

Does 10-Hz cathodal oscillating current of the parieto-occipital lobe modulate target detection?

1 Sarah S. Sheldon^{1,*} and Kyle E. Mathewson^{1,2}

2 ¹Department of Psychology, Faculty of Science, University of Alberta, Edmonton, Alberta, Canada

3 ²Neuroscience and Mental Health Institute, Faculty of Medicine and Dentistry, University of Alberta,
4 Edmonton, Alberta, Canada

5 **Correspondence*:**

6 Sarah S. Sheldon

7 ssheldon@ualberta.ca

8 **Keywords: alpha oscillations, transcranial current stimulation, entrainment, detection,**
9 **negative findings**

10 **ABSTRACT**

11 The phase of alpha (8-12 Hz) brain oscillations have been associated with moment to moment
12 changes in visual attention and awareness. Previous work has demonstrated that endogenous
13 oscillations and subsequent behavior can be modulated by oscillating transcranial current stimulation
14 (otCS). The purpose of the current study is to establish the efficacy of cathodal otCS for modulation
15 of the ongoing alpha brain oscillations, allowing for modulation of individual's visual perception.
16 Thirty-six participants performed a target detection with sham and 10-Hz cathodal otCS. Each
17 participant had two practice and two experimental sets composed of three blocks of 128 trials per
18 block. Stimulating electrodes were small square sponges (20 cm²) placed on the participant's head
19 with the anode electrode at Cz and the cathode electrode at Oz. A 0.5 mA current was applied at the
20 cathode electrode every 100 ms (10 Hz frequency) during the otCS condition. The same current and
21 frequency was applied for the first 10-20 s of the sham condition, after which the current was turned
22 off. Target detection rates were separated into ten 10-ms bins based on the latency between the
23 stimulation/sham pulse and target onset. Target detection rates were then compared between the
24 sham and otCS experimental conditions across the ten bins in order to test for effects of otCS phase
25 on target detection. We found no significant difference in target detection rates between the sham and
26 otCS conditions, and discuss potential reasons for the apparent inability of cathodal otCS to
27 effectively modulate visual perception.

28 **1 INTRODUCTION**

29 Oscillating neural activity enables the brain to communicate and coordinate across different areas in
30 order to carry out important cognitive functions. Over the last decade, there has been a resurgence of
31 interest in oscillatory activity due to recent technological advances that enable non-invasive
32 modulation of these brain oscillations (Fröhlich, 2015; Fröhlich et al., 2015; Herrmann et al., 2013).
33 In particular, transcranial current stimulation (tCS) has become a popular method because it provides
34 the possibility to modulate the phase, amplitude, and frequency of ongoing oscillatory activity
35 (Paulus, 2011).

36 The most common applications of tCS involves the delivery of the electrical stimulation as either a
37 direct current (i.e., current of a constant intensity and polarity) or an alternating current (i.e., current

38 that oscillates between negative and positive polarity). Anodal (positive polarity) and cathodal
39 (negative polarity) transcranial direct current stimulation (tDCS) can modulate the neuronal response
40 threshold by inducing depolarization or hyperpolarization, respectively (Jackson et al., 2016; Paulus
41 et al., 2016). On the other hand, transcranial alternating current stimulation (tACS) can modulate
42 ongoing neuronal activity in a frequency-specific manner. It is thought that tACS effects response
43 thresholds in a manner similar to tDCS except that alternating between positive (anodal) and negative
44 (cathodal) current results in the neural oscillations becoming entrained to the timing of the alternating
45 current (Antal and Paulus, 2013; Herrmann et al., 2013; Reato et al., 2013; Vosskuhl et al., 2015).
46 This means that tACS can be used to manipulate oscillatory activity in an experimental setting to
47 understand the relevance of such induced oscillations for cognition.

48 Although numerous studies have demonstrated that these electrical stimulation methods can effect
49 perception (Antal et al., 2004; Antal and Paulus, 2008; Helfrich et al., 2014; Neuling et al., 2012a)
50 and cognition (Antonenko et al., 2016; Marshall et al., 2006; Simonsmeier and Grabner, 2017;
51 Zaehle et al., 2011), it seems that many other studies have found little to no evidence supporting the
52 efficacy of these techniques (Brignani et al., 2013; Horvath et al., 2015; Marshall et al., 2016;
53 Tremblay et al., 2014; Veniero et al., 2017). Therefore, here we used a well studied paradigm of alpha
54 oscillations affecting visual perception as a test of the feasibility of using tACS to manipulate
55 oscillations and cognition.

56 Using tACS with a DC-offset is referred to as oscillating transcranial current stimulation (otCS). This
57 technique can be thought of as a combination of tDCS and tACS., and this combination of tDCS and
58 tACS has been shown to be effective for boosting memory (Marshall et al., 2006), and pulsed current
59 stimulation has been shown to affect corticospinal excitability (Jaberzadeh et al., 2014). We therefore
60 utilized otCS here to manipulate posterior parietal alpha oscillations and test if there was any
61 influence on target detection.

62 Brain oscillations within the alpha (8-12 Hz) frequency band have emerged as a marker of visual
63 perception and selective attention (Mathewson et al., 2011). We and others have shown that target
64 detection depends on the phase of alpha oscillations at the moment of target onset (Mathewson et al.,
65 2009), which we have explained due to alpha acting as a pulsating inhibition in the brain. We have
66 found using fast optical imaging that these alpha oscillations relevant for detection can be localized to
67 the posterior parietal cortex (Mathewson et al., 2014). We have found support for this theory in a
68 series of studies in which we rhythmically entrain alpha oscillations with visual stimulation and
69 observe subsequent rhythmic modulation in target detectability (Kizuk and Mathewson, 2017;
70 Mathewson et al., 2012, 2014). We find that 12-Hz rhythmic visual stimulation induces phase
71 locking at the same frequency in the EEG, as well as these fluctuations in target detection. In
72 comparison to the classical rhythmic sensory stimulation protocols which entrain the entire visual
73 system, the use of tCS offers the advantage of directly stimulating cortical targets (Brignani et al.,
74 2013).

75 The aim of the current study was to provide a proof of principle that the entrainment of ongoing
76 neural oscillations by rhythmic visual stimulation can be replicated with cathodal otCS at the same
77 frequency. The present study aims to address this issue by attempting to control the phase alpha
78 oscillations in the posterior parietal cortex during visual perception. We chose otCS because it has
79 been associated with modulation of parieto-occipital alpha activity and subsequent behavior (Kasten
80 and Herrmann, 2017).

81 **2 MATERIALS AND METHODS**

82 2.1 Participants

83 Thirty-six participants from the University of Alberta community participated in the study (mean age
84 = 21; age range = 17-32, 10 males). Participants were all right-handed, and had normal or corrected
85 normal vision and no history of neurological problems. All participants gave informed written
86 consent, were either compensated at a rate of \$10/hr or given research credit for their time, whichever
87 was applicable. The study adhered to the tenets of the Declaration of Helsinki and was approved by
88 the Internal Ethics Board at the University of Alberta.

89 2.2 Target Detection Task

90 Participants were seated 57 cm away from a 1920 x 1090 pixel² ViewPixx/EEG LCD monitor
91 (VPixx Technologies, Quebec, Canada) with a refresh rate of 120 Hz, simulating a CRT display with
92 LED backlight rastering. The rastering, along with 8-bit digital TTL output triggers yoked to the
93 onset and value of the top left pixel, allowed for submillisecond accuracy in pixel illumination times,
94 which were confirmed with a photocell prior to the experiment. Stimuli were presented on a 50%
95 gray background using a Windows 7 PC running MATLAB R2012b with the Psychophysics toolbox
96 (Version 3; Brainard, 1997; Pelli, 1997). See Figure 1A for the stimulus dimensions. Video output
97 was sent to the ViewPixx/EEG with an Asus Striker GTX760 (Fremont, CA) graphics processing
98 unit.

99 Each trial began with a black fixation cross presented at the center of the monitor for 400 ms. The
100 fixation cross was followed by a blank screen. The blank screen remained for 200, 230, 300, 320,
101 370, 410, or 450 ms (target stimulus onset asynchrony; tSOA) after which the target appeared for
102 8.33 ms (one monitor refresh). The target was followed by a backward mask lasting for 8.33 ms with
103 a constant 41.7 ms target-mask SOA (mSOA). Following the mask offset, the participant had 1000
104 ms to respond before the next trial began. There were 128 trials per block, and three blocks per
105 experimental condition. On 20% of trials, the target was omitted to assess false alarms. A summary
106 of the task sequence can be seen in Figure 1B.

107 In the first two conditions, the target luminance value was adjusted throughout the task based on a 3-
108 up/1-down staircasing procedure that was chosen because it targeted a 0.5 target detection rate for
109 each individual (García-Pérez, 1998; Kingdom and Prins, 2016). The target luminance value in the
110 final two conditions remained constant and determined for each participant by taking the average
111 target luminance value across the last two blocks of trials in the second staircasing block.

112 2.3 Electrical Stimulation

113 A battery-driven stimulator (Oasis Pro, Mind Alive, Canada) was used to deliver a 10-Hz oscillating
114 cathodal transcranial electrical current via rubber electrodes encased in sponges (5×4 cm; Oasis Pro,
115 Mind Alive, Canada) and soaked in saline solution. The electrodes were attached to the head
116 underneath an EEG Recording Cap (EASYCAP, Herrsching, Germany) with the cathodal electrode
117 (where the current was applied) at Oz and the anodal electrode placed at Cz. These positions were
118 chosen for maximal stimulation intensity in the parieto-occipital cortex (Neuling et al., 2012b). The
119 stimulation current had a rounded square waveform that was delivered at a 10-Hz frequency. The
120 onset of each stimulation pulse was recorded by the amplifier via a customized trigger output added
121 to the Oasis Pro stimulator by the manufacturer with the accuracy confirmed with oscilloscopes prior
122 to the experiment.

123 The intensity of the stimulation current was adjusted for each participant to ensure that they did not
124 experience pain, tingling or other unpleasant sensations. To obtain this threshold, we started with an
125 intensity level of 0.50 mA (peak-to-peak). If the participant indicated unpleasant sensations, we
126 decreased the intensity in steps of 0.02 mA until the participant reported little to no skin sensation.
127 The obtained threshold level ranged between 0.34-0.50 mA ($M = 0.46$, $SD = 0.05$) was used as
128 stimulation intensity in the tCS condition.

129 The sham condition consisted of a 10 s fade-in and 20 s of stimulation at 0.50 mA. The current was
130 then shut off by disconnecting the Oasis Pro stimulator from the stimulating electrodes out of sight of
131 the sign of the participant. Disconnecting the stimulating device from the electrodes did not interrupt
132 the stimulation triggers sent to the amplifier, which can therefore be used as control timings. The
133 experimental condition also consisted of a 10 s fade-in and 20 s of stimulation at 0.50 mA, after
134 which the current intensity was decreased to the individual's obtained threshold level.

135 **2.4 EEG Recording**

136 During the target detection task, EEG data was recorded using a 16-channel V-amp amplifier (Brain
137 Products, München, Germany) from 15 scalp locations (O1, O2, P7, P3, Pz, P4, P8, T7, C3, Cz, C4,
138 T8, F3, Fz, F4; 10/20 system), a ground electrode at position Fpz, and two reference electrodes,
139 placed at the right and left mastoids, with Ag/AgCl sintered ring electrodes (EASYCAP, Herrsching,
140 Germany) in a 20-channel electrode cap (EASYCAP). SuperVisc electrolyte gel and mild abrasion
141 with a blunted syringe tip were used to lower impedances to less than 5 k Ω for all electrode sites
142 except Cz which did not have direct contact with the head because it was on top of the stimulating
143 electrode sponge. EEG was recorded online referenced to an electrode attached to the left mastoid.
144 Offline, the data were re-referenced to the arithmetically derived average of the left and right mastoid
145 electrode.

146 In addition to the 15 EEG sensors, two reference electrodes, and the ground electrode, the vertical
147 and horizontal bipolar EOG was recorded from passive Ag/AgCl Easycap disk electrodes affixed
148 above and below the left eye, and 1 cm lateral from the outer canthus of each eye. Prior to placement
149 of electrodes, the participant's skin was cleaned using Nuprep (an exfoliating cleaning gel) and
150 electrolyte gel was used to lower the impedance of these EOG electrodes to under 5 k Ω in the same
151 manner as previously mentioned. The bipolar vertical and horizontal EOG was recorded using a pair
152 of BIP2AUX converters in the V-amp auxiliary channels (Brain Products). The EOG electrodes had
153 a separate ground electrode affixed to the central forehead.

154 Data were digitized at 2000 Hz with a resolution of 24 bits (0.049 μ V steps). Data were collected
155 inside a sound and radio frequency-attenuated chamber (40A-series; Electro-Medical Instruments,
156 Mississauga, Ontario, Canada), with copper mesh covering a window. The lights were left on, and
157 the window was covered during experiments. The only electrical devices inside the chamber were the
158 amplifier, powered from a battery powered laptop located outside the chamber, speakers, keyboard,
159 and mouse, all powered from outside the room, the ViewPixx monitor, powered with DC power from
160 outside the chamber, and a battery-powered intercom. Nothing was plugged into the internal power
161 outlets, and any electrical devices (e.g., cell phones) were removed from the chamber during
162 recording.

163 **2.5 Design and Procedure**

164 For all the participants, the study consisted of one session and took approximately 90 minutes. We
165 implemented a single-blind sham-controlled design in which participants underwent two

166 experimental conditions (otCS and sham) in a counterbalanced order. EEG data was simultaneously
167 recorded during both conditions.

168 The procedure started with the participants performing three practice blocks of the staircased version
169 of the target detection task while the experimenters set-up the EEG cap and electrical stimulation
170 electrodes. After the practice blocks and set-up, the electrical stimulation intensity was determined
171 for each participant using the procedure described above. Next, the participant performed the
172 staircased version of the target detection task a second time under the stimulation sham condition.
173 The average luminance value of the target in the last two blocks of trials was calculated for each
174 participant. Finally, participants performed the target detection task under the otCS and sham
175 experimental conditions (counterbalanced across subjects) using the previously calculated target
176 luminance value.

177 Although EEG data was recorded throughout the final three conditions, attempts to remove the otCS
178 stimulation artifact with both traditional and advanced multi-step procedures (Helfrich et al., 2014;
179 Kohli and Casson, 2015; Liu et al., 2012) were unsuccessful. This was most likely due to the
180 presence of small fluctuations of stimulation intensity caused by the stimulating device. Therefore,
181 we were not able to examine possible psychophysiological effects.

182 **2.6 Questionnaire**

183 To obtain possible adverse effects for otCS, a version of a questionnaire introduced by Brunoni et al.
184 (2011) was used. The following side-effects were inquired: headache, neck pain, scalp pain, tingling,
185 itching, burning sensation, skin redness, sleepiness, trouble concentrating and acute mood change.
186 Participants were asked to indicate the intensity of the side-effect (1, absent; 2, mild; 3, moderate; 4,
187 severe) and if they attributed the side-effect to the tACS (1, none; 2, remote; 3, possible; 4, probable;
188 5, definite).

189 The most reported adverse effects (intensities rated higher than 1) after the experiment were trouble
190 concentrating (70.0%), sleepiness (66.7%) and scalp tingling (56.7%). Ratings for intensity of
191 adverse effects were generally relatively low, except for sleepiness ($M = 2.12$) and trouble
192 concentrating ($M = 2.10$). For the ratings on whether subjects attributed the adverse effects to the
193 stimulation, only tingling achieved an average score above 2 ($M = 2.20$).

194 **2.7 Data Analyses**

195 Data analysis was performed using MATLAB R2017a (The MathWorks Inc, Natick, MA, USA) and
196 EEGLAB 13.6.5b (Delorme and Makeig, 2004). All statistical analyses were conducted using SPSS
197 11.5.0 (Chicago, IL) and R 3.3.1 (R Core Team, 2013).

198 **2.7.1 Target detection performance**

199 First, the trials from the non-staircased version of the target detection task were subdivided into 10
200 ms bins based on the time between the preceding stimulation pulse and the onset of the target (pulse
201 to target SOA; see Figure 1B). This was our main independent variable, since we predict that if alpha
202 oscillations are being entrained by the electrical stimulation their phase should influence detection.
203 Because a stimulation pulse was every 100 ms, this meant that there was a total of ten bins. Target
204 detection rates (proportion of targets participants detected) of each participant was calculated for
205 these ten 10 ms bins after excluding catch trials (where no target appeared) and trials without a valid
206 response. These calculations were performed separately for each stimulation condition (otCS and
207 sham). A test of the mean detection rates across bins between otCS and sham conditions was

208 conducted using a mixed ANOVA where the 10 ms bins and stimulation condition were within-
209 subject factors, condition order (otCS before sham or sham before otCS) was a between-subject
210 factor, and the participants were treated as a random variable. The ANOVA was performed in R
211 using the built-in `aov` function and the `ezANOVA` function from the `ez` package (Lawrence, 2016).
212 The analysis yielded a significant interaction between stimulation condition and order of conditions
213 indicating the presence of a sequence effect (see Results section and Figure 3A). The sequence effect
214 was not relevant to the hypothesis that target detection rates will vary in a sinusoidal manner relative
215 to otCS stimulation pulses but not the sham pulses. Therefore, the target detection rates were
216 normalized for each participant in each condition separately and then re-tested with the mixed
217 ANOVA.

218 Finally, the behavioral data was subdivided into twelve bins of 32 consecutive trials across the three
219 blocks of each stimulation condition and submitted to a repeated-measures ANOVA. This was done
220 to investigate whether there was a change in target detection rates across the condition, since if alpha
221 power increases with stimulation time target detection should get worse.

222 2.7.2 Sinusoidal model of detection rates

223 For each participant and stimulation condition, the sinusoidal function

$$224 \quad x(t) = \alpha_0 + \alpha_1 \sin(\omega t + \phi) \quad (1)$$

225 with intercept α_0 , amplitude α_1 , and phase ϕ was estimated for the standardized target detection rates
226 of the ten 10-ms bins in each stimulation condition. The routine to fit the parameters was initialized
227 with random start values, and used a nonlinear least-squares method. The parameters were limited by
228 the following constraints: $\phi \in (-\pi, \pi)$; $\alpha_1 \in (0, \infty)$; and, frequency ω was fixed at 0.06 bins/cycle
229 (100 Hz). To compare the influence of the otCS and sham stimulation pulses on target detection
230 rates, a paired Student's *t* test was performed on the estimated amplitude (α_1) and a Wilcoxon
231 signed-ranks test was performed on the goodness-of-fit measure adjusted r-square (R_{adj}^2).

232 2.7.3 EEG data

233 The average voltage in the 300 ms baseline prior to the target was subtracted on each trial for every
234 electrode. Trials with absolute voltage fluctuations on any channel greater than 1000 μV were
235 discarded, and data was segmented into 1800 ms epochs aligned to target onset (-800 ms pre-target
236 onset to 1000 ms post-target onset). Eye movements were then corrected with a regression-based
237 procedure developed by Gratton, Coles, and Donchin (1983). After a second baseline subtraction
238 with 300 ms pre-target, trials with remaining absolute voltage fluctuations on any channel greater
239 than 500 μV were removed from further analysis.

240 3 RESULTS

241 The mixed ANOVA on the mean detection data yielded no significant main effects or interactions
242 (Figure 2A) except for the interaction between stimulation condition and stimulation condition order
243 ($F(1,646) = 38.20, p < 0.001$). This indicates that there was a sequence effect in that mean target
244 detection rates were greater in the second stimulation condition compared to the first, regardless of
245 whether sham came before otCS (sham condition: $M = 0.46, SE = 0.05$; otCS condition: $M = 0.51, SE$
246 $= 0.04$) or otCS came before sham (sham condition: $M = 0.49, SE = 0.05$; otCS condition: $M = 0.45,$
247 $SE = 0.04$). All other main effects and interactions had an *F*-value of less than 1.

248 To compensate for this sequence effects, target detection rates were normalized for each participant
249 in each condition separately and were tested again with the same ANOVA. The statistical test also
250 yielded no significant main effects or interactions including the interaction between stimulation
251 condition and stimulation condition order (Figure 2B). There were no main effects or interactions
252 with a p -value less than 0.20.

253 Contrary to our hypothesis, the sinusoidal pattern of the target detection rates did not seem to be
254 strongly modulated by the cathodal otCS stimulation pulses compared to the sham (Figure 3A). This
255 is supported by a paired t test which indicates that there is no significant difference in the estimated
256 amplitude parameters (α_1) from the fitted sine functions to the otCS and sham behavioral data ($t(35)$
257 = 0.65, $p = 0.52$; Figure 3B). Furthermore, a Wilcoxon signed-ranks test indicated that the amount of
258 variability in the target detection rates accounted for by the sinusoidal model (adjusted R^2 value) did
259 not differ significantly between the sham and otCS stimulation conditions ($Z = -0.58$, $p = 0.56$;
260 Figure 3C).

261 Finally, the mean target detection rates across each experimental condition was examined to see if
262 there was an effect of the otCS stimulation over the course of the trials. Mauchly's test indicated that
263 the assumption of sphericity was violated for the stimulation condition x bins interaction, $W = 0.065$,
264 $p < .01$, $\epsilon = .66$. The degrees of freedom were corrected using Greenhouse-Geisser estimates of
265 sphericity. There was a significant main of bin on target detection rates ($F(11,385) = 4.78$, $p <$
266 0.001). There was no significant main effect of stimulation condition ($F(1,35) < 1.00$), nor a
267 significant interaction between stimulation condition x bins ($F(7.23,253.19) = 0.65$, $p = 0.72$). As can
268 be seen in Figure 4, there was a change in target detection rates across the duration of the task, but
269 this change was about the same in both conditions. A post hoc test using the Holm procedure to
270 control for Type I errors revealed that the first 32 trials (bin 1; $M = 0.57$, $SE = 0.03$) had significantly
271 better target detection rates than the set of trials in bin 4 ($M = 0.46$, $SE = 0.03$), bin 7 ($M = 0.47$, $SE =$
272 0.02), and bin 8 ($M = 0.48$, $SE = 0.02$). Because participants performed the task in three blocks of
273 128 trials, the end of the first block corresponds to bin 4 and the end of the second block corresponds
274 to bin 8. Therefore, the most likely explanation for these results is that the participants got fatigued
275 towards the end of each block.

276 4 DISCUSSION

277 The current studied aimed to provide a proof of principle that the entrainment of ongoing neural
278 oscillations by rhythmic visual stimulation can be replicated with cathodal otCS at the same
279 frequency. To this end, we attempted to modulate the phase alpha oscillations in the posterior parietal
280 cortex during a well-established visual detection task. Contrary to our hypothesis, there was no
281 evidence that cathodal otCS stimulation pulses modulated target detection rates. We found that mean
282 target detection rates during the otCS stimulation did not change as compared to sham stimulation.
283 Furthermore, the sinusoidal pattern of the target detection rates did not seem to be strongly
284 modulated by the cathodal otCS stimulation pulses compared to the sham. Together, these results did
285 not provide significant evidence for 10 Hz cathodal otCS directly inducing modulation of alpha
286 oscillations that can influence visual perception in a target detection task.

287 To the best of our analysis, cathodal otCS stimulation was not observed to modulate alpha
288 oscillations and subsequent target detection rates. A major limitation of this study is that the efficacy
289 of cathodal otCS can only be inferred from the perceptual and behavioural consequences of electrical
290 stimulation during the target detection task. Although EEG was recorded throughout the experiment,
291 we were not able to remove the otCS-induced artifacts. As a result, we have no direct

292 electrophysiological evidence that the cathodal otCS stimulation interacted with the ongoing brain
293 oscillations. Therefore, we cannot eliminate technical or methodological issues as the explanation for
294 a lack of measurable behavior effects. For example, it is possible that the stimulation intensity or
295 duration was not sufficient for inducing modulation of endogenous alpha oscillation. However, it is
296 unlikely that stimulation intensity was too low to induce effects because previous studies have used
297 similar intensities with observable effects (Moliadze et al., 2012; Neuling et al., 2015). Insufficient
298 stimulation duration is also an unlikely explanation because there was no change in target detection
299 rates compared to sham over course of the target detection task (see Figure 4). Furthermore, the three
300 blocks of the target detection task took at least 10 mins which is considered enough time to induce
301 effects in the ongoing oscillations (Antal et al., 2008; Thair et al., 2017).

302 It is also possible that using a 10 Hz stimulation frequency for all participants rather than matching
303 the otCS frequency to each individuals' peak alpha frequency reduced the efficacy of cathodal otCS.
304 Several lines of evidence have shown that effective modulation of endogenous oscillations by
305 periodic brain stimulation depends on matching the stimulation frequency to the rhythmic activity.
306 For example, a study using optogenetic stimulation and multichannel slice electrophysiology found
307 that a weak sine-wave electric field can enhance ongoing oscillatory activity, but only when the
308 stimulation frequency was matched to the endogenous oscillation (Schmidt et al., 2014).
309 Furthermore, a meta-analysis of fifty-one sham controlled experiments that investigated the effects of
310 tACS on perception and cognitive performance, Schutter and Wischniewski (2016) found that
311 performance is more likely to increase when tACS is administered based on individual spectral
312 information. Together, these results suggest that the efficacy of cathodal otCS in the current study
313 might have been greatly reduced because we did not control for inter-individual differences of
314 endogenous alpha oscillations. However, using a 10 Hz stimulation frequency rather than matching
315 the otCS frequency to individual peak frequencies might not have been as important a factor as it
316 might seem. Specifically, even in the same participant, individual endogenous oscillatory activity
317 varies during the course of a given task which could decrease the effects of stimulation even when
318 the individual peak frequency was applied (Woods et al., 2016).

319 Another factor that could have reduced the efficacy of this method was that we did not control the
320 timing of the otCS stimulation with regards to the target detection task. As a result, state-dependent
321 differences in cortical activity across individuals prior to otCS may influence the effects of
322 subsequent stimulation, introducing a possible source of variability (Silvanto and Pascual-Leone,
323 2008). However, this is an unlikely explanation because much of the variability due to differences
324 across individuals would have been accounted for in the sham condition and by blocking on
325 participants in the statistical analysis. Therefore, it is unlikely that state-dependent differences in
326 cortical activity could significantly contribute to the lack of behavioral differences between the otCS
327 and sham conditions in the target detection task.

328 In addition to the technical and methodological limitations mentioned above, individual differences
329 in the brain's susceptibility to otCS is another factor that may contribute to the lack of an observable
330 effect. Anatomical variation including scalp-brain distance, gyral folding of the cerebral cortex, and
331 thickness of corticospinal fluid layer and skull can have a significant impact on the effects of
332 transcranial current stimulation (Nitsche et al., 2008; Opitz et al., 2015).

333 The results of the current study suggest that 10-Hz cathodal otCS stimulation does not directly induce
334 modulation of alpha oscillations that can influence visual perception in a target detection task. Part of
335 this null result might be explained by individual differences in peak alpha frequency, state-dependent
336 changes in cortical activity, and susceptibility to otCS stimulation. However, technical and

337 methodological issues might also contribute a lack of observable differences in visual perception. In
338 the absence of electrophysiological evidence, it is important to be cautious about forming any firm
339 conclusions based on the current study. Further research is needed to convincingly eliminate cathodal
340 otCS stimulation as a means of modulating endogenous alpha oscillations in the posterior parietal
341 area. However, the current study provides the first evidence supporting that conclusion.

342 **5 CONFLICT OF INTEREST**

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

345 **6 AUTHOR CONTRIBUTIONS**

346 SSS and KEM contributed conception and design of the study. SSS performed the statistical analysis.
347 Both authors interpreted the data and wrote the article. Both authors approved the final version of the
348 manuscript.

349 **7 FUNDING**

350 This work was supported by a Natural Science and Engineering Research Council of Canada
351 (NSERC) discovery grant (#04792) to Kyle E. Mathewson.

352 **8 ACKNOWLEDGMENTS**

353 The authors would like to thank Anna Kim for assistance with data collection.

354 **9 REFERENCES**

- 355 Antal, A., Boros, K., Poreisz, C., Chaieb, L., Terney, D., and Paulus, W. (2008). Comparatively weak
356 after-effects of transcranial alternating current stimulation (tACS) on cortical excitability in
357 humans. *Brain Stimul.* 1, 97–105. doi:10.1016/j.brs.2007.10.001.
- 358 Antal, A., Nitsche, M. A., Kruse, W., Kincses, T. Z., Hoffmann, K.-P., and Paulus, W. (2004). Direct
359 Current Stimulation over V5 Enhances Visuomotor Coordination by Improving Motion
360 Perception in Humans. *J. Cogn. Neurosci.* 16, 521–527. doi:10.1162/089892904323057263.
- 361 Antal, A., and Paulus, W. (2008). Transcranial direct current stimulation and visual perception.
362 *Perception* 37, 367–74. doi:10.1068/P5872.
- 363 Antal, A., and Paulus, W. (2013). Transcranial alternating current stimulation (tACS). *Front. Hum.*
364 *Neurosci.* 7, 317. doi:10.3389/fnhum.2013.00317.
- 365 Antonenko, D., Fixel, M., Grittner, U., Lavidor, M., and Flöel, A. (2016). Effects of Transcranial
366 Alternating Current Stimulation on Cognitive Functions in Healthy Young and Older Adults.
367 *Neural Plast.* 2016. doi:10.1155/2016/4274127.
- 368 Brainard, D. H. (1997). The Psychophysics Toolbox. *Spat. Vis.* 10, 433–436. Available at:
369 <http://www.ncbi.nlm.nih.gov/pubmed/9176952> [Accessed October 5, 2017].
- 370 Brignani, D., Ruzzoli, M., Mauri, P., and Miniussi, C. (2013). Is Transcranial Alternating Current
371 Stimulation Effective in Modulating Brain Oscillations? *PLoS One* 8, e56589.

- 372 doi:10.1371/journal.pone.0056589.
- 373 Brunoni, A. R., Amadera, J., Berbel, B., Volz, M. S., Rizzerio, B. G., and Fregni, F. (2011). A
374 systematic review on reporting and assessment of adverse effects associated with transcranial
375 direct current stimulation. *Int. J. Neuropsychopharmacol.* 14, 1133–1145.
376 doi:10.1017/S1461145710001690.
- 377 Delorme, A., and Makeig, S. (2004). EEGLAB: an open source toolbox for analysis of single-trial
378 EEG dynamics including independent component analysis. *J. Neurosci. Methods* 134, 9–21.
379 doi:10.1016/J.JNEUMETH.2003.10.009.
- 380 Fröhlich, F. (2015). “Chapter 3 – Experiments and models of cortical oscillations as a target for
381 noninvasive brain stimulation,” in *Progress in Brain Research*, ed. S. Bestmann, 41–73.
382 doi:10.1016/bs.pbr.2015.07.025.
- 383 Fröhlich, F., Sellers, K. K., and Cordle, A. L. (2015). Targeting the neurophysiology of cognitive
384 systems with transcranial alternating current stimulation. *Expert Rev. Neurother.* 15, 145–167.
385 doi:10.1586/14737175.2015.992782.
- 386 García-Pérez, M. A. (1998). Forced-choice staircases with fixed step sizes: asymptotic and small-
387 sample properties. *Vision Res.* 38, 1861–1881. doi:10.1016/S0042-6989(97)00340-4.
- 388 Gratton, G., Coles, M. G. ., and Donchin, E. (1983). A new method for off-line removal of ocular
389 artifact. *Electroencephalogr. Clin. Neurophysiol.* 55, 468–484. doi:10.1016/0013-
390 4694(83)90135-9.
- 391 Helfrich, R. F., Schneider, T. R., Rach, S., Trautmann-Lengsfeld, S. A., Engel, A. K., and Herrmann,
392 C. S. (2014). Entrainment of Brain Oscillations by Transcranial Alternating Current Stimulation.
393 *Curr. Biol.* 24, 333–339. doi:10.1016/j.cub.2013.12.041.
- 394 Herrmann, C. S., Rach, S., Neuling, T., and Strüber, D. (2013). Transcranial alternating current
395 stimulation: a review of the underlying mechanisms and modulation of cognitive processes.
396 *Front. Hum. Neurosci.* 7, 279. doi:10.3389/fnhum.2013.00279.
- 397 Horvath, J. C., Forte, J. D., and Carter, O. (2015). Evidence that transcranial direct current
398 stimulation (tDCS) generates little-to-no reliable neurophysiologic effect beyond MEP
399 amplitude modulation in healthy human subjects: A systematic review. *Neuropsychologia* 66,
400 213–236. doi:10.1016/J.NEUROPSYCHOLOGIA.2014.11.021.
- 401 Jaberzadeh, S., Bastani, A., and Zoghi, M. (2014). Anodal transcranial pulsed current stimulation: A
402 novel technique to enhance corticospinal excitability. *Clin. Neurophysiol.* 125, 344–351.
403 doi:10.1016/j.clinph.2013.08.025.
- 404 Jackson, M. P., Rahman, A., Lafon, B., Kronberg, G., Ling, D., Parra, L. C., et al. (2016). Animal
405 models of transcranial direct current stimulation: Methods and mechanisms. *Clin. Neurophysiol.*
406 127, 3425–3454. doi:10.1016/j.clinph.2016.08.016.
- 407 Kasten, F. H., and Herrmann, C. S. (2017). Transcranial Alternating Current Stimulation (tACS)
408 Enhances Mental Rotation Performance during and after Stimulation. *Front. Hum. Neurosci.* 11,
409 2. doi:10.3389/fnhum.2017.00002.

- 410 Kingdom, F. A. A., and Prins, N. (2016). “Chapter 5 – Adaptive Methods,” in *Psychophysics* (San
411 Diego: Academic Press), 119–148. doi:10.1016/B978-0-12-407156-8.00005-0.
- 412 Kizuk, S. A. D., and Mathewson, K. E. (2017). Power and Phase of Alpha Oscillations Reveal an
413 Interaction between Spatial and Temporal Visual Attention. *J. Cogn. Neurosci.* 29, 480–494.
414 doi:10.1162/jocn_a_01058.
- 415 Kohli, S., and Casson, A. J. (2015). Removal of Transcranial a.c. Current Stimulation artifact from
416 simultaneous EEG recordings by superposition of moving averages. in *2015 37th Annual
417 International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*
418 (Milan: IEEE), 3436–3439. doi:10.1109/EMBC.2015.7319131.
- 419 Lawrence, M. A. (2016). ez: Easy Analysis and Visualization of Factorial Experiment. Available at:
420 <https://cran.r-project.org/package=ez>.
- 421 Liu, Z., de Zwart, J. A., van Gelderen, P., Kuo, L.-W., and Duyn, J. H. (2012). Statistical feature
422 extraction for artifact removal from concurrent fMRI-EEG recordings.
423 doi:10.1016/j.neuroimage.2011.10.042.
- 424 Marshall, L., Helgadóttir, H., Mölle, M., and Born, J. (2006). Boosting slow oscillations during sleep
425 potentiates memory. *Nature* 444, 610–613. doi:10.1038/nature05278.
- 426 Marshall, T. R., Esterer, S., Herring, J. D., Bergmann, T. O., and Jensen, O. (2016). On the
427 relationship between cortical excitability and visual oscillatory responses — A concurrent
428 tDCS–MEG study. *Neuroimage* 140, 41–49. doi:10.1016/j.neuroimage.2015.09.069.
- 429 Mathewson, K. E., Beck, D. M., Ro, T., Maclin, E. L., Low, K. A., Fabiani, M., et al. (2012).
430 Dynamics of Alpha Control: Preparatory Suppression of Posterior Alpha Oscillations by
431 Frontal Modulators Revealed with Combined EEG and Event-related Optical Signal. *J. Cogn.
432 Neurosci.* doi:10.1162/jocn.
- 433 Mathewson, K. E., Beck, D. M., Ro, T., Maclin, E. L., Low, K. A., Fabiani, M., et al. (2014).
434 Dynamics of Alpha Control: Preparatory Suppression of Posterior Alpha Oscillations by Frontal
435 Modulators Revealed with Combined EEG and Event-related Optical Signal. *J. Cogn. Neurosci.*
436 26, 2400–2415. doi:10.1162/jocn_a_00637.
- 437 Mathewson, K. E., Gratton, G., Fabiani, M., Beck, D. M., and Ro, T. (2009). To See or Not to See:
438 Prestimulus Phase Predicts Visual Awareness. *J. Neurosci.* 29, 2725–2732.
439 doi:10.1523/JNEUROSCI.3963-08.2009.
- 440 Mathewson, K. E., Lleras, A., Beck, D. M., Fabiani, M., Ro, T., and Gratton, G. (2011). Pulsed out of
441 awareness: EEG alpha oscillations represent a pulsed-inhibition of ongoing cortical processing.
442 *Front. Psychol.* 2, 99. doi:10.3389/fpsyg.2011.00099.
- 443 Moliadze, V., Atalay, D., Antal, A., and Paulus, W. (2012). Close to threshold transcranial electrical
444 stimulation preferentially activates inhibitory networks before switching to excitation with
445 higher intensities. *Brain Stimul.* 5, 505–511. doi:10.1016/J.BRS.2011.11.004.
- 446 Neuling, T., Rach, S., Wagner, S., Wolters, C. H., and Herrmann, C. S. (2012a). Good vibrations:
447 Oscillatory phase shapes perception. *Neuroimage* 63, 771–778.

- 448 doi:10.1016/j.neuroimage.2012.07.024.
- 449 Neuling, T., Ruhnau, P., Fuscà, M., Demarchi, G., Herrmann, C. S., and Weisz, N. (2015). Friends,
450 not foes: Magnetoencephalography as a tool to uncover brain dynamics during transcranial
451 alternating current stimulation. *Neuroimage* 118, 406–413.
452 doi:10.1016/J.NEUROIMAGE.2015.06.026.
- 453 Neuling, T., Wagner, S., Wolters, C. H., Zaehle, T., and Herrmann, C. S. (2012b). Finite-Element
454 Model Predicts Current Density Distribution for Clinical Applications of tDCS and tACS.
455 *Front. Psychiatry* 3, 83. doi:10.3389/fpsyt.2012.00083.
- 456 Nitsche, M. A., Cohen, L. G., Wassermann, E. M., Priori, A., Lang, N., Antal, A., et al. (2008).
457 Transcranial direct current stimulation: State of the art 2008. *Brain Stimul.* 1, 206–223.
458 doi:10.1016/j.brs.2008.06.004.
- 459 Opitz, A., Paulus, W., Will, S., Antunes, A., and Thielscher, A. (2015). Determinants of the electric
460 field during transcranial direct current stimulation. *Neuroimage* 109, 140–150.
461 doi:10.1016/J.NEUROIMAGE.2015.01.033.
- 462 Paulus, W. (2011). Transcranial electrical stimulation (tES – tDCS; tRNS, tACS) methods.
463 *Neuropsychol. Rehabil.* 21, 602–617. doi:10.1080/09602011.2011.557292.
- 464 Paulus, W., Nitsche, M. A., and Antal, A. (2016). Application of Transcranial Electric Stimulation
465 (tDCS, tACS, tRNS). *Eur. Psychol.* 21, 4–14. doi:10.1027/1016-9040/a000242.
- 466 Pelli, D. G. (1997). The VideoToolbox software for visual psychophysics: transforming numbers into
467 movies. *Spat. Vis.* 10, 437–442. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/9176953>
468 [Accessed October 5, 2017].
- 469 R Core Team (2013). R: A language and environment for statistical computing.
- 470 Reato, D., Rahman, A., Bikson, M., and Parra, L. C. (2013). Effects of weak transcranial alternating
471 current stimulation on brain activity—a review of known mechanisms from animal studies.
472 *Front. Hum. Neurosci.* 7. doi:10.3389/fnhum.2013.00687.
- 473 Schmidt, S. L., Iyengar, A. K., Foulser, A. A., Boyle, M. R., and Fröhlich, F. (2014). Endogenous
474 Cortical Oscillations Constrain Neuromodulation by Weak Electric Fields. *Brain Stimul.* 7, 878–
475 889. doi:10.1016/j.brs.2014.07.033.
- 476 Schutter, D. J. L. G., and Wischniewski, M. (2016). A meta-analytic study of exogenous oscillatory
477 electric potentials in neuroenhancement. *Neuropsychologia* 86, 110–118.
478 doi:10.1016/j.neuropsychologia.2016.04.011.
- 479 Silvanto, J., and Pascual-Leone, A. (2008). State-dependency of transcranial magnetic stimulation.
480 *Brain Topogr.* 21, 1–10. doi:10.1007/s10548-008-0067-0.
- 481 Simonsmeier, A. B. A., and Grabner, R. H. (2017). Electrical Brain Stimulation (tES) Improves
482 Learning More Than Performance: A Meta-Analysis. *Neurosci. Biobehav. Rev.*
483 doi:10.1016/j.neubiorev.2017.11.001.

- 484 Thair, H., Holloway, A. L., Newport, R., and Smith, A. D. (2017). Transcranial Direct Current
485 Stimulation (tDCS): A Beginner's Guide for Design and Implementation. *Front. Neurosci.* 11,
486 641. doi:10.3389/fnins.2017.00641.
- 487 Tremblay, S., Lepage, J.-F., Latulipe-Loiselle, A., Fregni, F., Pascual-Leone, A., and Théoret, H.
488 (2014). The Uncertain Outcome of Prefrontal tDCS. *Brain Stimul.* 7, 773–783.
489 doi:10.1016/J.BRS.2014.10.003.
- 490 Veniero, D., Benwell, C. S. Y., Ahrens, M. M., and Thut, G. (2017). Inconsistent Effects of Parietal
491 α -tACS on Pseudoneglect across Two Experiments: A Failed Internal Replication. *Front.*
492 *Psychol.* 8, 952. doi:10.3389/fpsyg.2017.00952.
- 493 Voskuhl, J., Strüber, D., and Herrmann, C. S. (2015). Transcranial alternating current stimulation:
494 Entrainment and function control of neuronal networks. *Nervenarzt* 86, 1516–1522.
495 doi:10.1007/s00115-015-4317-6.
- 496 Woods, A. J., Antal, A., Bikson, M., Boggio, P. S., Brunoni, A. R., Celnik, P., et al. (2016). A
497 technical guide to tDCS, and related non-invasive brain stimulation tools. *Clin. Neurophysiol.*
498 127, 1031–1048. doi:10.1016/j.clinph.2015.11.012.
- 499 Zaehle, T., Sandmann, P., Thorne, J. D., Jäncke, L., Herrmann, C. S., Engel, A., et al. (2011).
500 Transcranial direct current stimulation of the prefrontal cortex modulates working memory
501 performance: combined behavioural and electrophysiological evidence. *BMC Neurosci.* 12, 2.
502 doi:10.1186/1471-2202-12-2.

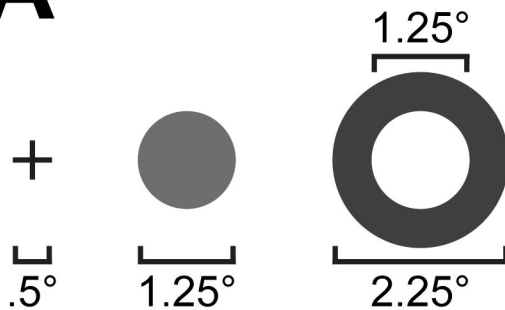
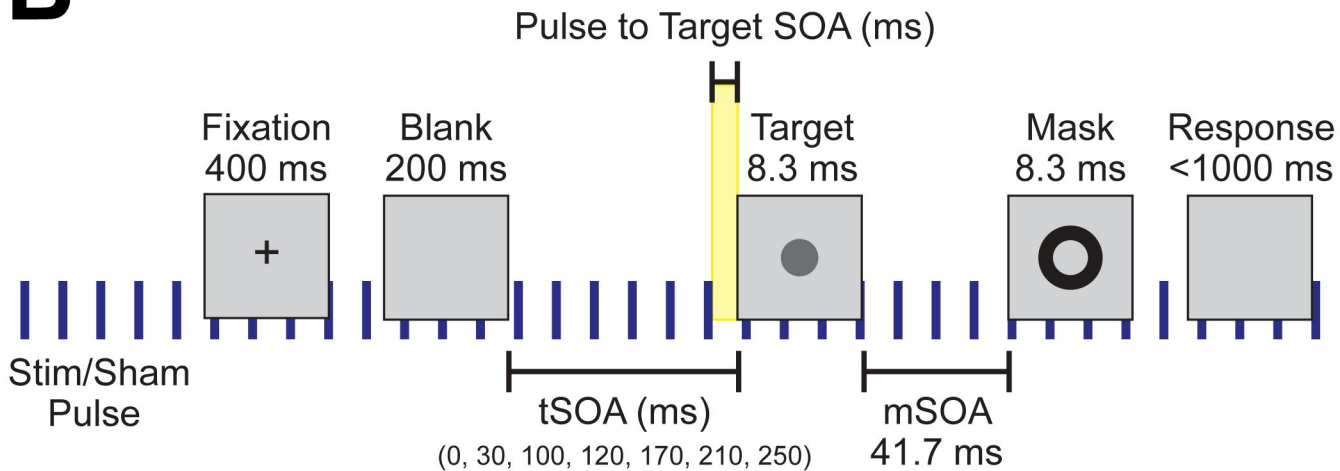
503 10 FIGURE CAPTIONS

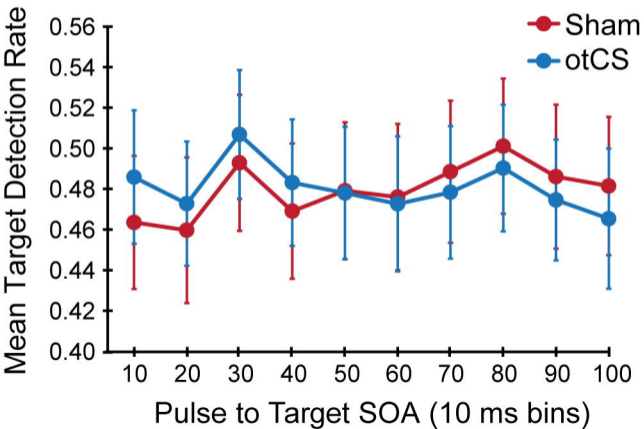
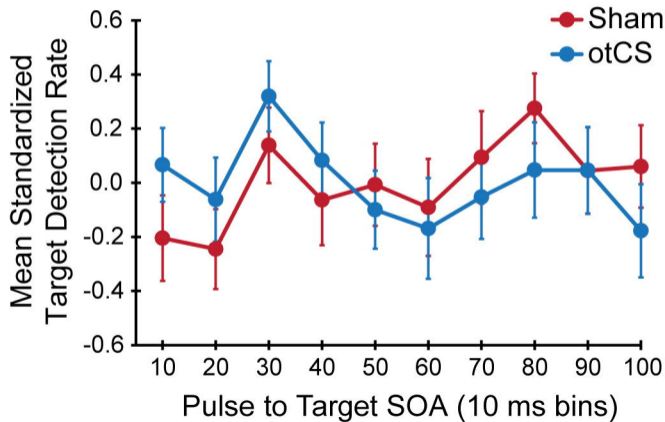
504 **Figure 1.** Experimental setup and design. **(A)** Spatial dimensions of the stimuli, which were
505 presented to subjects at the center of the screen. **(B)** Individual trial timeline with durations of each
506 screen presentation. Blue vertical lines indicate the continuous application of the 10 Hz sham or otCS
507 stimulation pulse throughout the task. Highlighted yellow area was the time range between the
508 preceding stimulation (sham or otCS) pulse and the onset of the target which was used to subdivide
509 the trials into 10 ms bins.

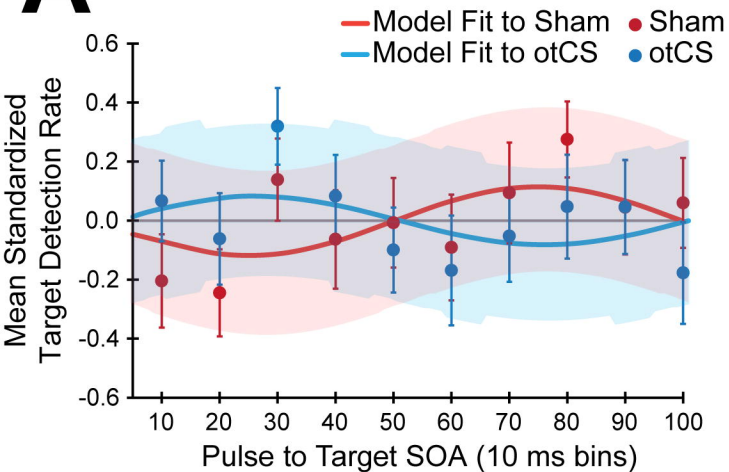
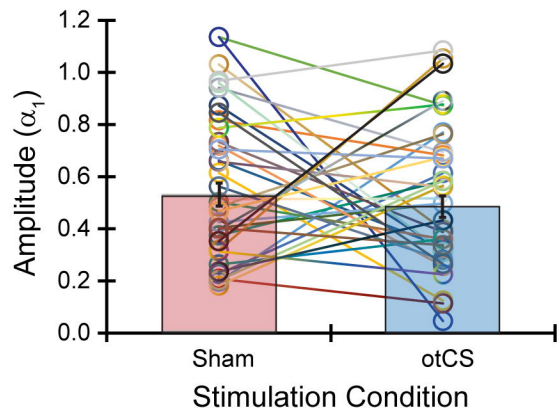
510 **Figure 2.** **(A)** Mean target detection rates and **(B)** mean standardized target detection rate in each 10
511 ms bin during the sham and otCS stimulation conditions. Error bars indicate the standard error (*SE*).

512 **Figure 3.** **(A)** The mean standardized target detection rates in each 10 ms bin for the sham and otCS
513 stimulation conditions overlaid by each fitted sine functions for the sham and cathodal otCS
514 stimulation conditions. Error bars and shaded color regions indicate the *SE* of the mean standardized
515 detection rates and model fits, respectively. **(B)** The open circles denote the individual amplitude (α_1)
516 estimates for each participant in the sham and otCS conditions. Lines connect the data points from
517 the same participant. The red and blue bars are the group averages in the sham and otCS conditions,
518 respectively. The error bars are the *SE*. **(C)** Histograms of the goodness-of-fit measure, adjusted R^2 ,
519 of the sinusoidal model to the mean standardized target detection rates in sham (left) and otCS (right)
520 stimulation conditions. The larger the adjusted r-square value, the more variability in the detection
521 rates explained by the model. Grey line marks a value of zero.

522 **Figure 4.** Mean target detection rates rate in each bin of 32 consecutive trials across the three
523 experimental blocks during the sham and otCS stimulation conditions. Error bars indicate the *SE*.

A**B**

A**B**

A**B****C**