Enhancing Anger Perception in Older Adults by Stimulating Inferior Frontal Cortex with High Frequency Transcranial Random Noise Stimulation

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Abstract

Extensive behavioural evidence has shown that older people have declined ability in facial emotion perception. Recent work has begun to examine the neural mechanism that contribute to this, and potential tools to support emotion perception during aging. The aim of this study was to investigate whether high frequency tRNS applied to the inferior frontal cortex would enhance facial expression perception in older adults. Healthy aged adults (60+ years) were randomly assigned to receive active high-frequency or sham tRNS targeted at bilateral inferior frontal cortices. Each group completed tests of facial identity perception, facial happiness perception and facial anger perception. These tasks were completed before and after stimulation. The results showed that, compared to the sham group, the active tRNS group showed greater gains in performance after stimulation in anger perception (relative to performance before stimulation). The same tRNS stimulation did not significantly change performance on the two other face perception tasks assessing facial identity and facial happiness perception. Examination of how inter-individual variability related to changes in anger perception following tRNS indicated that the degree of performance change in anger perception following active tRNS to inferior frontal cortex was predicted by baseline ability and gender of older adult participants. The findings suggest that high frequency tRNS may be a potential tool to aid anger perception in typical aging, but flag that performance variability and gender may interact with stimulation leading to different outcomes.

Keywords:

transcranial random noise stimulation (tRNS); facial emotion perception; aging; inferior frontal cortex; anger perception

Introduction

Emotional facial expression perception plays an important role in interpersonal communication. Difficulties with emotion perception are associated with specific types of social impairment, including poor interpersonal interaction, reduced social competence, loneliness, and inappropriate social behaviours (e.g., Spell and Frank, 2000; Kanai et al. 2012). Numerous studies have focused on establishing how emotion perception is affected as a function of normal adult aging, as well as the extent and implications of any observed difficulties (e.g. Sullivan and Ruffman, 2004; Isaacowitz et al., 2007; Ebner et al., 2013; Ebner and Fischer, 2014). The overall pattern of results regarding age group differences in facial expression perception is quite consistent: a recent meta-analysis reviewed papers examining age differences in emotion perception and concluded that older adults (60+) have increased difficulty in perceiving at least some basic emotions (particularly anger, sadness, and fear) from faces, but that others remain spared (e.g. disgust perception; Ruffman et al. 2008).

Although many studies have investigated the cognitive and neural basis of decline in emotion perception during typical aging, little attention has been directed towards improving face emotion processing in these individuals. In other areas of research one tool that has proved to be useful in aiding social perception is transcranial electrical stimulation (tES). TES is a safe and noninvasive technique for brain stimulation that can be used to increase or decrease brain activity under a targeted brain region. It refers to a range of techniques, including transcranial direct current stimulation (tDCS), transcranial random noise stimulation (tRNS), and transcranial alternating current stimulation (tACS), which involve passing a weak current between electrodes placed on the scalp (Miniussi, Harris, and Ruzzoli, 2013). For instance, in high-frequency tRNS, an alternating current ranging randomly between 100-640Hz is passed between electrodes leading to bilateral increases in cortical excitability under two stimulating electrodes (Terney et al., 2008).

Prior work has shown that tES can be effective in improving performance on several tasks in young adults, including memory, perception, social cognition, social perception, learning and motor abilities (e.g. Cohen Kadosh et al., 2010; Snowball et al., 2013; Fertonani et al., 2011; Sellaro et al., 2016; Romanska et al., 2015). While tES has been employed to study young adults, it has been used less frequently to study older adult participants (see Tatti et al., 2016 for review). This is surprising given a) the psychosocial consequences of reduced emotion perception ability (Spell and Frank, 2000), b) the consistent pattern of age-related declines in emotion perception ability (e.g. Ruffman et al., 2008), and c) prior work showing that social processing (including emotion perception) can be improved following tES in young adult participants (e.g. Santiesteban et al., 2012, 2015; Hogeveen et al., 2014, 2016; Janik et al., 2015; Romanska et al., 2015; Barbieri et al., 2016; Liepelt et al., 2016; Sellaro et al., 2016). Indeed, in other domains (e.g. memory, motor performance) non-invasive brain stimulation techniques have been shown to offer promise in enhancing performance of healthy older adults. For instance, Hsu et al. (2015) investigated the effect of non-invasive brain stimulation on healthy older adults by conducting a meta-analysis of fourteen studies with a total of 331 healthy older adults. The meta-analysis revealed that applying a single session of non-invasive brain stimulation typically positively influenced older adults' performance. With this in mind, assessing the effect of using non-invasive brain stimulation as a tool to improve older adults emotion perception seems an important avenue of investigation.

One form of tES that might be particularly useful in the context of aging is the use of high-frequency tRNS, which can induce bilateral changes in cortical excitability. This is important because age-related neural functions are often associated with shifts from unilateral functional brain activation to bilateral activation. For instance, the compensation-related utilisation of neural circuits hypothesis (CRUNCH) suggests that older people shift from unilateral functional brain activation to bilateral activation to achieve similar performance output as younger people who might only use unilateral neural activation (Reuter-Lorenz and Cappell, 2008). Similarly, aging has been linked with hemispheric asymmetry reductions and the recruitment of compensatory mechanisms (e.g. the hemispheric asymmetry reduction in older adults model [HAROLD], Cabeza, 2002). In this context high frequency tRNS may be useful to increase compensatory potential by inducing greater bilateral functional brain activation.

Prior work also suggests that age-related declines in emotion perception are related to changes in perceptual strategies employed by old relative to young adults; for example, older adults tend to use perceptual information from upper parts of the face (e.g. eye region) less often and less efficiently (i.e. they are worse at detecting changes in this region) than young adult participants (Circelli et al., 2013; Murphy and Isaacowitz, 2010; Sullivan et al., 2007; Slessor et al., 2013; Chaby et al., 2011; Wong et al., 2005). This perceptual strategy of privileging information from lower parts of the face appears to predict patterns of change in older adult emotion perception (Wong et al., 2005; Mather, 2016). In this regard, it has been argued that older adults have weaker perceptual representations of emotions that typically rely more heavily on information from the top half of the face (e.g. fear, sadness, and anger; Mather, 2016). One way in which high frequency tRNS is thought to aid performance is via mechanisms of stochastic resonance, with random noise amplifying weak neural signals (e.g. Moss et al., 2004). With this in mind, tRNS may offer a useful intervention to amplify weak signals in brain regions associated with emotion processing in older adults.

One brain region commonly linked with emotion perception is the inferior frontal cortex. For instance, a number of meta-analyses point to the involvement of inferior frontal cortex during expressive face perception (e.g. Sabatinelli et al., 2011; Fusar-Poli et al., 2009). Of particular interest in the context of aging is that activation within inferior frontal cortex has commonly been linked with the perception of facial emotions that older adults show impairments in perceiving (e.g. fear, sadness, and anger; Fusar-Poli et al., 2009; Fischer et al., 2010). Indeed in the meta-analysis by Fusar-Poli and colleagues (2009) it was found that bilateral inferior frontal cortex activity was most prominently associated with processing anger perception (an emotion that is typically linked with impaired perception in older adulthood). With this in mind, the inferior frontal cortex is a particularly interesting target region to assess whether high frequency tRNS could improve the emotion perception.

When investigating the utility of non-invasive brain stimulation for improvement, it is also important to consider individual variation within the target cohort and how this might interact with stimulation effects. One key feature that can interact with the effects of brain stimulation is baseline performance (e.g. Feurra et al., 2013; Hsu et al., 2014; Hsu et al., 2015; Hsu et al., 2017; Tseng et al., 2012). This is particularly important in aging research, since a number of studies point to differences in the functional brain networks recruited between high and low performing older adults (Cabeza et al., 2002, Reuter-Lorenz and Cappell, 2008). For example, in the context of face processing it has been shown that high performing older adults show activation in compensatory brain networks (i.e. different brain networks) when compared to young adults and when compared to low-performing older adults (Lee et al., 2011). These findings are often interpreted with the suggestion that low-performing older adults recruit similar brain networks as young adults but in an inefficient manner, whereas high-performing older adults show greater plastic reorganization of neurocognitive networks (and therefore compensate for deficiencies associated with typical aging; Cabeza et al., 2002, Reuter-Lorenz and Cappell, 2008). This highlights an important consideration for non-invasive brain stimulation studies since identifying a target brain region based on young adult or low-performing older adult brain networks may lead to differential patterns of behavioural change in low-performing versus high-performing older adults (i.e. low performing older adults may benefit from stimulating brain regions that younger adults use, but high performing older adults may benefit from stimulating a compensatory brain network).

To our knowledge no studies to date have examined a) if high-frequency tRNS can modulate emotion perception or b) if any effect can differ across older adults depending on baseline performance (i.e. high versus low performing older adults). With this in mind, this study sought to examine whether high-frequency tRNS targeted at the inferior frontal cortex could modulate older adults' abilities to perceive facial emotion (anger and happiness perception) and facial identity. We also assessed the extent to which any changes in performance following stimulation would be influenced by pre-stimulation (i.e. baseline) perceptual abilities. Based on prior work highlighting the involvement of bilateral inferior frontal cortex activity in anger perception (Fusar-Poli et al., 2009) and work suggesting that low-performing older adults tend to recruit similar brain networks as young adult participants (but high performing older adults tend to recruit compensatory brain networks) we predicted a specific improvement in low-performing older adults in anger perception.

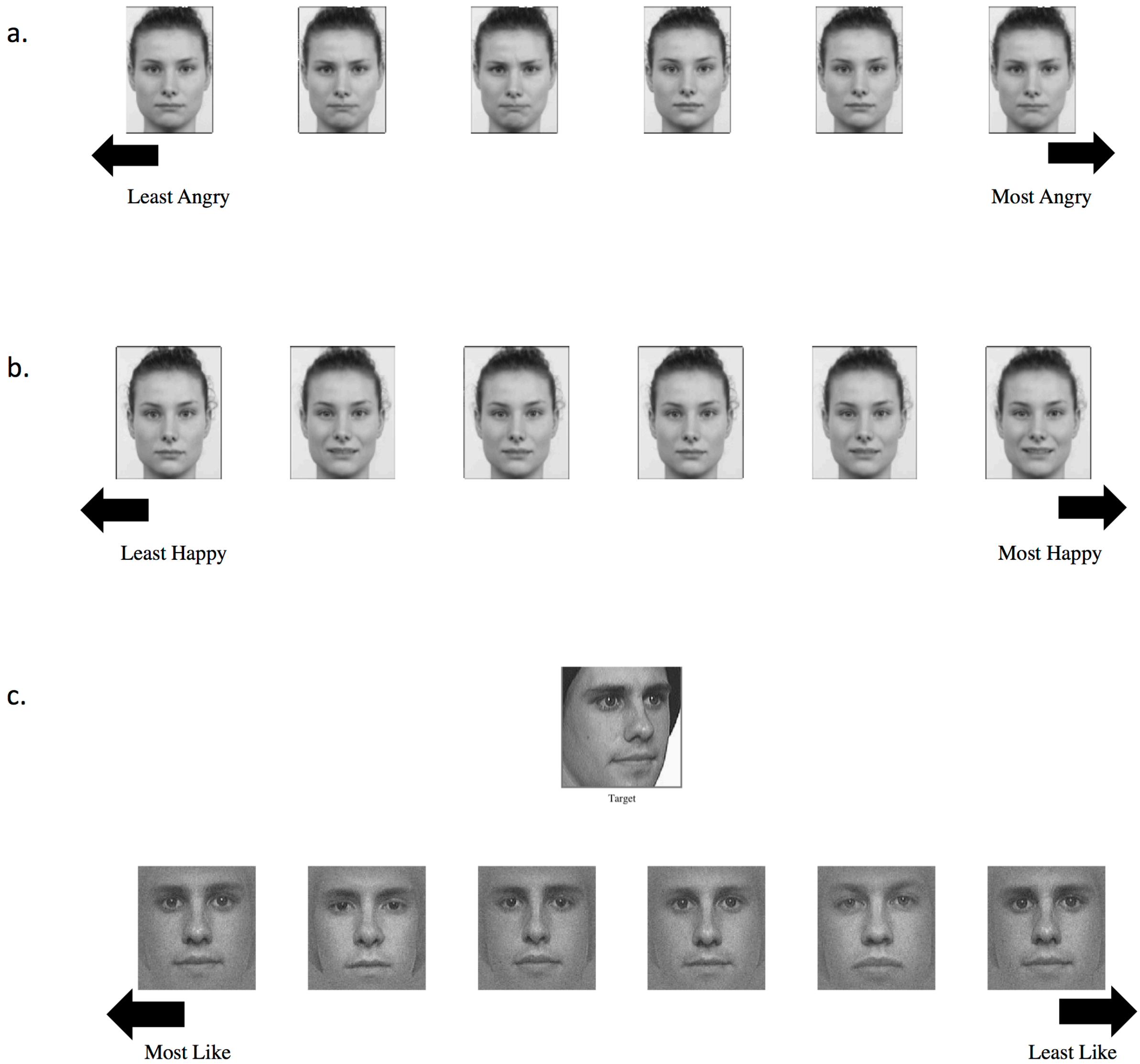
Methods

Participants

Thirty-two healthy older adult volunteers (mean age = 70.1 years, SE = 2.8 years; fourteen males) participated in this study. Participants were randomly assigned to the active high frequency tRNS (n = 16, mean age = 69.2 years, SE = 1.5 years; eight males) or sham stimulation (n = 16, mean age = 70.9 years, SE = 2.28 years; six males) groups.

Participants were recruited from the community using fliers in, for example, retirement communities or senior citizen centers. All participants were native-English Caucasians, with normal or corrected-to-normal vision, with no known history of neurological problems, dyslexia or other language-related problems. Information on handedness, education level, and National Adult Reading Test (NART) score (Nelson and Willison, 1991) were obtained and recorded from each subject. All participants were asked to complete mini-mental state examination (MMSE) (Folstein et al., 1975) to evaluate mental states, and none of them scored lower than 24. Informed consent from all participants were obtained prior to beginning the experiment who were fully informed about the experimental procedure. The experimental protocol was approved by the Ethics Committee of Goldsmiths (University of London).

Figure 1. Example trials on a) CFPT-Angry, b) CFPT-Happy, and c) CFPT-Identity.



Equipment and Procedure

Participants completed three tests before and after tRNS. The tests were the Cambridge Face Perception Angry (CFPT-Angry; Janik et al., 2015), Cambridge Face Perception Happy (CFPT-Happy; Janik-McErlean et al., 2016) and the Cambridge Face Perception Identity (CFPT-Identity; Duchaine et al., 2007a, 2007b) tests (Figure 1). During each test participants were shown a series of six faces and asked to sort them in order from most to least like a given target (either emotion or identity; further task details are provided below). Performance on each task was firstly measured by an error score, which was calculated by summing the deviations from the correct position for each face, with one error reflecting each position that a face must be moved to be in the correct location. For instance, if the image was three spaces from its correct position the error score for that trial would be three. Error scores on the trials were summed to determine the total number of errors. The total number of errors made was subtracted from the total number of possible errors on a given task. This was divided by the total number of errors made to give a proportion of correct responses, which was converted into percentage of correct responses. This approach is consistent with prior work using CFPT measures (e.g. Janik et al., 2015; Janik-McErlean et al., 2016; Romanska et al., 2015; Rezlescu et al., 2014). All participants completed the tasks before stimulation to measure their baseline performance and after stimulation to measure post-stimulation performance change. The order of the tasks was randomised for each subject. The approximate completion time for all tests was 30 minutes, after which they received 20 minutes of brain stimulation (see details below), followed by the post-stimulation tests. Further details of each test and the brain stimulation parameters can be found below.

CFPT-Angry

In the CFPT-Angry participants were presented six faces (from a frontal view) morphed between the expression of ‘anger’ and a ‘neutral’ expression in varying proportions (40%, 32%, 24%, 16%, 8%, 0%). All faces were of young adult participants and were adapted from the Radbound Facial Database (Langner et al., 2010). These six faces were presented simultaneously on the screen in fixed pseudo-random order. Memory demands are minimal in this task because faces are presented simultaneously; it is therefore an ideal measure to assess facial identity perceptual abilities. Participants were required to sort the faces according to how angry they appeared, from the face that looks least angry on the left to the face that looks most angry on the right. The time limit for each trial was 60 seconds, but participants could move on to the next trial earlier if they completed the trial before the time limit expired. Participants completed ten trials in total.

Performance was measured using percentage of correct responses. Chance performance is 36% (Janik et al., 2015; Janik-McErlean et al., 2016).

CFPT-Happy

In the CFPT-Happy task participants were presented six faces (from a frontal view) morphed between the expression of 'happiness' and a 'neutral' expression in varying proportions (15%, 12%, 9%, 6%, 3%, 0%; lower morphs were used than CFPT-Angry in order to avoid ceiling effects that commonly occur with happiness perception tasks). All faces were of young adult participants and were adapted from the Radbound Facial Database (Langner et al., 2010). The six faces were presented simultaneously on the screen in a fixed pseudo-random order. Memory demands are minimal in this task because faces are presented simultaneously; it is therefore an ideal measure to assess facial identity perceptual abilities. Participants were required to sort the faces according to how happy they appeared, from the face that looks least happy on the left to the face that looks most happy on the right. The time limit for each trial was 60 seconds, but participants could move on to the next trial earlier if they completed the trial before the time limit expired. Participants completed ten trials in total. Performance was measured using percentage of correct responses. Chance performance is 36% (Janik-McErlean et al., 2016).

CFPT-Identity

To investigate facial identity perception the CFPT-Identity was used in the experiment (previously called CFPT; Duchaine et al., 2007a, 2007b). This test assessed participants' ability to perceive differences between facial identities. During the task, participants were shown a target face (from a 3⁄4 viewpoint) and six faces (from a frontal view) morphed between the target and a distractor face (six unique distractors per target) in varying proportions (88%, 76%, 64%, 52%, 40%, 28%) so that they vary systematically in their similarity to the target face. All faces stimuli used were young adults. In each trial, participants were asked to sort the six faces by similarity to the target face within 60 seconds. If the participant completed the trial before the end of the one-minute time window they had the option to click on a button to begin the next trial (i.e. the task was self-paced). Memory demands are minimal in this task because faces are presented simultaneously; it is therefore an ideal measure to assess facial identity perceptual abilities. Normally, the CFPT contains, eight upright and eight inverted trials that alternated in a fixed pseudo-random order (Duchaine at al., 2007a, 2007b), but for the purpose the present study eight upright trials were completed (i.e. there were no inverted trials). Performance was measured using percentage of correct responses. Chance performance is 36% (Romanska et al., 2015; Janik et al., 2015; Janik-McErlean et al., 2016).

Brain Stimulation Parameters

Participants were randomly assigned to two groups for different stimulation conditions: active high frequency tRNS or sham stimulation. For each group, participants were seated in a comfortable chair, in front of a computer screen and a keyboard. In the active high frequency tRNS group 20-minute of brain stimulation was administered using a pair of saline-soaked surface sponge electrodes and a battery- driven, programmable, constant current DC-Stimulator (neuroConn). The stimulation electrodes were placed over both sides of the inferior frontal cortex, which has been previously identified as F7 and F8 (international 10–20 system for electrode placement sites; Towle et al., 1993). The size of both stimulation electrodes were 5 × 5 cm and they were fixed by rubber straps. High frequency tRNS (100-640 Hz) was applied for 20-minutes with a current strength of 1000 µA, 15s fade in/out. For sham stimulation the current was applied for 5s with a 15s fade in/out. This length of stimulation does not lead to changes in cortical excitability beyond the period of stimulation. It has been shown that participants cannot distinguish between active and sham stimulation (Ambrus et al., 2011). During the 20-minute brain stimulation, all participants were shown a neutral video to ensure consistency of personal activity during stimulation and to reduce boredom before continuing to the next stage of the experiment. Participants were blind to the stimulation group that they were assigned to.

Results

Preliminary Analyses and Baseline Characteristics

Prior to the statistical analysis, two participants (one from the Sham Group and one from the Active tRNS Group) were identified as outliers (using a criteria of > 3 standard deviations from the mean on any individual variable of interest; and significance using Grubb's Test). Following removal of these outliers the mean age of Sham and Active tRNS Groups did not significantly differ from each other [t(28) = .702, p = .489] (Active-tRNS: mean = 68 years, SE = 1.56 years; Sham: mean = 71 years, SE = 2.15 years). This was also the case for years of education (Active-tRNS: mean = 14 years, SE = 0.92 years; Sham: mean = 15 years, SE = 0.95 years; t(28) = .341, p = 736), and NART scores (Active-tRNS: mean = 118, SE = 3.80; Sham: mean =121, SE =1.56; t(28) = .372, p = 713). Handedness (14 Right Handed in Active Group, 15 Right Handed in Sham Group) and gender (8 Females / 7 Males in Active Group and 9 Females / 6 Males in Sham Group) was also similar between two groups.

To assess whether pre-test performance was similar across the tasks for each group we conducted a 3 (Task) x 2 (Group) mixed ANOVA. The main effect of Group [F(1, 28) = .201, p = .658, η^2 = .007] and Group x Task interaction [F(2,56) = 1.22, p = .303, η^2 = .042] did not reach significance, indicating that baseline performance on the three face perception tasks did not significantly differ between two groups. There was, however, a main effect of Task [F(2,56) = 3.91, p = .026, η^2 = .123], which was due to better overall performance on the anger task relative to the identity task [p = .030 Bonferroni corrected] (see Supplemental Table 1 for descriptive statistics of performances in pre- and post-tests).

Group Level Performance Differences following tRNS

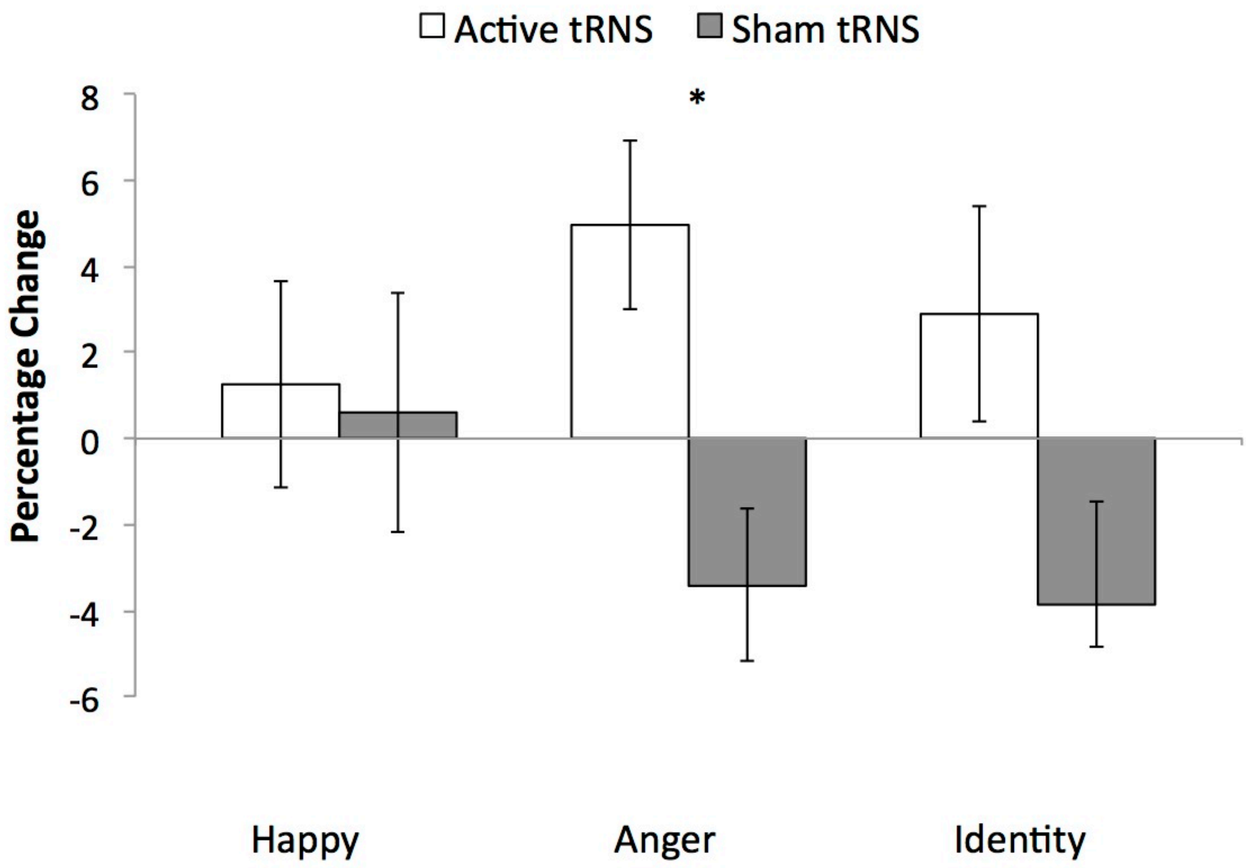
To examine the extent to which performance on each task was modulated by active or sham tRNS a performance change score was calculated by subtracting performance following tRNS (active or sham) from baseline performance (i.e. performance before stimulation). This provides a measure of the degree of change in performance following stimulation with positive values indicating an improvement in performance and negative values indicating a reduction in performance.

To compare whether the degree of change following stimulation differed between Active and Sham tRNS groups across each task (happy, anger, identity) we conducted a 2 (Group) x 3 (Task) mixed ANOVA. This revealed a main effect of Group due to the Active Group showing larger gains in performance following stimulation compared to sham stimulation [$F(1,28) = 8.47$, $p = .007$, $\eta_p^2 = .232$]. The main effect of Task [$F(2,56) = .213$, $p = .809$, $\eta_p^2 = .008$] and interaction [$F(2,56) = 1.46$, $p = .242$, $\eta_p^2 = .049$] did not reach significance. In this regard, active tRNS to IFC lead to greater improvements in performance across tasks, but this effect was not task specific.

Although, the interaction above was not significant, based on prior predictions regarding the potential for IFC stimulation to influence emotion perception a series of planned Bonferroni corrected paired comparisons were also conducted. This revealed that for anger perception participants in the Active tRNS group showed larger gains in performance than participants in the Sham tRNS group [$t(28) = 3.18$, $p = .012$ (Bonferroni corrected)]. This pattern of results was not found for happiness perception [$t(28) = .181$, $p = .858$] or identity perception [$t(28) = 1.95$, $p = .183$ (Bonferroni corrected)] where no significant differences were observed (Figure 2).

In addition, as descriptively there was a tendency for the Sham Group to show a decrement in performance between pre- and post-test, but the Active Group to show an increase in performance between pre- and post-test we also compared whether difference scores for each group were significantly different from zero using a one-sample t-test. This revealed that the Active Group anger performance score was significantly different from zero [$t(14) = 2.55$, $p = .023$], but that the Sham Group score was not significantly different from zero [$t(14) = -1.98$, $p = .076$].

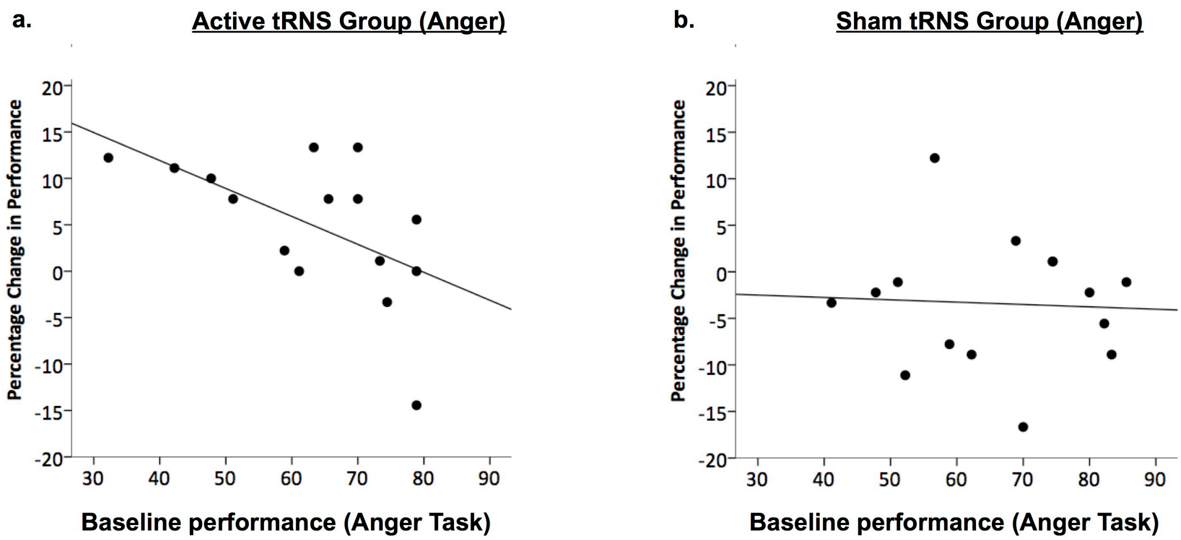
Figure 2. Percentage change (Post-Stimulation minus Pre-Stimulation Task Performance) significantly differed between older adults in the Active tRNS Group and Sham tRNS Group for anger perception, but not happiness or identity perception.



Contribution of individual differences to performance change following tRNS

Given that prior work has linked the efficacy of brain stimulation effects to baseline performance we also sought to examine the extent to which performance in the pre stimulation test was related to performance change following stimulation across all tasks. To do so we correlated pre-tests scores with performance change for the Active tRNS and Sham tRNS groups separately. This revealed that for the Active tRNS Group there was a significant negative relationship between pre-test performance and performance change following stimulation [r = - .572, p = .026], indicative of lower performance in the pre-test being associated with larger performance gains following active tRNS (Figure 3a). This pattern was not observed for the Sham tRNS group, where no significant relationship was found between pre-test performance and performance change scores [*r* = -.052, *p* = .854] (Figure 3b). Similarly, no significant relationship was observed between pre-test performance and performance change scores for either the active tRNS or sham stimulation group on the CFPT-Happy or CFPT-Identity (i.e. happiness pre-test performance did not significantly relate to performance change in happiness perception [Active tRNS Group – *r* = -.085, *p* = .764; Sham Group – *r* = -.297, *p* = .282]; identity pre-test performance did not significantly relate to performance change in identity perception [Active tRNS Group – *r* = -.282, *p* = .309; Sham Group – *r* = -.034, *p* = .906]).

Figure 3. Baseline performance in anger perception was significantly related to the degree of change following stimulation (Post-Stimulation minus Pre-Stimulation Task Performance) for the Active tRNS Group, but not the Sham tRNS Group.



Simple linear regression indicated that pre-test performance was a significant predictor of performance change following stimulation in the Active tRNS Group [*β* = -.572, *t* = 2.51*; F* (1, 14) = 6.31*, p* =.026*;* Adjusted R Square = .275]. In addition to baseline performance, prior work has suggested that brain stimulation effects may be influenced by gender (e.g. Chaieb et al., 2008; Lapenta et al., 2012; Russell et al., 2014). Adding gender (male = 1, female = 2) as secondary predictor in a hierarchical regression model alongside pre-test performance significantly improved the model [F (1, 12) = 9.30, p = .013; Adjusted R Square = .542)], with both pre-test performance [β = -.674, t = 3.66, p = .003] and gender [β = .540, t = 2.93, p = .013; females showing larger change relative to males] acting as significant predictors of performance change in anger perception following stimulation in the Active tRNS Group only.

Discussion

The aim of the present study was to investigate whether high-frequency tRNS targeted at the inferior frontal cortex would enhance older adults' ability to process facial emotion, and in doing so explore the importance of the inferior frontal cortex in older adults' emotion perception. Facial emotion perception (happiness and anger perception) and facial identity perception were assessed before and after active or sham tRNS targeted at the inferior frontal cortex. The results showed that there was a significant improvement for anger perception following high-frequency tRNS relative to sham stimulation. In contrast, the same tRNS parameters did not significantly change the ability to perceive facial identity or happiness. These results indicate that tRNS targeted at inferior frontal cortex enhanced older adults' ability to detect fine grained changes in the expression of anger, and add strength to previous proposals suggesting that the inferior frontal cortex is particularly sensitive to processing anger rather than positive emotions (Fusar-Poli et al., 2009).

By providing evidence of a link between inferior frontal cortex activity and anger perception in older adult participants, the neuromodulatory approach adopted in the current study could provide avenues for the development of novel approaches to intervention aimed at overcoming age-related declines in anger perception. In this context it is important to be aware of factors that might interact with stimulation efficacy. In addition to showing group level differences between active and sham tRNS targeted at inferior frontal cortex on anger perception, the results also showed that the degree of improvement in anger perception displayed by older adults receiving active tRNS to inferior frontal cortex was influenced by both baseline ability (i.e. pretest score) and gender. This pattern was not observed in the sham stimulation group. It was also not found for facial happiness or facial identity perception. These results are in line with recent findings showing that the effects of noninvasive brain stimulation are to some degree dependent on individual differences in susceptibility (e.g. modulation by gender - Chaieb et al., 2008; Lapenta et al., 2012; Russell et al., 2014; modulation by performance variability – Hsu et al., 2014; Hsu et al., 2015; Hsu et al., 2017; Krause and Cohen-Kadosh, 2014; Sarkar et al., 2014; Tseng et al., 2012). For instance, Hsu and colleagues (2014; 2017) have shown that variability in baseline abilities can influence the efficacy of modulation of visual memory following anodal tDCS applied to posterior parietal cortex.

To our knowledge, no studies have examined the relationship between inter-individual variability in baseline ability and performance change in emotion perception following tRNS in older adult participants. In other domains, there is some evidence for a similar pattern of data to our own. For example, using fMRI in conjunction with transcranial magnetic stimulation (TMS; a different type of non-invasive brain stimulation) to study memory, Solé-Padullés et al. (2006) found that TMS modulates low performing older adults' neural activation patterns (from unilateral to bilateral neural activation), and this change coincides with significant improvements in memory performance. The present finding (and findings of prior work in other domains using other forms of brain stimuation, e.g. TMS; Solé-Padullés et al. 2006; Hsu et al., 2015) suggests that future brain stimulation studies with older adult participants should measure and examine the impact of baseline performance on stimulation efficacy. An additional broader implication of this is that prior studies that found little or small brain stimulation effects in older adults might have been related to the possible recruitment of high performing older adults who have a relatively small capacity for cognitive improvement, which could potentially mask the effect of noninvasive stimulation on lower performing individuals. In future studies there is a need to further clarify the relationship between the effect of brain stimulation and different levels of ability, and the underlying neural compensation mechanisms.

The relationship between gender and change performance in anger perception following active tRNS is consistent with prior work that has shown that gender can influence performance change following tES (Chaieb et al., 2008; Lapenta et al., 2012; Russell et al., 2014). This has commonly been interpreted in two ways: 1) hormonal differences (Chaieb et al., 2008; Lapenta et al., 2012) or 2) differences in brain structure (cranial bone density differences between males and females; Russell et al., 2014). To date work assessing how gender influences the efficacy of tES has been focused on young / middle-aged adults[1], therefore future studies will need to assess whether and how gender is likely to act as a moderator of performance change following non-invasive brain stimulation in older adults.

While our findings highlight the importance of stimulation targeted at the inferior frontal cortex in anger perception in older adult participants, it is important to note that we cannot fully conclude that the improvement on anger perception was only due to the after-effect of stimulating this region, as there is evidence showing that noninvasive transcranial brain stimulation can spread to surrounding neural regions of the targeted stimulation regions (Zheng et al., 2011; Summers et al., 2016). The role of the inferior frontal cortex in processing negative emotions and its inter-connection with other brain regions involved in emotion perception (e.g. amygdala, Nomura et al., 2004; Nakamura et al., 1999; Narumoto et al., 2000) during aging is not clear. To investigate these questions, future studies will need to combine brain stimulation with brain imaging techniques (e.g. EEG, fMRI) to reveal more about network dynamics underlying changes in emotion processing following stimulation of inferior frontal cortex and consider how these might vary according to baseline performance (e.g. see Hsu et al., 2014 for a similar approach in younger adults). Models of the interaction between aging and performance suggest that low-performing older adults recruit similar brain networks as young adults but in an inefficient manner, whereas high-performing older adults show greater reorganization of neurocognitive networks leading greater compensation

[1] The mean age from Russell et al. (2014) was 53 years for males [range 34-68 years] and 50.5 years [range 21-75 years] for females, however this was tested on 12 males and 12 females thus testing on a larger sample of older adult participants is required.

(Cabeza et al., 2002; Reuter-Lorenz and Cappell, 2008). In the context of the findings reported here one might speculate that high-performing older adults have successfully applied compensatory strategies and recruited additional neural regions, leading to stimulation being less likely to induce additional benefits. In contrast, low-performing older adults (i.e. those that are inefficient in recruiting additional neural regions) have a greater capacity for stimulation to induce additional benefits. Combining tRNS with neuroimaging techniques may help to address this possibility.

In addition, it will be important for future work to assess the extent to which performance change in emotion perception following stimulation to inferior frontal cortex extends to other emotions that were not tested in the current study (e.g. fear, sadness), and to other emotion processing tasks (e.g. emotion discrimination; tasks involving the older adult rather than younger adult target faces). Further, as we did not observe a significant interaction between group and task performance, conclusions regarding the task specificity of the effects reported here require further investigation. In particular, while participants showed a significantly greater improvement in anger perception following active stimulation relative to sham that was not observed for facial identity or happiness perception, the lack of interaction means that the task specific nature of this improvement remains unclear.

As we only tested older adult participants in the current investigation it also remains important to consider whether the pattern of effects is specific to older adults or evident across different age groups. Prior brain imaging work suggests that the inferior frontal cortex plays a role in younger and older adult emotion perception (Sabatinelli et al., 2011; Fusar-Poli et al., 2009). In this regard, one may expect a similar pattern of results, but whether the effects would be specific to anger versus other emotional cues and perceptual abilities remains unclear. Younger adults tend to outperform older adults in emotion perception, but this can vary according to the emotion type - anger, sadness, and fear emotions are regularly found to be impaired, but others remain spared (e.g. Ruffman et al. 2008). The reasons for why these emotions are impaired, but the others tend to be spared are unclear. Commonly functions that are spared from decline in aging can be related to activity in different neural correlates to younger adults (e.g. Cabeza et al., 2002; Reuter-Lorenz and Cappell, 2008), thus one may not expect an identical pattern of results between younger and adults. This remains an important question for future investigation.

In summary, here we assessed the impact of high-frequency tRNS targeted at the inferior frontal cortex on older adults' facial emotion and facial identity perception abilities. We find that high-frequency tRNS targeted at the inferior frontal cortex improved anger perception in older adults, but that the degree of improvement was influenced by baseline ability and gender. In contrast, the same tRNS stimulation did not significantly change the performance on happiness perception or identity perception. The finding highlights high frequency tRNS as a potential tool to aid facial emotion perception in typical aging, but that there are gender and performance specific moderators of this effect that should be considered prior to application.

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Supplementary Table 1: Descriptive Statistics for Pre- and Post-Test Task Performance

Task	*Group*	*N*	*Mean (%)*	*S.E.M (%)*
CFPT-Happy Pre-Test	All	30	60.22	2.67
CFPT-Happy Pre-Test	Active	15	61.19	3.82
CFPT-Happy Pre-Test	Sham	15	59.26	3.84
CFPT-Happy Post-Test	All	30	61.14	2.92
CFPT-Happy Post-Test	Active	15	62.44	4.34
CFPT-Happy Post-Test	Sham	15	59.85	4.02
CFPT-Angry Pre-Test	All	30	64.52	2.58
CFPT-Angry Pre-Test	Active	15	63.11	3.70
CFPT-Angry Pre-Test	Sham	15	65.93	3.67
CFPT-Angry Post-Test	All	30	65.29	2.52
CFPT-Angry Post-Test	Active	15	68.07	3.04
CFPT-Angry Post-Test	Sham	15	62.52	3.99
CFPT-Identity Pre-Test	All	30	58.45	2.16
CFPT-Identity Pre-Test	Active	15	56.02	3.83
CFPT-Identity Pre-Test	Sham	15	60.89	1.93
CFPT-Identity Post-Test	All	30	57.96	2.44
CFPT-Identity Post-Test	Active	15	58.88	3.94
CFPT-Identity Post-Test	Sham	15	57.04	3.01