2010; Sheehan et al., 1998). Following previous published protocols (Beste et al., 2016; Sellaro et al., 2015; Steenbergen et al., 2015) participants took part in the experiment only if they met the following criteria: (i) age between 18 and 30 years; (ii) no history of neurological or psychiatric disorders; (iii) no history of substance abuse or dependence; (iv) no history of brain surgery, tumors, or intracranial metal implantation; (v) no chronic or acute medications; (vi) no pregnancy; (vii) no susceptibility to seizures or migraine; (viii) no pacemaker or other implanted devices. Given that after the completion of the study 24 participants reported to have took part to another tVNS study two weeks before the testing, they were not included in this study. From the remaining 80 participants tested (50 females, 30 males, mean age = 20.96 years, range 17–33; mean RMSSD = 40.35, range 12–91), none of the participants experienced tVNS before this study. Before the beginning of the testing session, participants were given a verbal and written description of the procedure and of the usual adverse effects (i.e., itching and tingling skin sensation, skin-reddening, and headache). Participants received no information about the different types of stimulation (active vs. sham) or about the assumptions regarding the study. The experiment conformed to the ethical standards of the Declaration of Helsinki and the protocol was approved by the local ethical committee (Leiden University, Institute for Psychological Research). Written informed consent was obtained from all participants.

### 2.2. Transcutaneous vagus nerve/vagal nerve stimulation (tVNS)

We employed the NEMOS® tVNS neurostimulating device. This device is composed of a stimulation unit and a dedicated ear electrode, which can be worn like an earphone. Following previous published protocols for optimal stimulation (Colzato et al., 2017a, 2017b; Sellaro et al., 2015; Steenbergen et al., 2015), the tVNS® device was programmed to a stimulus intensity of 0.5 mA, delivered with a pulse width of 200–300  $\mu$ s at 25 Hz. Stimulation alternated between on and off periods every 30 s. In the active condition, the stimulation

electrodes were applied to the concha in the left ear. In the sham (placebo) condition, the stimulation electrodes were placed on the center of the left ear lobe. Indeed, the ear lobe has been found to be free of cutaneous vagal innervation (Fallgatter et al., 2003; Peuker and Filler, 2002) and a recent fMRI study found that this sham condition produced no activation in the cortex or brain stem (Kraus et al., 2013).

Further, following safety criteria to avoid cardiac side effects, the stimulation was always applied to the left ear (Cristancho et al., 2011; Nemeroff et al., 2006). Indeed, although efferent fibers of the vagus nerve affect cardiac function, such an impact seems to relate only to the efferent vagal fibers connected to the right ear (Nemeroff et al., 2006). Consistent with this picture, a clinical trial reported no arrhythmic effects of tVNS when applied to the left ear (Kreuzer et al., 2012).

### 2.3. Creativity tasks

#### 2.3.1. Divergent thinking

**2.3.1.1. Alternate Uses Task (AUT).** In the Alternate Uses Task (Guilford, 1967), participants were asked to list as many possible uses for a brick. In this study we considered five scores. (i) Fluency corresponds to the total amount of all responses, (ii) flexibility concerns the number of different categories used, (iii) creativity concerns the general impression of how creative an idea is, (iv) originality regards the novelty and uniqueness of an idea, and (v) usefulness is determined by the effectiveness and feasibility of an idea. Creativity, usefulness, and originality were scored on a scale ranging from 1 to 5. All five AUT measures were scored by two independent raters who were blinded to the type of stimulation (interrater reliability as reflected by Cronbach's alpha = 1.00 [fluency]; 1.00 [flexibility]; 0.82 [creativity]; 0.96 [usefulness]; 0.94 [originality]). Final AUT scores are represented by the means of both ratings.

#### 2.3.2. Convergent thinking

**2.3.2.1. Idea Selection Task (IST).** In the idea selection task, the participant's ability to select the most creative ideas from a pool of available ideas is measured (de Buissonjé et al., 2017). Participants were presented with a societal problem (e.g., "How can children be motivated to eat vegetables and fruit") and with 18 ideas to solve the problem (e.g., "Make the packaging of vegetables and fruits colourful and fun to attract children's attention in the store.", "Apply reverse psychology by telling children that they can't have vegetables and fruits.", and "Integrate more vegetables and fruits into school lunches."). Upon having read all ideas, participants were instructed to select the three most creative ideas from the idea pool. For each of the 18 ideas presented in the idea pool, expert ratings of creativity, originality, effectiveness and feasibility are available, allowing the researchers to assign each of the selected ideas the corresponding expert score. For each of the dimensions, per participant an average score of the three selected ideas was calculated. The higher the average score, the better a participant's selection ability on the specific idea selection dimension.

**2.3.2.2. Remote Associates Test (RAT).** In this task, participants were presented with three unrelated words (such as "bar", "dress", and "glass") and asked to find a common associate ("cocktail"). The version used in this study comprised of 8 previously validated items (Akbari Chermahini et al., 2012). The score in this task corresponds to the number of correct responses.

**2.3.2.3. Creative Problem Solving Task (CPS).** The candle-problem and the two-cord problem were used to assess performance on this task. The candle problem (Duncker, 1945) consists of an illustration of a taper type candle, a box of drawing pins, and a matchbook enclosing a complete set of matches. All three items are positioned on a table positioned in the corner of a room. Performance is assessed by the answer participants give to the question how to attach the candle to the

wall in such a way that, once the candle is lit, the wax does not drip on the table or the floor. For the two-cord problem (Maier, 1930), participants are given an illustration of two ropes hanging from the ceiling of which a person needs to tie the ends with the help of a chair, four sheets of paper, a wrench, and a jar full of nails. For both illustrations, scores were calculated by assigning 1.0 point for correct answers; 0.5 point for partly correct answers, and 0 points for incorrect answers. The final score is the mean of both assignment scores.

## 2.4. Personality questionnaires

### 2.4.1. Quick Big Five Personality Questionnaire

The Quick Big Five Personality Questionnaire (Vermulst and Gerris, 2005) is based on the big five personality markers by Goldberg (1992): conscientiousness, extraversion, agreeableness, emotional stability, and openness to experience. Answers to 30 statements were given on a 5-point Likert scale ranging from 1 (*disagree strongly*) to 5 (*agree strongly*). Participants were asked to describe their current self in an average situation as accurately as possible, based on each of the 30 adjectives.

### 2.4.2. Regulatory Focus Proverb Questionnaire

A short version of the RFQ-proverb (Van Stekelenburg, 2006) consisting of 14 proverbs was administered to assess participants' regulatory focus. Participants were asked to rate on a 7-point Likert scale to what extent the following proverb would be chosen as their personal motto (1 = *not at all*, 7 = *very much*). Seven proverbs were promotion-oriented (e.g. "Nothing ventured, nothing gained") and the other 7 were prevention-oriented (e.g. "Better safe than sorry").

## 2.5. Heart rate variability

Following Colzato and Steenbergen (2017), a Polar H7 elastic chest-belt heart rate monitor manufactured by Polar Electro Oy, Kempele, Finland was used to measure resting state baseline heart rate variability (and therewith vagal tone). This Polar heart rate monitor has been demonstrated to provide data with reliability comparable to that of ambulatory ECG systems (Weippert et al., 2010). The Polar H7 consists of a plastic case containing two ECG electrodes, an electronic processing unit, and a Bluetooth transmitter to send the output to an external device. For optimal conduction, the electrodes of the Polar were moistened before attaching the elastic belt to the chest of the participant. Participants then rested in a seated position for 5 min before initiating a 5 min heart rate measurement while still sitting down. The smartphone application Elite HRV, developed by Elite HRV LLC, was used to transmit and process the output from the Polar heart rate monitor to a Samsung Galaxy Table 4 or Apple iPad Mini. Elite HRV provides the root mean square of the successive differences (RMSSD) as an indicator of HRV alterations and a measure of short-term PNS activity.

## 2.6. Procedure

A single-blind, sham/placebo-controlled, randomized between-group design was used to assess the effect of on-line (i.e., participants performed creativity tasks while being stimulated) tVNS on creativity performance in healthy young volunteers. Following screening for eligibility, all participants took part in a single session and were tested individually. Upon arrival, participants read and signed the informed consent, and were subsequently asked to remain seated and try to relax for 5 min, after which their resting-state HRV was recorded for 5 min to assess baseline vagal tone. After that, the tVNS electrodes were applied and stimulation was started. Fifteen minutes after the onset of stimulation, participants performed the following creativity tasks and personality questionnaires for 25 min: the Alternate Uses Task (Guilford, 1967), Idea Selection Task (de Buissonjé et al., 2017), Remote Associates Test (Akbari Chermahini et al., 2012; Mednick, 1962), Creative

**Table 1**

Mean scores and descriptive statistics for divergent and convergent thinking tasks as a function of stimulation group (Active tVNS vs. Sham).

Outcome	95% CI for mean difference	<i>t</i> (78)	Cohen's <i>d</i> =	Observed Power	Bayes factor <sub>10</sub>
<b>Divergent thinking</b>					
AUT Fluency	1.63, 6.77	3.26** <sup>^</sup>	0.72	0.89	19.70
AUT Flexibility	0.90, 3.65	3.30** <sup>^</sup>	0.74	0.90	22.27
AUT Creativity	0.03, 0.51	2.25*	0.52	0.60	2.01
AUT Usefulness	-0.73, -0.17	-3.20** <sup>^</sup>	0.71	0.88	17.02
AUT Originality	0.13, 0.62	3.07** <sup>^</sup>	0.67	0.85	12.23
<b>Convergent thinking</b>					
RAT	0.11, 1.69	2.27*	0.51	0.61	2.11
CPS	0.05, 0.30	2.73**	0.63	0.77	5.52
IST Creativity	-.07, 0.31	1.27	0.28	0.24	0.47
IST Originality	0.03, 0.46	2.28*	0.50	0.61	2.13
IST Effectiveness	-.09, 0.15	0.44	0.11	0.07	0.25
IST Feasibility	-.13, 0.52	1.20	0.26	0.22	0.43

AUT (Alternative Uses Task); RAT (Remote Associates Test); CPS (Creative Problem Solving Task); IST (Idea Selection Task).

\*  $p < .05$  (significant group difference).

\*\*  $p < .01$  (significant group difference).

<sup>^</sup>  $p < .0045$  (significant group difference after Bonferroni correction .05/11).

Problem Solving Task (Duncker, 1945; Maier, 1930), the Quick Big Five Personality Questionnaire (Vermulst and Gerris, 2005), and the Regulatory Focus Proverb Questionnaire (Van Stekelenburg, 2006). None of the participants reported major complaints or discomfort during or after tVNS. Participants were explicitly asked if they could guess the stimulation received, but none reported to be aware of it (i.e. they indicated that they did not feel any difference between sham and active tVNS).

## 2.7. Statistical analysis

For each participant the scores for each creativity task were calculated. To infer a causal relation between the stimulated vagal nerve and creativity performance, independent *t*-tests were performed to compare the two groups with regard to creativity performance. A significance level of  $p < 0.05$  was adopted for all statistical tests. Bonferroni correction was applied to the creativity outcomes to correct for multiple comparisons, see Table 1. In addition to standard statistical methods, we also analyzed our data within a Bayesian framework, which allows researchers to quantify and compare the relative likelihood of the data under two competing hypotheses, namely, the alternative (H1) and the null (H0) hypothesis, as indexed by the Bayes factor (Morey and Rouder, 2015; Rouder et al., 2012). Analyses were performed using JASP 0.8.2.0 software (available on <https://jasp-stats.org/>). Bayesian *t*-tests (using the default setting) were carried out to quantify evidence for the presence of a tVNS on our divergent and convergent task indicators, see Table 1.

## 3. Results

### 3.1. Participants

Participants were randomly assigned to one of two experimental groups: sham stimulation (N = 40; 16 males; mean age = 20.53, SD = 2.4; mean RMSSD = 39.86, SD = 20.71), or active stimulation (N = 40; 14 males; mean age = 21.40, SD = 3.5; mean RMSSD = 40.84, SD = 20.09). Groups did not differ in terms of age,  $t(78) = 1.29$ ,  $p = .20$ , baseline vagal tone (as assessed with HRV),  $t(78) = 0.21$ ,  $p = .83$ , or gender,  $\chi^2 < 1$ ,  $p = .82$ . Furthermore, no significant group differences were revealed for personality traits, as indexed by the Quick Big Five

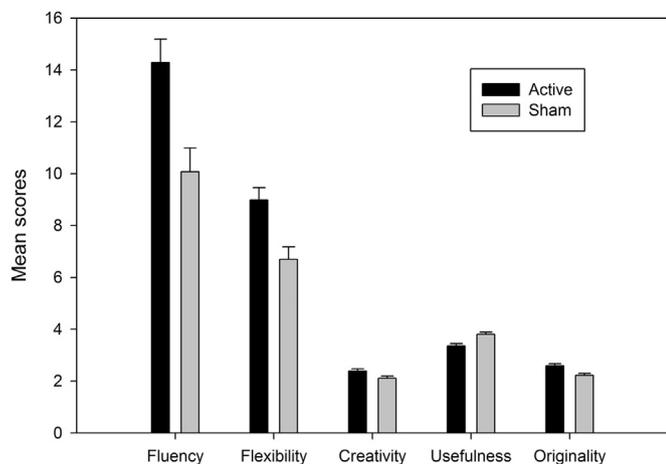


Fig. 1. Mean scores for divergent thinking task (AUT, Alternative Uses Task) as a function of stimulation group (Active tVNS vs. Sham).

Personality Questionnaire,  $t_s \leq -1.558$ ;  $p_s \geq 0.12$ , and the Regulatory Focus Proverb Questionnaire,  $t_s \leq -0.264$ ;  $p_s \geq 0.79$ .

### 3.2. Creative performance

Table 1 summarizes descriptive statistics for the divergent and convergent thinking tasks for the Active tVNS and Sham groups. Active tVNS enhanced creative performance in divergent thinking (as indexed by the Alternative Uses Task (AUT), except for the usefulness score), see Fig. 1, but not in convergent thinking tasks (as indexed by the Remote Associates Test (RAT), Creative Problem Solving Task (CPS) and the Idea Selection Task (IST)), see Fig. 2.

#### 3.2.1. Divergent thinking

Fluency scores were significantly higher in the active ( $M = 14.28$ ,  $SD = 6.06$ ) as compared to sham ( $M = 10.08$ ,  $SD = 5.46$ ) conditions, demonstrating that participants in the active tVNS condition were able to generate more AUT answers than participants in the sham condition. With regard to flexibility scores, participants in the active condition generated answers in significantly more different categories ( $M = 8.98$ ,  $SD = 3.09$ ) than participants in the sham condition ( $M = 6.7$ ,  $SD = 3.07$ ). Regarding creativity scores, the between-group difference was not significant, indicating that participants in the active condition did not generate more creative ideas ( $M = 2.39$ ,  $SD = 0.5$ ) than participants receiving sham stimulation ( $M = 2.11$ ,  $SD = 0.57$ ). Regarding originality, participants in the active condition ( $M = 2.59$ ,  $SD = 0.62$ ) scored significantly higher than participants in the sham condition ( $M$

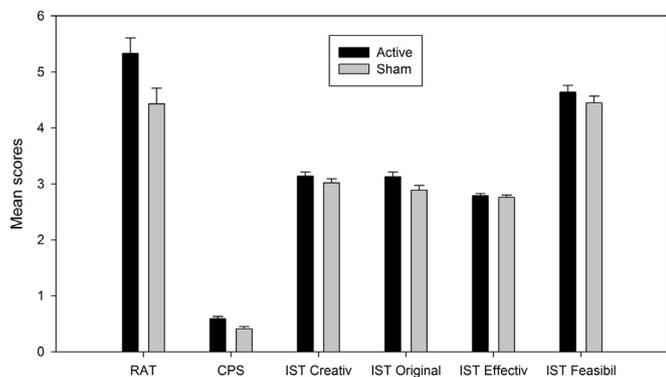


Fig. 2. Mean scores for convergent thinking tasks (RAT, Remote Associates Test; CPS, Creative Problem Solving Task; IST, Idea Selection Task (Creativ, Creativity; Original, Originality; Effectiv, Effectiveness; Feasibil, Feasibility)) as a function of stimulation group (Active tVNS vs. Sham).

$= 2.22$ ,  $SD = 0.55$ ). In contrast, with regard to usefulness, participants ideas in the active condition were rated significantly lower ( $M = 3.35$ ,  $SD = 0.62$ ) than those in the sham condition ( $M = 3.80$ ,  $SD = 0.64$ ).

#### 3.2.2. Convergent thinking

After correcting for multiple comparisons the statistical analysis revealed no significant effect of tVNS on the three convergent thinking tasks (RAT, CPS and IST). Along the same lines the analysis within the Bayesian framework found no evidence in supporting  $H_0$  or  $H_1$ . This means that with respect to convergent thinking, our data are inconclusive in providing an account for the effect of tVNS on convergent thinking, see Table 1 and Fig. 2.

## 4. Discussion

Our findings show that tVNS enhances creativity in selective ways. Indeed, when actively stimulated, compared to sham, participants demonstrated increased performance in terms of divergent thinking. However, analysis within the Bayesian framework found our data to be inconclusive in providing an account for the effect of tVNS on convergent thinking. The observation that tVNS promotes performance on well-established diagnostic indexes of creative potential (Duncker, 1945; Guilford, 1967; Maier, 1930; Mednick, 1962) provides considerable support for the idea of a crucial role of the vagus nerve in creativity, at least for divergent thinking.

First, patients suffering from pathologies associated with dysfunction of the vagus nerve, such as autism (Cheshire, 2012), also demonstrate worse performance in creativity tasks (Craig and Baron-Cohen, 1999). Therefore, the potential of tVNS to enhance creativity might be helpful not only for healthy individuals, as demonstrated in the current study, but perhaps also for people suffering from autism by promoting cognitive flexibility – an important creative thinking style (Ritter et al., 2012).

Second, even though we did not measure GABA levels directly in this study, we speculate that the positive effects of tVNS on divergent thinking might be attributed to a transient increase of GABA concentration. Indeed, animal and clinical studies revealed that VNS enhances levels of GABA (Ben-Menachem et al., 1995; Marrosu et al., 2003) in the brain. tVNS has been demonstrated to enhance intracortical inhibition in healthy humans (Capone et al., 2015), suggesting that tVNS might modulate and likely augment behavioral performance related to the GABAergic systems. Increased GABA concentration seems to facilitate the ability to select among competing options under conditions of high selection demand, a crucial skill to carry out creative processes in divergent thinking. Via a modulation of intracortical inhibition and cortical signal-to-noise ratio, a higher GABA concentration is prone to weaken competition between behavioral alternatives and hence promotes the selection of the correct response while withholding an inappropriate alternative in high selection demand (i.e., divergent thinking) but not in low selection demand (i.e., convergent thinking; de la Vega et al., 2014; Munakata et al., 2011).

Given the causal nature of the stimulation technique used in the current study, our findings provide a first direct demonstration for a causal link between the vagus nerve and creativity. We used a between-participants design to avoid possible practice effects on task performance. Given that our groups were matched in terms of gender, age, personality traits and baseline HRV (i.e. a marker of vagal tone) and that none of the participants reported major complaints or discomfort during or after tVNS and sham condition and that none could guess the stimulation received (i.e. they indicated that they did not feel any difference between sham and active tVNS), we can rule out an explanation of our results in those terms.

Some limitations and considerations concerning these results need to be discussed here. First, we did not verify tVNS effectiveness in increasing vagal activity. Therefore, it would be optimal for future studies to include such an assessment, for instance, by measuring vagus-evoked potentials (Fallgatter et al., 2003). Second, future studies should

include questionnaire such as the Creative Achievement Questionnaire (Carson et al., 2005) as a control measure to ensure groups do not differ in their baseline creativity ability. Third, follow-up studies should include a control task not related to GABAergic function in order to conclude without doubt that tVNS enhanced creativity via GABA involvement.

To conclude, our observation that the vagus nerve plays a causal role in creativity may stimulate new research to further extend our understanding of the specific role of the vagus nerve in the processing of divergent thinking, and supports the idea that tVNS is a promising non-invasive brain stimulation technique for modulating mental processes in healthy humans (van Leusden et al., 2015).

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