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## Abstract

Transcutaneous vagus nerve stimulation (tVNS) has been shown to promote inferences of emotional states based on eye-related information provided by facial expressions of emotions. Eye gaze direction can influence the allocation of attentional sources when processing facial emotional stimuli. Here we sought for further evidence indicating whether tVNS effects would be specific to emotional expressions or to gaze - both socially relevant stimuli - and whether they reflect the enhancement of attention. In two separate sessions receiving either active or sham tVNS, forty-three healthy young volunteers completed a Rapid Serial Visual Presentation task in which participants identified the gender of a target face (T1) with direct (salient social cue) or averted gaze (subtler social cue) with different emotional expressions or a neutral expression, and then judged the orientation of a landscape (T2) that appeared at different temporal lags after T1. Active tVNS, compared to sham stimulation, enhanced conditional T2 accuracy for both neutral and emotional faces and independently of the temporal lag, but only when gaze was directed at the participant. This suggests that tVNS modulates attention to a direct gaze (salient social cue) irrespective of the expressed emotion. We interpret that the effects of tVNS seem to reflect enhanced perception of gaze direction, which in turn attracts attention, making the observer more sensitive and increasing the impact of the socially relevant facial cue. We conclude that tVNS is a promising technique for enhancing social information processing in healthy humans.

*Keywords*: transcutaneous vagus nerve stimulation, perception, facial emotion recognition, gaze direction, social cues

## 1. Introduction

Other's emotions are important social cues, which provide us with ample information on how to respond in social situations. Without the ability to recognize and react to other's emotions, successful social interactions would not be possible (Frijda and Mesquita, 2004; Frith, 2009). An evolutionary perspective on emotion recognition has suggested that the vagus nerve is the key phylogenetic element underlying social engagement with the environment (Porges, 2007, 2003, 2001). The vagus nerve is the tenth cranial nerve and controls, among other functions, how humans are nodding their head and how they allocate their gaze towards other people, in fact modulating facial expressions, listening, and vocalizing (Porges, 2001; Stifter et al., 1989; Thayer and Lane, 2000; Yang and Immordino-Yang, 2017); all functions known to regulate social engagement. Following Porges' polyvagal theory, mammals (in contrast to other species) mature a ventral, myelinated, branch of the vagus. Whereas energy conservation is related to the primitive, dorsal vagal branch, the activation of the later developed ventral vagal branch has been connected to the ability to adapt and regulate complex behaviors such as attention, emotion, and communication (Porges, 2007, 2003, 2001). A number of studies confirm that activity of the vagus is associated with social cognitive abilities like empathy, recognizing and regulating emotions (Thayer and Lane, 2000), as well as prosocial traits (Kogan et al., 2014), cooperation (Beffara et al., 2016), and other forms of altruistic prosocial behaviors (Bornemann et al., 2016).

The vagus nerve is composed of around 75% afferent and 25% efferent fibers, which defines the vagus as an important conductor of sensitive and somatic signals (Berthoud and Neuhuber, 2000). One way to study the causal role of the afferent vagus in cognitive and emotional functions is transcutaneous vagus nerve stimulation (tVNS), a novel and noninvasive brain stimulation technique which imaging studies have shown to activate the afferent vagus (Badran et al., 2018; Frangos et al., 2015; Yakunina et al., 2017) and the insula

(Dietrich et al., 2008; Kraus et al., 2007), a crucial neural structure for emotion recognition (Adolphs, 2002). For safety reasons – to not interfere with cardiac innervation – tVNS is provided to the left afferent branch of the vagus towards the brain (Van Leusden et al., 2015). The left and right vagus nerve innervate the heart differently (Ardell and Randall, 1986) and due to the low intensity of tVNS, stimulating the afferent vagus is not a necessary requirement for efferent parasympathetic effects.

Several behavioral studies have demonstrated the causal role of the vagus nerve in emotion recognition by applying tVNS to the afferent branch of the vagus (Colzato et al., 2017; Sellaro et al., 2018). Although the evidence for tVNS-effects on the processing of socially relevant stimuli is still emerging, there is consistent support for the role of the vagus in emotion recognition and social functioning (Geisler et al., 2013; Kemp et al., 2012; Kok and Fredrickson, 2010; Quintana et al., 2012). Therefore, the use of tVNS allows us to provide further evidence on the causal role of the vagus in the mechanisms of social perception.

Colzato et al. (2017) showed that tVNS promoted the ability of inferring people's emotional state based on images of the eye region - at least if the emotional state was well-discriminable. In other words, tVNS-induced increase of afferent activity of the ventral vagal complex enhanced the ability to recognize salient social cues. People's fight/flight response strategies are a sympathetic response likely to depend on salient and recognizable social cues, and the homeostatic adjustment between sympathetic and parasympathetic responses relies heavily on the vagus nerve (Damasio et al., 1991). Taken together, the findings converge and support the role of the vagus nerve in regulating social engagement via emotion recognition (Porges, 2007, 2003, 2001).

However, while the findings of Colzato et al. (2017) do suggest an interesting connection between vagal activity and the processing of socially relevant stimuli, the particular design that was used still leaves open different interpretations regarding the nature of this connection. For one, the stimulus set was only comprised of faces expressing specific emotions, so it remains unclear whether tVNS might also enhance the processing of faces not expressing an emotion. For another, the stimulus faces had varying gaze directions, straight towards the participant or averted to either the right or the left. Because in the results from Colzato et al. (2017) gaze was not systematically manipulated, this does not allow to disentangle the impact of the expressed emotion on the one hand, and the social relevance depicted by the gaze on the other. Gaze direction is a critical component of facial processing and emotion recognition (Hamilton, 2016; Kleinke, 1986) and it has been shown that the direction of the gaze influences the allocation of attentional sources when processing facial expressions (Palermo and Rhodes, 2007; Ricciardelli et al., 2012). Finally, it remains unclear whether the tVNS-induced enhancement was attentional in nature. Although not directly manipulated, given that the task required perceptual identification, increased vagal activation might have improved performance by speeding up the perceptual interpretation of the stimuli. However, there is ample evidence that affective stimuli also attract visual attention (Schwabe et al., 2011; Vuilleumier and Schwartz, 2001), which means that performance might also have benefited from vagus-induced increases of attentional resources on processing the affective stimuli.

The main goal of the current study was twofold: first, to disentangle the impact of gaze and emotional expression, and so to test whether tVNS impacts the processing of faces expressing particular emotions, or the processing of faces of particular social relevance to the observer (as manipulated by comparing direct and averted gaze) or both, we varied these two factors orthogonally. And second, we tried to assess the degree to which facial stimuli make use of attentional resources by measuring their after-effects on the processing of a subsequent non-facial stimulus. To achieve our goal, we employed a Rapid Serial Visual Presentation

(RSVP) paradigm, a well-established tool to assess the allocation of attention over time, allowing us to investigate how tVNS impacts attentional deployments. If two visual targets appear close in time in a RSVP task, the first target (T1) is typically easy to report, but report of the second target (T2) is dramatically impaired. The shorter the temporal distance between T1 and T2 (the so-called lag), the greater the impairment - a phenomenon known as Attentional Blink (AB; Raymond et al., 1992).

Most theories explain the AB by assuming that processing and consolidating T1 uses so many attentional resources that too little is left for processing and consolidating T2 if it appears too early (Chun and Potter, 1995; Jolicœur and Dell'Acqua, 1998; Vogel et al., 1998). Indeed, manipulating the amount of attentional resources needed to process T1 has been shown to systematically impact the size of the AB (Jackson and Raymond, 2006; Müsch et al., 2012), and individuals that tend to allocate more attentional resources to the processing of T1 exhibit a stronger AB (Colzato et al., 2008a, 2007; Dale and Arnell, 2010; Martens et al., 2006; Martens and Valchev, 2009; Shapiro et al., 2006). Of particular importance for our purposes, the affective salience of the stimuli has been demonstrated to systematically affect the size of the AB (de Jong et al., 2009; Milders et al., 2011; Schwabe et al., 2011) and the AB is shown to be sensitive to the emotional content/meaning (Schwabe and Wolf, 2010, Schwabe et al., 2011) and to gaze direction of T1 (Ricciardelli et al., 2016, 2012). More specifically, when emotional expressions are manipulated at both T1 and T2, a neutral T1 indeed attenuates the AB for emotional T2s but an aversive T1 prolongs the AB (Schwabe and Wolf, 2010, Schwabe et al., 2011). However, it must be noted that the emotional stimuli presented in T1 were words in the studies of Schwabe and Wolf, (2010) and Schwabe et al., (2011) - with emotional vs. neutral meaning - while the stimuli used in Ricciardelli et al., (2016, 2012) were pictures of faces. Although the level of processing is across studies is different – more semantic for words (Schwabe et al., 2011; Schwabe and Wolf, 2010) and more visual/perceptual for pictures (Ricciardelli et al., 2016, 2012) - what both groups of results have in common is the emotional meaning of the stimuli and its social relevance. The finding that an emotional T1 eliminates the blink-reducing effect of an emotional T2 suggests that emotionality of T1 is a critical factor in the emotional modulation of the AB (Schwabe and Wolf, 2010). Ricciardelli et al. (2016, 2012) reported that even neutral T2s were found to escape the AB (i.e., showed equal, unimpaired accuracy at all lags), if T1 was an angry face with a gaze that was directed at the participant, but not if the gaze was averted. The authors attributed this effect pattern to the biological significance of T1: due to the arguably stronger bottom-up salience of angry faces with direct gaze, less top-down attention was necessary to process the T1, which left more capacity to process T2 even at short lags.

At the physiological level, evidence suggests that norepinephrine (NE) and cortisol have a regulatory role in modulating attention to emotional stimuli (De Martino et al., 2008; Schwabe and Wolf, 2010) and both markers of noradrenergic function have been shown to be affected by tVNS (Ventura-Bort et al., 2018; Warren et al., 2019). Accordingly, tVNS-induced changes in the allocation of attentional resources devoted to processing T1 would be expected to affect the size of the AB (i.e., should impair T2 processing more for short than for longer temporal distances between T1 and T2), while possible changes of T1 perception should affect T2 processing independently of the temporal distance.

In the current study, we used an emotional RSVP paradigm in which participants were explicitly asked to first discriminate the gender of the target face (T1) with direct (salient social cue) or averted gaze (subtler social cue) when its expression was angry, fearful or neutral, and then to judge the orientation of a landscape (T2) (Ricciardelli et al., 2012; Ricciardelli et al., 2016) that was rotated either clockwise or anticlockwise. Gaze direction and emotional expressions were task-irrelevant to control for the spontaneous allocation of attention in processing the facial expression. Formally, our study consisted of the crossing of four independent variables: the emotion that the facial stimuli used as T1 were displaying (angry vs. fearful vs. neutral), the gaze direction of these faces (averted vs. direct), the temporal distance (lag) between T1 and T2 (2 vs. 4 vs. 7), and tVNS stimulation (active vs. sham). We used the same experimental paradigm as in the third experiment described in Ricciardelli et al., (2016), adding tVNS as the main factor of interest for the current study. Because it was not part of our main hypothesis, we had no specific predictions regarding the findings observed in Ricciardelli et al., (2016) and, therefore, we expected to find similar results.

To address our predicted effect of tVNS, statistical tests were guided by the three questions underlying the present study: First, we were interested to see whether tVNS-induced changes in performance, as compared to the sham condition, would differ for angry or fearful versus neutral faces, which would indicate that the effect is specific to emotional stimuli. Second, we were interested in the role of social relevance, which would suggest that tVNS effects would be restricted to stimuli showing direct gaze. And, third, we were interested to see whether tVNS would target attention to social stimuli that are particularly relevant for the observer (i.e., direct gaze), which should lead to an interaction involving lag, or whether, if effects are independent of lag, tVNS could be modulating mechanism of perception.

## 2. Material and Methods

### 2.1. Participants

An a-priori sample size calculation was performed using G*Power 3.1.7 (Faul et al., 2007) to estimate the approximate number of participants required, considering 0.01 as criterion for statistical significance (the traditional alpha = 0.05 slightly corrected for multiple testing) and a desired power of 0.90 in a within-subjects design with 2 groups and measurements. Based on prior results (Colzato et al., 2017) evidencing the effect of tVNS on emotion recognition, medium effect sizes (r≈0.20) were anticipated for the current study. Results of the sample size calculation estimated that the total number of participants needed was 40. Although our planned number of participants was 40, three additional participants were tested considering the possibility to exclude potential outliers. All the participants tested provided valid useful data.

As a result, 43 Leiden University undergraduate students (39 females/4 males, $M_{age}$ = 20.00, $SD_{age}$ = 2.34, range 18–30) took part in the study. Participants were enrolled via the university online recruiting system as well as via flyers distributed through the campus advertising the opportunity to participate in a two sessions study on the effects of tVNS on social decision-making for course credit compensation. All participants were screened individually by the same lab-assistant using a screening questionnaire based on the MINI International Neuropsychiatric Interview (M.I.N.I.; Sheehan et al., 1998), which is a short, structured interview to screen for several psychiatric disorders and drug use, often used in clinical and pharmacological research (Colzato et al., 2017, 2008a).

Following previous published protocols (Beste et al., 2016; Colzato et al., 2017; Sellaro et al., 2018, 2015; Steenbergen et al., 2015) the following inclusion criteria were considered for participation: (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. All participants were naïve to tVNS. Prior to the testing session, they received verbal and written explanation of the procedure and of the typical adverse effects (i.e., itching and tingling skin sensation, skin-reddening, and headache). To avoid expectation effects, no information was provided about the different types of stimulation (active vs. sham) or about the hypotheses concerning the experiment. In the first session, written informed consent was obtained from all participants prior to the start of the experiment. The study conformed to the ethical standards of the Declaration of Helsinki (World Health Organisation, 2013) and the protocol was approved by the local ethical committee (Leiden University, Institute for Psychological Research) under the reference CEP17-1220427.

### 2.2. Apparatus and procedure

#### 2.2.1. **Design**

A single-blind, sham/placebo-controlled, randomized cross-over within-subjects design with counterbalanced order of conditions was used to assess the effect of online (stimulation overlapping with the performance of the critical task) tVNS on RSVP performance in healthy young volunteers. All participants took part in two sessions (active vs. sham) separated at least by 7 days and were always tested individually. In both sessions, following previous protocols (Beste et al., 2016; Colzato et al., 2017; Sellaro et al., 2018; Steenbergen et al., 2015), stimulation was applied for 15 minutes before the start of the tasks until finishing the tasks. Consistent with Sellaro et al. (2018), during the 15 minute waiting period, participants filled out a number of personality questionnaires to infer mood (i.e. using the positive and negative affect scale, PANAS; Watson et al., 1988), interpersonal reactivity (i.e. using the Interpersonal Reactivity Index, IRI; (Davis, 1983, 1980), empathy (i.e. using the Empathy Quotient, EQ; Baron-Cohen and Wheelwright, 2004), autistic traits (i.e. using the Autistic Quotient, AQ; Baron-Cohen et al., 2001) and alexithymia (i.e. using the Bermond-Vorst Alexithymia Questionnaire, BVAQ; Vorst and Bermond, 2001). Whereas the PANAS was filled out in both sessions, the other questionnaires are assumed to reflect trait measures and were filled out only once.

After the 15-minute waiting period, participants completed the RSVP and two other tasks to measure emotion recognition, which are not reported in this paper. The order of the tasks was counterbalanced but kept constant across the sessions. After the cognitive tasks, the stimulation was terminated with the total experimental session lasting approximately 60 minutes. After completion of each session, participants were asked to complete a tVNS adverse effects questionnaire requiring them to rate, on a 5-point (1–5) scale, how much they experienced (1) headache, (2) neck pain, (3) nausea, (4) muscle contraction in face and/or neck, (5) stinging sensation under the electrodes, (6) burning sensation under the electrodes, (7) uncomfortable (generic) feelings, and (8) other sensations and/or adverse effects. At the end of the second session, participants were debriefed and compensated for their participation.

#### 2.2.2. **Questionnaires**

The *IRI* is a self-report questionnaire that assesses perceived individual differences in the tendency to be empathetic. It consists of 28 Likert-type items on a response scale with five alternatives ranging from 0 (does not describe me well) to 4 (describes me very well). It comprises four subscales assessing affective (empathic concern and personal distress) and cognitive (fantasy and perspective taking) components of empathy (Davis, 1983, 1980). The *EQ* is a self-report questionnaire designed to assess empathy in normal adult populations (Baron-Cohen and Wheelwright, 2004). It comprises 60 questions (20 items are filler questions) that, taken together, provide an overall measure of cognitive perspective taking, affective empathy, and social skills (range 0–80, higher scores indicating more empathy). The *AQ* is a self-report questionnaire aimed at detecting the presence of autistic traits in normal adult populations (Baron-Cohen et al., 2001). The questionnaire is made of 50 items that, taken together, provide a measure of the degree to which an adult with normal intelligence has traits associated with the autistic spectrum (range 0-50, higher scores indicating autistic-like behavior). The *BVAQ-40* (Vorst and Bermond, 2001) is a questionnaire to measure difficulties in one’s ability to identify own emotions (i.e. alexithymia). It consists of 40 items.

Participants rate, on a scale from 1 (completely) to 5 (not at all), to what extent a certain statement applies to them. Importantly, higher scores indicate a more difficulty in identifying one's own emotions. The PANAS is composed by two 10-item mood scales (i.e. 20 in total), which measure positive and negative affect. Using a 5-point scale, participants are required to rate how they experience each of the 20 presented emotions at this moment, using a 5-point scale: 1 'very slightly or not at all', 2 'a little', 3 'moderately', 4 'quite a bit' and 5 'very much'. A positive and a negative mood score is achieved by adding the respective items, both ranging from 10 to 50.

### 2.2.3. transcutaneous Vagus Nerve Stimulation (tVNS)

We used the NEMOS® tVNS neurostimulating device consisting of two titan electrodes attached to a gel frame and connected to a wired neurostimulating device (CM02, Cerbomed, Erlangen, Germany). Following previous protocols (Beste et al., 2016; Colzato et al., 2017; Sellaro et al., 2018; Steenbergen et al., 2015), this device was applied to stimulate vagal afferents, located at the cymba concha, of the left ear, to avoid possible arrhythmic effects given that vagal fibers to the heart originate from the right site (Nemeroff et al., 2006). The tVNS® device was programmed to a stimulus intensity at 0.5 mA, delivered with a pulse width of 200–300 μs at 25 Hz and stimulation alternated between on and off periods every 30 s. In the sham (placebo) condition, the stimulation electrodes were placed on the center of the left ear lobe which is not innervated by vagal afferents (Fallgatter et al., 2003; Peuker and Filler, 2002), and is known to produce no activation in the cortex and brainstem (Frangos et al., 2015; Yakunina et al., 2017).

#### 2.2.4. **RSVP**

We used the same materials employed in experiment 3 of the study by Ricciardelli et al. (2016), with stimuli being grayscale photographs of four different Caucasian faces and 14 landscapes. The landscape photographs were chosen from open-access internet images. Face stimuli were picked from the Karolinska Directed Emotional Faces set (KDEF; Lundqvist et al., 1998) which portrayed unfamiliar images of two women and two men displaying a neutral, angry or fearful facial expression with direct or averted gaze pointing to the left or right, see Figure 1A. The experiment consisted of 384 trials divided in two blocks of 192 trials one for angry vs. neutral and the other for scared vs. neutral faces. Trials consisted of an RSVP of 16 images, each displayed at the center of the computer screen for 135 ms. All images were upright landscape photos except for two images consisting of angry, fearful, neutral faces (T1) with direct or averted (50% direct gaze, 25% gaze averted right, and 25% gaze averted left, respectively) gaze direction and the rotated (90 degrees to the right or to the left) landscape target (T2) stimulus. Thus, trial types across gaze and facial emotion were equiprobable.

- Please, insert Figure 1 here -

T2 was presented one, three or six items after T1 (Lag 2, 4, 7, respectively; see Figure 1B for the sequence of events of one trial and an example of a Lag 2 trial). Hence, stimulus onset asynchronies (SOAs) between T1 and T2 were 270 ms (Lag2), 540 ms (Lag4), and 945 ms (Lag7). Participants commenced each trial by pressing the space bar. At the end of the trial, a first question appeared on the screen asking participants to categorize the gender of the T1 face by pressing the F-key, labelled with a tag ‘‘F’’ (female) and the K-key, labelled with a tag ‘‘M’’ (male). A second question was then displayed demanding participants to react to the orientation of the T2 landscape by pressing the M-key, labelled with a tag ‘‘O’’ (clockwise) and the V-key, labelled with a tag ''A'' (anticlockwise). Participants were permitted to take a short break between the blocks.

### 2.3. Statistical analyses

Statistical analyses were performed using SPSS software version 25.0 (IBM, Armonk, NY, USA). To examine whether active tVNS, as compared to sham (placebo) stimulation, enhanced the ability to decode salient social cues, 2 (tVNS stimulation: active vs. sham) × 3 (emotional facial expressions: angry vs. fearful vs. neutral) × 2 (gaze direction: averted vs. direct) × 3 (lag: 2 vs. 4 vs. 7) separate repeated-measures analysis of variance (rmANOVA) were carried out with T1 and T2 accuracy as dependent variables, even though only the T2 analyses were relevant for testing our predictions. As usual, T2 accuracy was based only on those trials in which T1 was correctly reported (T2|T1).

A significance level of $p < 0.05$ was adopted for statistical tests. In case of violation of the sphericity assumption, Greenhouse–Geisser correction was applied and corrected *p* values were reported. Post-hoc paired samples *t*-tests were performed to clarify mean differences in case of significant interactions, and Bonferroni correction was applied to control for multiple testing. Hedges's $g_{av}$ effect sizes measures for paired-sample *t*-tests are calculated following Lakens (2013), and reported in addition to within-subjects confidence intervals.

## 3. Results

### 3.1. Personality questionnaires

Participants' scores on the personality questionnaires were comparable to previous reports (Sellaro et al., 2018), with the average measures of empathy [$IRI_{Total\ score}$ (*M* = 73.12, *SD* = 12.13), $IRI_{Perspective\ taking}$ (*M* = 20.30, *SD* = 4.02), $IRI_{Fantasy\ scale}$ (*M* = 18.81, *SD* = 5.80), $IRI_{Empathic\ concern}$ (*M* = 21.12, *SD* = 4.70), $IRI_{Personal\ distress}$ (*M* = 12.88, *SD* = 3.62), EQ (*M* =

49.26, *SD* = 10.71)], autistic traits [AQ (*M* = 17.26, *SD* = 6.83)] and alexithymia [$BVAQ_{Total\ score}$ (*M* = 89.58, *SD* = 18.44), $BVAQ_{Affective\ dimension}$ (*M* = 35.44, *SD* = 7.87), $BVAQ_{Cognitive\ dimension}$ (*M* = 54.14, *SD* = 15.11)] falling into the normal range.

### 3.2. Mood and after-tVNS effects

A significant difference in positive ($t(42) = 2.05$, $p = 0.05$, 95% CI [0.03 3.37], Hedges's $g_{av} = 0.22$) and negative mood ($t(42) = 2.03$, $p = 0.05$, 95% CI [0.00 2.78], Hedges's $g_{av} = 0.30$) was observed between active and sham tVNS sessions. In relation to the after-effects, participants experienced more muscle contractions ($t(42) = 2.32$, $p = 0.02$, 95% CI [0.04 0.61], Hedges's $g_{av} = 0.37$) and burning feelings ($t(42) = 2.07$, $p = 0.04$, 95% CI [0.01 0.92], Hedges's $g_{av} = 0.40$) in the active compared to the sham stimulation. No other comparisons reached the level of significance (all $p_s \geq 0.05$). (see Table 1).

| | Active tVNS | Sham tVNS |
|---|---|---|
| Positive affect* | 25.88 ± 7.12 | 27.58 ± 8.03 |
| Negative affect* | 15.02 ± 5.52 | 13.63 ± 3.66 |
| Headache | 1.72 ± 1.03 | 1.70 ± 0.94 |
| Neck pain | 1.65 ± 0.99 | 1.62 ± 1.02 |
| Nausea | 1.25 ± 0.72 | 1.25 ± 0.62 |
| Muscle contractions* | 1.83 ± 0.97 | 1.51 ± 0.80 |
| Stinging sensation | 2.62 ± 1.38 | 2.65 ± 1.49 |
| Burning sensation* | 2.25 ± 1.19 | 1.79 ± 1.14 |
| Generic uncomfortable feeling | 2.21 ± 1.16 | 2.09 ± 1.25 |
| Accuracy reporting stimulation type | 0.51 ± 0.50 | 0.39 ± 0.49 |

**Table 1.** Mean ± standard deviations of self-reported positive and negative affect and after tVNS effects as observed in both sessions. After effects rating ranged on a scale from 1 (not at all) to 5 (very much) $^*p < 0.05$.

### 3.3. RSVP

T1 accuracy independent of T2 performance (T1 unconditional) is shown in Figure 2 and descriptive data are summarize in Table 2. rmANOVA on T1 accuracy including tVNS stimulation (active, sham), emotional facial expression (angry, fearful, neutral), gaze direction (averted, direct) and Lag (2, 4, 7) as within-subjects factors, revealed a non-significant four-way interaction between the factors ($F(2.97, 124.74) = 1.86$, $p = 0.14$, $\eta^2_p = 0.04$), as well as non-significant three-way (all *p*s > 0.05), two-way interactions (all *p*s > 0.17), or main effects (all *p*s > 0.13). Together, results suggest that tVNS did not modulate T1 performance.

- Please, insert Figure 2 here -

T2 accuracy rates were calculated only for T1 correct trials (96%) and submitted to within-subjects rmANOVA like the procedure used for accuracy in T1. Descriptive data of the different conditions are shown in Table 2. Analyses revealed six different sources of variance. First, replicating previous findings (Ricciardelli et al., 2016, 2012) and numerous other AB tasks, we observed significant main effect of Lag ($F(1.56, 65.67) = 38.40$, $p < 0.01$, $\eta^2_p = 0.48$). As usual, accuracy was significantly lower for Lag2 ($M = 0.76$, $SD = 0.19$) than for Lag4 ($M = 0.80$, $SD = 0.19$) and Lag7 ($M = 0.82$, $SD = 0.19$), indicating the presence of a robust AB. Post hoc paired-samples *t*-tests, Bonferroni corrected for multiple comparisons, showed significant differences between Lags 2 and 4 ($t(42) = 5.47$, $p < 0.01$, 95% CI [0.02 0.05], Hedges's $g_{av} = 0.20$), between Lags 2 and 7 ($t(42) = 7.35$, $p < 0.01$, 95% CI [0.04 0.07], Hedges's $g_{av}$ = 0.28), and between Lags 4 and 7 ($t(42)$ =3.84, $p$ < 0.01, 95% CI [0.01 0.02], Hedges's $g_{av}$ = 0.09).

| | **Active tVNS** | | | **Sham tVNS** | | |
|---|---|---|---|---|---|---|
| | Lag2 | Lag4 | Lag7 | Lag2 | Lag4 | Lag7 |
| T1 | | | | | | |
| *Averted gaze* | | | | | | |
| Angry | 0.96±0.05 | 0.96±0.07 | 0.97±0.05 | 0.97±0.06 | 0.95±0.10 | 0.96±0.07 |
| Neutral | 0.97±0.06 | 0.96±0.06 | 0.96±0.06 | 0.95±0.08 | 0.96±0.09 | 0.96±0.07 |
| Fearful | 0.96±0.06 | 0.95±0.06 | 0.95±0.07 | 0.94±0.09 | 0.96±0.09 | 0.96±0.09 |
| *Direct gaze* | | | | | | |
| Angry | 0.96±0.05 | 0.96±0.06 | 0.96±0.06 | 0.97±0.06 | 0.96±0.08 | 0.97±0.05 |
| Neutral | 0.96±0.05 | 0.96±0.06 | 0.96±0.05 | 0.95±0.07 | 0.96±0.07 | 0.95±0.08 |
| Fearful | 0.96±0.08 | 0.95±0.07 | 0.97±0.06 | 0.96±0.10 | 0.97±0.09 | 0.95±0.09 |
| T2\|T1 | | | | | | |
| *Averted gaze* | | | | | | |
| Angry | 0.74±0.23 | 0.81±0.20 | 0.82±0.20 | 0.73±0.19 | 0.77±0.23 | 0.81±0.21 |
| Neutral | 0.75±0.21 | 0.81±0.18 | 0.81±0.20 | 0.75±0.20 | 0.79±0.20 | 0.81±0.21 |
| Fearful | 0.78±0.21 | 0.80±0.21 | 0.85±0.20 | 0.76±0.24 | 0.82±0.21 | 0.81±0.23 |
| *Direct gaze* | | | | | | |
| Angry | 0.80±0.20 | 0.82±0.19 | 0.82±0.20 | 0.74±0.22 | 0.79±0.22 | 0.78±0.20 |
| Neutral | 0.79±0.21 | 0.81±0.20 | 0.83±0.19 | 0.75±0.21 | 0.78±0.20 | 0.81±0.21 |
| Fearful | 0.80±0.21 | 0.83±0.20 | 0.85±0.21 | 0.79±0.23 | 0.79±0.24 | 0.82±0.22 |

**Table 2.** Mean ± standard deviations of T2 accuracy scores given T1 in RSVP task as a function of tVNS stimulation, lag, gaze direction and emotional expression.

Second, a main effect of facial expressions was observed ($F$(1.58, 66.30) = 6.10, $p$ < 0.01, $\eta^2_p$ = 0.13). Accuracy was significantly higher for the fearful ($M$ = 0.81, $SD$ = 0.20) than for the angry ($M$ = 0.79, $SD$ = 0.18) and the neutral facial expression ($M$ = 0.79, $SD$ = 0.19). Corrected for multiple comparisons, post hoc paired-samples $t$-tests showed significant differences between fearful and angry ($t$(42) =2.65, $p$ = 0.01, 95% CI [0.00 0.03], Hedges's $g_{av}$ = 0.10), and between fearful and neutral faces ($t$(42) =3.23, $p$ < 0.01, 95% CI [0.01 0.03], Hedges's $g_{av}$ = 0.08), but no difference between angry and neutral faces ($t$(42) =0.64, $p$ = 0.52, 95% CI [-0.01 0.01], Hedges's $g_{av}$ = 0.02). Third, a main effect of gaze direction was observed ($F$(1,42) = 7.09, $p$ = 0.01, $\eta^2_p$ = 0.14). Accuracy was significantly higher for the direct ($M$ = 0.80, $SD$ = 0.19) than for the averted gaze ($M$ = 0.79, $SD$ = 0.19).

Similar to Ricciardelli et al., (2016) in experiment 3, the gaze effect interacted with lag ($F$(1.82, 76.79) = 3.81, $p$ = 0.03, $\eta^2_p$ = 0.08), and post hoc paired-sample $t$-test Bonferroni corrected showed that, in Lag2, accuracy in the direct gaze ($M$ = 0.77, $SD$ = 0.19) was higher than for the averted gaze ($M$ = 0.75, $SD$ = 0.19) ($t$(42) =3.89, $p$ < 0.01, 95% CI [0.01 0.04], Hedges's $g_{av}$ = 0.13). However, while Ricciardelli et al., (2016) found higher accuracy for the averted than the direct gaze in Lag 4, we observed no significant gaze effect in Lag4 ($M_{Averted}$ = 0.80, $SD_{Averted}$ = 0.19, $M_{Direct}$ = 0.80, $SD_{Direct}$ = 0.19, $t$(42) =0.63, $p$ = 0.53, 95% CI [-0.01 0.02], Hedges's $g_{av}$ = 0.03) or Lag7 ($M_{Averted}$ = 0.82, $SD_{Averted}$ = 0.19, $M_{Direct}$ = 0.82, $SD_{Direct}$ = 0.19, $t$(42) =0.02, $p$ = 0.98, 95% CI [-0.01 0.01], Hedges's $g_{av}$ = 0.00). One could speculate that, because tVNS seems to enhance the perception of direct gaze, it could be processed more efficiently in the shorter lags. However, the interaction between gaze, lag and stimulation did not reach significance ($F(2,84) = 0.11$, $p = 0.90$, $\eta^2_p < 0.01$) and therefore, we cannot confirm that this might be due to a tVNS effect.

The interaction between emotion and gaze ($F(2,84) = 0.01$, $p = 0.99$, $\eta^2_p < 0.01$), emotion and lag ($F(4,168) = 0.51$, $p = 0.72$, $\eta^2_p = 0.01$) were not significant and, in contrast to Ricciardelli et al., (2016), we do not replicate the emotion × gaze × lag interaction ($F(3.31,138.97) = 1.26$, $p = 0.29$, $\eta^2_p = 0.03$). The current design differs from Ricciardelli et al., (2016) in the number of factors, given that tVNS stimulation adds contextual variability that might explain why we fail to replicate previous findings. To further explore this possibility, we ran exploratory rmANOVA with emotion, gaze, and lag as factors, separately for the active and sham conditions. While the three-way interaction between emotion, gaze and lag is not observed during active tVNS ($F(3.20, 134.47) = 1.44$, $p = 0.23$; $\eta^2_p = 0.03$), it is close to significance in the sham condition ($F(4, 168) = 2.09$, $p = 0.08$; $\eta^2_p = 0.05$), partially replicating the results from Ricciardelli et al., (2016). Further research is needed to corroborate the present and previous results.

Most importantly, we obtained a significant main effect of tVNS stimulation ($F(1,42) = 7.72$, $p < 0.01$, $\eta^2_p = 0.15$), indicating that accuracy was significantly higher in the active ($M = 0.80$, $SD = 0.18$) than in the sham condition ($M = 0.78$, $SD = 0.19$), and a significant interaction between stimulation and gaze ($F(1,42) = 5.43$, $p = 0.02$, $\eta^2_p = 0.11$). Bonferroni corrected post-hoc paired-samples *t*-test indicated that, for the sham session, no significant gaze effects occurred ($M_{Direct} = 0.78$, $SD_{Direct} = 0.20$, $M_{Averted} = 0.78$, $SD_{Averted} = 0.20$), $t(42) = 0.24$, $p = 0.81$, 95% CI [-0.01 0.01], Hedges's $g_{av} = 0.01$). In contrast, in the active session, accuracy was significantly higher in the direct ($M = 0.82$, $SD = 0.19$) than in the averted gaze condition ($M = 0.80$, $SD = 0.19$, $t(42) = 3.90$, $p < 0.01$, 95% CI [0.01 0.03], Hedges's $g_{av} = 0.10$), see Figure 3.

The remaining interaction effects with tVNS did not reach the level of significance: stimulation × emotion ($F$(1.70,71.68) = 0.81, $p$ = 0.43, $\eta^2_p$ = 0.02); stimulation × gaze × emotion ($F$(1.49,62.69) = 0.03, $p$ = 0.93, $\eta^2_p$ < 0.01); stimulation × lag ($F$(2,84) = 0.07, $p$ = 0.93, $\eta^2_p$ < 0.01); stimulation × emotion × lag ($F$(3.17,133.34) = 0.84, $p$ = 0.48, $\eta^2_p$ = 0.02); stimulation × gaze × emotion × lag ($F$(3.35,140.99) = 2.24, $p$ = 0.08, $\eta^2_p$ = 0.05).

- Please, insert Figure 3 here -

### ***3.3.1. Additional analysis***

As reported above, we observed a difference between active and sham tVNS sessions in positive and negative mood, as well as in muscle contractions and burning sensations reported after the stimulation. In order to control that these differences were not influencing our results; we calculated a difference score between active and sham sessions in the four variables and introduced them as covariates in a within subjects rmANCOVA with the same factors as reported before. We observed that none of the main effects of the covariates was significant (positive mood: $F$(1,38) < 0.01, $p$ = 0.95, $\eta^2_p$ < 0.01; negative mood: $F$(1,38) = 0.02, $p$ = 0.88, $\eta^2_p$ < 0.01; muscle contractions: $F$(1,38) = 0.09, $p$ = 0.76, $\eta^2_p$ < 0.01; burning sensations: $F$(1,38) = 2.07, $p$ = 0.16, $\eta^2_p$ = 0.05). Moreover, the main effect of the stimulation ($F$(1,38) = 10.87, $p$ < 0.01, $\eta^2_p$ = 0.22) and the key interaction between session and gaze ($F$(1,38) = 4.85, $p$ = 0.03, $\eta^2_p$ = 0.11) remained significant when controlling for the covariates. Further, none of the covariates interacted with it (stimulation × gaze × positive mood: $F$(1,38) = 0.07, $p$ = 0.79, $\eta^2_p$ < 0.01; negative mood: $F$(1,38) = 0.92, $p$ = 0.34, $\eta^2_p$ = 0.02; muscle contractions: $F$(1,38) = 0.03, $p$ = 0.87, $\eta^2_p$ < 0.01; burning sensations: $F$(1,38) = 1.50, $p$ = 0.23, $\eta^2_p$ = 0.04). Therefore, we can rule out the possibility that the difference between active and sham sessions in positive, negative mood, muscle contractions and burning sensations explained our results.

## 4. Discussion

The aim of this study was to provide more insight with respect to three issues that were left open by the study of Colzato et al. (2017). First, we asked whether tVNS-induced changes in performance are specific to emotional faces (faces showing emotional expressions) or whether they also occur for neutral faces. While we found general performance to be better with fearful faces, which might be due to a general increase of arousal induced by these faces, facial expression did not interact with any other variable, including the tVNS manipulation. It is important to note that our interest in attention made us use a different task than the one used in Colzato et al. (2017), so that strictly speaking we cannot exclude the possibility that facial expression plays a role in tVNS effects on emotion recognition; but what we can say is that the present task fails to provide any evidence for expression-specific effects of tVNS-induced enhancement.

Second, we tested whether tVNS effects would be sensitive to the social relevance of facial stimuli, as manipulated by direct versus averted gaze. We observed that the gaze manipulation interacted with tVNS, showing that tVNS-induced enhancement was only obtained with direct-gaze stimuli but not with averted-gaze stimuli. We note that, given the particular experimental task we were using, this does not provide direct evidence for improved processing of the face stimuli themselves, which would have produced an effect on T1 but not T2. On the one hand, the very good performance on T1 is close to ceiling, so that we do not consider the absence of a T1 effect as evidence against the possibility that tVNS improves face processing. On the other hand, however, finding an impact on T2 does not provide direct evidence for that either. Rather, the outcome seems to suggest that active tVNS sped up or otherwise improved T1 processing, so that more capacity was left for processing T2.

This brings us to our third question, which asks whether improvements are due to enhanced attention allocation. Even though our task produced a healthy AB, as indicated by the lag effect, it did not interact with tVNS. Given that the attentional origin of the AB is uncontroversial, this provides rather direct evidence against the possibility that tVNS is targeting attentional control. Therefore, we interpret that the tVNS effect is likely to be driven by enhanced perception rather than attention. One possibility to more closely address whether the tVNS enhancement that we observed is triggered by perceptual or attentional processing would be to use, in a future follow-up study, a RSVP task introducing socially relevant stimuli presented both at T1 and T2 (Milders et al., 2011; Schwabe and Wolf, 2010).

It is worth mentioning that some of the effects observed in the study of Ricciardelli et al., (2016) have not been replicated in the current study. Even if we used the same experimental task, adding the stimulation to our design introduces an important contextual factor that has not been tested before, and may explain the differences in the pattern of results. We interpret that the presence of main effects of gaze and emotion (in contrast to what was observed in Ricciardelli et al., 2016) could be explained by contextual factors (see i.e., de Jong et al., 2009). Moreover, individual differences or mood induced-changes due to the stimulation could have also played a role. As reported in our additional analysis, covariates (mood and stimulation after-effects) do not explain the present results but may have contribute to not completely replicate the previous effects observed in Ricciardelli et al., 2016. Because in Ricciardelli et al., (2016) no measures of mood or personality were taken and the effect of tVNS in relation to this paradigm had not been tested before, we can’t rule the possibility that these factors might have had an effect.

Ricciardelli et al., (2016) observed a three-way interaction between emotion, gaze and lag, showing a lack of AB when T1 was an angry face with direct gaze and a presence of AB when T1 was a fearful face, independent of the direction of the gaze. In the current study, we did not observe such an interaction. We observed a main effect of stimulation, suggesting that the tVNS improves general facial processing including all aspect of the face. Ricciardelli et al., (2016) interpreted that fearful faces with direct gaze are less socially salient (Adams and Kleck, 2003; Sander et al., 2005). One might expect that if in our study fearful faces became more salient due to the stimulation, they might be equal to angry faces with a direct gaze, requiring less attentional resources and thus cancelling out the significant three-way interaction. The interesting gaze by stimulation interaction that we observed might mean that, by enhancing the processing of direct gaze, tVNS could have made both facial emotions more salient for the observer, requiring less attentional resources and being less sensitive to AB. If the mechanism implies that the more socially salient the stimulus is for the observer (bottom up processing), the less attentional resources are needed (top-down deployment of attention), tVNS might be a contextual factor modulating the social salience of the stimulus, by an enhancement of its perceptual processing.

An alternative interpretation of our findings could be the possibility that tVNS reduces the processing of relevant stimuli, allowing a better detection of T2. Recent findings suggest a null effect of tVNS on the AB (Burger et al., 2020) and it has been demonstrated that emotionality in T1 affects recognition of T2 (Schwabe et al., 2011; Schwabe and Wolf, 2010). Because we do not observe an interaction with emotion, it could be that gaze directed faces (those affected by tVNS) are less important for task execution and, during tVNS, less resources are invested in their processing and more are allocated in the detection of non-relevant targets (T2). However, because previous findings suggest a beneficial effect of tVNS in recognizing relevant cues coming from the eyes (Colzato et al., 2017) and due to the importance of gaze as a salient social cue (Kleinke, 1986; Milders et al., 2011; Ricciardelli et al., 2012), we consider more plausible that tVNS might be facilitating the processing of direct gaze, as a socially relevant stimuli.

We thus conclude, at least tentatively, that tVNS is likely to improve the perceptual processing of facial stimuli (irrespective of their expression: in this case, fear, anger, or neutral) with direct social relevance (i.e., with direct gaze). We acknowledge that social relevance of events can be signaled by other cues than direct gaze, but there is converging evidence that direct gaze is a particularly important social cue that provides information of high biological importance, such as whether the observer is the focus of the viewer's attention (Ricciardelli et al., 2016, 2012). Therefore, detecting a direct gaze in a fast and accurate way is crucial for survival given that it can trigger adaptive responses such as detecting a threat and consequently a fight/flight response.

Our current finding converges with previous results (Colzato et al., 2017; Sellaro et al., 2018) showing that tVNS can enhance key functions for emotion recognition. However, while in Colzato et al., (2017) we observed an effect in the easy items – interpreted as salient social cues – in the case of Sellaro et al., (2018) the tVNS-induced enhancement was observed in the difficulty items. It is worth mentioned that both tasks are different in nature and because difficulty is defined based on performance within the tasks, the difficulty levels are not directly comparable. While Sellaro et al., (2018) used pictures of the whole faces, Colzato et al., (2017) used pictures restricted to the eye region. Although in the current study the stimuli included pictures of whole faces, the key gaze manipulation was restricted to the eyes, similar Colzato et al., (2017), and whose key social relevance has been consistently reported (Hamilton, 2016; Kleinke, 1986; Palermo and Rhodes, 2007; Ricciardelli et al., 2012).

Taken altogether, our findings support the evolutionary role of the vagus nerve in regulating social interactions (Porges, 2007, 2003, 2001). In fact, we provide further evidence supporting that not only the vagus involved in in allocating their gaze towards other people (Porges, 2001), but it can also speed up the perceptual processing of other's gaze. Eye contact and gaze behavior are essential aspects of the human interaction and the eye region is used as an adaptive and informative signal to interpret mental states and intentions of other individuals (Hamilton, 2016; Kleinke, 1986; Ricciardelli et al., 2016). Given that, we did not observe any significant interaction between tVNS stimulation and type of emotion, our findings highlight that the role of the vagus is mainly related to the processing of relevant features of facial expressions, such as the gaze, rather than to the emotion expressed.

We also found active tVNS, as compared to sham stimulation, to enhance overall conditional T2 accuracy (T2|T1). Why should this be the case? It is known that performance in the Attentional Blink task relies on working memory and working memory capacity (Akyürek et al., 2007; Colzato et al., 2007). Although effects of tVNS on working memory have not yet been reported, previous findings have shown enhanced associative episodic memory followed by tVNS stimulation. Jacobs and colleagues (2015) showed that tVNS improves memory performance in healthy older individuals, which raises the possibility that the increase of overall T2 accuracy was due to a possible effect of tVNS in modulating the consolidation of T1. It has been proposed that T1 and T2 consolidate into episodically distinct representations within working memory (Wyble et al., 2015, 2009), and that the presence of an AB seems to delay consolidation of T2 (Vogel and Luck, 2002). Thus, if tVNS enhances working memory consolidation, it may improve T2 accuracy in multiple, not mutually exclusive ways. First, better WM performance may imply more, or more efficient, parallel processing. More parallelism would allow the concurrent processing and, consequently, the correct report of both T1 and T2 (Kessler et al., 2005). Second, higher WM performance may permit a more efficient suppression of distractor-induced interference (Kane and Engle, 2002). More efficient distractor-suppression could have supported T2 accuracy by helping to disentangle T1 and T2 from the distractors. Third, a higher WM performance may allow, or at least be associated with, longer integration windows; that is, increased WM functioning may produce attentional gates to be longer open, allowing both T1 and T2 to appear (Colzato et al., 2007). Last, better WM functioning might support also a smarter attentional allocation policy avoiding over-investing resources into T1 processing (in the sense of Olivers and Nieuwenhuis, 2006) and, thus, leave more capacity for T2 processing. Along these lines, despite our positive effect on T2 based on the direction of the gaze and tVNS stimulation, we did not observe a modulation of T1 accuracy, consistent with previous findings showing effects in T2 but not in T1 (Colzato et al., 2008b, 2007; Dale and Arnell, 2010; Martens et al., 2006; Martens and Valchev, 2009).

Besides that, recent evidence has shown that tVNS modulates levels of NE (Ventura-Bort et al., 2018) and hormonal levels of salivary cortisol (Warren et al., 2019), and both neuromodulators have been shown to play a role in the AB effect when using emotional stimuli (De Martino et al., 2008; Schwabe and Wolf, 2010). In our results, neither the tVNS-induced perceptual enhancement nor the main AB effect interacted with the emotional expression, and given that we did not directly measure physiological markers, we are not able to conclude whether our tVNS manipulation had an effect on noradrenergic function. Future studies should attempt to replicate the current findings in combination with physiological measurements for NE such as pupil dilation, salivary alpha amylase and cortisol (Warren et al., 2019).

Some possible limitations of our study are noteworthy. Namely, our sample was not completely balanced in terms of gender. Even if the sample of Ricciardelli et al., (2016 experiment 3) was also unbalanced, the number of males was considerably lower in our study. Because females are more sensitive to social stimuli and process them better, in addition to the stimulation, fearful faces with direct gaze may have benefit more from the processing enhancement than angry faces with direct gaze already processed with little attentional resources. Given the evidence for gender differences in the ability to empathize and recognize emotions, tVNS could have differently modulate emotion recognition in males and females (Sellaro et al., 2018). Future studies might devote more systematic attention to gender effects and possible effects of the match between the gender of the participant and the gender of facial stimuli. Finally, because previous findings have reported a different role of gaze in processing approach (positive) or avoidance-oriented (negative) emotions (Adams and Kleck, 2003), future research should explore and compare the role of the vagus nerve in detecting expressions indicating benevolence or hostility.

To conclude, our findings suggest that tVNS does not have an impact on attention allocated to faces or facial expressions but rather, it seems to enhance the perceptual processing of socially relevant face stimuli. We thus provide converging evidence for a causal role of the vagus nerve in the recognition of socially relevant others (Colzato et al., 2017). These findings stimulate future research aiming to extend our knowledge on the use of tVNS as a safe and useful tool to enhance emotion recognition and social functioning.

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## Author contribution

The design of the study was developed by all authors. RH carried out data collection. MJM performed the analysis. LSC, MJM, and BH wrote the first draft of the article. All authors revised the first draft and approved the last version of the manuscript.

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## Figure captions

**Figure 1. Schematic illustration of a rapid serial visual presentation (RSVP) trial.**

**A)** Example of face stimuli showing angry and neutral facial expressions with a direct or an averted (left or right) gaze. **B)** Example of part of the sequence of events of a rapid serial visual presentation (RSVP) trial. Here, the face target (T1) is an angry face with direct gaze and the rotated landscape target (T2) appears one item after it (270 ms, Lag 2).

**Figure 2. T1 performance.** T1 (unconditional) accuracy for direct and averted gaze directions as a function of active and sham tVNS stimulation. Vertical capped lines indicate standard error of the mean.

**Figure 3. T2 performance.** Accuracy for T2 given T1 correct (T2|T1) shown separately for direct and averted gaze directions as a function of active and sham tVNS stimulation. Vertical capped lines indicate standard error of the mean.