

# Transcutaneous Vagus Nerve Stimulation May Enhance Only Specific Aspects of the Core Executive Functions. A Randomized Crossover Trial

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### *Conflict of interest statement*

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest

### *Author contribution statement*

UB and SL contributed to conceiving the design of the study. LK led the data collection, with the help of UB. SL realized the statistical analysis with the help of SL. UB wrote the first draft of the manuscript and SL, MR and SK provided critical comments to improve it. Final adjustments on the manuscript were suggested by SL and MR. All authors agreed on the final version.

### *Keywords*

tVNS, Vagus Nerve Stimulation, HRV, Heart rate variability, Cardiac vagal activity, task switching, Neurovisceral integration model

### *Abstract*

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**Background:** Individuals are able to perform goal-directed behaviors thanks to executive functions. According to the neurovisceral integration model, executive functions are upregulated by brain areas such as the prefrontal and cingulate cortices, which are also crucially involved in controlling cardiac vagal activity. An array of neuroimaging studies already showed that these same brain areas are activated by transcutaneous vagus nerve stimulation (tVNS). Despite evidence towards effects of tVNS on specific executive functions such as inhibitory control, there have been no studies investigating what type of inhibition is improved by tVNS by systematically addressing them within the same experiment. Furthermore, the effect of tVNS on another core executive function, cognitive flexibility, has not yet been investigated.

**Objective:** We investigated the effects of tVNS on core executive functions such as inhibitory control and cognitive flexibility.

**Methods:** Thirty-two participants (nine women, Mage = 23.17) took part in this study. Vagally-mediated heart rate variability parameters (root mean square of successive differences, RMSSD, and high frequency, HF) were measured while participants performed four different cognitive tasks that mainly rely on different aspects of both the aforementioned executive functions.

**Results:** Despite clear conflict effects in the four tasks, only performance on the task used to measure set-shifting paradigm was improved by tVNS, with switch costs being lower during tVNS than during sham stimulation. Furthermore, HF increased during each of the cognitive flexibility tasks, although HF during tVNS did not differ from HF during sham stimulation.

**Conclusion:** The results indicate for the first time a) that tVNS can increase cognitive flexibility in a set-shifting paradigm, and b) that tVNS may exert a stronger effect on cognitive flexibility than inhibition. The present study provides only partial evidence for the neurovisceral integration model. Future studies should address further paradigms that demand cognitive flexibility, thus investigating this new hypothesis on the specificity of the tVNS effects on cognitive flexibility.

### *Contribution to the field*

This manuscript investigates the effect of transcutaneous vagus nerve stimulation (tVNS), a technology used to non-invasively modulate vagal activity, on executive functions and on cardiac vagal activity. Regarding executive functions, we focused on inhibitory control and cognitive flexibility, core executive functions that are necessary for higher-order cognitive functioning. The present study is the first to consider different aspects of inhibitory control and cognitive flexibility in an integrative manner. To achieve this, we make use of an integrative theoretical background, namely the neurovisceral integration model, and use four cognitive tasks within the same study setup. These tasks are thought to rely mainly on different subtypes of both these executive functions. Results showed that only performance on task-switching was improved by tVNS, with switch costs being lower during tVNS than during sham stimulation. Furthermore, high frequency (HF) heart rate variability, an index of cardiac vagal activity, increased during each of the cognitive flexibility tasks, although HF during tVNS did not differ from HF during sham stimulation. These results indicate for the first time a) that tVNS can increase cognitive flexibility in a task-switching paradigm, and b) that tVNS may exert a very specific influence on core executive functions.

*Ethics statements*

*Studies involving animal subjects*

Generated Statement: No animal studies are presented in this manuscript.

*Studies involving human subjects*

Generated Statement: The studies involving human participants were reviewed and approved by Ethics Committee of the German Sport University Cologne (120/2018). The patients/participants provided their written informed consent to participate in this study.

*Inclusion of identifiable human data*

Generated Statement: No potentially identifiable human images or data is presented in this study.

In review

*Data availability statement*

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In review

# **Transcutaneous Vagus Nerve Stimulation May Enhance Only Specific Aspects of the Core Executive Functions. A Randomized Crossover Trial**

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## Abstract

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**Keywords:** tVNS, vagus nerve stimulation, HRV, heart rate variability, cardiac vagal activity, task switching, neurovisceral integration model

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## 32 1 Introduction

33 Transcutaneous vagus nerve stimulation (tVNS) is a technology used to electrically and non-  
34 invasively modulate vagal activity through the auricular branch of the vagus nerve. There has  
35 been an increasing amount of studies using tVNS to enhance cognitive processes that rely on  
36 prefrontal activity. An array of these studies addressed specific aspects of inhibitory control  
37 separately (e.g., Keute, Ruhna, Heinze, & Zaehle, 2018; Ventura-Bort et al., 2018), whereas  
38 others investigated more complex cognitive functioning such as creativity (Colzato, Ritter, et  
39 al., 2018) and implicit spiritual self-representation (Finisguerra et al., 2019). Attempts  
40 motivated by theory-driven hypotheses to systematically investigate the effects of tVNS on  
41 different aspects of basic cognitive functions are still scarce. Based on the predictions  
42 outlined in the neurovisceral integration model (Thayer et al., 2009), the current study aimed  
43 at investigating the effects of tVNS on the core executive functions inhibitory control and  
44 cognitive flexibility (Diamond, 2013). Furthermore, and also in line with the neurovisceral  
45 integration model, we measured cardiac vagal activity during tVNS and cognitive  
46 performance, a parameter suggested to reflect the effectiveness of executive functioning.

47 Executive functions refer to top-down mental processes that serve goal-directed  
48 behavior (Diamond, 2013). Inhibitory control and cognitive flexibility are considered core  
49 executive functions, meaning that they are necessary components for building higher-order  
50 executive functions (Diamond, 2013; Miyake & Friedman, 2012). Inhibitory control involves  
51 the ability to override dominant or prepotent responses by controlling one's attention and  
52 behavior, and can be distinguished between selective attention and response inhibition  
53 (Diamond, 2013). Selective attention is expressed by the inhibitory cognitive control of  
54 attention, which occurs by suppressing prepotent mental representations on the level of  
55 perception. Response inhibition is a behavioral inhibition that keeps a person from acting  
56 impulsively. Cognitive flexibility consists in quickly and flexibly switching between tasks or  
57 mental sets (Diamond, 2013). It can be broken down into task switching and set shifting.  
58 Task switching differs from set shifting in the type of conflict: task switching is related to  
59 switching between tasks with different instructions involving different stimuli. Set shifting, in  
60 turn, consists of shifting attention between different features of the same stimuli to follow a  
61 given instruction (Dajani & Uddin, 2015).

62 Executive functioning is linked to prefrontal activity (Arnsten & Li, 2004). According  
63 to the neurovisceral integration model (Smith et al., 2017; Thayer et al., 2009), cardiac vagal  
64 activity—the activity of the vagus nerve regulating cardiac functioning—reflects the output  
65 of the central autonomic network, which links the prefrontal cortex to the heart (Thayer et al.,  
66 2009). The optimal activation of the neural pathways within this network is crucial for  
67 performing a given task that requires cognitive effort and for showing flexible responses to a  
68 changing environment (Thayer et al., 2009). Because cardiac vagal activity and executive  
69 functioning share common underlying neurovisceral self-regulation mechanisms, higher  
70 cardiac vagal activity is associated with improved executive functioning. Cardiac vagal  
71 activity can be indexed via heart rate variability (HRV), the difference in the time interval  
72 between adjacent heartbeats (Malik, 1996), and specifically by the root mean square of the  
73 successive differences (RMSSD) and by high-frequency (HF).

74 There is a large body of empirical evidence linking higher levels of cardiac vagal  
75 activity to higher executive performance (Inhibitory control: Alderman & Olson, 2014;  
76 cognitive flexibility: Colzato, Jongkees, de Wit, van der Molen, & Steenbergen, 2018;  
77 Johnsen et al., 2003). Based on the evidence of the relationship between executive  
78 functioning and cardiac vagal activity as indexed by HRV (RMSSD and HF), in the present  
79 study we will consider the executive functions described here to investigate if tVNS can

80 improve different types of inhibitory control and cognitive flexibility as well as cardiac vagal  
81 activity.

82 The expected link between tVNS and executive functions can be understood by  
83 considering the neuroanatomical pathways of the vagus nerve. The electrical signal, starting  
84 in the auricular branch of the vagus nerve (ABVN), reaches the nucleus tractus solitarius,  
85 which is a crucial structure that projects to a variety of brain areas, including cortical  
86 regions such as the anterior cingulate cortex and the prefrontal cortex (Aihara et al., 2007).  
87 As shown by several functional magnetic resonance imaging (fMRI) studies (Badran et al.,  
88 2018; Frangos, Ellrich, & Komisaruk, 2015; Kraus et al., 2013; Yakunina & Kim, 2017),  
89 tVNS evoked, in contrast to sham stimulation, higher activity in the nucleus tractus  
90 solitarius (Frangos et al., 2015; Yakunina & Kim, 2017), in the left prefrontal cortex and in  
91 cingulate areas (Badran et al., 2018). Importantly, these brain areas affected by tVNS  
92 correspond to the areas described by the neurovisceral integration model as regulating both  
93 executive and cardiac regulation, such as the prefrontal cortex and cingulate areas (Thayer  
94 et al., 2009, 2012).

95 So far, there are studies showing that tVNS affects the types of inhibitory control  
96 (Table 1). These studies used varying cognitive paradigms, which comprise different  
97 dependent variables, and addressed the inhibitory control types only separately and in  
98 different study designs (see Table 1 for an overview of design-related characteristics of  
99 studies investigating inhibitory control using tVNS). Thus, an integrating, evidence-based  
100 discussion on the interplay between tVNS and these types of inhibitory control has not been  
101 possible.

102 Table 1 here

103 As stated above, executive functions and cardiac vagal activity share overlapping  
104 neurological structures, with both being upregulated by cortical areas, including the  
105 prefrontal cortex (Thayer et al., 2009). Given that the tVNS signal is sent afferently to the  
106 prefrontal cortex via ABVN, cardiac vagal activity has also been thought to be affected by  
107 tVNS (Murray et al., 2016). Using RMSSD to measure the effect of tVNS on cardiac vagal  
108 activity, different studies did not find any differences between active and sham stimulation  
109 (Burger, Van der Does, Thayer, Brosschot, & Verkuil, 2019; Burger et al., 2016; De Couck  
110 et al., 2017). One study showed in three experiments that tVNS consistently increased  
111 RMSSD; however, this increase was similarly observed during both active and sham  
112 stimulation, with this possibly indicating that tVNS sends non-specific signals at the  
113 brainstem level that similarly influence cardiac vagal activity in both active and sham  
114 stimulation (Borges et al., 2019). Nonetheless, this study did not take any cognitive  
115 paradigm into account, which might have contributed to understanding if this possible  
116 signal non-specificity—identified as an increase in cardiac vagal activity during both active  
117 and sham stimulation—can also be observed in cognitive functions. This possibility would  
118 challenge the use of earlobe sham stimulation, which has widely been used in current  
119 research with tVNS. Therefore, further studies on the effect of active as well as sham tVNS  
120 on cardiac vagal activity are still needed.

121 To summarize, there is evidence towards the modulation of inhibitory control by  
122 tVNS; however, these findings refer to different cognitive phenomena that have been found  
123 in different samples and in the context of different study designs. So far, there is no study that  
124 has systematically investigated the effects of tVNS on different aspects of core executive  
125 functions, and importantly, there is a lack of studies whose hypotheses were explicitly  
126 motivated by a theory. To address different aspects of executive functioning in an integrative  
127 way, it is crucial to use the same study design and setup. This way it is possible to control for



128 possible experimental variations such as length of resting and of stimulation periods, daytime,  
 129 and other factors that might influence measurement of cardiac vagal activity. Confounders  
 130 related to study design, e.g., instructions, laboratory setup, and differences in sample size, can  
 131 also be considered. Thus, going beyond existing literature, the present study aims at  
 132 investigating the effects of tVNS on inhibitory control, cognitive flexibility, and cardiac vagal  
 133 activity. To achieve this, it uses an integrative theoretical background, namely the  
 134 neurovisceral integration model (Thayer et al., 2009), and applies the same study design  
 135 across these target executive functions. Based on the evidence on neurophysiological  
 136 pathways related to tVNS, addressing cognitive processes that mainly rely on different  
 137 executive functions might help to further understand how tVNS affects basic cognitive  
 138 processes involved in goal-directed behavior.

139 Against this background, it was hypothesized that the performance on the four  
 140 cognitive tasks is higher during active tVNS, compared to sham stimulation (H1a for  
 141 selective attention, H1b for response inhibition, H1c for task switching, and H1d for set  
 142 shifting; this assignment of the subtypes of executive functions to the letters is also valid for  
 143 the next hypotheses). Furthermore, we expected that cardiac vagal activity increases  
 144 relatively to the resting phase only during active stimulation and not during sham stimulation,  
 145 with cardiac vagal activity during the tasks being higher in the active tVNS condition (H2a-  
 146 d). Moreover, we hypothesized that cardiac vagal activity during tVNS and before each  
 147 cognitive task is positively associated with task performance only in the active tVNS  
 148 condition (H3a-d). Finally, we expected cardiac vagal activity during the tasks to have a more  
 149 strongly positive relationship to task performance in the active condition than in the sham  
 150 condition (H4a-d).

## 151 2 Materials and Methods

### 152 2.1 Participants

153 As it is not possible to run power analyses for multi-factorial repeated-measures designs with  
 154 G\*Power 3.1 (Faul et al., 2007), we followed the same procedure found in previous studies  
 155 with similar study design (e.g., Liepelt, Porcu, Stenzel, & Lappe, 2019). Accordingly, we  
 156 matched the average number of participants in the studies that investigated executive  
 157 functions with tVNS using a within-subject design (summarized in Table 1). Since we also  
 158 measured cardiac vagal activity, we additionally considered the average sample size in  
 159 Borges et al. (2019), because this study systematically investigated the effect of tVNS on  
 160 cardiac vagal activity in different experiments. Twenty-nine participants were calculated to  
 161 be necessary to find an effect. Anticipating possible exclusions due to drop-outs and after  
 162 data cleaning, we recruited 35 participants. Thirty-two participants (nine female) were  
 163 included in the analysis due to technical problems with the electrocardiogram (ECG) signal  
 164 of three participants. Mean age was 23.17 years old ( $SD = 4.08$ ), whereby female participants  
 165 had  $M_{age} = 21.11$ ,  $SD = 1.27$ , and male participants had  $M_{age} = 24.87$ ,  $SD = 5.87$ ). Consort  
 166 flowchart (Dwan et al., 2019) is presented in Figure 1.

167 Figure 1 here

168 The sample consisted of healthy students at the local university. Participants were  
 169 eligible if they were not pregnant at the time of the experiment and free of cardiovascular or  
 170 neurological diseases, or major mental disorders, for example severe depression or anxiety  
 171 disorder. They were asked not to smoke, exercise, or consume food, alcohol, or caffeine for at  
 172 least 2 h before participation. These potentially confounding variables as well as tVNS  
 173 safety-related questions were assessed by means of an adapted version of the demographics

174 questionnaire for experiments using HRV developed by Laborde, Mosley, and Thayer (2017).  
 175 All participants gave written informed consent prior to the experiment, which was approved  
 176 by the local ethical committee (ethics approval number 120/2018).

## 177 **2.2 Transcutaneous vagus nerve stimulation**

178 We employed the NEMOS tVNS device developed by Cerbomed (Erlangen, Germany). Two  
 179 titan electrodes found in a structure similar to an earphone are placed in the cymba conchae  
 180 of the left ear, an area thought to be exclusively innervated by the ABVN (Peuker & Filler,  
 181 2002), in order to electrically stimulate these vagal fibers (Ellrich, 2011). In the sham  
 182 stimulation, the electrodes are placed on the left earlobe, which is thought to be free of vagal  
 183 innervation (Peuker & Filler, 2002) and has abundantly been used as a sham stimulation in  
 184 research with tVNS (van Leusden et al., 2015). The tVNS device delivers a stimulation with a  
 185 pulse width of 200–300  $\mu$ s at 25 Hz and an on–off cycle of 30 s. Regarding the adjustment of  
 186 the stimulation intensity, cardiac vagal activity may be similarly influenced by electrical  
 187 afferent stimuli that are triggered by different methods to stipulate stimulation intensity  
 188 (Borges et al., 2019). Therefore, we followed procedures found in previous research with  
 189 tVNS that allow participants to choose their individual intensity (Fischer et al., 2018;  
 190 Ventura-Bort et al., 2018). Accordingly, in each session participants received increasing and  
 191 decreasing series of 10-s stimulation trials, and rated the subjective sensation of the  
 192 stimulation on a 10-point scale, ranging from nothing (0), light tingling (3), strong tingling  
 193 (6), to painful (10). The increasing series of trials started from an intensity of 0.01 mA and  
 194 increased by 0.01 mA on a trial-by-trial basis until participants reported a tingling sensation  
 195 of 9. Before starting the decreasing series, the same intensity was repeated and then reduced  
 196 trial by trial in 0.01 mA until a subjective sensation of 6 or below was experienced. This  
 197 procedure was repeated a second time. The final stimulation intensity used for the  
 198 experimental procedure was calculated based on the average of the four intensities rated as 8  
 199 (two from the increasing and two from the decreasing series). The average chosen stimulation  
 200 intensity in the active condition was  $M = 2.19$  mA ( $SD = 0.93$ ) and  $M = 2.20$  mA ( $SD = 1.06$ )  
 201 in the sham condition. These stimulation intensities did not differ significantly from each  
 202 other,  $t(31) = 0.063$ ,  $p = .950$ .

## 203 **2.3 Cardiac vagal activity**

204 To assess cardiac vagal activity, we used the Faros 180° device from Mega Electronics  
 205 (Kuopio, Finland) with a set sampling rate of 500 Hz. This device enables users to measure  
 206 the ECG signal as recommended by current guidelines on HRV measurement for  
 207 psychophysiological experiments (Laborde et al., 2017). We placed two disposable ECG pre-  
 208 gelled electrodes (Ambu L-00-S/25, Ambu GmbH, Bad Nauheim, Germany) on the chest, the  
 209 positive electrode on the right infraclavicular fossa and the negative one on the left anterior  
 210 axillary line below the 12<sup>th</sup> rib.

211 RMSSD, as well as HF (0.15 Hz to 0.40 Hz band) transformed with autoregressive  
 212 modeling, were chosen as indicators of cardiac vagal activity in the main analyses (Malik et  
 213 al., 1996). From ECG recordings, we extracted HRV with Kubios software (University of  
 214 Eastern Finland, Kuopio, Finland), visually inspected the full ECG recording, and manually  
 215 corrected artifacts (Laborde et al., 2017). Since HF is only influenced by breathing when  
 216 breathing cycles are between nine cycles per minute (0.15 Hz) and up to 24 cycles per minute  
 217 (0.40 Hz) (Malik et al., 1996), participants with a respiration rate of less than nine cycles per  
 218 minute and more than 24 cycles per minute were excluded from analyses with HF. The  
 219 respiration rates (the number of respiratory cycles per minute) was obtained multiplying the

220 ECG-derived respiration value obtained via the Kubios algorithm by 60 (Tarvainen,  
 221 Niskanen, Lipponen, Ranta-aho, & Karjalainen, 2013) and was also separately analyzed. We  
 222 considered for analysis measurements in blocks of 4 min, which is in accordance with the  
 223 range suggested by recommendations for experiment planning in psychophysiological  
 224 research (Laborde et al., 2017). Given that the cognitive tasks differed greatly from one  
 225 another regarding time length, with the tasks lasting between 5 and 15 minutes, for the  
 226 analysis within task blocks we chose a time window of the last 4 minutes respectively for  
 227 each cognitive task.

## 228 **2.4 Cognitive tasks**

229 In order to standardize the tasks and therefore avoid response mistakes, all tasks used the  
 230 keys “S” and “K” as responses for left and right, respectively. The participants were  
 231 instructed to press the buttons with their index fingers, and the stimuli were presented in  
 232 white against a grey background (except for the set-shifting task). We used a 24-in. flat-  
 233 screen monitor (1,920 x 1,080 pixels at 60 Hz) at a viewing distance of 60 cm to present the  
 234 tasks and ran all of them with PsychoPy3 Version 3.0.0 (Peirce et al., 2019). The participants  
 235 performed four tasks which are thought to mainly rely on inhibitory control (selective  
 236 attention and response inhibition), and cognitive flexibility (task switching and set shifting).  
 237 These tasks were chosen according to two criteria: First, we followed recommendations from  
 238 influential reviews on executive functions (Diamond, 2013; Miyake & Friedman, 2012). For  
 239 the choice of the cognitive task, we considered the task impurity problem: according to  
 240 Miyake and Friedman (2012), because executive functions necessarily manifest themselves  
 241 by operating on other cognitive processes, any executive task strongly implicates other  
 242 cognitive processes that are not directly relevant to the target executive function.  
 243 Consequently, we chose the tasks that are thought to minimize demands of other executive  
 244 functions (Diamond, 2013). Second, we performed a literature search to find studies that used  
 245 the tasks recommended by the aforementioned reviews and also provided evidence on the  
 246 relationship with a) tVNS, b) cardiac vagal activity, and c) prefrontal activity (imaging  
 247 studies). The tasks chosen are the following:

### 248 **2.4.1 Flanker task**

249 Following recommendations from Diamond (2013), to measure selective attention we used a  
 250 modified version of the Flanker task (Eriksen & Eriksen, 1974). We used the Flanker task as  
 251 reported by Alderman and Olson (2014). With this version, it could be shown that individuals  
 252 with higher fitness levels expressed higher HF values during the task, and that these  
 253 individuals had lower RT than the less fit group. A trial consists of five arrows in which the  
 254 third one is the target arrow. Participants were asked to press the left key on the computer  
 255 keyboard when the target arrow pointed to the left and the right key when the target arrow  
 256 pointed to the right. Participants were instructed to respond as quickly and accurately as  
 257 possible for each trial. After a practice block of 30 trials, two experimental blocks of 120  
 258 trials each were presented, each separated by 30 s. Each block consisted of congruent and  
 259 incongruent stimuli presented in random order. The congruent trials consisted of the target  
 260 arrow being flanked by arrows facing the same direction, while incongruent trials involved  
 261 the target arrow being flanked by arrows facing the opposite direction. Each stimulus was  
 262 presented for 100 ms (to increase task difficulty) with a response window of 1,500 ms. A  
 263 random inter-stimulus time interval of 1,100, 1,300 or 1,500 ms was also used between each  
 264 50 ms visual fixation (+) and the stimulus in order to increase task difficulty (Figure 2a).

265

## 266 2.4.2 Spatial Stroop task

267 The task for measuring response inhibition was the Spatial Stroop task, as this task is thought  
268 to minimize memory demands compared to other classical tasks such as the Simon task  
269 (Diamond, 2013). This response inhibition task was designed according to Marotta, Román-  
270 Caballero, and Lupiáñez (2018), from which we only took the arrow part of the task, and  
271 consisted of a practice and two experimental blocks. During the practice block, 15 trials were  
272 presented, and feedback was provided. The practice block was followed by two experimental  
273 blocks of 64 experimental trials each. Participants were instructed to fixate a fixation cross  
274 presented in the center of the screen. A directional arrow appears randomly on the left or on  
275 the right side of the fixation point, and this arrow points randomly to the right or the left side.  
276 Participants are required to indicate the direction of the arrow by pressing the left key if the  
277 arrow points to the left and the right key if the arrow points to the right, while ignoring its  
278 location. They were instructed to respond as quickly and accurately as possible for each trial.  
279 The arrow was presented either left or right of the fixation cross for 2,000 ms. Feedback for  
280 incorrect key presses was provided to participants in the form of a 220-Hz tone presented for  
281 1,500 ms. This design produced trials that were congruent (e.g., a right-indicating target  
282 presented on the right) or incongruent (e.g., a left-indicating target presented on the right, see  
283 Figure 2b).

## 284 2.4.3 Number-Letter task

285 We used the Number-Letter task (NLT) as described in Colzato, Jongkees, et al. (2018),  
286 which found that participants with higher resting-state cardiac vagal activity showed greater  
287 flexibility than individuals with lower resting-state cardiac vagal activity. Throughout the  
288 task, a 10-cm square divided into four quadrants was displayed on the computer screen.  
289 During each trial, a character pair consisting of letters, numbers or symbols was presented in  
290 the center of one quadrant. Participants had to either perform a letter task in which they  
291 classified the letter in the stimulus pair as a consonant or a vowel, or they had to perform a  
292 number task in which they classified the number in the pair as odd or even. They were  
293 instructed to respond as quickly and accurately as possible for each trial. After their response  
294 or after 2,000 ms had passed, a new stimulus pair was displayed in the next quadrant  
295 following a clockwise pattern. The upper quadrants were assigned to the letter task and the  
296 lower quadrants to the digit task, so that the display location served as a task cue and the task  
297 changed predictably. Depending on the task, the relevant character in the stimulus pair was  
298 either a letter or a digit, whereas the second and irrelevant character was either a member of  
299 the other category, so that the response afforded by this character could be congruent or  
300 incongruent with the task-relevant response, or was drawn from a set of neutral characters.  
301 This design produced switch trials in Quadrants 1 and 3, and non-switch trials when the  
302 stimuli appeared in Quadrants 2 and 4. Consonants were sampled randomly from the set <G,  
303 K, M, R>, vowels from the set <A, E, I, U>, even numbers from the set <2, 4, 6, 8>, odd  
304 numbers from the set <3, 5, 7, 9>, and neutral characters from the set <#, ?, \*, %>, with the  
305 restriction that a stimulus could not be repeated on successive trials. The position of the task-  
306 relevant character within a pair (left or right) was randomly determined on each trial. The  
307 participants pressed the left key to indicate “even” or “consonant” and the right key to  
308 indicate “odd” or “vowel”. Participants completed a practice set of 9 blocks, each with 16  
309 trials, before entering the experimental phase. This consisted of a set of 15 blocks, with each  
310 block again consisting of 16 trials. A short response stimulus interval (RSI) of 150 ms was  
311 chosen which remained constant within a given set. A short RSI, the so-called preparation  
312 component, has been shown to provoke more pronounced switch costs than long RSI, also

313 known as residual component. This is because shorter intervals usually hamper the  
 314 reconfiguration process before the stimulus is presented (Colzato, Jongskees, et al., 2018).  
 315 Stimuli were response-terminated or presented for a maximum duration of 2,000 ms (Figure  
 316 2c).

#### 317 2.4.4 Dimensional Change Card Sorting task

318 The Dimensional Change Card Sorting task (DCCS) based on Zelazo and colleagues (2014)  
 319 was used in the present study to measure set shifting, as recommended by Diamond (2013).  
 320 This version is part of the NIH Toolbox Cognition Battery and was validated with 268 adults  
 321 (Zelazo et al., 2014). DCCS makes use of two different styles of bivalent cards, displaying a  
 322 red rabbit on the left and a blue truck on the right side at the bottom of the screen throughout  
 323 the task. The participants are then asked to respond to a centrally-presented bivalent stimulus  
 324 (blue/red rabbit/truck) regarding either its shape or color. Pressing the left key sorts the  
 325 stimulus to the location of the left target (i.e., the red rabbit); pressing the right key sorts the  
 326 stimulus to the location of the right target (i.e., the blue truck). The DCCS task consists of  
 327 four blocks (practice, pre-switch, post-switch, and mixed). During the practice block with 24  
 328 trials (12 for each dimension), participants receive a feedback whether the response was  
 329 correct or false. At the beginning of each trial, a fixation cross was shown for 1,000 ms, being  
 330 followed by the cue (the word “color” or “shape”) they had to respond to. This cue was  
 331 presented for 1,000 ms. The stimulus was then presented and disappeared only after a  
 332 response was recorded. Test trials started with a pre-switch block consisting of 15 trials that  
 333 had the same sorting dimension (color or shape) that was used in the preceding practice  
 334 block. After that, participants were cued to the other dimension, and a post-switch block with  
 335 15 trials took place. When those two blocks are finished, the mixed block begins. Participants  
 336 are then instructed to sort the stimuli to the dimensions and they are presented with 50 mixed  
 337 trials that are presented in a pseudorandomized order. This mixed block includes 40  
 338 “dominant” and 10 “non-dominant” trials. The dominant dimension, which could be shape or  
 339 color, was always the sorting dimension that participants were presented to in the post-switch  
 340 block. The arrangement for all three test blocks is the same as for practice trials, but no  
 341 feedback is provided. The order of the pre- and post-switch blocks as well as the task version  
 342 with one of the dominant dimensions was counterbalanced across participants (Figure 2d).

343 Figure 2 here

#### 344 2.5 Procedure

345 The experiment had a sham-controlled, single-blinded, randomized crossover within-subject  
 346 design. For each stimulation condition (active or sham stimulation), the participants  
 347 underwent all tasks within one session. The order of the tasks was randomized for each  
 348 participant beforehand. After determining the individual stimulation intensity (familiarization  
 349 phase), a total of four task blocks were presented, one per task. Each block consisted of one  
 350 cognitive task and a total of three measurements: The first one was done to take only resting  
 351 cardiac vagal activity into account (resting period, 4-min measuring interval), the second to  
 352 measure cardiac vagal activity during the stimulation (tVNS period, 4-min period), and the  
 353 third to measure cardiac vagal activity during the stimulation simultaneously with the  
 354 cognitive tasks (task period, 4 min). The tVNS period was included because there is a lack of  
 355 evidence on the temporal latency of the effects of tVNS (Borges et al., 2019). Thus, a built-up  
 356 period of four minutes of the effects of tVNS and sham stimulation was used, as done in  
 357 previous studies (e.g. Burger et al., 2019). Between each test block, the participants could  
 358 take a 30-s break and were then asked to continue with the next task (Figure 3).

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Figure 3 here

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The data collection took place on two different dates with approximately one week between the two sessions. During the sessions, either active or sham stimulation was administered to each participant. According to the crossover design, all participants underwent both stimulation conditions. The order of stimulation condition (active-sham; sham-active) was counterbalanced across participants. After taking a seat, signing the informed consent, and answering questions from a body check which included questions related to the exclusion criteria, the ECG and the tVNS electrodes were positioned. The participants then performed the four cognitive tasks across the four blocks. The HRV resting measure was taken in a sitting position with the eyes looking at a grey screen, knees at 90°, and hands on the thighs. The same body position was kept for all measurement periods, and the participants were asked to move as little as possible during the experiment. The order of the tasks was counterbalanced, however the course of events in both conditions was identical. At the end of the second testing session, the participants were debriefed and thanked.

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## 2.6 Data analysis

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Outliers in the HRV data (less than 1% of the data) were winsorized, meaning that values higher/lower than two standard deviations from the mean were transformed into a value of two standard deviations from the mean. Since the HRV data as well as the tasks data were afterwards still positively skewed, they were log-transformed to obtain a normal distribution. We ran the analyses with the log-transformed values; however, we indicate the raw data as descriptive values, given that they can be more easily interpreted. We excluded incorrect and missed responses for all RT analyses, and for all error percentage analyses, incorrect and missed responses were included. We defined the same cut-off values to exclude outliers in the four cognitive tasks, namely responses faster than 200 ms and greater than 2,000 ms.

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To test H1a-d, we ran 2x2 repeated-measures analyses of variance (rmANOVAs) with stimulation condition (active vs. sham stimulation) and congruency (congruent vs. incongruent trial) for inhibitory control tasks, and stimulation condition (active vs. sham stimulation) and trial type (switch vs. non-switch trial) for cognitive flexibility tasks as within-subject factors. The relevant task parameters are RT and percentage error for all four tasks, and additionally switch costs for the cognitive flexibility tasks. Only for the effect of tVNS on switch costs (RT on switch trials minus RT on repeated trials), paired samples t-tests were run. To investigate H2a-d, we ran a 2 (active and sham stimulation) x 3 (resting, single tVNS, and task period) rmANOVA for each task block. Relevant dependent variables were RMSSD, HF, and respiratory frequency. To address H3a-d, we ran separated Pearson product-moment correlation matrices, one for active and one for sham stimulation, for all tasks. We investigated the correlation between RMSSD and HF during the single tVNS period and RT and percentage error, while controlling HF for respiration. In the analysis of the cognitive flexibility tasks, we additionally included switch costs. Finally, to test H4a-d, we did the same analysis as for H3a-d, but considering RMSSD and HF during the tasks instead of during the single tVNS period. To control for false discovery rate (FDR) due to multiple correlation testing, for all correlation matrices we applied the Benjamini–Hochberg procedure which adjust the *p* value (Benjamini & Hochberg, 1995). For all rmANOVAs, Greenhouse–Geisser correction was used when sphericity was violated. In the case of a significant main or interaction effect, post hoc paired sample t-tests with aggregated means were conducted using Bonferroni correction. To quantify evidence for the hypotheses found, we ran Bayesian statistics using Bayesian information criteria (Wagenmakers, 2007) for all analyses. Terms used to discuss the reported Bayes factors are based on Wetzels and

406 colleagues' recommendations (2011). Accordingly, values higher than 1 provide evidence for  
 407 alternative hypotheses, whereas values lower than 1 provide evidence for null hypotheses.  
 408 The Bayes factor can have the following meanings: anecdotal or worth no more than a bare  
 409 mention ( $0.333 < B_{10} < 3$ ), substantial ( $0.100 < B_{10} \leq 0.333$  or  $3 \leq B_{10} < 10$ ), strong ( $0.033 <$   
 410  $B_{10} \leq 0.100$  or  $10 < B_{10} < 30$ ), very strong ( $0.010 < B_{10} \leq 0.033$  or  $30 \leq B_{10} < 100$ ), and  
 411 decisive ( $B_{10} \leq 0.010$  or  $B_{10} \geq 100$ ) evidence. To control for carry-over effects on RMSSD  
 412 and HF, which potentially arose in the current block due to the previous block, we tested the  
 413 effect of position (i.e., first, second, third and fourth resting periods arranged chronologically)  
 414 on each testing day. We also took the testing days (Day 1 and Day 2) into account in the same  
 415 analysis and checked if there was a difference in RMSSD and HF from the first to the second  
 416 day. We ran two separated 2 (Day 1 and Day 2) x 4 (Resting period 1, Resting period 2,  
 417 Resting period 3, and Resting period 4) rmANOVAs, one for each vmHRV parameter.  
 418 Furthermore, we checked whether there was a learning effect in the cognitive tasks from one  
 419 testing day to the other by running 2 (Day 1 and Day 2) x 2 (congruent and incongruent or  
 420 non-switch and switch trials, depending on the task) rmANOVAs, one for each behavioral  
 421 measurement. Finally, to check whether tVNS affects task performance more strongly when  
 422 its trials are novel, we split the trials of the tasks into first and second half, whereby first half  
 423 would correspond to novel trials, and collapsed the congruent/non-switch with the  
 424 incongruent/switch trials. We then ran 2x2 rmANOVAs with stimulation (active and sham  
 425 stimulation) and novelty (first and second half of the task) as factors, and RT and percentage  
 426 error of all tasks as dependent variables. The results of these additional analyses can be found  
 427 as a supplemented material (data sheet 1). To report the results of the present study, we  
 428 followed the CONSORT statement, which stands for Consolidated Standards of Reporting  
 429 Trials (Dwan et al., 2019). We used IBM SPSS Statistics 26 to prepare the data and JASP  
 430 0.11.1 to analyze it. Significance level was  $\alpha = .05$ .

### 431 3 Results

#### 432 3.1 Effects of tVNS on executive functions

433 Descriptive statistics are presented in Table 2, and complete results of the hypothesis testing  
 434 can be found in Table 3 (inhibitory control tasks) and Table 4 (cognitive flexibility tasks),  
 435 here we will mainly focus on significant results as well as on results of Bayesian estimations  
 436 for effects of stimulation. The rmANOVAs revealed that, regarding RTs in the Flanker task,  
 437 there was an effect of congruency,  $F(1, 31) = 95.788, p < .001, \eta_p^2 = .755$ , with RTs in the  
 438 congruent trials ( $M = 475.93$  ms,  $SD = 52.14$ ) being significantly shorter than in the  
 439 incongruent trials ( $M = 555.38$  ms,  $SD = 72.28$ ),  $t(31) = 9.100, p < .001, d = 1.609$ . No effect  
 440 of active stimulation compared to sham stimulation could be found, ( $p = .283$ ). Regarding  
 441 percentage error in the Flanker task, there was an effect of congruency,  $F(1, 31) = 8.202, p =$   
 442  $.007, \eta_p^2 = .209$ , with congruent trials ( $M = 4.40\%$ ,  $SD = 4.40$ ) presenting less errors than  
 443 incongruent trials ( $M = 6.80\%$ ,  $SD = 7.12$ ),  $t(31) = 3.157, p = .004, d = 0.558$ . No effect of  
 444 active stimulation compared to sham stimulation could be found, ( $p = .760$ ). According to the  
 445 estimated Bayes factors (alternative/null), data provided substantial evidence for null effects  
 446 of stimulation condition on RT ( $B_{10} = 0.311$ ) and substantial evidence of null effects in  
 447 percentage error ( $B_{10} = 0.196$ ).

448 Tables 2, 3, and 4 here

449 For RT in the Spatial Stroop task, there was an effect of congruency,  $F(1, 31) =$   
 450  $39.001, p < .001, \eta_p^2 = .557$ , with RTs in the congruent trials ( $M = 504.08$  ms,  $SD = 51.73$ )  
 451 being significantly shorter than in the incongruent trials ( $M = 531.64$  ms,  $SD = 56.21$ ),  $t(31) =$   
 452  $6.245, p < .001, d = 1.104$ . No effect of active stimulation compared to sham stimulation

453 could be found, ( $p = .361$ ). Regarding percentage error, there was an effect of congruency,  
 454  $F(1, 31) = 37.673, p < .001, \eta_p^2 = .549$ , with congruent trials ( $M = 1.47\%, SD = 1.48$ )  
 455 presenting less errors than incongruent trials ( $M = 4.39\%, SD = 3.63$ ),  $t(31) = 6.138, p < .001,$   
 456  $d = 1.085$ . No effect of active stimulation compared to sham stimulation could be found, ( $p =$   
 457  $.756$ ). According to the estimated Bayes factors, data provided anecdotal evidence against the  
 458 alternative hypothesis for stimulation condition regarding RT ( $B_{10} = 0.344$ ) and substantial  
 459 evidence against evidence for effects of stimulation on percentage error ( $B_{10} = 0.201$ ).  
 460 Furthermore, Bayesian estimation indicated substantial evidence for an interaction effect  
 461 ( $B_{10} = 3.047$ ).

462 For NLT, an effect of trial type (switch trial vs. non-switch trial) could be found on  
 463 RT,  $F(1, 31) = 225.365, p < .001, \eta_p^2 = .879$ , with non-switch trials ( $M = 969.73$  ms,  $SD =$   
 464  $130.41$ ) having shorter RT than switch trials ( $M = 1,209.02$  ms,  $SD = 127.84$ ),  $t(31) = 15.012,$   
 465  $p < .001, d = 2.654$ . No effect of active stimulation compared to sham stimulation could be  
 466 found regarding RT ( $p = .505$ ). Switch costs during active stimulation ( $M = 225.23$  ms,  $SD =$   
 467  $107.14$ ) and during sham stimulation ( $M = 251.08$  ms,  $SD = 97.47$ ) did not differ from each  
 468 other,  $p = .140$ . Regarding percentage error, there was an effect of trial type,  $F(1, 31) =$   
 469  $59.615, p < .001, \eta_p^2 = .658$ , with non-switch trials ( $M = 22.68\%, SD = 2.91$ ) presenting more  
 470 errors than switch trials ( $M = 20.39\%, SD = 3.22$ ),  $t(31) = 7.721, p < .001, d = 1.365$ . There  
 471 was no main effect of stimulation ( $p = .168$ ). Bayes factor indicates substantial evidence  
 472 against the alternative hypothesis for stimulation condition regarding RT ( $B_{10} = 0.210$ ),  
 473 anecdotal evidence supporting the effect of stimulation on percentage error ( $B_{10} = 1.097$ ), and  
 474 anecdotal evidence against the effect of tVNS on switch costs ( $B_{10} = 0.529$ ).

475 For DCCS, an effect of trial type on RT could be found,  $F(1, 31) = 14.720, p = .001,$   
 476  $\eta_p^2 = .322$ , with non-switch trials ( $M = 969.73$  ms,  $SD = 130.41$ ) having shorter RT than  
 477 switch trials ( $M = 1,209.02$  ms,  $SD = 127.84$ ),  $t(31) = 15.012, p < .001, d = 2.654$ . There was  
 478 no effect of stimulation on RT ( $p = .904$ ), but there was an interaction effect between trial  
 479 type and stimulation conditions,  $F(1, 31) = 11.106, p = .002, \eta_p^2 = .264$ . Post-hoc analyses  
 480 (Bonferroni-corrected  $p = .0125$ ) revealed that RT in non-switch trials during the sham  
 481 stimulation condition ( $M = 557.51$  ms,  $SD = 113.56$ ) was significantly lower than RT in  
 482 switch trials during the sham condition ( $M = 614.01$  ms,  $SD = 138.65$ ),  $t(31) = 4.767,$   
 483  $p < .001, d = 0.843$ . Regarding percentage error, there was an effect of trial type,  $F(1, 31) =$   
 484  $15.343, p < .001, \eta_p^2 = .331$ , with non-switch trials having a lower percentage error ( $M =$   
 485  $17.49\%, SD = 11.39$ ) than switch trials ( $M = 28.00\%, SD = 17.30$ ),  $t(31) = 3.917, p < .001, d$   
 486  $= 0.692$ . There was no effect of stimulation on RT ( $p = .677$ ). Active and sham stimulation  
 487 differed significantly regarding switch costs, with switch costs during active stimulation ( $M =$   
 488  $4.77$  ms,  $SD = 39.75$ ) being lower than during sham condition ( $M = 37.54$  ms,  $SD = 45.39$ ),  
 489  $t(31) = 2.797, p = .009, d = 0.494$ . Bayes factor indicates substantial evidence against any  
 490 effects of stimulation condition on RT ( $B_{10} = 0.192$ ), against the alternative hypothesis for  
 491 percentage error ( $B_{10} = 0.233$ ), and substantial evidence for the differences in switch costs  
 492 ( $B_{10} = 4.916$ ). Furthermore, Bayesian estimation indicated substantial evidence for an  
 493 interaction effect ( $B_{10} = 3.047$ ).

### 494 3.2 Effects of tVNS on cardiac vagal activity

495 Descriptive statistics are presented in Table 5, and complete results of the hypothesis testing  
 496 can be found in Table 3 (inhibitory control tasks) and Table 4 (cognitive flexibility tasks), here  
 497 we will mainly focus on significant results as well as on results of Bayesian estimations for  
 498 effects of stimulation. Regarding changes of cardiac vagal activity within the test blocks (i.e.,  
 499 between resting, single tVNS, and tVNS with task periods, as well as between active and sham



500 stimulation), for Flanker task there was neither a main effect of stimulation condition ( $p =$   
 501  $.621$ ), nor of time on RMSSD ( $p = .065$ ). The same applies to the main effects on HF  
 502 (stimulation condition:  $p = .135$ ; time:  $p = .221$ ). There was no effect of stimulation on  
 503 respiratory frequency ( $p = .405$ ), but an effect of time,  $F(1.587, 49.206) = 3.518, p = .047, \eta_p^2$   
 504  $= .102$ . However, post-hoc analyses (Bonferroni-corrected  $p = .017$ ) revealed no significant  
 505 mean differences. According to the estimated Bayes factors, data provided substantial evidence  
 506 against the alternative hypothesis for stimulation condition regarding RMSSD ( $B_{10} = 0.215$ ),  
 507 and anecdotal evidence regarding HF ( $B_{10} = 0.664$ ).

508 Table 5 here

509 For the Spatial Stroop task, neither a main effect of stimulation on RMSSD, ( $p =$   
 510  $.926$ ), nor of time, ( $p = .084$ ), was found. There was an interaction effect between the  
 511 stimulation condition and RMSSD,  $F(2, 62) = 3.845, p = .027, \eta_p^2 = .110$ , however post-hoc  
 512 analyses revealed no effects after Bonferroni correction ( $p = .006$ ). There was no effect of  
 513 stimulation ( $p = .915$ ), and time ( $p = .132$ ) on HF and no effects on respiratory frequency  
 514 (stimulation:  $p = .648$ , time:  $p = .062$ ). Bayes factor indicates substantial evidence against the  
 515 alternative hypothesis for stimulation condition regarding RMSSD ( $B_{10} = 0.189$ ), HF ( $B_{10} =$   
 516  $0.196$ ), and respiratory frequency ( $B_{10} = 0.227$ ).

517 For the NLT, there was neither an effect of stimulation on RMSSD ( $p = .991$ ), nor on  
 518 time ( $p = .599$ ). Regarding HF, no effect of stimulation ( $p = .575$ ), but a main effect of time  
 519 was found,  $F(2, 46) = 4.689, p = .014, \eta_p^2 = .039$ . Post-hoc analyses (Bonferroni-corrected  $p$   
 520  $= .017$ ) revealed that HF during the resting period ( $M = 12.92, SD = 8.25$ ) was significantly  
 521 lower than during the task period ( $M = 18.31, SD = 9.39$ ),  $t(31) = 4.108, p < .001, d = 0.726$ .  
 522 According to the estimated Bayes factors, there is substantial evidence against the alternative  
 523 hypothesis for stimulation condition regarding RMSSD ( $B_{10} = 0.152$ ), regarding HF ( $B_{10} =$   
 524  $0.216$ ), and respiratory frequency ( $B_{10} = 0.159$ ).

525 For the DCCS, there was neither a main effect of stimulation condition on RMSSD, ( $p$   
 526  $= .877$ ), nor of time, ( $p = .212$ ). Regarding HF, there was no effect of stimulation, ( $p = .646$ ),  
 527 but a main effect of time,  $F(1.613, 38.708) = 6.821, p = .002, \eta_p^2 = .078$ . Post-hoc analyses  
 528 (Bonferroni-corrected  $p = .017$ ) revealed that HF increased from resting ( $M = 13.36, SD =$   
 529  $9.42$ ) to single stimulation phase, ( $M = 16.71, SD = 11.20$ ),  $t(31) = 3.205, p = .003, d = 0.566$ ,  
 530 and from resting to task phase, ( $M = 19.71, SD = 8.96$ ),  $t(31) = 4.708, p < .001, d = 0.832$ .  
 531 According to the estimated Bayes factors, data provided substantial evidence against the  
 532 alternative hypothesis for RMSSD regarding stimulation condition ( $B_{10} = 0.160$ ), regarding  
 533 HF ( $B_{10} = 0.186$ ), and regarding respiratory frequency ( $B_{10} = 0.168$ ).

### 534 3.3 Correlations between HRV and cognitive performance

535 We ran Pearson product-moment correlations to investigate if vmHRV parameters that were  
 536 measured during the single stimulation phase and the task phase predicted performance on  
 537 the cognitive tasks. Complete correlation matrices can be found in Tables 6 (for inhibitory  
 538 control tasks) and 7 (for cognitive flexibility tasks), here we will only present significant  
 539 results. None of the vmHRV parameters measured during the Flanker task correlated with the  
 540 cognitive parameters. Regarding the Spatial Stroop task, there was only significant  
 541 correlations between the parameters measured in the sham condition: RT in both congruent ( $r$   
 542  $= -.42, p = .018$ ) and incongruent trials ( $r = -.39, p = .027$ ) correlated negatively with  
 543 RMSSD during the single stimulation phase. HF correlated negatively with RT in the  
 544 congruent trials during the single stimulation phase ( $r = -.43, p = .038$ ), and positively with  
 545 percentage error of the incongruent trials during the single stimulation phase ( $r = .43, p =$

546 .032). In the NLT, RMSSD correlated positively with percentage error of non-switch trials  
 547 during the active condition ( $r = .40, p = .025$ ). In the active condition, HF during the single  
 548 stimulation phase correlated negatively with RT of both non-switch ( $r = -.44, p = .015$ ) and  
 549 switch trials ( $r = -.50, p = .005$ ), and HF during the task phase correlated negatively with  
 550 switch costs ( $r = -.42, p = .019$ ). In the sham condition, HF correlated positively with  
 551 percentage error during the task phase ( $r = .48, p = .015$ ). In the DCCS, switch costs in the  
 552 active condition correlated positively with RMSSD during the single stimulation phase ( $r =$   
 553  $.40, p = .024$ ), with RMSSD during the task phase ( $r = .37, p = .035$ ), and negatively with HF  
 554 during the task phase ( $r = -.42, p = .019$ ). HF during the task phase correlated positively with  
 555 RT of both non-switch ( $r = -.40, p = .026$ ) and switch trials ( $r = -.42, p = .018$ ). Importantly,  
 556 after adjusting the  $p$  values using the FDR correction, none of these correlations remained  
 557 significant.

#### 558 **4 Discussion**

559 The aim of this study was to investigate the effect of tVNS on performance in tasks  
 560 commonly used to measure inhibitory control and cognitive flexibility, core executive  
 561 functions on which higher-order executive functions rely. Based on the neurovisceral  
 562 integration model (Thayer et al., 2009), we hypothesized that executive performance would  
 563 be better during the active stimulation condition compared to the sham stimulation condition  
 564 (H1a-d). Conflict effects were found in all four tasks used. However, among the four tasks,  
 565 only in the DCCS a better performance could be directly linked to tVNS, with switch costs  
 566 being lower in the active condition than in the sham condition. For this reason, among the H1  
 567 hypotheses, only H1c was supported. On the physiological level, we expected vmHRV to be  
 568 higher in the active condition during both the single stimulation period and the task period  
 569 (H2a-d). During both cognitive flexibility tasks, HF increased from resting phase to task  
 570 phase, but no difference between active and sham stimulation could be detected. Therefore,  
 571 H2a-d could not be observed. Moreover, it was hypothesized that higher cardiac vagal  
 572 activity in the single stimulation phase (H3a-d) and in the task phase (H4a-d) would be  
 573 associated with better task performance only in the active condition. None of these  
 574 hypotheses could not be observed, because none of the correlations found remained  
 575 significant after adjusting the  $p$  values.

576 Tables 6 and 7 here

577 In the present study, we could provide a conceptual replication (Walker et al., 2017)  
 578 of the conflict effects previously observed in tasks that are thought to mainly demand  
 579 selective attention like the Flanker task (Alderman & Olson, 2014) and response inhibition  
 580 with the Spatial Stroop task (Marotta et al., 2018). In the same sense, findings towards dual-  
 581 task interference evoked by a task used to measure task switching with NLT (Colzato,  
 582 Jongkees, et al., 2018), as well as by a task thought to measure set shifting with DCCS  
 583 (Zelazo et al., 2014) could be replicated with large effect sizes. However, an effect of tVNS  
 584 could be found only on set shifting with DCCS. First, smaller switch costs during tVNS were  
 585 observed compared to the sham condition. Second, RT in non-switch trials did not differ from  
 586 RT in switch trials during active stimulation, but in the sham stimulation RT in switch trials  
 587 were higher than in non-switch trials. Possibly tVNS diminished the dual-task interference,  
 588 whereas sham stimulation did not, and this would explain this difference in switch costs  
 589 between tVNS and sham stimulation. Importantly, some results referring to a lack of  
 590 difference between active and sham stimulation were not substantially supported by Bayesian  
 591 estimations, namely for RT in the Spatial Stroop task, HF and respiratory frequency in the

592 Flanker task, and percentage error and switch costs in the NLT. Consequently, these findings  
 593 should be interpreted carefully.

594 The mixed nature of the results and the lack of correlation between cognitive  
 595 performance and cardiac vagal activity provide evidence against a generability of the  
 596 neurovisceral integration model (Thayer et al., 2009). These findings can be interpreted in  
 597 various manners. First, the present study indicates that tVNS may exert a circumscribed  
 598 influence on core executive functions. This suggests that the neurovisceral integration model  
 599 may be less generally applicable than previously outlined (Smith et al., 2017; Thayer et al.,  
 600 2009). This specificity is in line with previous findings involving executive functions and  
 601 cardiac vagal activity (Jennings, Allen, Gianaros, Thayer, & Manuck, 2015). Jennings and  
 602 colleagues (2015) found that cardiac vagal activity was not directly related to resting state  
 603 activity of intrinsic brain networks but rather to more localized connectivity. This implies that  
 604 the integration between autonomic and cognitive control is more limited than the general  
 605 integration originally suggested. Consequently, the neurovisceral integration model (Thayer  
 606 et al., 2009) might not apply to the full range of executive functions, but rather to specific  
 607 cognitive functions (Jennings et al., 2015).

608 It is not clear, however, whether the specificity of the integration between autonomic  
 609 and cognitive regulation shown in the present study is valid for executive functions in  
 610 general—i.e., independently of the method used to manipulate them—or whether tVNS  
 611 affects only specific cognitive regulation processes. One of the reasons for this possible  
 612 specificity related to tVNS might lie in the level of neurotransmission: tVNS sends a signal to  
 613 the locus coeruleus (Dietrich et al., 2008; Kraus et al., 2007), the primary source of  
 614 norepinephrine in the brain (Foote et al., 1983). Norepinephrine has been thought to be  
 615 engaged by tVNS (Beste et al., 2016; Steenbergen et al., 2015; van Leusden et al., 2015).  
 616 Locus coeruleus plays an important role in reorienting attention and cognitive flexibility, and  
 617 those neurons have been shown to have a task-related activation (Sara, 2015). Noradrenergic  
 618  $\alpha$ -1 and  $\alpha$ -2 receptors act in distinct cognitive processes: whereas  $\alpha$ -2 receptors engage at  
 619 moderate rates of norepinephrine release, thus promoting working memory,  $\alpha$ -1 receptors are  
 620 activated at higher rates, promoting both focused and flexible attention (Berridge & Spencer,  
 621 2016). It is not clear whether DCCS demands more flexible attention than NLT, and whether  
 622 the difference between the two could only be observed because tVNS evokes a stronger  
 623 release of norepinephrine, engaging  $\alpha$ -1 receptors that were necessary for the DCCS but less  
 624 so for the NLT. Hence, it is recommended for future studies to address the possible specific  
 625 efficacy of tVNS by considering an on-line measurement of norepinephrine such as pupillary  
 626 responses (Burger et al., 2020; Keute, Demirezen, et al., 2019; Warren et al., 2018). This  
 627 approach might complement and further specify the hypotheses based on the neurovisceral  
 628 integration model (Thayer et al., 2009).

629 Second, despite all efforts in taking well acknowledged recommendations into  
 630 account, task impurity (Miyake et al., 2000) may not have been ruled out. Consequently, the  
 631 question remains whether other cognitive processes underlying the specific task used to  
 632 measure set shifting, and not set shifting per se, are influenced by tVNS. For instance,  
 633 inhibitory processes have been thought to take place in cognitive flexibility. Accordingly, for  
 634 the efficient activation of another set in the context of set shifting, the inhibition of the  
 635 previous, no longer relevant task, is required. Therefore, backward inhibition is a process  
 636 highly involved in cognitive flexibility (Mayr & Keele, 2000). It remains unclear if a  
 637 comparable amount of backward inhibition is required for both tasks used to measure  
 638 cognitive flexibility. Similarly, rather than Spatial Stroop task being considered a good index  
 639 of response inhibition, possibly interference control, i.e. control at the level of perception, is  
 640 measured by means of this task (Tafuro et al., 2019). To overcome these concerns, it is

641 necessary to develop cognitive tasks that minimally vary from each other in the sense that the  
 642 additional cognitive processes necessary for performing a cognitive task can be minimized or  
 643 at least kept constant. This would enable a more accurate integrative assessment of the core  
 644 executive functions in future research with tVNS investigating executive performance.

645 Third, the lack of a difference between tVNS and sham stimulation regarding cardiac  
 646 vagal activity, which is in line with previous findings (Borges et al., 2019; Burger et al.,  
 647 2019; Burger et al., 2016; De Couck et al., 2017), could have contributed to the heterogeneity  
 648 of the findings. Despite ample evidence on the effects of tVNS on cognition (e.g., Sellaro,  
 649 Gelder, Finisguerra, & Colzato, 2017; Steenbergen et al., 2015), the evidence provided by the  
 650 present study on cardiac vagal activity substantiates the arguments against the suitability of  
 651 the earlobe as a sham stimulation, as discussed lately (Borges et al., 2019; Keute, Ruhnau, &  
 652 Zaehle, 2018; Rangon, 2018). At present, there is only one detailed description of the nerve  
 653 distribution of the human auricle and it shows that the earlobe is free from vagal innervation  
 654 (Peuker & Filler, 2002). However, it lacks substantial evidence that electrical stimulation on  
 655 the earlobe cannot stimulate brain center nuclei that trigger an increase in cardiac vagal  
 656 outflow (Rangon, 2018). This is especially relevant because the boundaries between  
 657 particular dermatomes often overlap (Butt et al., 2019), so that a clear understanding of the  
 658 nerve distribution of the human auricle is needed. Regardless of the suitability of the earlobe,  
 659 it has also been discussed whether vmHRV parameters are sensitive to afferent vagal changes  
 660 triggered by tVNS; it is not yet clear whether the electrical signal produced by tVNS is strong  
 661 enough to overcome body-related barriers such as skin and blood vessels, and therefore to  
 662 trigger vagal afferent firing in a way that would robustly increase prefrontal activity, thus  
 663 indirectly affecting cardiac vagal activity (Borges et al., 2019).

664 In the present study, the cognitive tasks themselves did not seem to have an impact on  
 665 the HRV parameters, since neither RMSSD nor HF decreased during the tasks when  
 666 compared to before the tasks. It is not clear whether this lack of a decrease—which would be  
 667 expected based on the neurovisceral integration model (Smith et al., 2017; Thayer et al.,  
 668 2009), given the conflict effects elicited by the tasks—was due to tVNS or not. Possibly, the  
 669 tasks were not cognitively demanding enough to evoke a decrease in cardiac vagal activity.  
 670 The lack of cognitive demand could also explain why we found no effect of tVNS on  
 671 inhibitory control, whereas an array of previous studies provided evidence in this direction  
 672 (see Table 1). Importantly, none of these previous studies used the same paradigms that were  
 673 used in the present study. It is possible that the paradigms for measuring inhibitory control  
 674 used here, at least concerning the amount of trials and instructions used in the present study,  
 675 are not sensitive to effects that might otherwise be elicited by tVNS. Moreover, none of the  
 676 previous studies investigating the effects of tVNS on inhibitory control found overall  
 677 enhanced performance, measured by means of RT and percentage error (see Table 1).  
 678 Instead, they addressed inhibitory control in specific contexts, such as backward inhibition  
 679 when working memory is more strongly demanded (Beste et al., 2016), or response selection  
 680 during action cascading (Steenbergen et al., 2015). Regarding cognitive demand, future  
 681 studies should incorporate measures of the cognitive demand of the tasks, for instance by  
 682 means of subjective questionnaires or imaging techniques such as functional near-infrared  
 683 spectroscopy (fNIRS) and fMRI to measure prefrontal activity during task performance.

684 As the only vmHRV parameter to show changes in the present study, HF increased  
 685 during the NLT and DCCS when compared to the resting phase. Since both tasks are  
 686 cognitively demanding due to the dual-task interference, based on the neurovisceral  
 687 integration model (Thayer et al., 2009) HF should decrease compared to both resting and  
 688 single stimulation phases. At the same time, this increase of HF was not associated with a  
 689 better performance in the DCCS, as it would be predicted by the neurovisceral integration

690 model. Although there was no difference between tVNS and sham stimulation regarding HF  
 691 in the present study, the increase in HF during the DCCS might be linked to the positive  
 692 effect of tVNS found on switch costs. So far, there has been no other study investigating the  
 693 effect of tVNS on respiration, and whether respiration, when affected by tVNS, moderates  
 694 executive performance. Future studies should address this question in order to further  
 695 investigate the mechanisms of action behind tVNS.

#### 696 **4.1 Limitations**

697 There are limitations to our study that should be mentioned. First, RMSSD increased within  
 698 the experimental sessions (see supplementary material). It is not clear, however, whether this  
 699 carry-over effect emerged from the stimulation itself, or simply from the fact that the  
 700 participants were sitting during the experiment. Thus, this increase during the experimental  
 701 sessions may represent a relevant confounder that renders it difficult to interpret cardiac vagal  
 702 activity measurements. Second, despite considering inhibitory control and cognitive  
 703 flexibility differentially by taking different aspects into account, the present study did not  
 704 consider other types of cognitive flexibility. Creatively thinking outside the box, seeing  
 705 something from different perspectives (Diamond, 2013), or stochastic reversal learning  
 706 (Colzato, Jongkees, et al., 2018) could be aspects of cognitive flexibility prone to be  
 707 influenced by tVNS. Third, respiratory frequency was obtained via a dedicated algorithm  
 708 from Kubios (Tarvainen et al., 2013). However, a more precise assessment of respiratory  
 709 frequency such as a respiration belt or a pneumotachograph is recommendable (Quintana et  
 710 al., 2016). Fourth, the sample has a misbalance regarding gender, with male participants  
 711 being vast majority. Given that sex differences can influence cardiac vagal activity (Koenig  
 712 & Thayer, 2016), this misbalance may have been an issue for the analysis. Finally, as stated  
 713 above, the tasks are not comparable to each other. For example, the Flanker task used here  
 714 has, when compared to the Spatial Stroop task, a shorter stimulus presentation time and  
 715 random intertrial interval. This can provoke different cognitive processes that deviate from  
 716 the ones we aimed at measure. A further difference is the length of the tasks, ranging from  
 717 five (DCCS) to 15 (Flanker task) minutes. The amount of trials also greatly varies between  
 718 the tasks. Due to a lack of measurement of task difficulty, it was not possible to investigate  
 719 whether the difficulty level differed strongly between the tasks, as stated above. Furthermore,  
 720 the DCCS uses colorful pictures, whereas all other tasks are bicolored and involve time  
 721 pressure. The impact of these differences on the cognitive tasks should be considered when  
 722 use them in future studies with tVNS.

#### 723 **4.2 Conclusion**

724 The present study is the first to investigate different core executive functions with their  
 725 different subtypes in an integrative manner. Additionally, this is the first study to investigate  
 726 the effect of tVNS on cognitive flexibility. On the one hand, it was shown that tVNS can lead  
 727 to less switch costs in set shifting, possibly explained by diminished the dual-task  
 728 interference due to tVNS. On the other hand, the present study provided evidence that tVNS  
 729 may have only very specific effects on cognitive processes. By addressing the different  
 730 aspects of core cognitive functions in one standardized study design, the present study  
 731 contributes to a better understanding of the effects of tVNS by further delineating what kind  
 732 of cognitive and physiological mechanisms might be influenced by this neuroenhancement  
 733 tool. Future studies investigating the effect of tVNS on executive functions should further  
 734 investigate cognitive flexibility and consider task characteristics as well as address different  
 735 types of executive functions.

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### **Authors Contributions Statement**

744 UB and SL contributed to conceiving the design of the study. LK led the data collection with  
745 the help of UB. UB realized the statistical analysis with the help of SL. UB wrote the first  
746 draft of the manuscript and SL, MR and SK provided critical comments to improve it. Final  
747 adjustments on the manuscript were suggested by SL and MR. All authors agreed on the final  
748 version.

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### **Conflict of Interest Statement**

751 The authors declare that the research was conducted in the absence of any commercial or  
752 financial relationships that could be construed as a potential conflict of interest.

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In review

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In review

981 Table 1

982 *Summary of the studies with tVNS addressing different types of inhibitory control*

Study	Dependent variable	Cognitive paradigm	Study design	Sample size	Results
Beste et al., 2016	Response inhibition and working memory	Backward inhibition and mental workload inhibition paradigm	Between-subjects	51	Higher response inhibition processes only when working memory processes are needed
Fischer et al., 2018	Selective attention, N2 and P3 amplitudes	Simon	Within-subject	21	Adaptation to conflict was enhanced, N2 amplitude higher
Keute et al., 2019	Automatic motor response inhibition, readiness potentials	Subliminal motor priming	Within-subject	16	Increased NCE; effects on readiness potentials only in compatible trials
Steenbergen et al., 2015	Response selection as a consequence of response inhibition	Stop-change	Between-subjects	30	Faster responses when two actions were executed in succession
Ventura-Bort et al., 2018	Selective attention, sAA, P3a and P3b amplitudes	Oddball	Within-subject	20	Increased sAA after tVNS; easy trials produced larger P3b amplitudes

*Note.* NCE = negativity comparability effect; sAA = salivary alpha-amylase; tVNS = transcutaneous vagus nerve stimulation

983

Table 2

*Mean scores and standard deviations for the performance-relevant parameters of the four cognitive tasks used in the study*

		RT (ms)		Percentage error (%)		Switch costs (ms)	
		Active Stimulation	Sham Stimulation	Active Stimulation	Sham Stimulation	Active Stimulation	Sham Stimulation
Flanker Task	Congruent trials	482.29 (68.19)	469.57 (48.91)	4.50 (4.68)	4.64 (4.45)		
	Incongruent trials	562.54 (88.48)	548.21 (73.63)	7.65 (10.59)	5.95 (5.32)		
Spatial Stroop Task	Congruent trials	501.55 (52.93)	506.60 (60.88)	1.13 (1.40)	1.80 (2.26)		
	Incongruent trials	526.08 (60.86)	537.20 (64.90)	4.45 (3.98)	4.32 (4.24)		
NLT	Non-switch trials	984.11 (164.33)	955.35 (126.00)	21.96 (4.25)	23.41 (2.44)		
	Switch trials	1,212.09 (148.21)	1,205.95 (141.31)	20.12 (4.20)	20.65 (3.85)	225.23 (107.14)	251.08 (97.47)
DCCS	Non-switch Trials	600.16 (138.69)	577.51 (113.56)	18.31 (16.01)	16.68 (15.48)		
	Switch Trials	603.90 (137.04)	614.01 (138.65)	28.24 (23.92)	27.76 (24.32)	4.77 (39.75)	37.54 (45.39)

*Note.* RT = reaction times; NLT = Number Letter task; DCCS = Dimensional Card Sorting task

Table 3

*Inhibitory control tasks: Results of repeated measures analysis of variance for the performance-related as well as heart rate variability parameters, with Bayesian analyses ( $B_{10}$ )*

	Flanker task				Spatial Stroop task			
	<i>F</i> -value	<i>p</i> -value	$\eta_p^2$	$B_{10}$	<i>F</i> -value	<i>p</i> -value	$\eta_p^2$	$B_{10}$
RT								
Congruency	95.788	< .001	.755	2.018E +13	39.001	< .001	.557	2,732.297
Stimulation condition	1.192	.283		0.311	0.860	.361		0.344
Stimulation x congruency	0.001	.992		0.280	0.754	.392		3.047
Percentage error								
Congruency	8.202	.007	.209	3.796	37.673	< .001	.549	4.204E+7
Stimulation condition	0.095	.760		0.196	0.098	.756		0.201
Stimulation x congruency	0.511	.480		0.278	2.626	.115		0.596
RMSSD								
Stimulation condition	0.250	.621		0.215	0.009	.926		0.189
Time measurements	2,862	.065		0.220	2.576	.084		0.154
Time x condition	0.351	.645		0.048	3.845	.027	0.110	0.372
HF								
Stimulation condition	1.669	.211		0.664	0.012	.915		0.196
Time measurements	2.291	.135		0.632	2.146	.132		0.726
Time x condition	3.038	.059		0.158	0.681	.512		0.203
Respiratory frequency								
Stimulation condition	0.714	.405		0.617	0.213	.648		0.227
Time measurements	3.518	.047	0.102	0.102	2.917	.062		0.099
Time x condition	0.855	.430		0.010	0.109	.897		0.087

*Note.* RT = reaction times; RMSSD = root mean square of the successive differences; HF = high frequency

Table 4

*Cognitive flexibility tasks: Results of repeated measures analysis of variance for the performance-related as well as heart rate variability parameters, with Bayesian analyses ( $B_{10}$ )*

	NLT				DCCS			
	<i>F</i> -value	<i>p</i> -value	$\eta_p^2$	$B_{10}$	<i>F</i> -value	<i>p</i> -value	$\eta_p^2$	$B_{10}$
<b>RT</b>								
Trial type	225.365	< .001	.879	1.446E+22	14.720	.001	.322	0.314
Stimulation condition	0.454	.505		0.210	0.015	.904		0.192
Stimulation x congruency	1.670	.206		0.411	11.106	.002	.264	0.339
<b>Percentage error</b>								
Trial type	59.615	< .001	.658	602.764	15.343	< .001	.331	0.491
Stimulation condition	1.996	.168		1.097	0.177	.677		0.233
Stimulation x congruency	3.214	.083		0.382	0.552	.463		0.250
Switch costs <sup>1</sup>	1.513	.140		0.529	2.797	.009	.494	4.916
<b>RMSSD</b>								
Stimulation condition	< 0.001	.991		0.152	0.024	.877		0.160
Time measurements	0.517	.599		0.073	1.590	.212		0.133
Time x condition	0.810	.449		0.011	1.269	.288		0.150
<b>HF</b>								
Stimulation condition	0.324	.575		0.216	0.217	.646		0.186
Time measurements	4.689	.014	.039	12.853	6.821	.002	.078	260.327
Time x condition	1.061	.355		0.163	0.391	.679		0.130
<b>Respiratory frequency</b>								
Stimulation condition	0.021	.885		0.159	0.010	.920		0.168
Time measurements	0.657	.522		0.078	1.516	.228		0.078
Time x condition	0.508	.604		0.100	0.545	.582		0.083

*Note.* <sup>1</sup>The depicted results are from t-tests, i.e. for switch costs, instead of *F* and  $\eta_p^2$ , the results are for *t*-values and Cohen's *d*, respectively. RT = reaction times; RMSSD = root mean square of the successive differences; HF = high frequency



Table 5

*Mean scores and standard deviations for the heart rate variability parameters over time in the four cognitive task blocks*

		RMSSD		HF		Respiratory frequency	
		Active Stimulation	Sham Stimulation	Active Stimulation	Sham Stimulation	Active Stimulation	Sham Stimulation
Flanker Task	Resting	48.43 (22.38)	52.34 (26.56)	13.81 (8.78)	13.71 (12.45)	12.36 (2.06)	12.19 (2.68)
	tVNS	52.56 (28.53)	54.66 (25.02)	15.27 (11.26)	19.59 (13.94)	12.51 (2.40)	12.10 (2.91)
	Task	55.44 (29.81)	55.26 (24.66)	14.44 (9.60)	16.16 (11.56)	12.23 (2.33)	11.66 (3.03)
Spatial Stroop Task	Resting	52.38 (27.64)	53.48 (21.52)	12.97 (10.05)	14.12 (10.80)	14.70 (9.61)	15.85 (10.79)
	tVNS	54.47 (25.99)	58.85 (26.31)	18.74 (13.19)	17.31 (13.60)	19.60 (11.82)	19.16 (15.58)
	Task	55.93 (26.89)	50.70 (19.28)	15.65 (8.45)	17.45 (13.91)	16.25 (9.12)	20.32 (16.48)
NLT	Resting	51.82 (24.75)	50.07 (22.2)	18.06 (12.22)	13.83 (10.98)	12.20 (2.03)	12.02 (2.33)
	tVNS	49.91 (21.12)	51.82 (20.44)	18.51 (12.56)	18.85 (15.07)	12.27 (2.05)	12.38 (2.64)
	Task	50.28 (25.77)	48.78 (18.45)	17.78 (12.13)	17.547 (9.40)	12.06 (1.88)	12.17 (2.48)
DCCS	Resting	54.26 (24.46)	51.82 (22.46)	14.93 (10.11)	16.24 (14.98)	13.52 (8.82)	15.66 (13.96)
	tVNS	54.90 (25.86)	57.4 (24.75)	17.56 (12.57)	19.59 (13.11)	17.95 (12.18)	19.23 (12.80)
	Task	56.36 (24.52)	55.41 (23.24)	19.83 (13.16)	17.55 (11.14)	20.76 (11.75)	19.90 (10.07)

*Note.* RMSSD = root mean square of the successive differences; HF = high frequency; tVNS = transcutaneous vagus nerve stimulation (single stimulation phase); NLT = Number Letter task; DCCS = Dimensional Change Card Sorting task

Table 6

*Pearson product-moment correlations between cognitive performance-relevant parameters and vagally-mediated heart rate variable parameters during the single stimulation phase (tVNS) and the task phase (task) for active and sham conditions. Coefficients for the inhibitory control tasks*

			Active stimulation				Sham stimulation			
			RT		Percentage error		RT		Percentage error	
			Congruent trials	Incongruent trials	Congruent trials	Incongruent trials	Congruent trials	Incongruent trials	Congruent trials	Incongruent trials
Flanker task										
RMSSD	tVNS	Pearson's r	.02	-.05	-.21	-.22	-.29	-.23	.26	.197
		<i>p</i> value	.935	.768	.243	.233	.114	.207	.144	.280
	Task	Pearson's r	-.06	-.08	-.25	-.28	-.24	-.24	.16	.27
		<i>p</i> value	.760	.666	.171	.115	.193	.189	.369	.140
HF	tVNS	Pearson's r	-.20	-.19	.16	.23	-.24	.01	.06	.03
		<i>p</i> value	.288	.334	.395	.237	.262	.991	.785	.906
	Task	Pearson's r	-.25	-.30	-.09	-.17	-.34	-.18	-.01	.07
		<i>p</i> value	.189	.119	.647	.378	.109	.394	.987	.760
Spatial Stroop task										
RMSSD	tVNS	Pearson's r	.06	-.04	-.22	-.15	-.42*	-.39*	-.12	-.01
		<i>p</i> value	.755	.845	.227	.403	.018	.027	.532	.987
	Task	Pearson's r	-.02	-.13	-.18	-.34	-.34	-.31	.19	.12
		<i>p</i> value	.907	.485	.318	.054	.059	.088	.311	.514
HF	tVNS	Pearson's r	-.25	-.27	-.11	.28	-.43*	-.32	.17	.45*
		<i>p</i> value	.175	.151	.579	.131	.038	.142	.437	.032
	Task	Pearson's r	-.20	-.07	-.17	.12	-.27	-.24	.11	.10
		<i>p</i> value	.302	.715	.376	.539	.219	.264	.623	.642

*Note.* \*  $p < .05$ , \*\*  $p < .01$ , \*\*\*  $p < .001$ . Non-adjusted *p* values. RT = reaction times; RMSSD = root mean square of successive differences; HF = high frequency; tVNS = transcutaneous vagus nerve stimulation (single stimulation phase)

Table 7  
*Pearson product-moment correlations between cognitive performance-relevant parameters and vagally-mediated heart rate variable parameters during the single stimulation phase (tVNS) and the task phase (task) for active and sham conditions. Coefficients for the cognitive flexibility tasks*

			Active stimulation					Sham stimulation				
			RT		Percentage error		Switch costs	RT		Percentage error		Switch costs
			Non-switch trials	Switch trials	Non-switch trials	Switch trials		Non-switch trials	Switch trials	Non-switch trials	Switch trials	
NLT												
RMSSD	tVNS	Pearson's r	-.28	-.24	.40*	.14	.13	.12	.15	.19	-.06	-.02
		<i>p</i> value	.132	.179	.025	.434	.434	.513	.430	.308	.727	.934
	Task	Pearson's r	-.06	-.03	.33	.31	.13	.10	.29	.22	-.02	.28
		<i>p</i> value	.732	.860	.070	.081	.475	.595	.113	.238	.909	.115
HF	tVNS	Pearson's r	-.44*	-.50**	.37*	.31	.14	.09	-.10	.11	-.23	-.28
		<i>p</i> value	.015	.005	.046	.099	.463	.677	.626	.599	.279	.170
	Task	Pearson's r	-.39*	-.24	.28	.22	.42*	-.10	-.02	.48*	.07	.15
		<i>p</i> value	.034	.204	.129	.242	.020	.621	.914	.015	.748	.482
DCCS												
RMSSD	tVNS	Pearson's r	-.27	-.17	.24	.29	.40*	.09	.04	-.03	-.01	-.10
		<i>p</i> value	.134	.351	.180	.103	.024	.623	.837	.869	.973	.603
	Task	Pearson's r	-.25	-.14	.16	.23	.37*	.06	.01	.03	.02	-.08
		<i>p</i> value	.177	.440	.385	.212	.035	.741	.953	.858	.920	.660
HF	tVNS	Pearson's r	-.40*	-.42*	.29	.31	-.08	.05	.04	-.19	-.14	.03
		<i>p</i> value	.026	.018	.110	.089	.684	.796	.835	.356	.483	.900
	Task	Pearson's r	.07	-.01	-.27	-.19	-.42*	-.05	-.03	.02	-.06	.10
		<i>p</i> value	.715	.970	.150	.314	.019	.819	.905	.931	.761	.619

*Note.* \*  $p < .05$ , \*\*  $p < .01$ , \*\*\*  $p < .001$ . Non-adjusted *p* values. RT = reaction times; RMSSD = root mean square of successive differences; HF = high frequency; NLT = Number Letter task; DCCS = Dimensional Change Card Sorting task; tVNS = transcutaneous vagus nerve stimulation (single stimulation phase)

991

### Figure captions

992 *Figure 1.* Consort (2019) diagram

993

994 *Figure 2.* Visual depiction of the four cognitive tasks used in the study. (a) Flanker task; (b)  
995 Spatial Stroop task; (c) Number Letter task (NLT); (d) Dimensional Change Card Sorting  
996 task (DCCS)

997

998 *Figure 3.* A) Experimental overview. B) Graphical depiction of the phases within each block.  
999 In total, the participants underwent four task blocks per testing day in a randomized order

1000

In review

Figure 1.TIFF

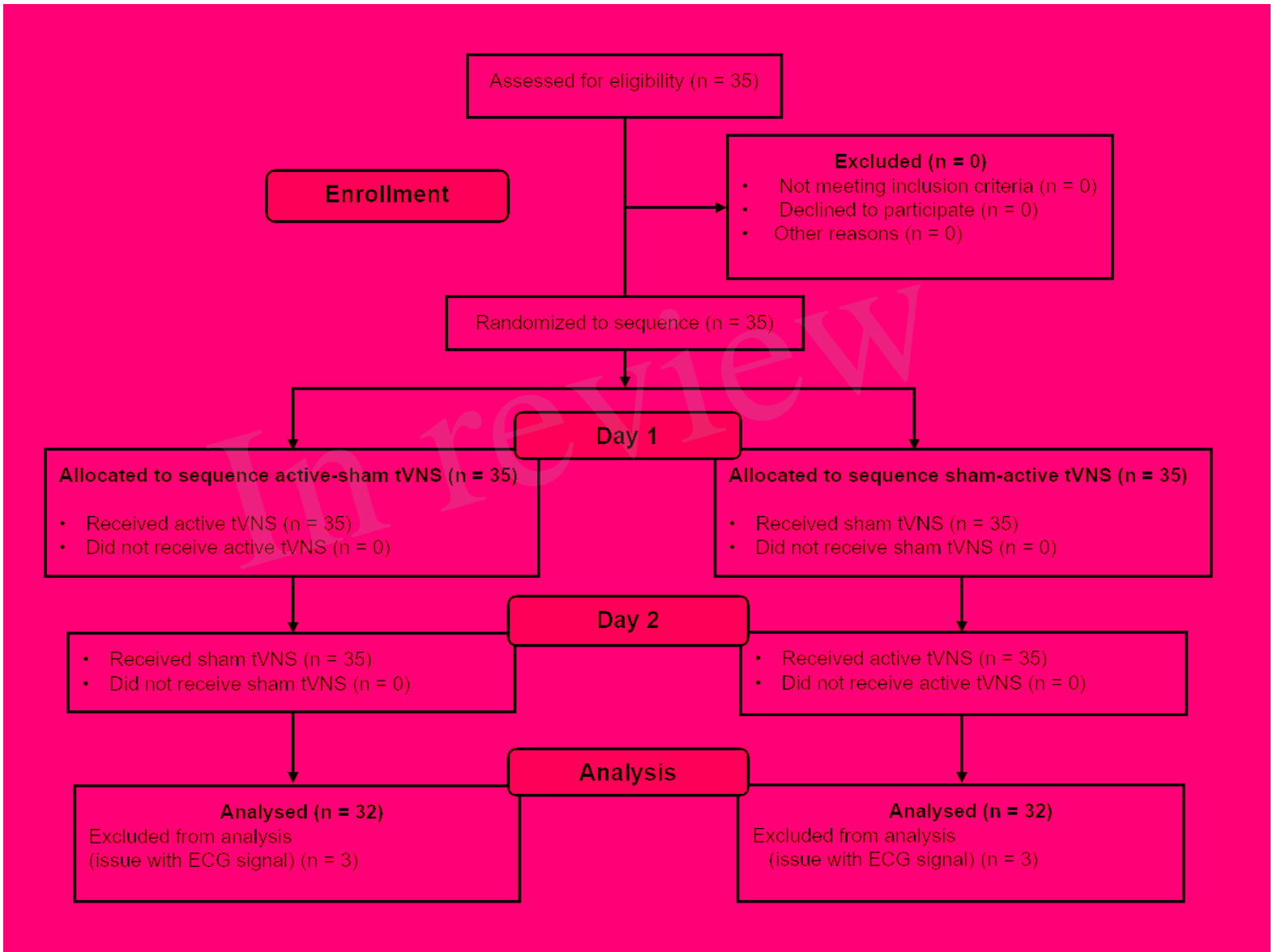
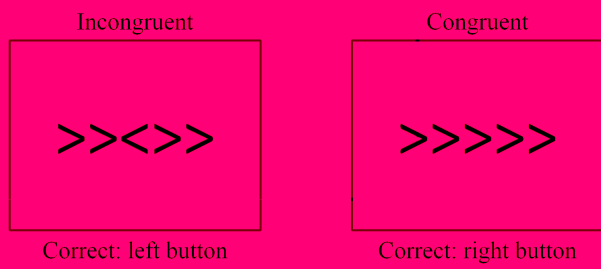
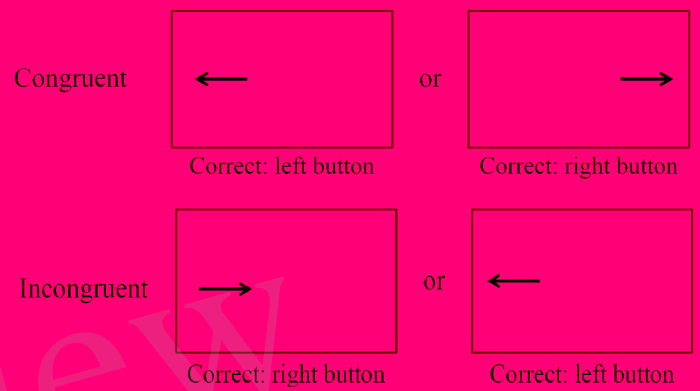


Figure 2.TIFF

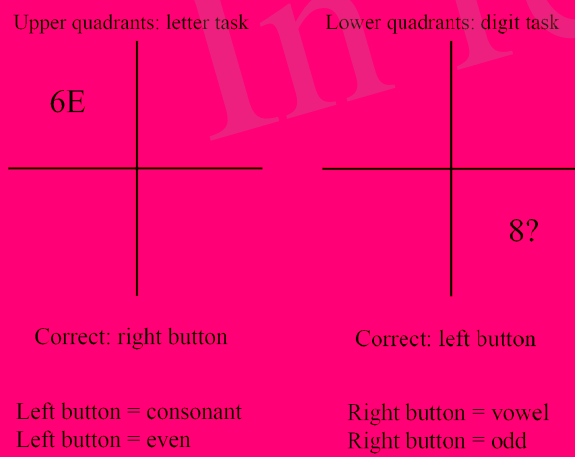
a) Flanker Task



b) Spatial Stroop Task



c) NLT



d) DCCS

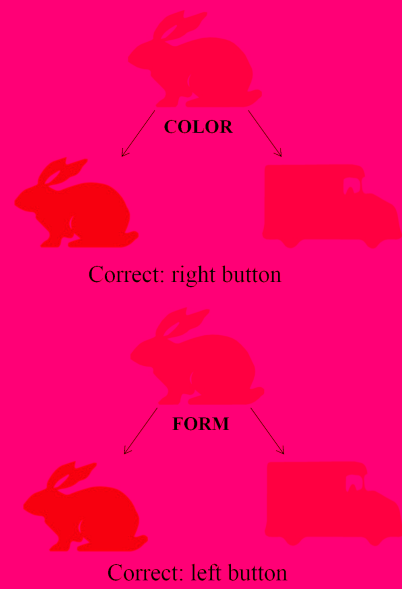
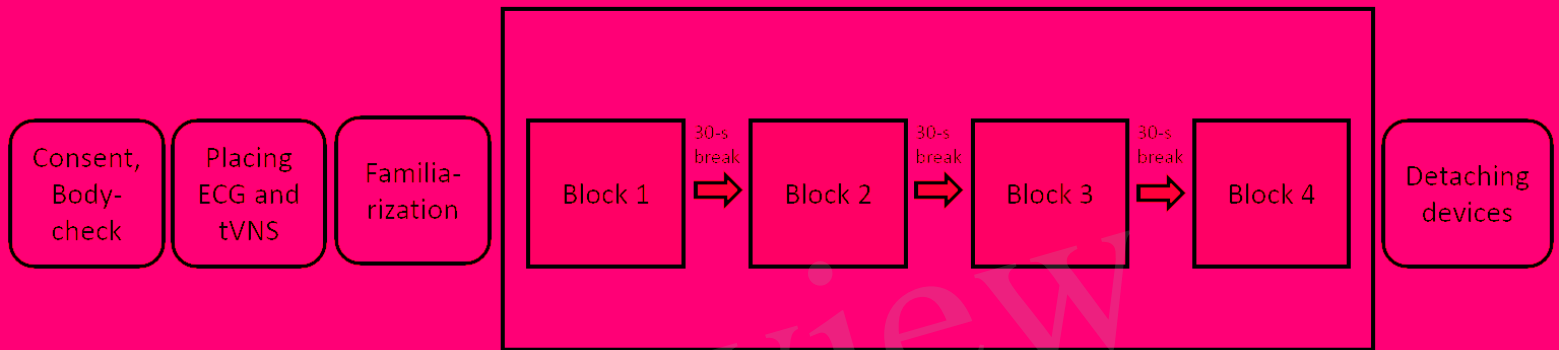


Figure 3.TIFF

A)



B)

Block

