Rhythmic Gamma Stimulation Affects Bistable Perception

Yuranny Cabral-Calderin[1,2], Carsten Schmidt-Samoa[1], and Melanie Wilke[1,2,3]

Abstract

■ When our brain is confronted with ambiguous visual stimuli, perception spontaneously alternates between different possible interpretations although the physical stimulus remains the same. Both alpha (8–12 Hz) and gamma (>30 Hz) oscillations have been reported to correlate with such spontaneous perceptual reversals. However, whether these oscillations play a causal role in triggering perceptual switches remains unknown. To address this question, we applied transcranial alternating current stimulation (tACS) over the posterior cortex of healthy human participants to boost alpha and gamma oscillations. At the same time, participants were reporting their percepts of an ambiguous structure-from-motion stimulus. We found that tACS in the gamma band (60 Hz) increased the number of spontaneous perceptual reversals, whereas no significant effect was found for tACS in alpha (10 Hz) and higher gamma (80 Hz) frequencies. Our results suggest a mechanistic role of gamma but not alpha oscillations in the resolution of perceptual ambiguity. ■

INTRODUCTION

Visual perception relies on a complex interplay between the analysis of incoming visual information and the integration of this input with ongoing processes and stored knowledge (Uhlhaas et al., 2009). The dynamic nature of our perceptual experience is underlined by the existence of visual illusions where perception falters into a sequence of alternating interpretations despite constant physical input. Familiar examples of such ambiguous patterns include the Necker cube, stroboscopic alternative motion, structure-from-motion (SfM), and binocular rivalry paradigms, which have proven to be valuable tools for studying the neural correlates of conscious visual perception (Boly et al., 2013; Sterzer, Kleinschmidt, & Rees, 2009; Leopold & Logothetis, 1999).

Previous studies have demonstrated the involvement of frontoparietal and extrastriate visual areas in bistable perception (Sandberg et al., 2014; Sterzer, Russ, Preibisch, & Kleinschmidt, 2002; Kleinschmidt, Buchel, Zeki, & Frackowiak, 1998; Lumer, Friston, & Rees, 1998). Synchronous oscillations between distributed neural populations in these regions have repeatedly been proposed to underlie perceptual states and their alternations (Tallon-Baudry, 2012; Fries, 2009; Engel & Singer, 2001). Supporting this notion, electrophysiological studies using local field potential recordings in monkeys have related perceptual states to the synchrony and power changes in the low/medium frequencies (9–30 Hz) in the visual cortex and thalamus (Wang, Maier, Logothetis, & Liang, 2009; Wilke, Mueller,

& Leopold, 2009; Wilke, Logothetis, & Leopold, 2006; Gail, Brinksmeyer, & Eckhorn, 2004) and power modulation in high frequencies (>30 Hz) in the lateral pFC, V4, and V5/MT (Panagiotaropoulos, Deco, Kapoor, & Logothetis, 2012; Wang et al., 2009; Wilke et al., 2006), although most of these studies confounded neural correlates of perceptual states with their alternations. In addition, EEG/MEG studies in humans that analyzed switch-related neural activity more directly have related perceptual switches to a decrease of alpha activity (Mathes, Pomper, Walla, & Basar-Eroglu, 2010; Struber & Herrmann, 2002; Isoglu-Alkac et al., 2000) and a widespread increase in gamma power and phase synchrony (Doesburg, Kitajo, & Ward, 2005; Strüber, Basar-Eroglu, Hoff, & Stadler, 2000; Basar-Eroglu, Struber, Kruse, Basar, & Stadler, 1996). Taking all these results together, it has been proposed that alpha activity might reflect a process of destabilization of the actual percept and gamma activity might be related to the binding of the new emerging percept (Doesburg et al., 2005; Struber & Herrmann, 2002).

Although the studies discussed above provide a correlative link between alpha and gamma oscillations and perceptual changes of bistable stimuli, the initiation of the perceptual switch and its possible substrate are often confounded with the preparation of the motor response. A pioneering human EEG study on this problem showed a focus of perceptual reversal-related alpha-band modulation at posterior (as opposed to central/frontal) sites when participants reported the switch with a temporal delay (Mathes et al., 2010). In addition, it has been shown in monkeys that the alpha local field potential modulation in the thalamus disappears when the animal is not required to report the percept (Wilke et al., 2009), thus

[1]University of Goettingen, [2]Leibniz Institute for Primate Research, Goettingen, Germany, [3]DFG Center for Nanoscale Microscopy and Molecular Physiology of the Brain (CNMBP)

casting doubt on whether the activity in the alpha band is related to perception itself or rather to decision/motor intentional processing accompanying the report.

Demonstrating a causal link between perceptual reversals and the activity in these frequency bands requires the possibility to interfere with these oscillations. With this aim, in this study we used transcranial alternating current stimulation (tACS). tACS is thought to interact with endogenous rhythmic neural activity in a frequency-specific manner, as suggested by cellular recordings in animals and EEG in humans (Helfrich et al., 2014; Ali, Sellers, & Frohlich, 2013; Ozen et al., 2010; Zaehle, Rach, & Herrmann, 2010). Thus, tACS represents a promising tool to investigate the relationship between oscillatory activity and bistable perception. Recent studies in humans reported frequency-specific effects of tACS on a wide range of brain functions including motor performance (Wach et al., 2013; Joundi, Jenkinson, Brittain, Aziz, & Brown, 2012), memory (Polania, Nitsche, Korman, Batsikadze, & Paulus, 2012), problem solving (Santarnecchi et al., 2013), as well as somatosensory (Feurra, Paulus, Walsh, & Kanai, 2011) and visual perception (Strüber, Rach, Trautmann-Lengsfeld, Engel, & Herrmann, 2014; Laczo, Antal, Niebergall, Treue, & Paulus, 2012; Kanai, Chaieb, Antal, Walsh, & Paulus, 2008).

In this study, we investigated whether alpha and gamma oscillations are causally involved in the initiation of spontaneous perceptual reversals of ambiguous visual stimuli. To this end, we applied tACS at alpha (10 Hz) and gamma (60 and 80 Hz) frequencies while human participants reported their percepts of an ambiguous SfM stimulus (Wallach & O'Connell, 1953). We chose these specific frequencies (including other frequencies applied in a pilot experiment) relying on the existing electrophysiological literature showing a decrease in alpha/beta frequencies with changing percepts and gamma power modulation in the 50–60 Hz band of an ambiguous SfM stimulus similar to the one we used here (Wang et al., 2009; Wang, Logothetis, & Liang, 2008). We hypothesized that if oscillations in a specific frequency band are causally related to perceptual reversals, then modulating the power of these oscillations with tACS would lead to measurable changes in the percept of the SfM stimulus. More specifically, we expected a decrease of reversal rates when tACS in the alpha range is applied and an increase in the reversal rates when gamma tACS is applied.

METHODS

Thirty-three participants (22 women, mean age = 27.9 ± 5.5 years) with normal or corrected-to-normal vision and without history of neurological or psychiatric disease took part in the study. From this sample, 10 individuals participated only in a pilot experiment, 23 participated in the main psychophysical experiment, and 11 participated in an additional control experiment.

All participants gave written informed consent. All procedures were performed according to the declaration of Helsinki and approved by the local ethics committee of the University Medical Center Göttingen. Participants were naive to the purpose of the experiments and were paid for their participation.

Experimental Setup

Stimuli were presented on a 27-in. monitor (Dell, Ultrasharp U2711b) with an eye–screen distance of 57 cm. The spatial resolution was 2560 × 1440 pixels, and the monitor had a refresh rate of 60 Hz. Observers sat in a dark room with their head position stabilized by means of a chin rest. They were instructed to maintain fixation on a central cross and to minimize blinking during stimulus presentations.

SfM Task

Stimuli were generated using MATLAB, version R2011b (The MathWorks, Inc., Natick, MA), and were presented using the Presentation software (version 14.9; Neurobehavioral System, Inc., www.neurobs.com). Two fields of moving dots (width and height, 8.0°, 400 dots), creating the illusion of a sphere rotating in depth around its vertical axis, were constructed (Figure 1A). One field of dots moved to the right, as the other field moved to the left. All dots were equal in luminance, making the rotation direction ambiguous. The sphere could be perceived to rotate either rightwards or leftwards, reversing direction spontaneously over time. Individual dots measured 4.2 arcmin in width and height. An example of such an SfM stimulus can be found in the supplemental materials (Video 1; see also www.michaelbach.de/ot/col_equilu/ for further references). The angular velocity of the sphere around the vertical rotational axis was 18°/sec. The task started with the central fixation cross for 2 sec, followed by the addition of the ambiguous SfM stimulus for 300 sec. Participants were instructed to fixate on the central cross and to press one button when the front surface was rotating rightwards and another button when it was rotating leftwards. A third button was assigned for reporting transition periods where participants could not decide the direction of rotation. To assure proper fixation, eye position was monitored at 60 Hz sampling rate via an Arrington Research ViewPoint EyeTracker (Arrington Research, Scottsdale, AZ). Participants were calibrated to a 16-point grid at the beginning of each task repetition.

Transcranial Alternating Current Stimulation

tACS was delivered by a battery-driven Eldith DC stimulator Plus (NeuroConn GmbH, Ilmenau, Germany) through a pair of conductive rubber electrodes attached with electrode paste (Weaver and Company, Aurora, CO). A smaller target electrode (16 cm^2) was placed over the inion (Oz), as determined by the International 10–20 EEG system (Figure 1B). The second electrode was positioned over

Figure 1. Stimulus display
and stimulation paradigm.
(A) Illustration of the
ambiguous SfM stimulus.
Moving dots presented on
a flat screen in the absence
of depth cues create the
percept of a sphere rotating
in depth. The perception
of the sphere fluctuates
between periods of rightward
and leftward horizontal
rotation. The rotating sphere
was presented continuously
for 5 min. (B) Placement of
tACS electrodes. Electrodes
were centered over Cz
and Oz. For illustration, the
electrodes are plotted on
a T1-weighted anatomical
MRI of a single participant.
(C) Schematic representation
of the structure of one
experimental session. Each

session started with a training run. The session was then divided into two blocks, separated by a 15-min break. In each block, tACS at a different
frequency (sham, 10 Hz, 60 Hz, or 80 Hz) was applied twice for 5 min. Each participant took part in two different sessions, in which two
different tACS frequencies were tested.
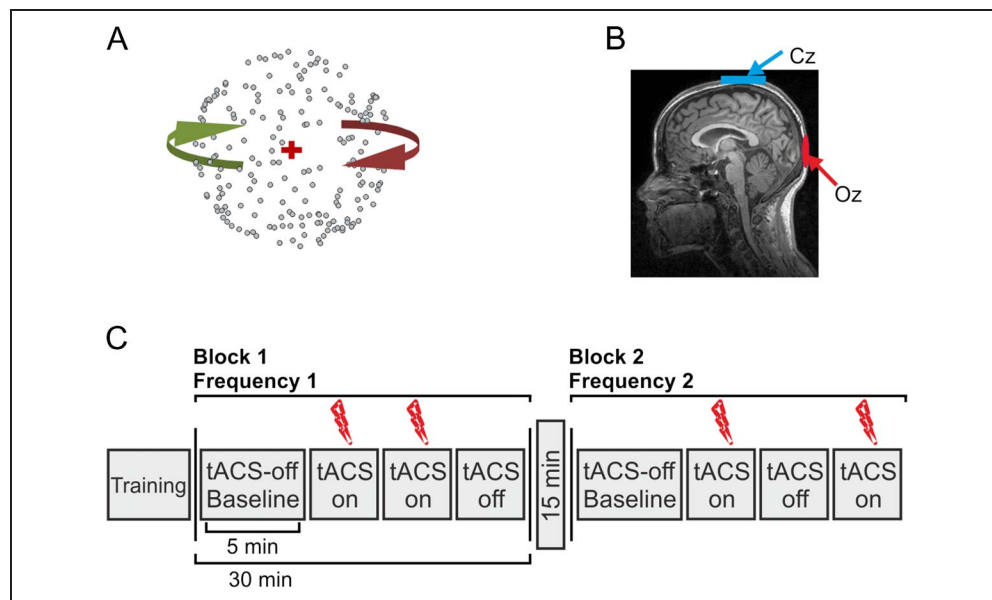
the vertex (Cz) and was larger than the inion electrode
(35 cm^2) in order to reduce current density and limit
stimulation effects under its surface. The stimulation site
over posterior cortex was chosen to induce oscillations
bilaterally in the occipital cortex, reaching up to thalamus
and parietal cortices (Neuling, Wagner, Wolters, Zaehle,
& Herrmann, 2012). Conceptually, we wanted to target
visual cortex because of previous electrophysiological
studies in monkeys showing perceptual modulation in
the alpha band in the visual cortex and gamma modulation
in V4 and MT (Wang et al., 2009; Maier et al., 2008; Wilke
et al., 2006) and because of a human EEG study that
demonstrated perceptual reversal-related alpha power
changes to be strongest at posterior sites when movement
preparation was controlled for (Mathes et al., 2010). tACS
was applied at 10 Hz, 60 Hz, and 80 Hz for 5 min while
the participant was performing the SfM task. The waveform
of the stimulation was sinusoidal without DC offset. The
current was fixed to 1.5 mA (peak to peak), resulting in a
mean current density of 0.094 mA/cm^2 under the Oz elec-
trode and 0.043 mA/cm^2 under the Cz electrode. The cur-
rent was ramped up and down over 1 sec. Impedance was
kept below 10 kΩ. For sham stimulation, 60 Hz tACS was
applied using the same parameters mentioned above, but
the stimulation was turned off after 3 sec. This procedure
was chosen to elicit the typical tingling sensation under the
electrodes at the beginning of the stimulation. Similar
methods of sham transcranial stimulation have been de-
scribed (Brignani, Ruzzoli, Mauri, & Miniussi, 2013). To
test the effectiveness of our sham stimulation, participants
were asked to report after each task repetition whether
they felt the electrical stimulation or not. According to

their reports, participants were not able to differentiate
the sham from the real stimulation. Each subject partici-
pated in two sessions, separated by at least 48 hr, in which
different tACS stimulation frequencies were tested in a
pseudorandomized order (Figure 1C). Two different fre-
quencies (sham, 10 Hz, 60 Hz, or 80 Hz) were tested in
each session in blocks separated by a 15-min break. In
each block, the visual task was repeated four times. The
first repetition was without tACS and was considered as
a baseline (tACS-off baseline). For the other three repeti-
tions, tACS was applied twice for the whole visual task
duration. The order of tACS-on/tACS-off within these three
repetitions was pseudorandomized. After each task repeti-
tion, participants were asked to verbally report whether
they perceived phosphenes while they performed the task.
In each session, the electrodes remained positioned on the
scalp all the time but tACS could be absent (tACS-off con-
dition) applied during 3 sec (sham condition) or during the
5 min of task performance (10 Hz, 60 Hz, and 80 Hz tACS).

Data Analysis

A reversal was detected each time the participant pressed
a new button to indicate a change in the perceived rota-
tion direction of the SfM stimulus. A perceptual domi-
nance period was defined as the time starting after the
participant reported the perceived direction until the next
button was pressed to indicate a new perceptual state.
The reversal rate per minute and the duration of the per-
ceptual dominance periods were analyzed for each tACS
condition. The data from the two repetitions with tACS-
on were pooled together for each tACS frequency. The

reversal rates were calculated by dividing the total number of reversals per stimulation condition by the total time (in minutes) that the condition was performed ($_{total}$ No. of Reversals/$_{total}$ Time). The effect of each tACS condition (sham, 10 Hz, 60 Hz, and 80 Hz) on the reversal rates was evaluated with nonparametric statistics because of the non-normal distribution of these data (Kolmogorov–Smirnov test for normality, $p < .05$). A Wilcoxon matched pairs test was implemented for comparing the reversal rates in the tACS-on versus tACS-off conditions for each frequency. Because of the high variability between participants in the reversal rates (a very well known phenomenon from the literature) and to facilitate the comparison between the different tACS frequencies (sham, 10 Hz, 60 Hz, and 80 Hz), the individual reversal rates in each tACS-on condition was normalized with respect to the tACS-off baseline condition within the block (e.g., normalized$_{reversals\ rate}$ = (reversal rate$_{tACS-on}$ − reversal rate$_{tACS-off\ baseline}$)/(reversal rate$_{tACS-on}$ + reversal rate$_{tACS-off\ baseline}$). The normalized values represent an index of how much the reversal rate changed for each tACS-on condition as compared with baseline. The data from the second tACS-off condition were not included in the analysis to avoid carry over. As the Kolmogorov–Smirnov test for normality did not indicate a non-normal distribution of the normalized reversal rates ($p > .20$), these values were included in a repeated-measures ANOVA (rANOVA) with the within-factor Frequency (sham, 10 Hz, 60 Hz, and 80 Hz). In case the rANOVA indicated a significant main effect of tACS condition, differences between the conditions were assessed with post hoc paired t tests. For assessing the distribution of the periods of perceptual dominance, for each participant the dominance durations in each tACS-on condition were normalized to its own mean (dominance duration$_{tACS-on}$/mean$_{dominance\ duration\ tACS-on}$). The resulting values were pooled and underwent a distribution fitting procedure where different distributions were tested (e.g., beta, exponential, extreme value, gamma, log-normal, normal, rayleigh, weibull). For examining the effect size, we used ANOVA partial eta-square and Cohen's d. The possible practice effect was assessed by comparing the reversal rates obtained in the tACS-off baseline conditions in the different sessions and blocks. For this analysis, nonparametric measures were used because of the non-normal distribution of the raw reversal rates (Kolmogorov–Smirnov test for normality, $p < .05$). A one-way rANOVA was implemented with the Friedman ANOVA (one factor with four levels: tACS-off baseline session1–block1, session1–block2, session2–block1, and session2–block2). The statistical analysis was implemented in STATISTICA 8.0 (Statsoft, 2007; Minneapolis, MN).

Control Experiment: Effects of tACS on Reaction Times

For investigating possible effects of tACS on the accuracy and RTs for detecting a perceptual switch, we also presented participants with unambiguous spheres. For the unambiguous spheres, the luminance of the dots that

ought to appear farther away from the observer was decreased to 30% with respect to the other dots, thus disambiguating its rotational direction toward a single perceived rotation direction. The other visual parameters were the same as described above for the ambiguous sphere. Participants observed the unambiguous rotating sphere for 5 min and were asked to report the direction of rotation by pressing one of two predefined buttons as fast as possible. The sphere could be rotating either rightwards or leftwards. The direction of rotation reversed 30 times within each task repetition. Perceptual dominance period durations were chosen from the group distribution of the main experiment in the ambiguous condition and were randomly presented. Participants were instructed to maintain fixation throughout the experiment by looking at a cross positioned at the center of the screen. Participants took part in one session, where tACS at 10 Hz and 60 Hz was applied in a pseudorandomized order. As in the main psychophysical experiment, the two frequencies were tested in different blocks separated by a 15-min break (Figure 1C). In each block, the visual task was repeated four times, twice with tACS-on and twice with tACS-off in a pseudorandomized order. The accuracy was calculated by dividing the number of switches correctly detected by the total number of switches presented. RTs for detecting a switch were calculated as the time between the physically induced direction reversal of the sphere and the recorded button press. The mean RT was calculated for each tACS condition including only the responses where the switch was correctly detected. For each of the two parameters, the values from the tACS-on for each frequency were compared with the tACS-off. Nonparametric Wilcoxon matched pairs test was used for the accuracy, and paired t test was used for the RT. The analysis was conducted as implemented in STATISTICA 8.0 (Statsoft, 2007; Minneapolis, MN).

RESULTS
### Effects of tACS on Spontaneous Perceptual Reversal Rates

Before performing the main psychophysical experiment, a pilot experiment was conducted with 10 participants testing the effect of five different tACS frequencies (5, 10, 16, 60, and 80 Hz) on the performance of the SfM paradigm. On the basis of the results (data not shown), we selected one frequency with a trend to decrease reversal rates (10 Hz), one with a trend to increase it (60 Hz), and another frequency showing no evident trend (80 Hz). Twenty-three individuals participated in the main experiment, aimed to evaluate the effect of tACS at alpha (10 Hz) and gamma (60 and 80 Hz) frequencies on the performance of an ambiguous SfM paradigm. From this sample, one participant was excluded from the final analysis because of high variability in the baseline conditions within sessions (up to 45% difference in reversal rates

between baselines, group median = 13%, range = 0–39%). Results refer to the data from 22 participants.

As depicted in the single participant examples in Figure 2A, tACS at 60 Hz increased the spontaneous perceptual reversal rates with respect to baseline (Wilcoxon matched pairs test for raw reversal rates in the group, $Z = 3.16$, $p = .001$), whereas sham ($Z = 0.40$, $p = .68$) or tACS in the other frequencies tested had either none or inconsistent effects across participants (10 Hz: $Z = 0.99$, $p = .32$; 80 Hz: $Z = 1.23$, $p = .21$). However, the
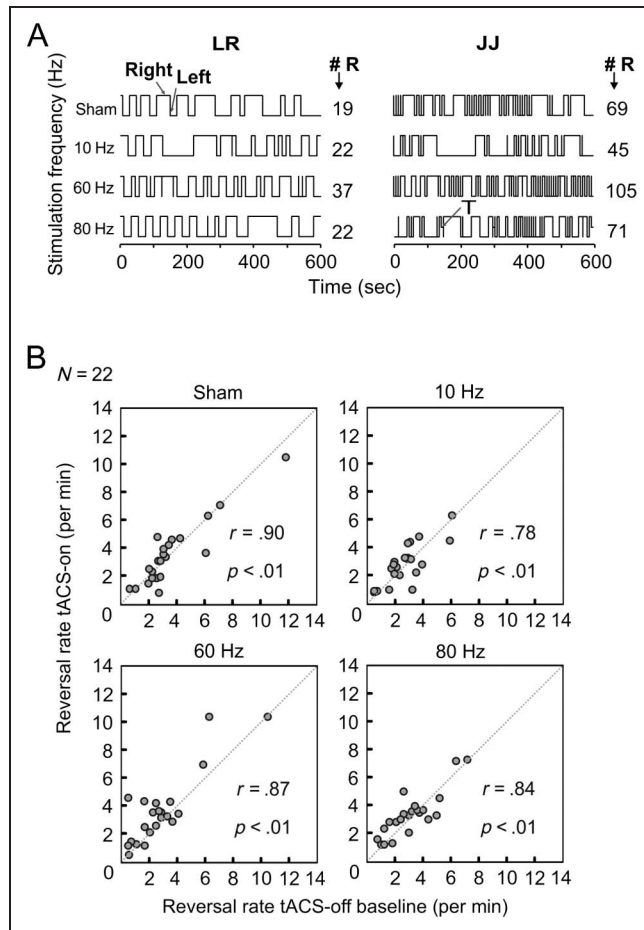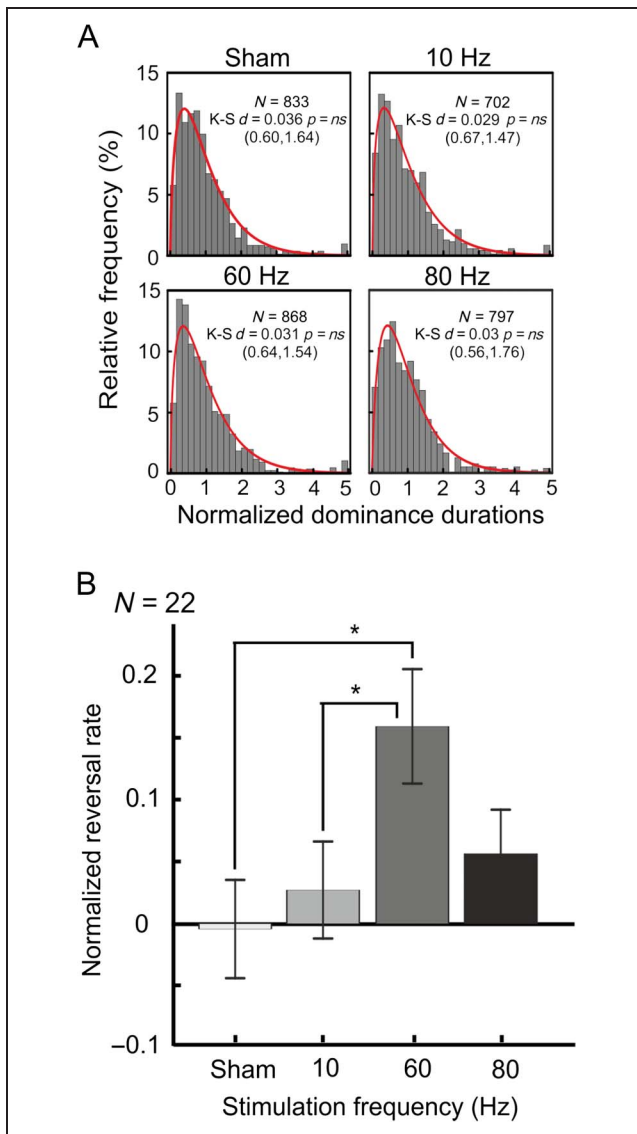

Figure 2. Behavioral results. Single participant data. (A) Perception of the SfM stimulus in two representative participants as a function of tACS frequency. Reversals of the perceived motion direction are represented as a fluctuation between upper and lower lines, corresponding to rightward and leftward rotation, respectively. Periods where the depicted line remains in the middle level represent transition phases (T) where the participant did not perceive a consistent direction of rotation of the sphere. The total number of spontaneous perceptual reversals (# R) during each tACS condition is shown on the right. LR and JJ refer to participants' code. (B) Correlation plots for each stimulation condition. For each frequency, the reversal rate per minute of each participant in the tACS-on condition is correlated with the reversal rate per minute in the baseline tACS-off condition. The unity regression line (gray dashed line) is shown. Pearson correlation coefficients (r) and associated p values are given in each graph. Equation of the regression line: sham ($y = 0.49 + 0.85 * x$), 10 Hz ($y = 0.69 + 0.78 * x$), 60 Hz ($y = 0.85 + 1.00 * x$), 80 Hz ($y = 0.86 + 0.80 * x$).

size of tACS-induced effects was variable between participants and between task repetitions. From the 22 studied participants, three did not show an increase but a decrease in the rate of spontaneous perceptual reversals during 60 Hz tACS. There was a high correlation between the individual reversal rates observed in each tACS condition (sham, 10 Hz, 60 Hz, and 80 Hz) and its own baseline (Figure 2B). As predicted from previous studies (Kleinschmidt, Sterzer, & Rees, 2012; Kanai, Bahrami, & Rees, 2010; Carter & Pettigrew, 2003; Struber & Herrmann, 2002), the baseline reversal rates differed considerably across participants, ranging from 0.4 to 11.8 reversals/min (Figure 2B). No significant difference was observed in the reversal rates between the different tACS-off baselines in the different blocks and sessions (Friedman ANOVA, $\chi^2 = 1.63$, $df = 3$, $p = .65$), suggesting no practice effect in the performance of the task (Figure S2). We further examined the temporal dynamics of the SfM stimulus by assessing the distribution of the durations of the periods of perceptual dominance. In each tACS condition (sham, 10 Hz, 60 Hz, and 80 Hz), the gamma function was the best fit for the distribution of the perceptual dominance periods, as previously reported for bistable stimuli (Kohler, Haddad, Singer, & Muckli, 2008; Brascamp, van Ee, Pestman, & van den Berg, 2005; Figure 3A).

To further quantify the tACS effects at the population level, we normalized the individual reversal rates observed in each tACS condition to the individual baselines (see Methods) and conducted a rANOVA with tACS condition (sham, 10 Hz, 60 Hz, and 80 Hz) as the within factor (Figure 3B). This analysis revealed a significant main effect of tACS condition [$F(3, 63) = 3.20$, $p = .029$, partial $\eta^2 = 0.13$]. Post hoc paired t tests revealed that this effect was attributable to the significant increase of spontaneous perceptual reversal rates observed with 60 Hz tACS that differed from the sham condition [$t(21) = 2.7$, $p = .013$, $d = 0.57$] and 10 Hz tACS [$t(21) = 2.20$, $p = .038$, $d = 0.46$]. The other comparisons between the different tACS conditions did not reach statistical significance.

We also tested for possible experimental confounds such as tACS-induced phosphenes and changes in RTs, which could account for the increase of spontaneous perceptual reversal rates during 60 Hz tACS. To test for the influence of tACS-induced phosphenes, participants were asked to report whether they perceived phosphenes after each task repetition. Consistent with a previous study (Kanai et al., 2008), none of the participants reported to perceive phosphenes during tACS at 60 Hz or 80 Hz, but 10 Hz evoked phosphenes in 7 of 22 participants. Participants were grouped by whether they perceived phosphenes or not and the normalized reversal rates for 10 Hz tACS were included in a t test for independent samples. No significant effect of phosphenes perception on the normalized reversal rates for 10 Hz stimulation was found [$t(20) = 0.96$, $p = .34$]. In a separate control experiment, we also evaluated accuracy and RTs for

Figure 3. Behavioral results. Group analysis. (A) Histograms and gamma fits for the normalized duration of perceptual dominance periods for every stimulation condition. In every stimulation condition, each participant's dominance durations were normalized to their mean and pooled (dominance duration$_{tACS-on}$/mean$_{dominance\ duration\ tACS-on}$). Different distributions were tested and the gamma distribution was always the most suitable model for the data. The results for the Kolmogorov–Smirnov (K-S) test are given in each graph. The numbers inside parentheses represent the fitted scale and shape parameters of the gamma fits. The red curve represents the best-fit gamma function. N refers to the number of dominance periods. (B) Change in the spontaneous perceptual reversal rates as a function of tACS condition. For each frequency, the mean change in spontaneous perceptual reversal rates relative to the baseline before tACS (normalized reversals rate = (reversals rate$_{tACS-on}$ − reversals rate$_{tACS-off\ baseline}$)/(reversals rate$_{tACS-on}$ + reversals rate$_{tACS-off\ baseline}$)) were computed for each individual participant and then averaged. Post hoc paired t tests revealed a significant increase of spontaneous perceptual reversal rates for the 60 Hz tACS compared with sham and 10 Hz. Error bars indicate SEM across 22 participants. *$p < .05$.

detecting physically induced reversals of a disambiguated version of the sphere (Figure 4A). Here, tACS at 10 Hz and 60 Hz was applied with the same parameters used in the main experiment. tACS condition had no significant effect either on the accuracy (Figure 4B; Wilcoxon matched pairs test: 10 Hz [$Z = 0.26, p = .78$], 60 Hz [$Z = 0.41, p = .67$]) or on the RTs for detecting the switch (Figure 4C; paired t test between tACS-off and tACS-on: 10 Hz [$t(10) = 1.6, p = .14$], 60 Hz [$t(10) = 0.96, p = .36$]).

Taken together, the psychophysical results suggest a causal relationship between oscillatory entrainment at 60 Hz and spontaneous perceptual reversals of the ambiguous SfM stimulus.

DISCUSSION

This study investigated the effects of tACS on bistable perception. Our main finding is that 60 Hz tACS increased the spontaneous perceptual reversal rates of a bistable SfM stimulus, whereas 10 and 80 Hz did not have any significant effect.

Although we did not record any electrophysiological data measuring the direct influence of tACS on brain oscillations in this study, we assume that tACS modulated the oscillatory activity at the applied frequencies. Support for this assumption can be derived from previous studies combining tACS with EEG that have shown increased power and coherence at the applied tACS frequency (Helfrich et al., 2014; Strüber et al., 2014).

Effects of tACS in the Gamma Range on Spontaneous Perceptual Reversal Rates

Gamma oscillations in neural circuits have long been hypothesized as a mechanism to facilitate the transient integration of distributed neuronal ensembles enabling cognitive functions such as visual attention and perception (Fries, 2009; Tallon-Baudry, 2009; Singer, 1999). The influence of tACS in the gamma range on bistable perception is in line with a large number of correlative studies in monkeys (Panagiotaropoulos et al., 2012; Wang, Logothetis, et al., 2008; Wilke et al., 2006) and humans (Doesburg et al., 2005; Strüber et al., 2000; Basar-Eroglu et al., 1996), showing robust correlations between perceptual changes of bistable stimuli and gamma power and/or coherence. We found that tACS at 60 Hz, but not at 80 Hz, increased reversal rates of the SfM stimulus. The effectiveness of the 60 Hz makes sense in respect to previous electrophysiological studies with the SfM stimulus as the stimulus-induced entrainment has been shown to peak at 50–60 Hz (Wang, Logothetis, & Liang, 2009b; Wang, Logothetis, et al., 2008; Wang, Maier, Logothetis, & Liang, 2008).

However, we do not claim a special relationship between 60 Hz and bistable perception in general, because it has been described that tACS at 40 Hz modulates apparent

Figure 4. Control experiment. (A) Schematic representation of the RT task. A replay condition was implemented taking into account the dominance period durations from the group distribution in the ambiguous condition. The contrast of one field of moving dots was decreased to 30%, rendering the sphere unambiguous. Participants had to detect the switch as soon as possible by reporting the direction of rotation (Methods). (B) Results of the accuracy in detecting a physically induced perceptual switch. For each tACS condition, the RTs are shown separated for the tACS-off baseline (light gray bar) and tACS-on (dark gray bar) condition. Each colored panel in the back represents a different frequency. Error bars indicate *SEM* across 11 participants. (C) Correlation plots for each stimulation condition. For each frequency, the RT for detecting a perceptual switch of each participant in the tACS-on condition is correlated with the reaction in the tACS-off condition. The unity regression line (gray dashed line) is shown. Pearson correlation coefficients (r) and associated p values are given in each graph. Equation of the regression line: 10 Hz ($y = -65.82 + 1.24 * x$), 60 Hz ($y = 260 + 0.56 * x$).
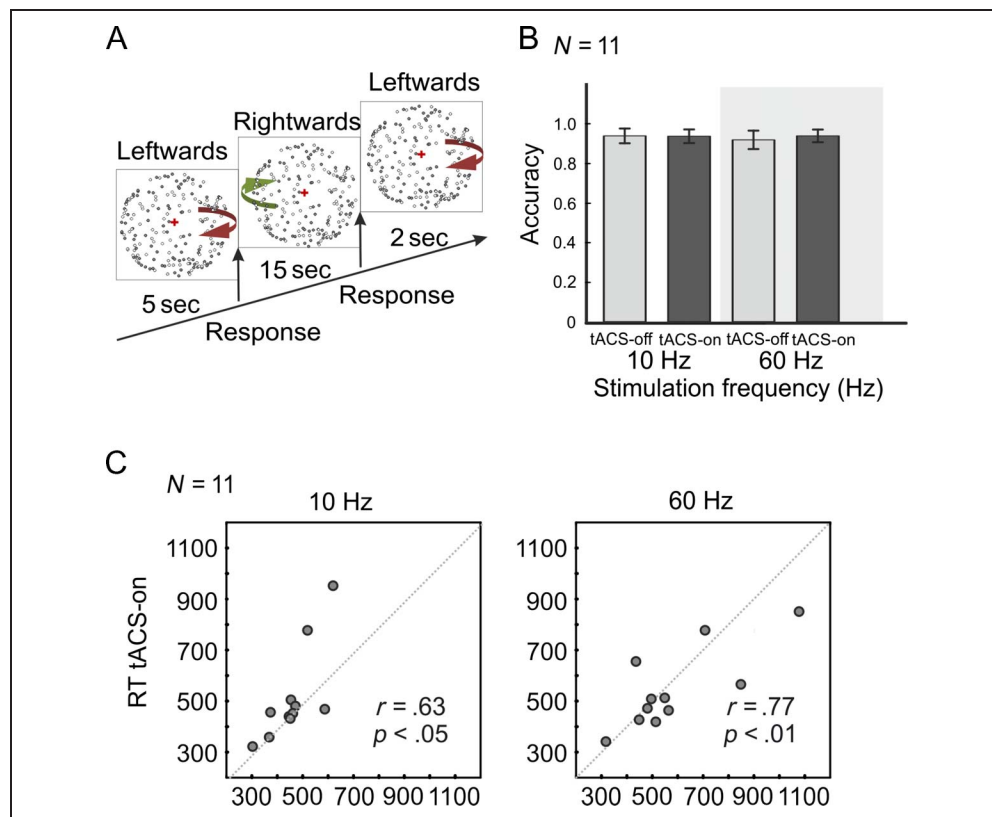
motion perception (Strüber et al., 2014). One could speculate that the effective gamma frequency is stimulus dependent. This notion is also supported by electrophysiological studies showing that the peak gamma frequency in a given brain area varies as a function of visual stimulus features such as contrast and eccentricity (Roberts et al., 2013; van Pelt & Fries, 2013; Ray & Maunsell, 2010).

The exact mechanism by which 60 Hz tACS affects the reversal rates of the SfM stimulus is hard to predict, partly because tACS seems to affect broad regions in the brain and is not focal. The choice of our tACS electrode positions was based on previous electrophysiological studies showing reversal-related alpha and gamma power modulation in the entire cortex including occipital and frontal sites (Strüber et al., 2000; Basar-Eroglu et al., 1996; Basar-Eroglu, Struber, Stadler, Kruse, & Basar, 1993). We thus cannot and do not claim region specificity of our tACS effects. However, the model of the electric field distribution of tACS proposed that using our electrode configuration it is possible to target regions in the occipital and parietal cortices (Neuling et al., 2012). It has been suggested that perceptual alternations rely on an interplay between feedforward and feedback processes such that weakened activity among sensory neurons in visual cortices that represent the currently dominant percept bias frontoparietal areas to initiate a

perceptual reorganization (Sterzer et al., 2009). In this context, one could speculate that gamma tACS simultaneously boosted activity in motion-sensitive neurons with different direction selectivity and thus disturbed local processes in visual cortices that underlie the formation of a coherent motion percept, prompting parietal areas to initiate a reinterpretation of the stimulus.

Our results are in agreement with Strüber et al. (2014), in the sense that both propose that gamma oscillations affect bistable perception. In particular, Strüber et al. (2014) showed that tACS-induced desynchronization of gamma oscillations (40 Hz) between hemispheres biases the perception of a bistable stroboscopic alternative motion stimulus toward the vertical motion. This result could be explained by a tACS-induced impairment of the interhemispheric motion integration needed for perceiving the horizontal motion (Strüber et al., 2014). However, they do not provide information about whether the reversal rates were affected as well. Our study shows that tACS in the gamma range (60 Hz) also disturbed the perceptual stability of the SfM stimulus, resulting in an increase in the reversal rates. However, the two studies also somewhat differ in respect to the scientific questions that were addressed as well as in respect to methodological details such as type of bistable stimulus, electrode configuration, and applied frequencies. To bring together the results

reported in both studies, it would be necessary to test for all these different conditions in the same design together with a verification of stimulus-induced neural frequency entrainment with the SfM versus the SAM stimulus.

Effects of tACS in the Alpha Range on Spontaneous Perceptual Reversal Rates

Apart from gamma activity, alpha-band power has also been repeatedly found to correlate (negatively) with perceptual changes of bistable patterns in monkeys (Wang, Logothetis, & Liang, 2009a; Wilke et al., 2006, 2009; Gail et al., 2004) and humans (Mathes et al., 2010; Struber & Herrmann, 2002; Isoglu-Alkac et al., 2000; Basar-Eroglu et al., 1996). We did not find an influence of tACS at 10 Hz on spontaneous perceptual reversal rates of the SfM stimulus. Thus, our hypothesis that alpha oscillations causally contribute to the formation of perceptual states of bistable stimuli was not confirmed. Although there is ample evidence for a causal influence of prestimulus, ongoing alpha oscillations on subsequent phosphenes perception, and detection of near-threshold stimuli (Dugue, Marque, & VanRullen, 2011; Romei, Gross, & Thut, 2010), there is additional evidence that argues against its causal role in respect to bistable perception. Specifically, modulation of alpha power was shown to be relatively modest when no active perceptual report was required (Panagiotaropoulos et al., 2012; Keliris, Logothetis, & Tolias, 2010; Wilke et al., 2009) and to occur later than changes in neuronal spiking or gamma power (Wilke et al., 2006). Taken together, our findings and those from previous studies are consistent with the view that alpha oscillations may not be causally linked to the perceptual switching process itself. Instead, alpha oscillations could represent task-related factors related to decision-making, motor preparation, and/or attention (Kanai & Tsuchiya, 2012). We shall stress that the lack of effect of 10 Hz tACS in our study should not be overinterpreted either, as it could be because of methodological limitations as well. Possible issues could be that we did not take into account the phase of endogenous alpha oscillations when applying tACS and that we did not stimulate at the endogenous peak frequencies of the participants. However, regarding the phase of the endogenous oscillations, animal studies suggest that, regardless of the phase relationship between ongoing oscillations and stimulation, tACS maximally entrains neuronal networks after only a few seconds (Ali et al., 2013). Because we applied tACS for a considerably longer time (5 min), we could assume that the network was entrained for at least most of the stimulation time. Regarding the endogenous peak frequency, several studies have reported that neural responses to weak electrical stimulation are maximal when neural populations are stimulated at their resonance frequency (Ali et al., 2013; Ozen et al., 2010). Thus, stimulating at frequencies outside the endogenous oscillation frequency might decrease the effectiveness of the entraining. However, a combined

tACS-EEG study recently showed that during tACS at 10 Hz the endogenous peak of the alpha band shifted toward the stimulation frequency (Helfrich et al., 2014). Future tACS studies may profit from closed-loop stimulation where tACS frequencies are dynamically adjusted in respect to endogenous or task-driven oscillations (Berenyi, Belluscio, Mao, & Buzsaki, 2012).

In summary, we propose that boosting neural activity in the gamma range influences the formation of bistable percepts. On the basis of the lack of an effect of tACS at 10 Hz, we suggest that future studies on conscious perception should tightly control other cognitive factors that could possibly explain percept-correlated activity such as attention, decision, confidence, and visuomotor variables.

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