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tRNS boosts perceptual learning in peripheral vision

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ABSTRACT

Visual crowding, the difficulty of recognizing elements when surrounded by similar items, is a widely studied perceptual phenomenon and a trademark characteristic of peripheral vision. Perceptual Learning (PL) has been shown to reduce crowding, although a large number of sessions is required to observe significant improvements. Recently, transcranial random noise stimulation (tRNS) has been successfully used to boost PL in low-level foveal tasks (e.g., contrast detection, orientation) in both healthy and clinical populations. However, no studies so far combined tRNS with PL in peripheral vision during higher-level tasks. Thus, we investigated the effect of tRNS on PL and transfer in peripheral high-level visual tasks. We trained two groups (tRNS and sham) of normal-sighted participants in a peripheral (8° of eccentricity) crowding task over a short number of sessions (4). We tested both learning and transfer to untrained spatial locations, orientations, and tasks (visual acuity). After training, the tRNS group showed greater learning rate with respect to the sham group. For both groups, learning generalized to the same extent to the untrained retinal location and task. Overall, this paradigm has potential applications for patients suffering from central vision loss but further research is needed to elucidate its effect (i.e., increasing transfer and learning retention).

1. Introduction

In peripheral vision, identification of targets among neighboring elements is much less efficient than in foveal vision, an effect known as visual crowding (Whitney and Levi, 2011). Crowding limits peripheral reading and peripheral letter identification (Chung, 2007; Mansfield et al., 1996) and, while almost absent in healthy foveal vision (Huurneman et al., 2012), it represents a major difficulty for clinical populations suffering from amblyopia (Levi et al., 1997) or central vision loss (macular degeneration (MD)), Stargardt syndrome, rods-cone dystrophy, etc. (Mansfield et al., 1996). Perceptual learning (PL), the improvement in a perceptual task as a product of repeated practice (Fahle and Poggio, 2002; Garner, 1970; Sagi, 2011), is a promising technique that has found its way into clinical practice due to its non-invasive and inexpensive approach (Campana and Maniglia, 2015). Several studies tested the efficacy of PL in reducing crowding, both in healthy and clinical populations (Astle et al., 2015; Chung, 2007; Chung and Truong, 2013; Hussain et al., 2012; Maniglia et al., 2011; Maniglia et al., 2016; Yashar et al., 2015). However, most of these protocols required a large number of sessions and in some cases the improvement remained specific to the trained task. Recently, non-invasive brain stimulation has been used, alone or coupled with PL, to enhance visual abilities (Camilleri et al., 2016, 2014; Campana et al., 2014; Fertonani et al., 2011; Pirulli et al., 2013; Thompson et al., 2008). In particular, transcranial random noise stimulation (tRNS), in which a weak electric current is delivered through the scalp on a cortical region at random frequencies, has shown promising results in boosting PL and reducing the number of sessions needed to observe significant improvements (Camilleri et al., 2014; Fertonani et al., 2011). In general, tRNS appears to boost both the early (within session - Fertonani et al., 2011) and late (between sessions/days - Camilleri et al., 2014) components of PL. So far, PL studies used tRNS coupled with lower-level perceptual tasks, such as contrast detection or orientation discrimination, rather than training directly higher-level visual abilities, such as visual acuity (VA) or crowding. Interestingly, tRNS during contrast detection training has been shown to induce

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greater transfer (the post-training improvement observed in an untrained task) to VA with respect to PL alone in both amblyopic and myopic patients (Camilleri et al., 2014; Campana et al., 2014). The working hypothesis of our study is that stimulation on early visual cortex would promote learning of low level features and trigger a trickle-down effect downstream of the visual processing, providing higher visual areas computing letter discrimination (e.g., the visual word form area (VWFA) in the left fusiform gyrus, Cohen et al., 2003, 2000) with a better input. Alternatively, tRNS might promote generalization of learning by reducing sensory adaptation, a phenomenon known to limit transfer of learning (Harris et al., 2012; Harris and Sagi, 2015). Consistently, Campana and colleagues (2016) showed that tRNS over V5 (a cortical area involved in the processing of visual motion, diminished the perceived duration of the motion after-effect, while tRNS over early visual areas allowed transfer of learning to an untrained visual task (visual acuity)) (Moret et al., 2018). Visual crowding is known to compromise object discrimination in general and letter/word discrimination in particular. In fact, reading under a crowded conditions is slower and less accurate. The exact location at which the pooling of features among neighboring items happens is still debated. Some authors propose that crowding occurs when elements are grouped into wholes, a process reflected in EEG by the N1 component (Chen et al., 2014; Chicherov et al., 2014; Tripathy et al., 2014) while others place the neural locus of crowding at an early cortical site, such as V1 or V2 (Freeman et al., 2012; Shin et al., 2017). Levi's (2008) review reconciles this in a multi-stage model where crowding occurs at both the detection of simple features (early lateral interactions) and integration of features downstream from V1. Online tRNS is particularly effective in enhancing performance when the stimulus is sub-threshold and only if the stimulation is applied over the neural population involved in the task (Fertonani et al., 2011; van der Groen et al., 2017; van der Groen and Wenderoth, 2016). In our training, we adopted an adaptive staircase procedure that moved up and down while tracking the threshold. This way, both supra and sub-threshold trials were interleaved and non-independent from each other since the level of each trial was chosen on the basis of all previous responses. We chose an adaptive procedure in order to ensure an adequate level of difficulty throughout the training and also to better exploit the effects of tRNS given its interaction with the task difficulty. In fact, while anodal and cathodal tDCS are mostly used before the task to profit from the after-effect of the stimulation (increased or reduced cortical excitability) (Clayton et al., 2016; Fertonani and Miniussi, 2017) we wanted to profit from both the ongoing modulation in the signal-to-noise ratio during the task and the general increase in the cortical excitability driven by the online tRNS, which is supposedly the best choice to induce cumulative neuroplastic changes over multiple sessions (Ho et al., 2013). Here, we aimed to test whether tRNS over the occipital cortex boosts PL during crowding reduction training. Moreover, in order to test whether tRNS increases generalization of learning, as observed in other cognitive (Cappelletti et al., 2013; Looi et al., 2017) and perceptual training studies (Camilleri et al., 2016, 2014, Campana et al., 2018), we tested five transfer tasks before and after the training. Generalization of learning is a highly desirable training outcome since it could inform rehabilitative interventions for clinical populations such as amblyopics or age-related macular degeneration (AMD) patients. Indeed, from a clinical point of view, task improvement is important but it remains of limited value if the effects are specific. We chose five transfer conditions (retinal location, orientation, task [VA] separately, and retinal location + orientation, retinal location + task [VA]) and we expected different levels of generalization based on the number of manipulated features (more transfer of learning for a single property manipulation and less transfer for combined manipulations).

Results indicate that coupling tRNS to the early visual cortex with PL of a peripheral crowding reduction task is effective in boosting between-session learning, but does not increase transfer of learning to untrained visual functions respective to PL alone (Sham condition).

2. Material and method

2.1. Apparatus

Stimuli were displayed on a 17″ Dell M770 CRT monitor with a refresh rate of 60 Hz. All stimuli were produced using the Psychtoolbox toolbox (Pelli, 1997) in MATLAB R2012a. The monitor (1024 × 768 pixels) was placed 57 cm in front of the participants and had a spatial resolution of 1.9 arcmin per pixel. Mean luminance was 47.6 cd/m^2, as measured with a Minolta CS110 (Konica Minolta, Canada). A chin-and-head rest was used to keep the head position fixed and the viewing was binocular. The experiment was conducted in a dark room.

2.2. Participants

Thirty-two participants (17 females) with normal or corrected-to-normal vision took part in the study (mean age 25, range 20–32 years). They were randomly assigned to one of two groups (tRNS or sham). All participants gave their written informed consent prior to their inclusion in the experiment and received compensation for their participation. The study was conducted in accordance with the Declaration of Helsinki (1964). The experimental protocol was approved by the ethical committee at Center National de la Recherche Scientifique with our institutional review board (CPP, Comité de Protection des Personnes, protocole 1301814/04/2014).

2.3. Visual acuity procedure

In order to define the size of the stimuli for the crowding task, we first measure VA individually for each participant. A central cross was displayed in the center of the screen and the participants were asked to fixate it and to identify a white single letter presented at 8° of eccentricity onto a black background. In order to avoid eye movements, stimulus position was randomized in a left/right manner and the presentation time was kept short (50 ms). In the absence of an eye-tracker, the use of these precautions greatly reduces (but not completely excludes) the impact of eye movements in the study. The target letter was randomly selected from a subset of 9 uppercase Sloan letters (D, S, R, Z, N, K, H, V, and C (Pelli and Robson, 1988). The size of the letters varied according to a one-up three-down adaptive staircase procedure (Levitt, 1971), with 0.1 log unit steps, leading to an 80% of correct letter identification threshold. An experimental run ended after 12 reversals or 100 trials. Each run typically lasted 60–90 trials. The threshold was obtained by averaging the last 6 reversals. If the number of 12 reversals was not reached after 100 trials, the first six reversals were always discarded and only the remaining ones were averaged. To reduce temporal uncertainty, a 50 ms sound was played prior to each target onset. At the end of each trial, participants reported verbally the letter to the experimenter who was sitting outside the experimental room in a position from where he was unable to see the monitor. The experimenter reported the answer by pressing the corresponding key on the keyboard.

2.4. Crowding procedure

The crowding procedure was similar to the visual acuity procedure with the difference that in each trial a trigram, rather than a single

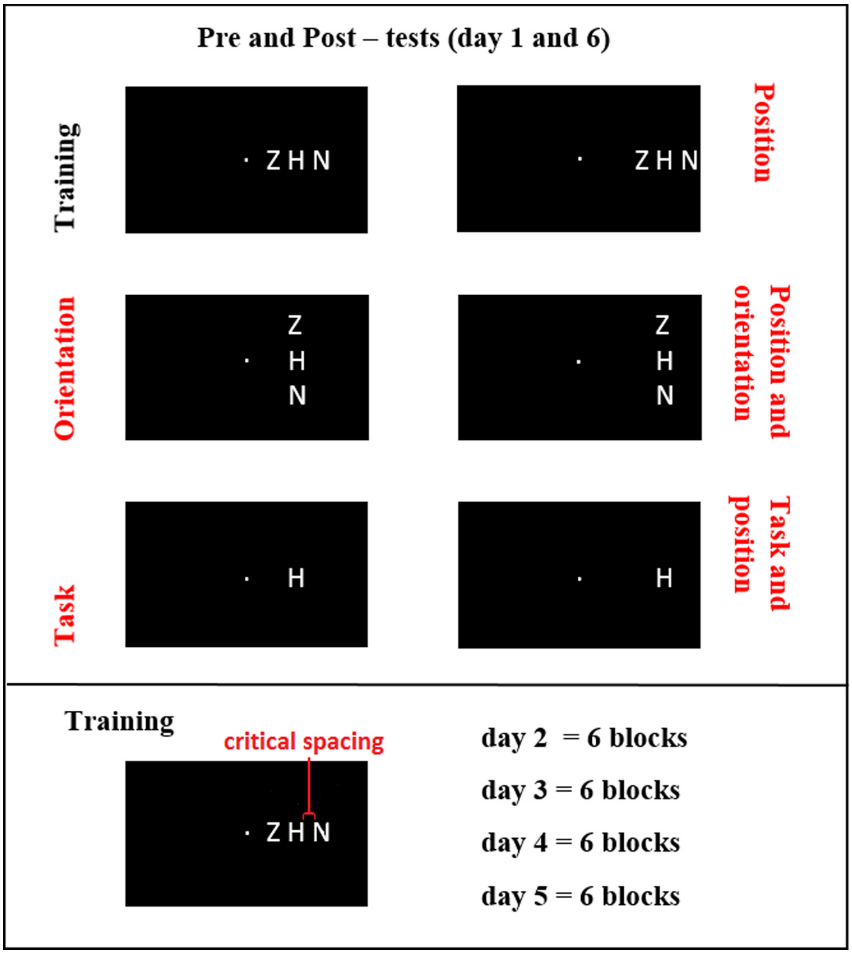

Fig. 1. Configurations used in the experiment. On the upper panel, the six tasks performed on the first and sixth day (pre- and post-tests): Training configuration (horizontal crowding 8° of eccentricity), Retinal position (crowding at 12°), Orientation (horizontal crowding at 8° with vertical orientation), Task (VA at 8°), Position and Orientation (vertical crowding tested at 12°), and Position and task (VA measured at 12°). On the lower panel, the training configuration (horizontal crowding 8° of eccentricity) tested six times during each daily session of the training. The letters in the figure are increased in size with respect to the actual stimuli and are arbitrarily displayed on the right for clarity. In the actual experiment, position was randomized between left and right.

letter, was presented (see Fig. 1, leftward panel). Participants were asked to identify the central letter of a peripheral trigram appearing at 8° of eccentricity (calculated from the center of the middle letter) either on the left or right of the central fixation. The trigrams were composed of randomly selected Sloan letters among a group of nine (D, S, R, Z, N, K, H, V, and C) with no repetitions within the same trigram. Participants were then asked to report the central letter of the trigram and to ignore the two flanking letters. Stimulus position was left/right randomized and the presentation time was 50 ms. To avoid any influence of the letter size on the task, we followed the common practice to increase the size of the letter 30% more than the acuity threshold of the participants (Barollo et al., 2017; Hussain et al., 2012; Maniglia et al., 2011). The spacing among the three letters was varied according to a one-up three-down adaptive staircase procedure (Levitt, 1971). The experimental setup and the stopping rule for the staircase was identical to the one adopted for the VA procedure. The measured threshold defined the Critical Spacing (CS) for letter recognition. At the end of each trial, participants verbally reported the letter to the experimenter who registered the answer on the keyboard. Since crowding is particularly relevant for reading, several studies used letters as stimuli. Some of these studies calculated CS as the Letter-to-Letter distance, some others as the Center-to-Center distance between letters (Hussain et al., 2012). An eventual overlap between target and flankers might reduce the validity of the measure since the task would then become a figure-ground segmentation task. On the other hand, measuring Letter-to-Letter spacing introduces inter-individual variability since the letter size varied according to the threshold of the participant, and the bigger the letter, the larger the center-to-center distance. We chose to avoid overlapping by defining CS as the letter-to-letter distance required by the participant for an 80% discrimination accuracy.

2.5. Transfer tasks

VA was measured to calibrate letter size in the crowding task at the same eccentricity to ensure that the size of the letter was large enough not to affect critical space measurement. VA before and after training was also used to determine whether learning transferred to an untrained but related task. In addition to VA, we measured four other transfer tasks (Fig. 1): crowding at 12° (retinal position transfer), vertical crowding at 8° (orientation transfer), 12° (retinal position and orientation transfer), and VA at 12° (retinal and task transfer) (see Fig. 1, upper panel). The procedure was the same as for crowding and VA. For pre-tests and post-tests, no brain stimulation (real or sham) was applied.

2.6. Training

The training was conducted on the horizontal crowding task (see Fig. 1, lower panel). Participants were divided into two groups: Group 1 (PL plus tRNS) and Group 2 (PL alone/sham). Each participant underwent three phases: pre-tests, training, and post-tests. During pre- and post-tests, thresholds for VA at 8° and 12°, horizontal crowding at 8° and 12°, and vertical crowding at 8° and 12° were estimated. Both groups underwent four training sessions, one per day during

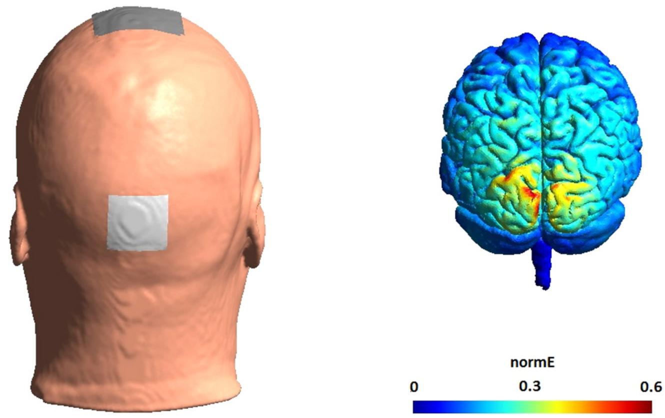

Fig. 2. Electrode positioning and modeled electrical field strength (normE). This estimate shows that the highest current density corresponded to the early visual cortices.

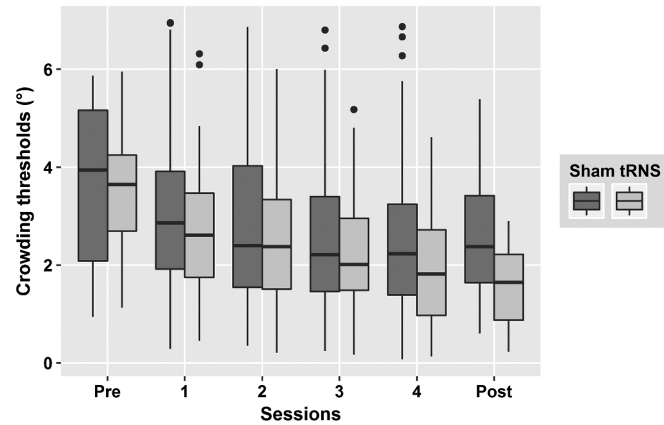

Fig. 3. Crowding thresholds (in degrees of visual angle) over days in the sham (in dark grey, n = 16) and tRNS (in light grey, n = 16) groups. For each day, the figure shows separated boxes for Sham and tRNS groups. From bottom to top, boxes provide the 5th, 25th, 75th, and 95th percentiles of the distributions. The horizontal bold lines provide the median values of the distribution and the black dots correspond to outliers.

four consecutive days. Each daily session consisted of six blocks, for a total of 24 blocks. Each session lasted approximately 30 min (~5 min per block). We did not provide direct auditory or visual feedback. However, participants were aware of the one-up three-down procedure so they could infer their performances from the trial-to-trial variation in spacing.

2.7. tRNS stimulation

Participants in Group 1 (PL + tRNS) were trained with concomitant electrical brain stimulation, while participants in Group 2 (PL alone) performed the training with sham stimulation. High-frequency tRNS was delivered using a battery-driven stimulator (BrainSTIM, EMS) through a pair of saline-soaked sponge electrodes. The tRNS consisted of an alternating current of 1.5 mA intensity with a 0 mA offset and maximal current density of 0.094 mA/cm^2. This type of stimulation is characterized by an alternating current of random intensity with zero offset and values ranging from -1.5 mA to 1.5 mA, with frequencies of fluctuation distributed across a range of 100–640 Hz with zero-mean (same as in Fertonani et al., 2011). The total duration of stimulation was 30 min to cover the entire training session. The active electrode had an area of 16 cm^2 and was placed over the occipital cortex measured at 3 cm above the inion. The reference electrode had an area of 27 cm^2 and was placed on the vertex. The current density was maintained well below the safety limits (always below 1 A/m^2; (Poreisz et al., 2007)). The electrodes were kept in place with non-conductive elastic bandages. For sham stimulation, we applied sponge electrodes in the same manner. At the beginning of the sham stimulation, current was ramped up over 15 s and then tapered off with an equal amount of time. The same procedure was performed at the end of the stimulation. To better understand the diffusion of the current through the cortex and the size of the stimulated area according to this setup, we calculated and visualized the expected current density with the SimNibs software (Saturnino et al., 2015, Fig. 2) which confirmed the current density was mostly localized in early visual areas.

2.8. Data analysis

Visual inspection of the data suggested a possible inhomogeneity in the variance of the training data between the two groups. We confirmed this by means of a Bartlett test (Bartlett's K-squared = 43.57, df = 11, p-value = 0.001), therefore we adopted non-parametric (distribution-free) inferential statistical methods. The Aligned Rank Transform for non-parametric factorial ANOVA (Wobbrock et al., 2011) allows a non-parametric analysis of variance to be conducted on factorial models with fixed and random effects for repeated measures. For the main effects, we performed this analysis using the "art" function of the ARTool package available at CRAN (Kay and Wobbrock, 2018). To test for interactions, we used another non-parametric ART test specifically developed to test for interactions of repeated measures design with one 'within' and one 'between' factors as described by Beasley and Zumbo (2009) and Higgins and Tashtoush (1994). This test was performed with the "npIntFactRep" function within the homonymous R package (Feys, 2015). However, because this package does not allow for testing interactions with more than one 'within' factor, we only ran interaction tests for the pre-post comparison in the trained and transfer tasks and for the between session learning but not for the between blocks learning. All the comparisons were pre-planned and we therefore reported their statistical significance without correcting for multiple comparisons. Given the number of performed comparisons (21), if all the null hypotheses were true, we should expect only 1.05 (5%) of the comparisons to have uncorrected P values less than 0.05. This consideration is important to better evaluate the strength of the reported results (Rothman, 1990).

3. Results

The reduction in critical space in the trained task was evaluated between sessions. We also evaluated transfer of learning to other untrained tasks between pre and post-test.

3.1. PL and tRNS effect between sessions

A two way Aligned Rank Transformation ANOVA performed on Group (tRNS vs Sham) and Sessions (pre-test, day1, day2 day3, day4, post-test) showed a main effect of Sessions ($F[5150] = 26{,}24$, $p < 0.0001$) and an interaction between Group and Sessions ($F[5150] = 2.72$, $p = 0.022$). It suggested that the tRNS group improved more than the Sham. However, since directly comparing levels of factors in a non-parametric model is not advised (Benavoli et al., 2015; Kay and Wobbrock, 2018), we did not run post-hoc analysis on this data (Fig. 3).

3.2. Trained and transfer tasks

We performed an Aligned Rank Transformation ANOVA for the trained and each of the transfer tasks. We tested Group (tRNS vs Sham) and Training (pre vs post) as factors plus their interaction. Results are reported below:

a) Trained task (horizontal crowding at 8°, Fig. 4a)	• Training (F[1,30] = 51.045, $p < 0.0001)^{*}$ • Group (F[1, 30] = 1.432, p = 0.241) • Interaction (F [1,30] = 4.885, $p = 0.0349)^{*}$
b) Retinal position transfer (horizontal crowding at 12°, Fig. 4b)	• Training (F[1, 30] = 10.216, $p = 0.003)^{*}$ • Group (F[1, 30] = 0.010, p = 0.920 • Interaction (F[1, 30] = 0.099, p = 0.754)
c) Orientation transfer (vertical crowding at 8°, Fig. 4c)	• Training (F[1, 30] = 2.27, p = 0.142) • Group (F[1, 30] = 3.19, p = 0.839) • Interaction (F[1, 30] = 2.089 p = 0.159)
d) Retinal position and orientation transfer (vertical crowding at 12°, Fig. 4d)	• Training (F[1, 30] = 3.968, p = 0.0585) • Group (F[1, 30] = 0.002, p = 0.961) • Interaction (F[1, 30] = 0.0756, p = 0.785).
e) Task transfer (VA at 8°, Fig. 4e)	• Training (F[1, 30] = 19.934, $p = 0.0001)^{*}$ • Group (F[1, 30] = 2.66, p = 0.609) • Interaction (F[1, 30] = 0.911, p = 0.347)
f) Retinal position and task transfer (VA at 12°, Fig. 4f)	• Training (F[1, 30] = 6.278, $p = 0.018)^{*}$ • Group (F[1, 30] = 3.611, p = 0.067) • Interaction (F[1, 30] = 0.454, p = 0.505)

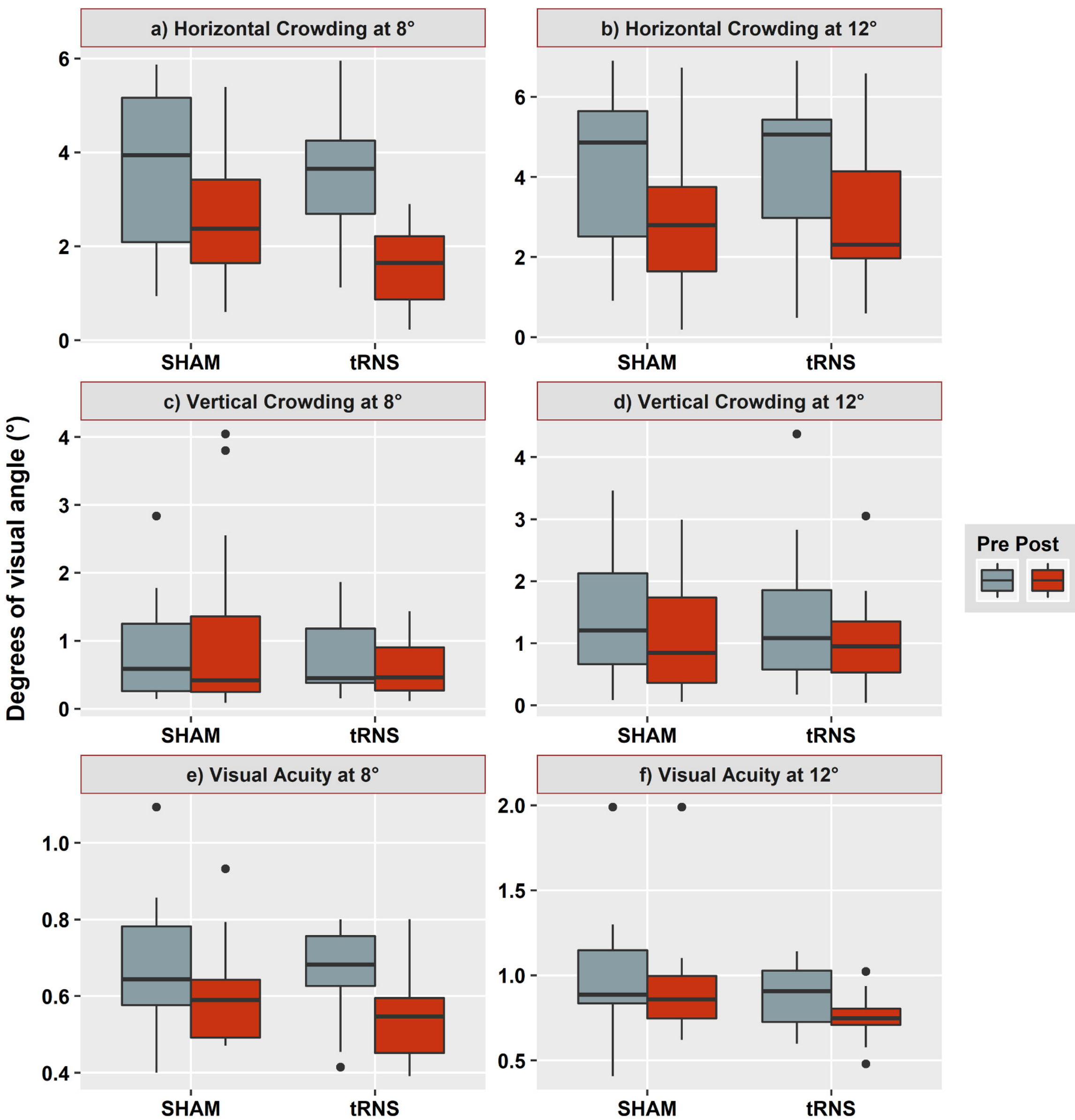

Fig. 4. Training and transfer tasks results for the sham and tRNS groups. Pre and post-training data are shown in grey and red, respectively. From bottom to top, boxes provide the 5th, 25th, 75th, and 95th percentiles of the distributions. The horizontal bold lines provide the median values of the distribution while the black dots correspond to outliers. a) Training task: crowding at 8° of eccentricity, b) Retinal transfer: horizontal crowding at 12°, c) Orientation transfer: vertical crowding at 8°, d) Position and orientation transfer: vertical crowding at 12°, e) Task transfer: VA at 8°, f) Position and task transfer: VA at 12° (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.).

4. Discussion

In the present study, we compared two training protocols for reducing visual crowding, one in which participants received online electric brain stimulation (i.e., tRNS) and the other in which no electric current was delivered during the task (i.e., sham). After four days of training, both groups improved in the trained task but the brain stimulation group reduced crowding significantly more than the sham group. Moreover, both groups showed transfer of learning to another retinal position and to visual acuity (VA). This is the first evidence of the efficacy of tRNS in boosting PL to improve performance during a peripheral vision task, a result consistent with previous studies in foveal vision (Camilleri et al., 2014; Campana et al., 2014).

4.1. Effect of tRNS on learning

Coupling tRNS and PL resulted in greater learning than PL alone, as observed in previous studies (Campana et al., 2014; Fertonani et al., 2011). The mechanisms underlying tRNS are still not completely understood: co-occurrence of stimuli in close succession and the temporal summation of small depolarizing currents induced by the random subthreshold stimulation (Terney et al., 2008) might facilitate the depolarization of cortical neurons, producing Hebbian LTP-like changes in the network that processes the task (Cappelletti et al., 2013; Fertonani et al., 2011; Miniussi et al., 2013; Snowball et al., 2013), improving in-turn performance over time (Terney et al., 2008). An alternative hypothesis is that the high stimulation frequency (100–640 Hz) prevents the homeostasis of stimulated neurons (Fertonani et al., 2011). Indeed, tRNS seems to induce greater improvements in performance than anodal tDCS, where the current flows constantly along the same direction, despite the fact that both stimulations produce an increase in cortical excitability (Fertonani et al., 2011; Pirulli et al., 2013). Finally, the introduction of external noise from the electric stimulation might alter the overall level of cortical excitability and the probability of discharge of each single unit, modifying in-turn the signal-to-noise ratio during stimulus processing (Fertonani et al., 2011). A model of *stochastic resonance* was previously proposed to explain the non-linear effects found in brain stimulation studies (Miniussi et al., 2013). This model takes into account the interaction between internal activity, externally induced noise, and stimulus-driven activity, predicting that in the case of a low target signal, an “adequate amount” of external noise (in our case the tRNS) can enhance the signal (alone) above the threshold. Some very recent studies investigated the relationship between the intensity of the tRNS stimulation and the performance in a visual task (van der Groen et al., 2017; van der Groen and Wenderoth, 2016). In particular, van der Groen and Wenderoth (2016) showed that the window of maximum efficacy in terms of stochastic resonance for a subthreshold visual stimulus has a peak at current intensities around 1 mA for an electrode of 35 cm^2 placed over the occipital cortex. This intensity is indeed lower than the one we used, but also the eccentricity of the task and the contact medium used to deliver the stimulation were different, and thus the expected peak efficacy of the stimulation is shifted towards higher intensities. Moreover, in other domains like auditory perception, improvement in perception attributable to stochastic resonance was achievable with intensities higher than 1 mA (Rufener et al., 2017). Given all these considerations, we suggest that the tRNS group in the present study might have benefited from both a general increase in cortical excitability and synaptic plasticity as well as a better signal-to-noise ratio throughout the course of the training, improving the performance between sessions, as suggested by the significant interaction.

4.2. Learning retention over time

Although our original design did not include any follow-up recording, we decided at the end of the experiment to collect additional data to further test learning retention in the trained task (horizontal crowding at 8°) over time. Ten participants (five in each group) were tested in follow-ups after three months. Because of this small sample size, the results of this follow-up experiment are tentative and are only succinctly reported here (the interested reader can, however, find all the details in the supplementary material). Interestingly, in this subsample only the tRNS group improved significantly between pre and post-test, in agreement with the main finding of the study which shows a larger learning effect for this group. For the sham group, despite a tendency to improve, the low statistical power due to the small sample size may have lead to a “false negative" finding. The main observed effect was that, after three months, the tested subjects had substantially lost their learning benefit. This is in contrast with previous studies that showed long-term learning retention after a crowding training (Hussain et al., 2012). Although this result might have been influenced by extreme values, it opens up an important reflection. It is possible that even if tRNS was able to speed up learning over a short number of trials, a larger amount of blocks or a different distribution of the training sessions needed to achieve a durable improvement in the task. Indeed, the number of trials used in our training is much lower than in previous studies. Given that consolidation of learning is a central aspect for future applications of PL in healthy and clinical populations, further research is needed to better determine the positive and negative aspects of tRNS over time.

4.3. Effect of tRNS on transfer

The tRNS group did not show greater transfer of learning to untrained visual tasks with respect to the sham group. An argument in favor of expecting a bigger transfer of learning for the tRNS group comes from the evidence that PL specificity can be overcome by removing the sensory adaptation that emerges after prolonged exposure to the same training configuration (Harris et al., 2012). Similarly, the randomly changing electric field induced by tRNS might prevent stimulated neurons from homeostasis, increasing their activity and thereby inducing a greater generalization. Indeed, Campana et al. (2016) showed a similar effect of reduced adaptation to motion for tRNS delivered over V5, while Campana et al. (2018) reported generalization to VA for a contrast detection training coupled with tRNS on the early visual cortex. The reason why we did not observe this effect might be related to the difficulty of the training we adopted. According to the stochastic resonance model (Miniussi et al., 2013), the interaction between task difficulty and intensity of the stimulation produces an inverted U shaped curve of performance and thus we opted for an adaptive task that could guarantee an adequate level of difficulty thorough the whole training regimen. A prolonged training at threshold (‘difficult’ training) was found to prevent learning from transferring to other retinal positions or tasks (Hung and Seitz, 2014). Easy trials during training, on the other hand, restored transfer of learning, consistent with the reverse hierarchy theory (Ahissar and Hochstein, 2000, 1997; Hochstein and Ahissar, 2002), according to which the difficulty of the task induces a shrinking of the attentional window and an increase in learning specificity. Since the beneficial effects of the tRNS are specific for difficult training conditions, this might prevent the stimulation from altering, in a positive or negative way, the amount of generalization. However, the relationship between training and generalization of learning appears complex, and might involve modifications in cortical areas beyond the ones we targeted with our stimulation (Maniglia and Seitz, 2018).

4.4. tRNS and crowding

Similarly to previous experiments combining visual PL and brain stimulation, our tRNS targeted the occipital cortex (Camilleri et al., 2014; Campana et al., 2014) and therefore mostly stimulated early visual areas (i.e., V1, V2/V3). The cortical substrate of crowding is a debated topic in vision science, with some studies implicating early cortical loci (Tripathy et al., 2014) and other higher level regions (Chicherov et al., 2014; Ronconi et al., 2016). It is likely that the reduction of crowding observed in PL studies results from neural changes at different levels of the visual processing hierarchy. However, the evidence that tRNS on occipital cortex induced a greater reduction of crowding is in line with the involvement of early cortical loci. Moreover, unlike previous studies (Camilleri et al., 2014; Fertonani et al., 2011), we stimulated upstream of the visual areas where the readout module for trained task (VWFA) is supposedly located. In this way, by applying the stimulation to some cortical areas involved in the early visual processing, we can potentially trigger a trickle-down effect that affects learning and discrimination of complex stimuli at later stages. However, given the absence of a control position for the stimulation, we cannot conclude that this result is specific for the protocol we adopted. We hope that future researchers will clarify this point.

4.5. Comparison with previous studies on crowding reduction

Previous studies reported crowding reduction through PL (Chung, 2007; Huckauf and Nazir, 2007; Hussain et al., 2012; Maniglia et al., 2011; Sun et al., 2010; Xiong et al., 2015). Chung (2007) showed a reduction of crowding of 38% (but no transfer to other tasks, i.e., reading speed). Hussain et al. (2012) trained adult amblyopic patients (in fovea) and healthy participants (4° of eccentricity) on a crowding task and reported similar reduction of critical space between the two groups (~20%) but no transfer to Maniglia et al. (2011) used a paradigm based on lateral masking and reported a transfer of learning to crowding reduction of about 16%. A similar paradigm used in AMD patients did produce improvements in VA, but not in crowding reduction (Maniglia et al., 2016b). More recently, Yashar et al. (2015) showed that a short training (600 trials) can reduce critical space of 32%. Our training, constituted by an average of 1600 trials, showed a similar reduction for the sham group (26%), but twice that amount for the tRNS group (63%). Moreover, it is worth noting that, on average, participants in the sham group reached their plateau at the end of the third day of training, while participants in the tRNS group reduced their critical space until the last session (Fig. 2).

Recently, Zhu et al. (2016) trained a group of healthy participants in a crowding task and reported a reduction of about 68% after 1700 trials. However, differences in task (orientation discrimination task in their study vs letter identification in the present one) and paradigm (fixed flanking distance and staircase-on-orientation discrimination accuracy in their study vs staircase-on-flanking distance in the present one) make the comparison between their results and ours less straightforward. In general, crowding can be reduced either by training on critical space reduction or by improving target identification for a fixed flanker distance.

5. Conclusion

The coupling of transcranial electrical stimulation and PL has shown to increase learning when compared with PL alone, offering a fast and effective method to improve peripheral visual functions. Future studies should verify its efficacy in clinical populations that might get practical advantages from crowding reduction, such as patients with amblyopia or central vision loss (Maniglia et al., 2016a). At the same time, its effect on brain networks should be further examined to increase our understanding in order to improve transfer and learning retention over time. Nonetheless, the present results supports the hypothesis that tRNS is a promising tool to improve visual training outcomes in general. These findings have potential implications for vision enhancement in both healthy individuals' periphery and patients suffering from central vision loss who cannot undergo the long training sessions typically needed in classic PL paradigms (Maniglia et al., 2016a).

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Disclosure statement

We wish to confirm that there are no known conflicts of interest associated with this publication and no financial/personal interest or belief that could affect our objectivity.

Credit author statement

Marcello Maniglia and Giulio Contemori (equal contribution authors) conceived and planned the experiments, developed the scripts for the data collection, built the experimental set up, collected and processed the experimental data.

Marcello Maniglia verified the statistical analysis and supervised the findings of this work.

Giulio contemori drafted the manuscript and designed the figures.

Yves Trotter encouraged Marcello Maniglia and Giulio Contemori to investigate the interaction between tRNS and learning, contributed to the design and implementation of the research, and commented on the manuscript.

Benoit R. Cottereau verified the analytical methods, aided in interpreting the results and worked on the manuscript.

All authors discussed the results and contributed to the final manuscript.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.neuropsychologia.2019.02.001.

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