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Reduction of excitability in the left inferior frontal gyrus by cathodal transcranial direct current stimulation facilitates emotion recognition

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List of abbreviations

ANOVA:	Analysis of variance
BA:	Brodmann area
cm:	Centimeters
cm^2:	Square centimeters
conc:	Concentration
DLPFC:	Dorsolateral prefrontal cortex
DMN:	Default mode network
DRD4:	D4 dopamine receptor polymorphism
DSM-IV:	Diagnostic and statistical manual of mental disorders - fourth edition
EEG:	Electroencephalogram
FDR:	False discovery rate
HbO_2:	Oxygenated hemoglobin
HHB:	Deoxygenated hemoglobin
Hz:	Hertz
IFG:	Inferior frontal gyrus
IQ:	Intelligence quotient
LQ:	Laterality quotient
NA:	Negative affectivity
NIRS:	Near-infrared spectroscopy
nm:	Nanometers
M:	Mean
mA:	Milliampere
min:	Minutes
M.I.N.I.:	Mini-international neuropsychiatric interview
mm:	Millimeters
mmol:	Millimoles
MRI:	Magnetic resonance imaging
ms:	Milliseconds
MWT-B:	Multiple-choice vocabulary intelligence test
PANAS:	Positive and negative affective schedule
PA:	Positive affectivity
RME:	Reading the mind in the eyes

ROI:	Region of interest
RT:	Reaction time
sec:	Seconds
SD:	Standard deviation
SPQ:	Schizotypal personality questionnaire
tDCS:	Transcranial direct current stimulation
TMS:	Transcranial magnetic stimulation
TMT A/B:	Trail making test A/B

1 Introduction

1.1 Emotion recognition and expression

Emotion recognition is a basic condition of successful social cognition and behavior. It is a prerequisite for correct attribution of mental states ('Theory of Mind'). Impaired emotion recognition is related to prominent deficits in social functioning. Deficits in emotion recognition have been observed in a variety of psychiatric disorders, such as affective diseases (Schaefer et al., 2010), eating disorders (Ridout et al., 2012) and different types of personality disorders (Dickey et al., 2011; Marissen et al., 2012). They are also central in schizophrenia (Chan et al., 2010) and in the case of autism they even are a key characteristic of the disease (Philip et al., 2010).

1.1.1 Emotion recognition and expression by facial expressions

The expression of feelings and emotion recognition is a part of psychological research since the beginning and a focal point of many studies and theories. One of the first emotion theories by Charles Darwin already put emotion expression in the center of attention (Darwin, 1872). In his theory, facial expression developed originating from motor processes in the process of phylogeny. These processes taking place in parallel with the development of facial muscles led to a differentiation of these muscles and finally to the ability of emotion communication. In this communication process at least two individuals are involved: one sender and one recipient. The emotional state of the sender is encoded to a facial expression, which can be interpreted with decoding mechanisms by the recipient. The ability to communicate emotional states in their environment led to an immediate selective advantage for respective individuals, since conspecifics could adjust better to resulting intended actions.

Emotion expression includes all behavioral changes associated with the accompanying emotion, and it can be divided into verbal and nonverbal expression. Nonverbal emotion expression consists of a variety of individual aspects (i.e., facial expression, gestures, posture, and more complex behavior). Thus, most of the studies confine the research to analyze aspects only. Ekman extended his studies from body movement to the face and undertook classical research on the universality of facial expressions (Ekman, 1971). He described facial expressions of emotions and the involved facial muscles (Facial Action Coding System) with changes in the different facial muscles, which occur during showing emotions (Ekman and Friesen, 1978). Thus, universal emotions exist, which are equally perceived and expressed regardless of cultural or geographical influences (Ekman and Friesen, 1975; Ekman, 1993). These so-called basic emotions include fear, anger, disgust, happiness, sadness, and surprise. According to the theory of basic emotions, for each of these six emotions, a specific facial expression exists and both expression and recognition of these emotions are congenital as part of the signal system resulting from evolutionary development. These primary emotions must be distinguished from secondary emotions like relief or hope, which are assumed to arise from higher cognitive processes, based on an ability to evaluate preferences over outcomes and expectations. Accordingly, secondary emotions are acquired during ontogenesis through learning processes in the social context (Becker-Asano and Wachsmuth, 2008).

Tomkins showed that biological dispositions for emotion expression exist from the day of birth and they influence the interaction between the child and parents (Tomkins, 1984). Over time the reaction tendencies become more differentiated, stronger internal and external regulated, and stabilized (Cicchetti and Hesse, 1983). Configural information within the face like characteristic features and their positional relation play a central role during the processing of facial expressions (Calder et al., 2000). There are two different automatisms when looking at a face: the assessment of whether it is a familiar face and the recognition of the relevant emotional content for social interaction. To establish and verify the identity of a familiar person through a face, individuals fall back on unchangeable characteristics in the opposing face. The recognition of the relevant emotional information for social interaction is based on varying structures (i.g., the eyes or the mouth) (Haxby et al., 2000).

Human facial expressions are a universally understood signal and a key component to interpret someone’s emotion correctly (Russell and Fernandez-Dols, 1997).

1.1.2 Reading the mind in the eyes

Especially the eye region is rich in information and an essential element for social communication (Rule et al., 2008). It captures more attention than do other areas of the face (Janik et al., 1978). For complex emotions, participants perform equally well at decoding mental states when shown just the eye region as when shown the whole face (Baron-Cohen et al., 1997). Based on these findings, a well-validated test of mental state decoding, the ‘reading the mind in the eyes’ (RME) test, was used. The RME test is an established method to measure emotion recognition and has been used for a large number of studies, including to modulate emotion recognition (Domes et al., 2007).

1.2 Cognitive model of emotion expression and recognition

1.2.1 Motoric representation of facial expressions

Facial expressions can be distinguished into two different kinds of mimic presentation, the voluntary presentation and the involuntary one. The latter being defined as the emotional mimic (Damasio, 2000). These two mimic presentations differ in their performance. As far back as the 19^{th} century Duchenne de Boulogne could show by electric stimulation of the mimic musculature that a spontaneous involuntary smile differs from a voluntary one by different activations of the mimic muscles. (Duchenne, 1876). During the voluntary one, the contraction of the musculus orbicularis oculi is missing.

Stroke patients with impairment of the motor cortex often cannot move the corners of their mouth to a voluntary smile, while performing a spontaneous smile completely symmetrical (Hopf et al., 1992). The opposite is the case considering patients with Parkinson’s disease and impairment of the basal ganglia. One of the clinical pictures is a mimic rigidity, resulting from a substantial reduction of spontaneous facial movements. Apart from that, they can show voluntary facial movements (Monrad-Krohn, 1924). Consequently, the motoric control of an emotional mimic movement is not located in the same brain region as the control of voluntary facial expressions. Voluntary facial expressions are mainly linked to the pyramidal system, whereas emotional, spontaneous facial expressions are associated with the extrapyramidal system (Frank and Ekman, 1997). However, it must be assumed that even if there are two separate control systems, these two systems work closely together in healthy individuals. The facial expression - whether it be a voluntary or a spontaneous one - always is a function between both systems (Rinn, 1984).

1.2.2 Cortical and subcortical network of emotion recognition

A network of cortical (i.e., frontotemporal regions) and subcortical structures (i.e., amygdala and basal ganglia) subserves the recognition of facial expressions (Castelli et al., 2010).

The first part of the cognitive processing of visual stimuli is taking place in primary and secondary visual areas located in occipital and temporal brain regions. After intake of the visual stimuli by the primary visual cortex (Brodmann area (BA) 17), the visual information gets to secondary visual areas (BA 18 and 19), where processing and integration of the information are taking place (Trepel, 2008). One region of the secondary visual cortex seems to be responsible specifically for facial recognition. The so-called fusiform face-area located in the gyrus fusiformis showed selective activation during looking at emotional faces (Vuilleumier and Pourtois, 2007; Schiltz, 2010).

Many studies showed the importance of the limbic system especially of the amygdala during emotion processing (Baron-Cohen et al., 1999; Adolphs, 2002; Stone et al., 2003; Castelli et al., 2010). The role of this system is the immediate perception and valuation of emotional stimuli (Phillips et al., 2003). This so-called bottom-up appraisal system is based on intrinsic or learned characteristics of stimuli to enhance or reduce behavior patterns. Through the hypothalamus and cores of the brain stem, the amygdala initiates endocrine and behavioral reactions so that the body can react adequately to emotional stimuli.

The limbic system also is connected to cortical areas. A decisive contribution to emotional control is performed by the connection between the amygdala and the prefrontal cortex (Ghashghaei et al., 2007). In this process, the prefrontal cortex represents the cortical control center of the subcortical development of emotions in

the amygdala and can influence the process by the revaluation of different situations (Banks et al., 2007).
Especially the left inferior frontal gyrus (IFG) is a crucial region for emotion recognition. It includes the motoric speech area (Broca Area), as well as mirror neuron activity (Fadiga et al., 2009). The mirror neuron system was first discovered in 1992 (di Pellegrino et al., 1992). The unique character of its discovery was that this system showed activity during both the performance and during the view of motor actions. After only considered an important role in the field of motor skills it became apparent that it is also essential for the processing of emotional-cognitive stimuli (Gallese et al., 2004). It is assumed that mirror neurons reflect perceived stimuli like facial emotional expressions and transfer them into an inner subjective perspective (Seitz et al., 2008). In this way, the emotional recognition becomes a cognitive representation. This allows people to share other's emotions and sympathize, a process generally known as empathy (Iacoboni, 2009).
The mirror neuron system was first localized in an inferior part of BA 6 (Rizzolatti et al., 1998). Later it could be demonstrated that mirror neurons also exist in other parts of the inferior prefrontal gyrus like in BA 44 (Rizzolatti and Craighero, 2004). BA 44 is considered a basic element of emotion recognition (Shamay-Tsoory et al., 2009).

1.2.3 The left inferior frontal gyrus (IFG) and its role in emotion recognition

Many studies showed the crucial role of the left inferior frontal gyrus (IFG) in emotion recognition, especially when it comes to reading the mind in the counterpart's eyes.
Compared to healthy controls, patients with schizophrenia performed less accurate in the RME test associated with less activation of the left IFG (Russell et al., 2000). Schizophrenic patients also showed a more significant reduction of gray matter in the left IFG associated with a significantly lower performance during the RME test (Hirao et al., 2008). Autistic individuals also showed worse performance on the RME test with lower activation of the left IFG compared to healthy controls (Baron-Cohen et al., 1999). Dal Monte et al. revealed that patients with penetrating traumatic brain injury performed worse in the RME test compared to non-head injured controls. They also showed that this impaired performance in the RME test was associated with lesions in the left IFG (Dal Monte et al., 2014). Healthy males scored lower while performing

the RME test and showed stronger activation in the left IFG than healthy females (Baron-Cohen et al., 2006). Older people had higher activation of the left IFG than younger people although the performance of the two groups did not differ on the RME test (Castelli et al., 2010). Furthermore, Moor et al. showed that younger adolescents (10-12 years) activated the left IFG more than older adolescents (14-16 years) while performing the RME test (Moor et al., 2012).

From the listed neuroimaging studies it can be shown that the left IFG is critically involved in emotion recognition and especially in the reading the mind in the eyes, but how and with which function is not yet fully resolved and still to explore and discuss in further studies.

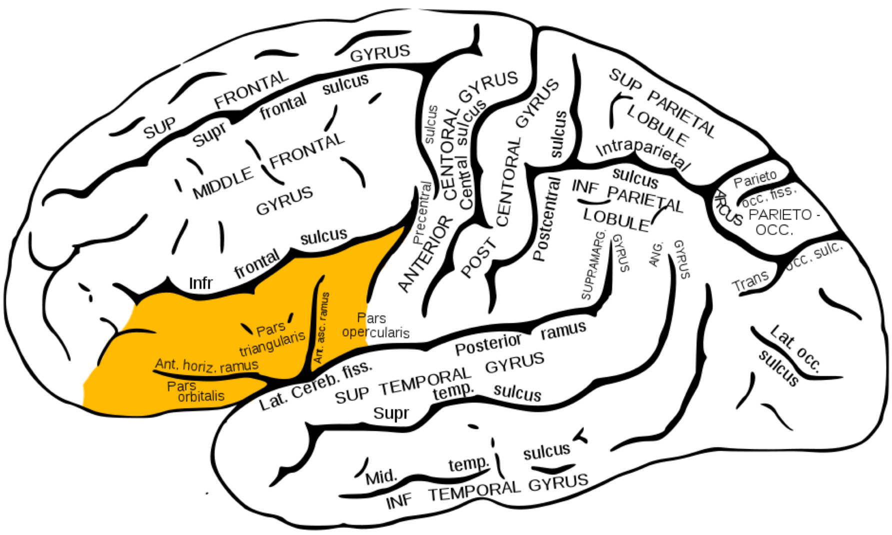

Figure 1: The left inferior frontal gyrus (IFG) marked in orange (Wikimedia Commons contributors, 2013).

1.3 Neural noise hypothesis

Hancock et al. described the neural noise as a random variability in the firing activity of neuronal networks and membrane voltage of single neurons (Hancock et al., 2017). It can come from many sources, i.e., physical fluctuations in the function of ion channels and the release of neurotransmitters into the synapse or synaptic activity from other neurons mediated by network connectivity. The authors interpret neural noise as a stochastic variability in the neuronal response to repeated presentations of the same stimuli, in contrast to non-stochastic response variability such as adaption effects. On the model of the neuronal network consisting of the balance of excitatory and inhibitory activity, the development of neural noise can be demonstrated. A local excitatory neuronal activity usually leads to neuronal feedback inhibition. The resulting rise in inhibitory synaptic conductance that is time-locked to the initial stimulus-dependent excitation increase provides the opportunity for a temporally precise and synchronized neuronal response by producing a narrow time window for neuronal firing (Wehr and Zador, 2003). An imbalance of the excitation and inhibition system can cause neural noise evoked by increased variability in neuronal firing and a loss of spike timing precision. Neural noise, in general, has not necessarily just negative aspects. Some level of neural noise can facilitate information transfer through stochastic resonance. Thereby weak periodic inputs, which generally would not be perceived, can reach the threshold for inducing neuronal activity by combining with synchronized firing neural noise (Stein et al., 2005). On the contrary neural noise can lead to spontaneous neuronal activity when stronger inputs are close to or above the firing threshold. This can reduce synchronization between neuronal activity within a network and external inputs.

1.4 Transcranial direct current stimulation (tDCS)

Transcranial direct current stimulation (tDCS) is a non-invasive technology for transient, polarity specific modulation of cortical activity and cognitive function (Dockery et al., 2009; Holland et al., 2011). It can induce changes in the resting membrane potential and the postsynaptic activity of cortical neurons by application of weak electrical currents directly to the scalp through a pair of electrodes. This current flow is generated by a direct current voltage source (e.g., a battery), whereby the electrodes flow from the negatively charged cathode to the positively charged anode without change of direction. An action potential consists of a characteristic depolarization of the neuronal membrane potential. Therefore, a depolarization of the resting membrane potential not exceeding the threshold of an action potential leads to enhanced excitability. Inversely hyperpolarization leads to decreased excitability. Accordingly, anodal stimulation increases the local cortical excitability, and cathodal stimulation leads to a decrease.

It should be noted that this is a simplified model. It is important to note that in response to an electric field, different compartments of the same neuron will simultaneously either depolarize or hyperpolarize. Thus the complex modulation by electric stimulation cannot necessarily be explained by a simple increase or decrease in excitability (Datta et al., 2008). Anodal stimulation is understood as the placement of the anode over the target area as the active electrode, while the cathode is placed over the reference area as the reference electrode. Inversed conditions correspond to cathodal stimulation. Plate-shaped electrodes made of conductive plastic are preferably used. Sponges soaked with physiological salt solution provide sufficient contact with the scalp and reduce skin resistance to a minimum.

In contrast to animal research tDCS on people is non-invasive. Therefore, the current flow must penetrate the skin, skull, and meninges. The consequence is a 50 percent reduction of the administered transcranial current density (Rush and Driscoll, 1968). Relevant parameters for the efficiency of the stimulation are the size of the stimulated area and the intensity of stimulation. Their quotient is the current density which determines the degree of potential deflection and thereby the influence on spontaneous activity and excitability (Nitsche and Paulus, 2000). Participants can be effectively blinded to the stimulation by comparison with placebo ('sham') stimulation (Gandiga et al., 2006). Bindman et al. stimulated the dissected cortex of anesthetized rats. Positive surface polarization with low current strength led to higher excitability and more spontaneous activity of cortical neurons, whereas negative surface stimulation led to decreased discharge frequency and with sufficiently high stimulation intensity even to reversible inactivity (Bindman et al., 1964). These results mostly matched the observations of Creutzfeld et al. on the dissected motor cortex of cats which showed a nearly linear relationship between induced current strength and discharge rate within the range of 250 to 1000 microamperes (Creutzfeldt et al., 1962). 40 years later Nitsche and Paulus showed on human experiments on the model of the motoric system that anodal stimulation increases and cathodal tDCS decreases cortical activity (Nitsche and Paulus, 2001).

1.4.1 Effects of non-invasive brain stimulation on emotion recognition

Nitsche et al. tested the effect of prefrontal tDCS on emotional face identification and showed improvements by a tDCS-driven excitability modulation of the prefrontal cortex, markedly by anodal tDCS of the left dorsolateral prefrontal cortex (DLPFC) for positive emotional content (Nitsche et al., 2012). Ferrucci et al. applied tDCS over the cerebellum and found a significantly enhanced sensory processing in response to negative facial expressions by anodal and cathodal stimulation (Ferrucci et al., 2012). Vonck et al. observed that the recognition of bodily emotions can be affected by tDCS depending on their valence. Anodal tDCS applied over the posterior superior temporal sulcus led to increased recognition performance for emotions with a negative emotional valence when it was compared with cathodal tDCS (Vonck et al., 2015). Boggio et al. could show the effect of anodal tDCS on the modulation of emotions. When applied over the left DLPFC ratings of unpleasantness and discomfort or pain were significantly decreased (Boggio et al., 2009). Peña-Gómez et al. found a similar result for the interference of anodal tDCS and emotional processing. Anodal stimulation of the left DLPFC showed a significant reduction of the perceived degree of emotional valence for negative stimuli (Peña-Gómez et al., 2011). Enticott et al. demonstrated the effect of tDCS on interpersonal motor resonance described as the activation of an individual's motor system during the observation of another's behavior (e.g., spontaneous mimicry when observing another's facial expression). Both anodal and cathodal stimulation of the left IFG significantly reduced the interpersonal motor resonance (Enticott et al., 2012). Martin et al. used high-definition tDCS applied over the dorsomedial prefrontal cortex to investigate the effects on emotion recognition depending on the sex of the participants. Only female participants showed a significant improvement in the RME test during anodal stimulation. Male participants presented an impaired performance whereby this decline was not significant (Martin et al., 2017). In prior experiments of our research group, both anodal and cathodal stimulation of the left IFG with a constant current of 1 mA showed no significant effects on the performance of emotion recognition (Klimm et al., 2013).

Transcranial magnetic stimulation (TMS), another regularly implemented non-invasive brain stimulation method, also was used to influence emotion recognition. Wölwer et al. showed a significant improvement of facial affect recognition after

repetitive TMS compared to sham stimulation over the left DLPFC of schizophrenic patients. This effect was independent of clinical improvement (Wölwer et al., 2014). Keuken et al. investigated the relationship between the mirror neuron system located in the left IFG and its reflection by EEG frequency bands. Additionally, they hypothesized an interference on emotion recognition after a temporary disruption of the left IFG with repetitive TMS. 8-12 Hz EEG μ rhythm was shown to be the most suitable indicator for mirror neuron activity. Repetitive TMS eliminated this index rhythm for mirroring activity and also led to a worse performance of emotion recognition resulting in increased reaction time during the emotion recognition task (Keuken et al., 2011). Enticott et al. used TMS to investigate the relationship between the mirror neuron system and facial emotion processing. An increased motor-evoked potential amplitude measured via electromyogram and seen as a marker of mirror neuron activity in the premotor cortex was associated with facial emotion recognition accuracy in static faces (Enticott et al., 2008).
It is possible to modulate emotion recognition with tDCS and TMS. But as the ambiguous current evidence shows it is not yet fully understood how exactly and in what manner non-invasive brain stimulation effects this process.

1.4.2 Interaction between tDCS and neural noise

The stimulation of non-motor cortical areas showed that behavioral effects are often not that obvious, with anodal stimulation usually inducing facilitation and cathodal stimulation inducing a range of effects (Jacobson et al., 2012). The effects of tDCS depend not only on the activity of the neurons that respond according to the task-goal but also on the activity of the neurons that are not associated with the final task-goal defined as neural noise (Miniussi et al., 2013). In the case of more background noise, for example during a novel task compared with a familiar task, anodal tDCS will not help task execution as it will increase the signal but also the noise, which is close to the threshold. In such a case cathodal tDCS can induce facilitation by reducing the general noise and helping the signal emerge (Dockery et al., 2009).
Antal et al. showed an improvement in the performance in a visuomotor coordination task by cathodal tDCS applied to the left visual middle temporal area when a large amount of visual noise was present in the visual stimulus (Antal et al., 2004). This

effect was explained by the role of cathodal tDCS acting as a neuronal filter and reducing the interfering neural noise. A similar mechanism can be observed in line with a neurophysiological process called lateral inhibition. This mechanism can reduce the neuronal activity to improve the excitatory response and therefore the final performance in the discrimination of non-relevant (noise) and relevant signals. Zwissler et al. also demonstrated the noise-reducing effects of cathodal tDCS on executive brain functions. They applied anodal and cathodal tDCS on the left dorsolateral prefrontal cortex while the participants performed a memory task. Thereby anodal tDCS increased the error rate in the memory task whereas cathodal tDCS led to a reduction of produced errors. In their opinion, the enhancement of excitability in the left dorsolateral prefrontal cortex by anodal tDCS caused 'blurred detail memory' like distracting neural noise. On the other hand, cathodal tDCS acted as a noise filter inhibiting the development of imprecise memory traces and reducing the false memory rate (Zwissler et al., 2014). Using a dichotic listening paradigm Alexander et al. could show the enhancing effects of cathodal tDCS on cognitive performance working as a noise-filter. When presented with auditory targets with different emotional valence participants showed better prosody comprehension during cathodal stimulation of the right IFC. Anodal stimulation showed no such effects (Alexander et al., 2012).

As stated by the mentioned studies above cathodal tDCS can reduce interfering neural noise and thereby help to produce a neuronal response for relevant sensory inputs which potentially would get lost in the general neural noise generated especially during unusual tasks.

1.5 Near-infrared spectroscopy (NIRS)

Near-infrared spectroscopy (NIRS) is an optical method to measure the regional brain tissue oxygenation. It has been developed in the 1970s (Jöbsis, 1977). The method is based on near-infrared light (650-1000 nanometers (nm) wavelength) penetrating 1-2 cm into the cortex and being reflected or absorbed in the process. In brain tissue, it is essentially absorbed by deoxygenated (HHb) and oxygenated hemoglobin (HbO_2), which have different absorption spectra. At wavelengths between 650 and 800 nm, HHb absorbs more light, whereas between 800 and 1000 nm the relation turns. As a result, we can evaluate the regional concentration changes of HHb and HbO_2 spectrophotometrically from the relationship of emitted and reflected near-infrared light with a modified Lambert-Beer’s law. Hemoglobin in its oxygenated and deoxygenated form is a reliable index for brain activity (Hoshi and Tamura, 1993). Changes in neuronal activity are associated with changes in cerebral blood flow. During neuronal activity, neurons need oxygen and glucose, which leads to a local increase in blood flow. As a result, significantly more oxygen accumulates which cannot be entirely absorbed by the brain cells. This leads to an increase of HbO_2 and a decrease of HHb, which can be measured with NIRS. The change in concentration of the chromophores HHb and HbO_2 reaches its peak within a few seconds and levels off to the base level. However, the curve progression varies slightly within an individual, within a collective and between the chromophores (Huppert et al., 2006). Fox and Raichle first described this typical perfusion pattern triggered by neuronal activation in a positron emission tomography study (Fox and Raichle, 1984) and it is also verifiable with NIRS (Hoshi and Tamura, 1993).

Further development of the method allowed the measurement of locally limited cortical activity and functional activation induced by motor (Obrig et al., 1996) and sensory stimuli (Meek et al., 1995) or cognitive tasks (Hoshi and Tamura, 1997; Herrmann et al., 2003). It has been shown that NIRS is sensitive enough to measure task-specific activation patterns during defined cognitive processes (Ehlis et al., 2007). The advantages of NIRS compared with magnetic resonance imaging (MRI) are the better temporal resolution and the relative insensitivity for motion artifacts. It usually comprises compact and mobile equipment with the possibility of long-term measurement. NIRS is particularly interesting to use in children and psychiatric patients (e.g., claustrophobic patients). It is considerably cheaper than MRI scans.

1.5.1 NIRS and emotion recognition

Platek et al. conducted the Schizotypal Personality Questionnaire (SPQ) on 21 participants and performed the RME test while wearing a NIRS probe. They observed significant positive correlations between SPQ total and maximum oxygenation values in both left and right hemispheres. These correlations were larger in the left hemisphere (Platek et al., 2005). Hoshi et al. showed that very unpleasant emotion was accompanied by an increase in HbO_2 in the bilateral ventrolateral prefrontal cortices while very pleasant emotion led to a decrease of HbO_2 in the left DLPFC (Hoshi et al., 2011). Kida and Shinohara exposed adult participants with tactile stimulation by velvet. This led to increased HbO_2 in the bilateral anterior prefrontal cortices (Kida and Shinohara, 2013). Minagawa-Kawai et al. let mothers and their infants perform a passive viewing of smiling faces. Interestingly they could demonstrate an increase in HbO_2 in the orbitofrontal cortex in response to own mother's or infant's smiling face in both mothers and infants (Minagawa-Kawai et al., 2009). Moghimi et al. presented emotional music excerpts to adult participants. Music excerpts rated as intense induced larger peaks of HbO_2 change in the prefrontal cortex (both left and right). The sharpness of HbO_2 peak was also linked to arousal and valence ratings (Moghimi et al., 2012). Hermann et al. found increased activity of the medial prefrontal cortex during an emotional induction paradigm that differed in the self-monitoring requirements. The task with the higher self-monitoring resulted in an increased concentration of HbO_2 (Herrmann et al., 2003).

In summary, NIRS could be successfully applied to measure brain activation during different tasks of emotion recognition.

1.6 Aim and hypothesis

This study aimed to determine the facilitation of tDCS on emotion recognition based on the interindividual differences in the activity of the left IFG during test performance on an emotion recognition task.

Considering the inconclusive study situation with very different effects of tDCS on emotion recognition stands to reason that there are interindividual differences how non-invasive brain stimulation affects network connectivity in brain regions responsible for emotion recognition.

Furthermore, prior experiments of our research group showed no significant effects of tDCS on emotion recognition with 1 mA both anodal and cathodal stimulation. This also indicated that interindividual differences in the underlying mechanisms of test performance and tDCS action have interacted with these effects.

It was hypothesized that the different interindividual activity in the left IFG predicts the effects of anodal and cathodal tDCS. To prove this hypothesis, the emotion-specific preactivation of the participants was measured with NIRS before testing the effects of anodal and cathodal tDCS on emotion recognition.

2 Materials and methods

2.1 *Participants*

Thirty-two healthy right-handed participants took part in the experiment (mean age 27,83; SD 7,36; range 21-53; 16 female). Handedness was assessed by a modified version of the Edinburgh handedness inventory (Oldfield, 1971). All participants gave informed consent and had no current neurological or psychiatric illness (verified with the mini-international neuropsychiatric interview (M.I.N.I.) (Sheehan et al., 1998)). All of them obtained the general higher education entrance qualification (Abitur). 15 participants were still undergoing vocational training, one completed a technical college, 13 accessed a university degree, and three were without a degree. Nine participants took medication on a regular basis (seven the contraceptive pill, one insulin, and one levothyroxine).

Furthermore, criteria for exclusion were pregnancy, foreign metal objects in the skull area and cardiac pacemakers. The participants received an expense allowance of € 10 per hour. The ethics committee of the Medical Faculty Tuebingen approved this study.

2.2 *Preliminary investigations*

2.2.1 *Mini-international neuropsychiatric interview (M.I.N.I.)*

The mini-international neuropsychiatric interview (M.I.N.I) (Sheehan et al., 1998), translated and adapted to German, contains modules that evaluate various Axis I disorders of the American psychiatric association's diagnostic and statistical manual of mental disorders - fourth edition (DSM-IV) (American Psychiatric Association, 1994), including major depressive episode, dysthymia, mania episode, hypomania episode, panic disorder, agoraphobia, social phobia, obsessive-compulsive disorder, posttraumatic stress disorder, alcohol dependence or abuse, psychoactive substance dependence or abuse, anorexia, and bulimia. Besides, it includes modules for psychotic syndromes and risk of suicide. It can be used for systematic data collection, to establish or confirm diagnostic hypotheses in primary care, following specific criteria.

2.2.2 Edinburgh handedness inventory

A modified version of the Edinburgh handedness inventory was used to verify the participants' handedness (Oldfield, 1971). It requires the participants' information with which hand they preferentially carry out activities like writing, drawing or brushing their teeth. For each activity, they should make two crosses into the corresponding column R (right hand) or L (left hand), in case of indecision one cross in each column. The laterality quotient (LQ) is calculated using the following equation, whereby R or L characterizes the sum of the crosses in the respective column:

$LQ = (R-L) / (R+L) \times 100$ $\qquad$ $-100 \geq LQ \geq 100$

An LQ of -100 stands for an absolute left-hander. The more positive the values of the LQ get, the more dominant the right hand becomes for the listed everyday activities. Handedness is seen as an indirect indicator for anatomic and physiologic cerebral asymmetry, and there are indications that psychiatric disorders like schizophrenia show a lower manifestation of right-handedness (Taylor and Amir, 1995). The degree of handedness and cerebral lateralization for language areas like the Broca's region show an almost linear correlation in healthy subjects. The frequency of left-hemispheric language dominance increases with the degree of right-handedness: 96% in strong right-handers (LQ of 100), 85% in ambidextrous individuals (LQ of -50 – 50) and 73% in strong left-handers (LQ of -100) (Knecht, 2000).

2.2.3 Multiple-choice vocabulary intelligence test (MWT-B)

The multiple-choice vocabulary intelligence test (MWT-B) is a performance test to measure the general verbal intelligence level. It consists of 37 word-rows with five words each row. Thereof, one word is known from colloquial or scientific language, and the other four are new fictitious word constructions. The participant is instructed to mark the familiar word. The evaluation is undertaken by transforming the number of correct choices into an IQ score based on a norm table. The official verification of this norm table was performed on a representative random sample of 20- to 64-year-old people. The norm table is uniform for all adults, and there are no differences in gender or age (Lehrl et al., 1995).

2.2.4 Trail making test A and B (TMT A and B)

The trail making tests A and B (TMT A and B) is testing the participants' visuomotor speed. The TMT A consists of the numbers 1-25 which have to be connected in ascending order as fast as possible without lifting the pen off the page. During the TMT B 13 numbers and letters, each has to be connected in their alternating ascending numerical and alphabetical order (1-A-2-B-3-C...). The time is measured for both tests by the investigator who also asks for immediate correction in the event of an error. In this way the time required for the test increases whereby the errors are not listed separately. The evaluation of these tests is made by normative scores based on the performance of healthy populations. Increasing age and a lower educational level were associated with poorer performance on the tests (Tombaugh, 2004).

2.3 Test methods

2.3.1 Positive and negative affective schedule (PANAS)

The positive and negative affective schedule (PANAS) is a questionnaire to assess the current emotional state. It was designed by Watson et al. in 1988. This questionnaire is a valid and established instrument to measure the positive affectivity (PA) as well as the negative affectivity (NA). It allows capturing brief mood fluctuations. High PA is correlated with energy, concentration, and enthusiasm whereas low PA shows a correlation with sadness and lethargy.

On the other hand, high NA is associated with negative tension like fear, anger, and nervousness. Low NA is characterized by inner peace and balance (Watson et al., 1988). The German version of the PANAS was tested for reliability by Krohne et al. The independence of the two scales PA and NA could be verified (Krohne et al., 1996). The questionnaire consists of 20 adjectives which in each case describe either 10 positive or 10 negative emotions. The participants were instructed to assess their current mental state with a five-tier scale (not at all – a little – intermediate – considerable – extreme). Before and after each of the three sessions of the experiment the participants had to fill in the PANAS questionnaire to measure their affectivity at the relevant time. A modified version of the PANAS was used for this study with PA: interested, excited, strong, impressed, proud, alert, inspired, determined, active, attentive and NA: distressed, worried, guilty, frightened, hostile, irritable, shamefully, nervous, fearful, scared.

2.3.2 Transcranial direct current stimulation (tDCS)

The stimulation was conducted with the NeuroConn 'DC-Stimulator Plus' (Ilmenau, Germany). There were three stimulation conditions: anodal and cathodal as the verum stimulation and sham as the placebo stimulation. Half of the participants experienced anodal and sham stimulation, and the other half was stimulated with cathodal and sham tDCS. The cathodal or anodal electrode was placed over the left IFG (EEG 10/20 system: between C3, F3, and F7) and the reference electrode supraorbital on the right. The size of both electrodes was 3×5 cm, and they were covered with sponges saturated with a physiological salt solution to lower the physiological skin impedance. The subjects wore a 10/20-Cap over their head to locate the points of interest and to fixate the electrodes. The verum stimulation was a constant current of 2 mA for 20 minutes each. During the sham stimulation, the electrodes remained also fixed for 20 minutes, but the stimulation lasted for only 40 seconds (again with 2 mA), so the participants experienced the typical initial tingling. Due to the short duration of the active stimulation under the sham condition, no relevant effects on the cortical excitability are expected.

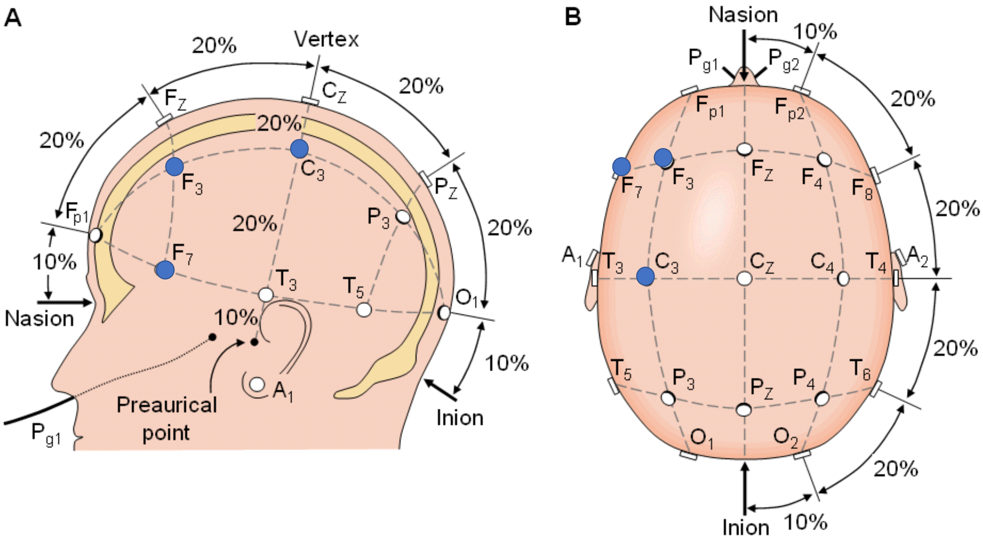

Figure 2: Electrode positioning between C3, F3 and F7 (marked with blue points) with the international EEG 10/20 system (Malmivuo and Plonsey, 1995)

2.3.3 The reading the mind in the eyes (RME) test

The original RME test consists of 36 black and white photographs depicting just the eye region of Caucasian individuals. A rectangular area of approximately 5 x 2 inches delineated the eye region, encompassing the entire width of the face from midway up the nose to right above the brow. Initially, the RME test was designed to measure the deficits of autistic adults on emotion recognition. All photographs were collected from magazines. Four mental state terms accompanied each stimulus (one target word and three foils) presented at each corner of the photograph (see Figure 3). Target words and foils were chosen by two of the original authors and pilot tested on groups of eight raters until each item met a criterion response of at least five raters choosing the target word. The resulting test was subjected to a nonclinical sample of 103 Cambridge University students, which yielded a 78% overall accuracy on the test (Baron-Cohen et al., 2001). The program used in this experiment was designed by Gregor Domes and Christoph Berger of the University of Rostock. The stimuli were the original pictures of the RME test designed by Baron-Cohen et al. They were presented in a random order. The program recorded mistakes and reaction time. At the beginning of each session, a sample stimulus was presented which was not included in the statistical analysis.

Figure 3: Sample image of the German version of the RME test (Baron-Cohen et al., 2001) designed by Gregor Domes and Christoph Berger of the University of Rostock.

2.3.4 Near-infrared spectroscopy (NIRS)

A flexible cap with two lateral probe-sets consisting of 44 measurement channels (22 on each frontotemporal hemisphere covering an area of 12 x 6 cm each) was fixated on the subjects' heads. Each of these sets included eight light emitters (semiconductor lasers) and seven photodetectors (avalanche photodiodes). The sets were arranged as 3×5 optode arrays for the left and right hemisphere. The most posterior channel of the lowest row (channel 1) was placed either over T7 for the left side or T8 for the right side, respectively, and oriented towards Fp1/Fp2 according to the international 10-20 system for EEG electrode placement (Jasper, 1958). A continuous wave system was used in this experiment (ETG-4000 Optical Topography System; Hitachi Medical Corporation, Tokyo, Japan). The 16 lasers (8 on each side) emitted near-infrared light in two different wavelengths (695 ± 20nm and 830 ± 20nm). The 14 detectors (7 on each side) measured the reflected light. Emitters and detectors were arrayed alternately with a constant inter-optode distance of 3 cm. Measurement was conducted with a resolution of 10 Hz. The measured light signal was converted into HbO_2 and HHb concentration changes using a modified Lambert-Beer law (Sassaroli and Fantini, 2004). The resulting values for HbO_2 and HHb do not reflect absolute concentrations due to a variety of factors such as varying penetration depth and scattering (Fallgatter *et al.*, 2004), but rather relative concentration changes for each measurement channel from a starting baseline.

2.4 Procedure

The participants had to complete three different sessions. The first session took place in the NIRS-Lab. During the NIRS measurement, they performed an own newly designed test which included the pictures from the RME test under three different conditions requiring them to either choose the right emotion (as in the actual RME test; task A) or the right gender (task B) or the right personal descriptive adjective (Task C) for a given face. All adjectives chosen for task C are listed in the German 'Duden' and were matched to the mental state terms used in the corresponding picture of the RME test based on their frequency in the German language with the help of the project 'dlexDB' from the Department of Psychology and Linguistics of the University of Potsdam (Heister et al., 2011). Each task comprised 36 pictures, which were split into 6 blocks. Every picture was shown for 10 sec. After each of the 18 blocks (1 min each) the participants had to fixate a black cross on a white screen for 30 sec until the next block was presented. The order of the blocks did not differ between the participants (task A- task B- task C- task A-…), but the task, to begin with, was counterbalanced. The test was designed with PsyScope X, a program to design and run psychological experiments. It has been developed at Carnegie Mellon by Jonathan Cohan, Matthew Flatt, Brian MacWhinney and Jefferson Provost in the '90s. Its code has been made public under the GNU GPL license. It is now being developed by the SISSA Language, Cognition and Development Lab at Sissa, the RICO group at the Universitat Pompeu Fabra and many other volunteers. Its development has been funded by the Regione Friuli-Venezia-Giulia (Bonatti, 2018). The presentation of this newly designed test was done on a Macintosh Laptop (15-inch MacBook Pro). The participants were sitting in a chair at a distance of around 70 cm in front of the Laptop. For each trial, they had to click the most suitable adjective with the mouse (task A: 4 possibilities, task B: 2 possibilities, task C: 4 possibilities). Before performing the task, a measurement of the participants' resting state was done with their eyes closed. To avoid motion artifacts, they were asked to move their head as little as possible. As external light sources can influence measurement results, the NIRS-Lab was darkened the complete time. Two small shielded lamps allowed the processing of the task.

After 21-28 days, they were invited to complete the second and third session. This period was chosen to keep training effects on the RME test at a minimum. In these sessions, tDCS was applied over the participants' left IFG while performing the RME test. In one session the participants received the verum stimulation (anodal or cathodal with a current of 2 mA each), in the other one the sham stimulation in a double-blind manner. The order of verum and sham stimulation was randomized and counterbalanced. After five minutes of stimulation at rest, the participants started the RME test on a Windows computer. The test was presented on a 22-inch widescreen TFT LCD-Monitor. The participants were sitting in a chair at a distance of around 70 cm in front of the monitor. They were instructed to work as quickly as possible but yet accurate. All of them were finished before the end of the 20 minutes stimulation. 16 participants received cathodal and sham stimulation, the other 16 anodal and sham stimulation. There was a gap of three to seven days between the two different stimulations to avoid after-effects of the verum stimulation on the second performance of the RME test. Monte-Silva et al. could show 60-120 minutes lasting after-effects in the form of induced changes of the cognitive excitability according to the duration of tDCS. The day after the stimulation no effects were detectable regardless of the duration of tDCS (Monte-Silva et al., 2013).

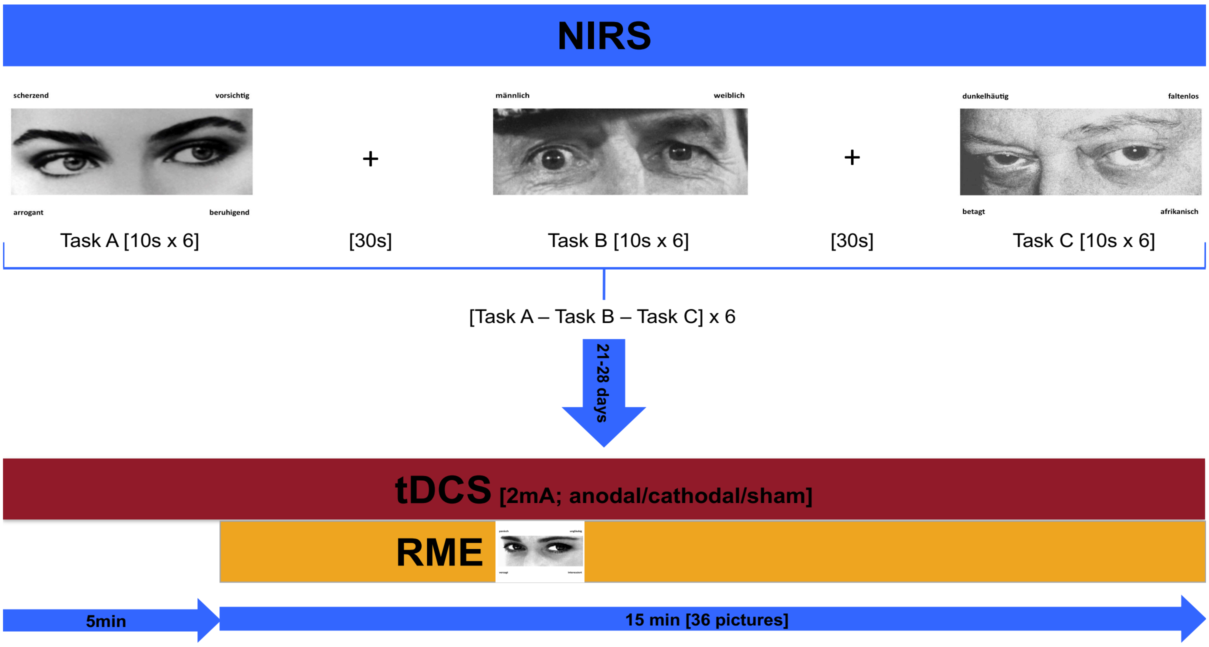

Figure 4: Experimental design of this study. First session: NIRS measurement during three different tasks (emotion recognition task A, gender recognition task B, personal descriptive adjective task C). Each task comprised 36 pictures, which were split into 6 blocks. Every picture was shown for 10 sec. After each of the 18 blocks (1 min each) the participants had to fixate a black cross on a white screen for 30 sec until the next block was presented. The order of the blocks did not differ between the participants (task A- task B- task C- task A-…), but the task, to begin with, was counterbalanced.
Second and third session after 21-28 days: tDCS (verum stimulation with 2mA (16 participants anodal and 16 cathodal) and sham stimulation with a gap of 3-7 days) over the left IFG during the RME test in a double-blind manner. The order of verum and sham stimulation was randomized and counterbalanced. After five minutes of stimulation at rest, the participants started the RME test including 36 pictures.

2.5 *Statistical Analysis*

For the calculation of the brain activation maps during the performance of the task in session one, changes in the concentration of HbO_2 and HHb were recorded from a starting baseline with the NIRS system. According to the task condition (Emotion recognition task, personal description task, gender recognition task) the data were individually averaged for the six repetitions of each task. Physiological signals unrelated to the task itself like spontaneous cerebral blood flow oscillations or whole body blood flow changes (Zhang et al., 2000) were corrected with a linear fitting function which was applied for baseline correction. Therefore, linear fitting was performed between the 10-sec baseline preceding all active task segments and a post-task baseline determined as the mean across the last 10 sec of the resting period in between active blocks. All task repetitions of the three conditions were averaged using this correction. The data obtained was further preprocessed by using customized Matlab scripts (The MathWorks, Inc., USA). More precisely, a low-pass filter was applied at 0.02 Hz followed by an interpolation of noisy channels based on the mean value of all adjacent channels. For statistical analysis, mean values between the 20-50 sec period of the individually averaged activation segments (of 60 sec total) were calculated for each condition, stimulation session, NIRS channel and participant (Ehlis et al., 2007, 2016).

Significant increases and decreases in HbO_2 and HHb concentration across the measurement array were tested using t-tests (against zero) for each condition. Due to the multiple testing situation, false discovery rate (FDR) corrections were applied (Benjamini and Hochberg, 1995; Singh and Dan, 2006), as known from the fMRI literature. As expected for task-related fNIRS data, concentration changes in HbO_2 and HHb showed a roughly anti-correlated signal course. Due to superior power and reproducibility, only HbO_2 data will be reported in the following results (Haeussinger et al., 2014).

Testing the effects of tDCS on the accuracy and the reaction time of the RME test, two mixed ANOVAs were calculated (for the dependent variables 'correctness' and 'reaction time') with the within-subjects factor 'stimulation setting' (verum/sham) and the between-subjects factor 'stimulation modus' (anodal/cathodal). Post-hoc tests were conducted using t-tests.

In order to test the correlation between the activation of the brain area relevant for the emotion recognition task and the task performance during the first NIRS session and the following two (tDCS) sessions, a region of interest (ROI) was defined, which consisted of channels 12, 13, 16 and 17 on the left side of the measurement array. These channels were located between C3, F3, and F7 (EEG 10/20 system), the same area we stimulated with tDCS in the second and third session. This area is located over the left IFG (Okamoto et al., 2004). The correlations between the NIRS activation patterns and the different task performances were calculated using Pearson`s R. One participant was excluded from further analysis due to extreme values. Furthermore, Pearson`s R was used again to calculate the correlation between the ROI-Activity during the NIRS session and the effect of cathodal and anodal tDCS on the performance of the RME test.

Additionally, the effects of tDCS on the participants' affectivity were determined using the PANAS. Therefore, ANOVAs with repeated measures were calculated for each of the two mood dimensions PA and NA depending on the ‘stimulation setting’ (verum/sham) and the ‘stimulation modus’ (anodal/cathodal).

The statistical analysis was performed using IBM SPSS Statistics version 25 for Macintosh.

3 Results

3.1 *Preliminary investigations*

3.1.1 *Edinburgh handedness inventory*

All participants showed a positive laterality quotient (LQ) which stands for lateralization in favor of the right hand (mean 79,69; SD 15,27; range 40-100).

3.1.2 *Multiple-choice vocabulary intelligence test (MWT-B)*

The participants obtained a mean of the MWT-B of 27,47. This value corresponds to the upper third of an as an average considered IQ (Lehrl, 2005). Overall, participants showed values in accordance with an average or high IQ in the range of 91-127 (mean 27,47; SD 3,71; range 21-33).

Table 1: MWT-B norms and level of intelligence (Lehrl, 2005)

Overall score	*Level of intelligence*	*IQ*
0 - 5	Very low intelligence	≤ 72
6 - 20	Low intelligence	73 - 90
21 - 30	Average intelligence	91 - 109
31 - 33	High intelligence	110 - 127
34 - 37	Very high intelligence	≥ 128

3.1.3 *Trail making test A and B (TMT A and B)*

The required time for the TMT A and B was in accordance with the collected data for normative scores based on the performance of healthy populations (TMT A: mean

20,51; SD 6,09; range 12,0-34,1; TMT B: mean 45,69; SD 14,07; range 20,7-78,8) (Tombaugh, 2004).

Table 2: Normative scores of TMT A and B based on the performance of healthy populations, subdivided according to age groups (Tombaugh, 2004).

Age groups	*TMT A*	*TMT B*
18 - 24	M 22,93; SD 6,87; range 12-57	M 48,97; SD 12,69; range 29-95
25 - 34	M 24,40; SD 8,71; range 10-45	M 50,68; SD 12,36; range 29-78
35 - 44	M 28,54; SD 10,09; range 12-50	M 58,46; SD 16,41; range 29-95
45 - 54	M 31,78; SD 9,93; range 18-56	M 63,76; SD 14,42; range 32-92

3.2 Effects of tDCS on positive affectivity (PA) and negative affectivity (NA)

A repeated measures ANOVA indicated an effect of anodal stimulation on PA *(F [3, 45] = 3.103; p = .036)*. But Bonferroni-adjusted post-hoc analysis revealed no significant difference of the different pairwise comparisons between PA before and after anodal compared to sham stimulation.

For cathodal stimulation there was no statistically significant difference between the different values for PA *(F [3, 45] = 1.673; p = .186)*.

Furthermore, there was no statistically significant effect of tDCS on NA. Neither for anodal stimulation *(F [3, 45] = 2.770; p = .052)* nor for cathodal stimulation *(F [3, 45] = 2.399; p = .080)*.

Table 3: Descriptive statistics for PA and NA before and after anodal and cathodal stimulation.
Note: pre verum = before verum stimulation, post verum = after verum stimulation, pre sham = before sham stimulation, post sham = after sham stimulation.

	Anodal/Sham Stimulation	*Cathodal/Sham Stimulation*
PA pre verum	Mean 2.98, SD .55	Mean 2.77, SD .73
PA post verum	Mean 3.11, SD .66	Mean 2.78, SD .79
PA pre sham	Mean 2.96, SD .63	Mean 2.99, SD .60
PA post sham	Mean 3.15, SD .65	Mean 2.80, SD .64
NA pre verum	Mean 1.16, SD .30	Mean 1.28, SD .31
NA post verum	Mean 1.03, SD .06	Mean 1.18, SD .30
NA pre sham	Mean 1.19, SD .36	Mean 1.23, SD .32
NA post sham	Mean 1.06, SD .14	Mean 1.13, SD .18

3.3 Performance of the RME test during tDCS stimulation

For the reaction times, the ANOVA showed a significant interaction between the stimulation setting (sham vs. verum) and the stimulation modus (anodal vs. cathodal) *(F [1, 30] = 7.78, p = .009)*. We found no significant main effects (stimulation setting: *F [1, 30] = 1.24, p = .274;* stimulation modus: *F [1, 30] = .59, p = .449)*.
The ANOVA calculated for the correctness of responses did not show significant main effects (stimulation setting: *F [1, 30] = .06, p = .803;* stimulation modus: *F [1, 30] = 1.14, p = .293)* or a significant interaction *(F [1, 30] = 2.03, p = .165)*.

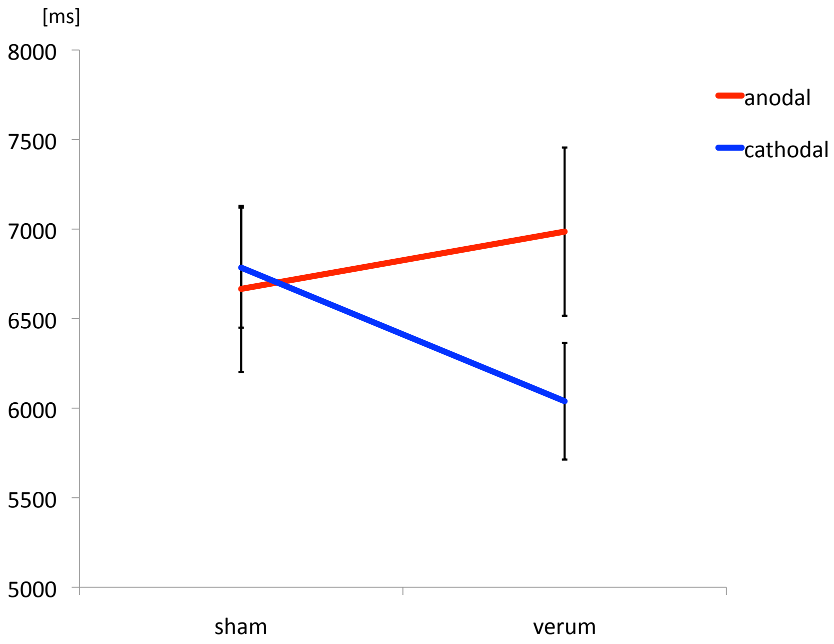

Figure 5: Significant interaction between the stimulation setting (sham vs. verum) and the stimulation modus (anodal vs. cathodal) for the reaction time in ms during the RME test.

The post-hoc t-tests showed, that the participants were significantly faster under cathodal stimulation than under sham stimulation *(t(15) = -3.92, p = .001)*. For the anodal stimulation, we found no significant difference on recognition speed *(t(15) = .97, p = .350)*.

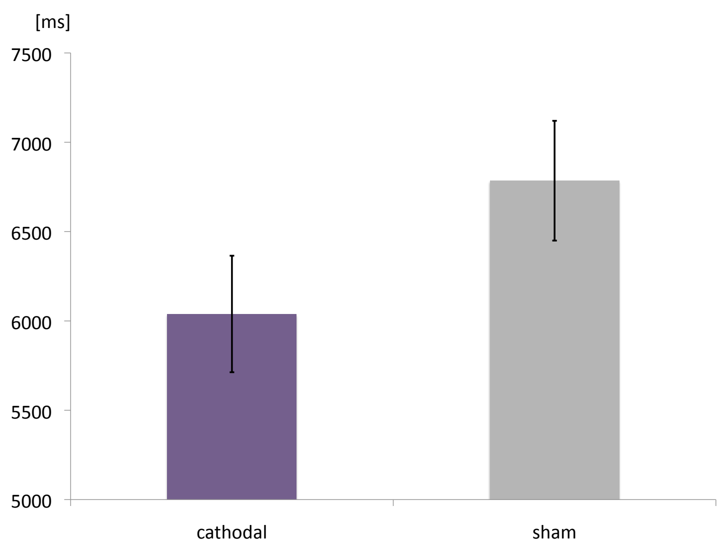

Figure 6: Post-hoc t-test with a significant difference between the effects of cathodal and sham stimulation on the recognition time in ms during the RME test.

3.4 NIRS activation patterns

For all three task conditions, significant changes in HbO_2 of the left hemisphere were detected, particularly within the superior-frontal part of the measurement array. Large – and overlapping – clusters of deactivation (as indicated by a decrease in HbO_2 concentration [and concomitant increase in HHb concentration]) were observed for all three task conditions following an FDR correction (significant channels for task A: 4, 8–10 and 12–22; task B: 4, 8–18, 21 and 22; task C: 5, 8–10, 12–14, 16–22; see Figure 7). Directly contrasting the three conditions at an uncorrected significance level revealed even stronger deactivation for the actual RME task (A) as compared to both the gender (B; channels 14, 19 and 21) and the adjective control task (C; channels 4, 8, 14, 15). No significant differences were found between the two control tasks.

When looking specifically at the chosen Region of Interest (ROI) consisting of channels 12, 13, 16 and 17 (comprising the stimulated area in the following sessions), all of these channels showed a statistically significant deactivation during all three tasks when compared with the baseline activation. However, no significant differences were found comparing the three task conditions among each other.

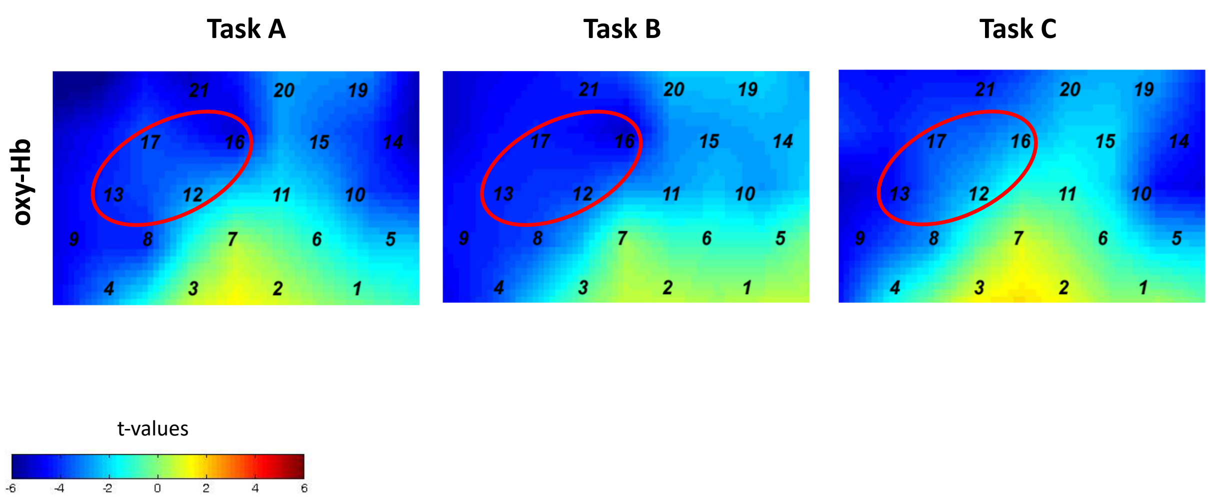

Figure 7: T-values of NIRS activation (left hemisphere) during task A (emotion recognition task), task B (gender control task) and task C (adjective control task) compared to baseline activation. The ROI is marked with a red circle.

3.5 *Correlation between brain activity over the left IFG and task performance during NIRS*

There was a significant correlation between the NIRS activity within the ROI during the emotion recognition task (task A) and the reaction time in task A during the first (NIRS) session *($r(29) = .36$, $p = .047$)*.

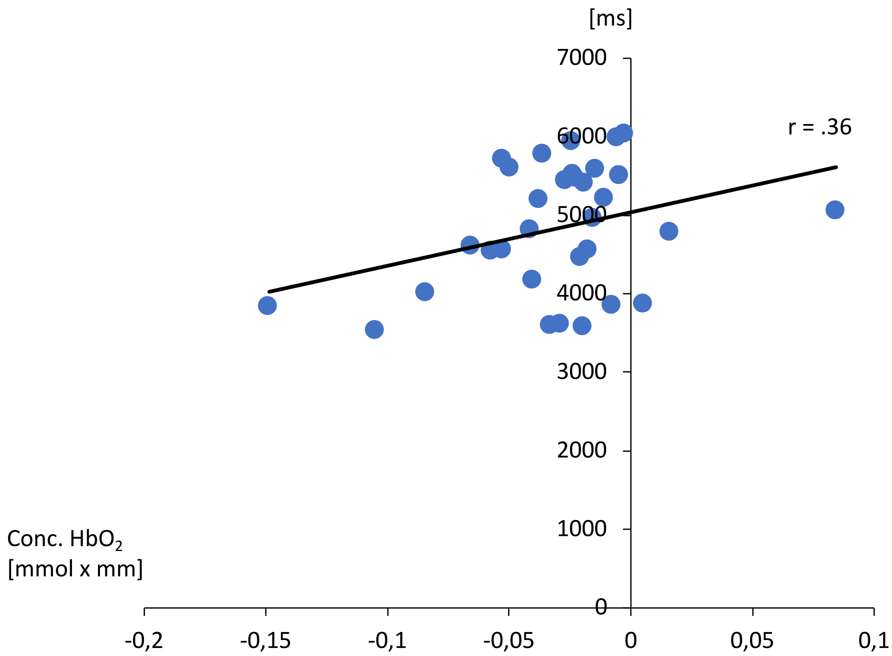

Figure 8: Significant correlation between ROI activity in concentration of HbO_2 (mmol x mm) during task A and reaction time in ms in task A. The more activity the participants showed in the left IFG during task A, the slower they made their decision for the most suitable emotion in task A.

Furthermore, a significant correlation between the NIRS activity during the personal description task (task C) and the reaction time in task C was found *($r(29) = .38$, $p = .035$)*.

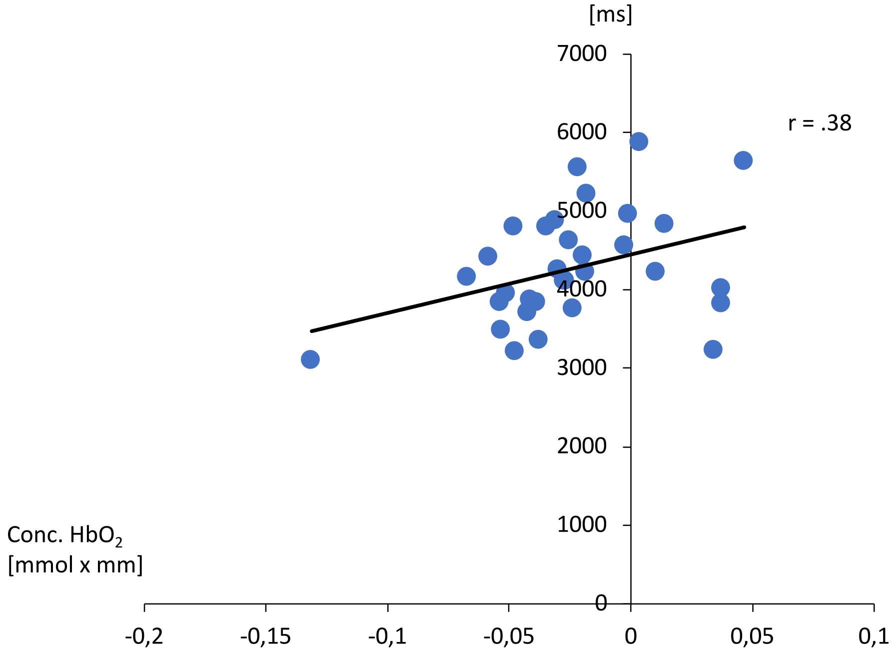

Figure 9: Significant correlation between ROI activity in concentration of HbO_2 (mmol x mm) during task C and reaction time in ms in task C. The more activity the participants showed in the left IFG during task C, the slower they made their decision for the most suitable personal description in task C.

A more detailed analysis for a correlation between an emotion-specific activity in the left IFG and the performance during task A revealed a statistically significant correlation between the activity difference during task A and the gender recognition task (task B) and the reaction time in task A *(r(29) = .41, p = .023)*. In contrast, we did not find a significant result when we correlated the difference between the activity during task A and the personal description task (task C) with the reaction time in task A *(r(29) = .03, p = .879)*.

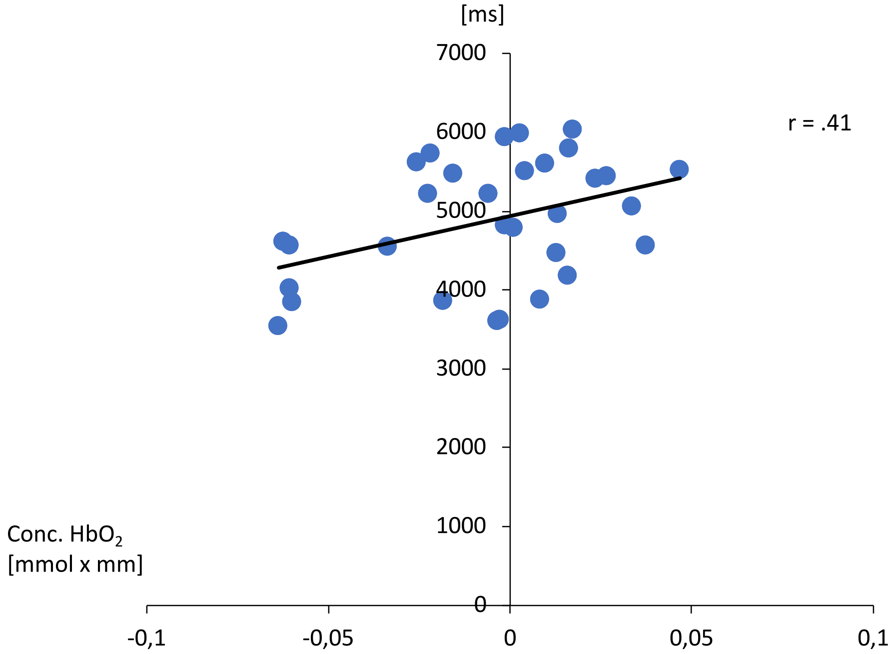

Figure 10: Significant correlation between ROI activity difference in concentration of HbO_2 (mmol x mm) of task A and task B (task A – task B) and reaction time in ms in task A. The more emotion-specific activity the participants showed in the left IFG, the slower they made their decision for the most suitable emotion in task A.

In summary, all significant correlations indicate a link between the task prolonged response time and higher IFG activity.

However, there was no significant correlation between the emotion-specific activity level (activity of task A - task C) and the RME performance.

The correlation between the activity level and the performance during the gender recognition task showed no significant results as well (for accuracy: $r(14) = .13$, $p = .485$; for reaction time: $r(14) = .12$, $p = .526$).

Moreover, no significant correlations were found for the correctness of responses (see table 4).

Table 4: Correlations between the ROI activity during NIRS (A: during task A, C: during task C, A-C: difference between task A and C, A-B: difference between task A and B) and the performance (Correctness/Reaction Time (RT)) of task A and C. Significant results are marked in bold.

	Correctness A	*RT A*	*Correctness C*	*RT C*
Activity A	*r = .064, p = .731*	***r = .360, p = .047***		
Activity C			*r = -.078, p = .677*	***r = .380, p = .035***
Activity A-C	*r = .227, p = .219*	*r = .028, p = .879*		
Activity A-B	*r = .024, p = .897*	***r = .406, p = .023***		

3.6 Linking tDCS-induced emotion recognition improvement and individual emotion specific brain activity

Correlating the difference of NIRS activity in the ROI between emotion recognition and the ‘adjective’ control condition (task A – task C) and the change of RME performance induced by cathodal tDCS (verum – sham) resulted in a significant negative correlation regarding the number of errors *(r(14) = -.51, p = .043)* and a non-significant correlation with respect to the reaction time *(r(14) = .21, p = .444)*.

Stronger emotion-specific NIRS IFG activation was associated with a more pronounced reduction of errors in the RME test under cathodal stimulation.

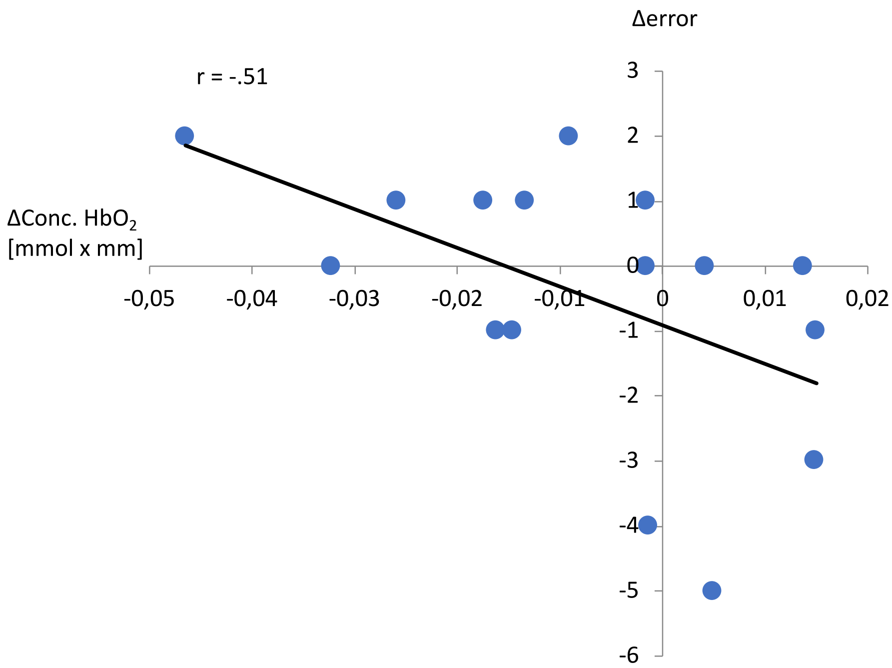

Figure 11: Significant negative correlation between ROI activity difference in concentration of HbO_2 (mmol x mm) of task A and task C (task A – task C) and the difference in errors made during cathodal tDCS and sham stimulation (cathodal – sham). The more emotion-specific activity the participants showed in the left IFG, the more they benefitted from cathodal tDCS regarding the correctness of responses.

The correlation between the ROI activity difference of task A and B and the performance on the RME test during cathodal tDCS showed no significant effect (see table 5).

There were no significant correlations between NIRS activity and anodal tDCS effects (Activity A-C with Δ Error anodal-sham: $r(14) = -.28$, $p = .298$; Activity A-C with Δ RT anodal-sham: $r(14) = .05$, $p = .850$; Activity A-B with Δ Error anodal-sham: $r(14) = -.11$, $p = .693$; Activity A-B with Δ RT anodal-sham: $r(14) = .17$, $p = .533$).

Table 5: Correlation between ROI activity during NIRS (A-C: difference between task A and C, A-B: difference between task A and B) and the effect of cathodal and anodal tDCS regarding the difference of performed errors compared to sham stimulation (Δ Error cath-sham) and the difference in the needed reaction time compared to sham stimulation (Δ RT cath-sham). Significant results are marked in bold.

	Activity A-C	*Activity A-B*
Δ Error cath-sham	***r = -.512, p = .043***	*r = .020, p = .942*
Δ RT cath-sham	*r = .206, p = .444*	*r = -.019, p = .945*

4 Discussion

This present study investigates the effects of tDCS on emotion recognition depending on the participants' brain activation level. It was hypothesized that the knowledge of the interindividual different brain activity is a prerequisite to interpret the effects of anodal and cathodal tDCS. To verify this hypothesis, the participants' preactivation over the left IFG was measured with NIRS before testing the effects of tDCS on emotion recognition. It was found that higher IFG activity was linked with longer response latencies in the RME test. Cathodal, inhibitory tDCS of 2mA clearly accelerated emotion recognition in the RME test. Moreover, the change in response correctness induced by cathodal tDCS was positively correlated with the emotion-specific IFG activity measured with NIRS during RME performance.

4.1 Facilitation of emotion recognition by cathodal tDCS depending on interindividual preactivation over the left IFG and on stimulation intensity

The participants were significantly faster during the RME test under cathodal tDCS with 2mA than under sham stimulation. Additionally, stronger emotion-specific NIRS IFG activation was associated with a more pronounced reduction of errors in the RME test under cathodal stimulation.

As already stated, tDCS not only has an impact on the neurons responding to the task goal but also on the neurons that are not associated with the final task-goal defined as neural noise (Miniussi et al., 2013). Planning ability can be improved using cathodal tDCS as a neural noise reducer. Deactivating non-invasive brain stimulation may be beneficial when paired with the inherent activation of brain regions of a new task or new condition (Dockery et al., 2009). This characteristic of cathodal tDCS acting as a neural noise filter is a frequently demonstrated evidence-based method. Cathodal tDCS applied to the left visual middle temporal area led to an improvement of visuomotor coordination when a large amount of visual noise was present in the visual stimulus (Antal et al., 2004).

Furthermore, contrary effects of tDCS with anodal stimulation leading to deterioration and cathodal stimulation causing an improvement of cognitive functions could be shown. When paired with a working memory task anodal tDCS increased the error rate whereas cathodal tDCS led to a reduction of produced errors. Combined with novel unfamiliar tasks anodal stimulation has the potential disadvantage by enhancing the already existing interfering neural noise whereas cathodal tDCS reduces this disruptive factor (Zwissler et al., 2014).

The IFG too can be affected according to a more efficient performance during cognitive tasks following the hyperpolarization generated by cathodal stimulation. Cathodal stimulation of the right IFG led to a better prosody comprehension when presented with auditory targets with different emotional valence (Alexander et al., 2012). Even the motor system seems to show facilitating or hindering tDCS effects during task execution depending on the activity pattern at the time of stimulation. Anodal tDCS can either reduce motor learning in tasks inducing a strong neuronal activation in the target area or enhance it when the task itself shows a lower neuronal activation (Bortoletto et al., 2015).

The significant correlation between the NIRS activity level and cathodal stimulation effects can, therefore, be explained by cathodal tDCS acting as a neural noise filter. The more activation the participants showed in the left IFG, the more they benefitted from deactivating cathodal tDCS. Considering the RME test as an unfamiliar novel task, it can be deduced that the resulting presence of interfering neural background noise allows cathodal tDCS to induce facilitation of emotion recognition by reducing this general noise and helping the target signal emerge.

Furthermore, cathodal tDCS with 2 mA showed a significant improvement of the reaction time of emotion recognition regardless of the interindividual IFG activation. Previous experiments with 1 mA tDCS showed no such effects (Klimm et al., 2013). It must therefore be assumed that the intensity of tDCS is also essential for the impact on emotion recognition.

Hoy et al. showed a dose dependence of tDCS on schizophrenic patients when applying it over the left DLPFC. Only 2 mA anodal tDCS led to a significant effect on cognitive performance on a working memory task (Hoy et al., 2014). In another experiment, they specifically looked at the effects of tDCS on gamma activity and its relationship to working memory performance. They found a significant increase in gamma event-related synchronization following 2 mA anodal stimulation of the left DLPFC along with a significantly improved working memory performance. There were no changes in either gamma or working memory performance following 1 mA stimulation (Hoy et al., 2015). Iyer et al. investigated the effect of tDCS on the

performance during a verbal fluency task. 2 mA anodal and cathodal tDCS applied over the left prefrontal cortex showed effects on the performance of verbal fluency while there were no such effects with 1 mA stimulation (Iyer et al., 2005). Boggio et al. let patients with Parkinson's disease perform a three-back working memory task during anodal tDCS over the left DLPFC. The results showed a significant improvement in working memory after 2 mA active anodal stimulation. 1 mA anodal stimulation, on the other hand, did not show significant effects on the performance in working memory (Boggio et al., 2006). Schwippel et al. investigated the effect of anodal tDCS of different intensities on working memory when applied over the right DLPFC of schizophrenic patients. In contrast to 1 mA stimulation, 2 mA anodal tDCS led to a significant improvement in the working memory task (Schwippel et al., 2018).
The dose dependence of tDCS can also be expected for the facilitating effects of cathodal stimulation on emotion recognition and explains the results of significantly faster emotion recognition during cathodal tDCS with 2 mA compared to no significant effects of 1 mA cathodal tDCS in previous experiments.
In the search for more differentiated explains for the influence of cathodal stimulation on cognitive processes, previous studies showed that the beneficial effects of cathodal tDCS of the left prefrontal cortex seems to be based on the influence on implicit neuronal processes like cognitive conflicts or distraction, whereas explicit distractions appear to remain unaffected (Schroeder et al., 2016). It can thus be assumed that during the attempt to interpret the emotion from external stimuli competing implicit neuronal processes like self-related thinking functions as a distractive factor which can be modified by cathodal stimulation leading to more focusing brain activation. These considerations are supported by the following discussions regarding the conducted brain imaging investigations with NIRS.

4.2 More focusing brain activation leads to better performance

All resulting significant correlations between the NIRS activity and the different task conditions showed an activity-dependent deterioration of the task performance particularly of the reaction time. The more activity the participants showed in the left IFG, the slower they decided for the, in their opinion, right choice.
Based on the neural noise theory a more efficient cerebral performance can be

explained by a lower energy input for the same or even a higher output, as training effects, for example, can also be defined. With increasing familiarity with newly learned tasks, the initial interfering neural noise can be gradually reduced allowing to reach the same performance with lower more focused brain activity. Missing strategies to reduce this noise or a predisposition for enhanced neural noise is accompanied by more inefficient task performance.

Herrmann et al. investigated the effect of D4 dopamine receptor polymorphism (DRD4) on prefrontal brain activation, by measuring brain tissue oxygenation with NIRS during the performance of two versions of a classical working memory task (n-back). Subjects with the 7-repeat allele of DRD4 showed signs of unspecific brain activation over the dorsolateral prefrontal cortex during a working memory task. Although this prefrontal noise did not impair behavioral performance in their sample, the results indicate that subjects with the 7-repeat allele of DRD4 showed a deficit in focusing their brain activation. In the opinion of Herrmann et al., this ineffective brain activation might lead to impaired performance in more difficult tasks (Herrmann et al., 2007). Increased variability of stimulus-induced prefrontal noise has been associated with genetic risk for schizophrenia. The level of prefrontal noise is in part regulated by the synaptic concentration of dopamine, which itself might be abnormal in schizophrenia (Winterer et al., 2006). Schizophrenia is associated with impaired emotion recognition, as already discussed (Chan et al., 2010).

These findings are in line with the results that the more activity the participants showed in the left IFG during the emotion recognition task in the NIRS session, the slower they made their decision for the most suitable emotion in task A. The theory of prefrontal neural noise acting as a negative factor considering the performance of emotion recognition is reinforced by the significant correlation between the activity difference during task A and the gender recognition task (task B) and the reaction time in task A. The more emotion-specific activity the participants showed in the left IFG, the worse they performed during the emotion recognition task.

Furthermore, a significant correlation between the NIRS activity during the personal description task (task C) and the reaction time in task C could be found. The more activity the participants showed in the left IFG during task C, the slower they made their decision for the most suitable personal description adjective. The left IFG has a critical role in semantic language processing too (Roskies et al., 2001).

The comparison of the significant correlation between the NIRS activity over the left IFG during task A or C and the reaction time in task A or C with the none significant correlation during the gender recognition task (task B) regarding the activity-dependent deterioration of the task performance supports the theory of ineffective brain activation leading to impaired performance in more difficult tasks. Task B with only two possibilities of choices between male and female is considered as the more familiar and thus the easier task.

Summarizing, as already indicated by the results of cathodal tDCS facilitating emotion recognition, an increasing focus of brain activity in the left IFG, which is represented by a deactivation during NIRS due to limited spatial resolution, and a corresponding suppression of neural noise leads to an improvement of more complex cognitive processes like reading the mind in other persons' eyes.

The idea of a required reduction of interfering cognitive processes to concentrate on external stimuli is further substantiated by the observed results of the task-related deactivation during NIRS.

4.3 Deactivation seen as a reduction of self-referential correlated brain activity

For all three task conditions, significant decreases in HbO_2 were detected during the NIRS session compared to the baseline condition, particularly also within the left frontal part of the measurement array including the ROI resulting in large and overlapping clusters of deactivation.

Critiques and discussions arose concerning the use of resting conditions as a low-level baseline to predict task-related brain activity. Certain cortical regions show a high level of activation during resting conditions (Morcom and Fletcher, 2007). This so-called default mode hypothesis is based on the finding of relative decreases in neuronal activity during task performance compared with a baseline state. Several studies have found that lower default mode network (DMN) activity is associated with more successful performance across a number of stimulus-driven goal-directed cognitive tasks (Daselaar et al., 2004; Anticevic et al., 2010). One hypothesis (Binder, 2012) suggests that such suppression during externally focused cognition might be necessary for adaptive disengagement from certain distracting cognitive operations such as mind-wandering (Antrobus et al., 1970), possibly imposing a filter (Anticevic et al., 2012). In addition, brain activity during resting conditions may be associated with self-referential processing (Gusnard et al., 2001).

Schulte-Rüther et al. investigated the link between dysfunctional brain networks and the disturbed empathic behavior of autistic patients. During functional MRI, autistic patients and healthy control subjects should identify the emotional state of a facial stimulus (other-task) or evaluate their emotional response (self-task). Both subject groups showed an equal performance during the other-task, but autistic patients presented less emotionally congruent responses in the self-task. Furthermore, significantly less activation inter alia in medial parts of the frontal cortex, which are associated with self-referential cognitive and emotional processes (Vogeley et al., 2001), was detected for autistic patients compared to healthy controls. However, these brain regions showed activation during both self- and other-conditions, implicating a link between the judgment of the emotional state of others and oneself based on a functional brain network. This theory was corroborated by the significant correlation between the performances of the self- and other-task in healthy controls. Autistic patients showed no such correlation (Schulte-Rüther et al., 2011).

Other brain regions, in particular, the left IFG showed an essential role during self-reflection tasks as well (Morin and Michaud, 2007), supporting the idea of participation of inner speech in self-related thinking (Morin and Hamper, 2012).

Considering these findings, the deactivation of left frontal brain regions compared to baseline activation may result from self-referential cognitive or emotional processes during the resting state used for the baseline condition. During these processes, healthy subjects might activate these brain regions, which then show less activation during the investigated task when compared with this baseline condition.

The ability to reduce the self-referential correlated brain activity towards a more efficient and focused level to deal with external tasks like identify other's emotional state, particularly demonstrated also by the activity-dependent impact on task performance during the NIRS session, could be seen as evidence for more efficient brain network abilities associated with higher empathic capacities. This hypothesis is confirmed by the even stronger deactivation for the actual RME task (A) as compared to both the gender (B; channels 14, 19 and 21) and the adjective control task (C; channels 4, 8, 14, 15). It seems to need a higher suppression of self-referential correlated brain activity to concentrate on emotional recognition than to deal with non-emotional external tasks. Even if there was no significant activity difference within the ROI during the different tasks, it could be supposed that a functioning network including the left IFG is necessary to change between the perspective of oneself and others. To put oneself in another person’s mind it appears to be a need for the suppression of introspection. The better this process works, the easier it is to interpret the counterpart’s emotion, as also indicated by the consistent behavioral data during the NIRS session.

Introspection seen as a distractor for emotion recognition can be considered in conformity with the neural noise hypothesis. It could be shown that more background noise is interfering with task performance (Dockery et al., 2009; Zwissler et al., 2014). Especially novel tasks produce more background noise (Dockery et al., 2009). The even stronger deactivation for the experimental task (task A) as compared to both control tasks (task B and C) also indicates increasing interfering background noise during novel more challenging tasks. Task A as the more unfamiliar and more difficult task compared to task B and C would need more focus and concentration on the task conditions and therefore better strategies to reduce interfering neural noise.

To concentrate on the relevant tasks, appropriate strategies to reduce the interfering neural noise are necessary to separate the relevant neuronal signals from the irrelevant ones. Consequently, more brain activity is not always an indicator for more efficiency and sometimes it even can be an interfering factor, especially during processing of novel tasks.

All in all, the large clusters of deactivation of the frontal brain regions observed for all three task conditions compared to the baseline state during NIRS can be explained by a more specific focus on the new task condition by reducing interfering neural noise activity in order to prevent distracting cognitive operations, which may correspond to self-referential processes.

4.4 Missing influence of tDCS on the participants’ mood

There were no significant effects of anodal or cathodal tDCS compared to sham stimulation on the participants’ emotional state regarding PA or NA. These results are consistent with previous studies investigating the mood modulation of tDCS using the PANAS by stimulating frontal brain regions of healthy participants. There too tDCS

showed no significant mood changes (Keeser et al., 2011; Peña-Gómez et al., 2011; Plazier et al., 2012).
Alternatively, it can be assumed that tDCS affects mood only under challenging conditions. Plewnia et al. showed a mood modulation of anodal stimulation regarding a smaller increase of negative mood after verum compared to sham stimulation. Additionally, a higher negative mood was correlated with less processing speed improvements in an adaptively challenging attention task during anodal stimulation (Plewnia et al., 2015).
In patients with depressive disorder, an influence of tDCS on the patients' mood could be proven. Brunoni et al. investigated the effect of tDCS applied over the DLPFC during a cognitive control therapy in patients with depressive disorder. Both, cognitive control therapy alone and combined with tDCS reduced depressive symptoms after the treatment. Older patients and those with a better cognitive task performance showed a greater improvement in depressive symptoms after the combined treatment with tDCS and cognitive control therapy (Brunoni et al., 2014).

4.5 Limitations and prospects

The investigated study collective shows a high level of education overall. All of the participants obtained the general higher education entrance qualification (Abitur). Furthermore, they achieved a mean of 27,47 in the MWT-B which is corresponding to the upper third of an as an average considered IQ (Lehrl, 2005). By this above average group data, a transfer of the study results to the general population can only be made to a certain extent.
The used task to measure emotion recognition (RME test) only consists of static stimuli which are not embedded in a social context. In contrast, everyday situations of emotion recognition include a dynamic setting with continually changing social conditions. As a consequence, the evaluation of emotion recognition using the RME test is only partially applicable to everyday situations.
With increasing age, the density of the human brain tissue rises. Using NIRS, this means that the mean path length of the emitted photon growing to the same extent, whereby the probability of absorption and dispersion of these emitted photons increases. Therefore the depth of penetration of NIRS decreases to about 2 cm in

adults' brains (Huppert et al., 2009). Consequently, only a part of the frontal brain regions can be mapped which limits an assertion concerning the functionality of the neuronal network in total.

The stimulation electrode which was used during the tDCS stimulation had a fixed size of 35 cm^2. Therefore, the spatial specificity is limited, and the stimulated area is relatively large which may result in a stimulation of different neuronal systems. This could lead to different neuronal effects which potentially influence each other.

As used in many study designs before, the reference electrode was placed supraorbital on the contralateral side (in this study on the right). Consequentially, the underlying brain tissue was stimulated with anodal direct current in the cathodal tDCS session or cathodal direct current in the anodal session. As a result, an involvement of these additionally stimulated brain regions cannot be excluded entirely for observed tDCS effects.

There is a great heterogeneity between the modulation effects of anodal or cathodal tDCS in cognitive studies (Jacobson et al., 2012). TDCS over the prefrontal cortex can modify a wide range of behaviors from various domains. It is difficult to confidently point to a general pattern describing the effects of prefrontal tDCS. Added to this, is the fact that the physiological effects of tDCS themselves are highly variable and dependent upon a variety of individual characteristics (Tremblay et al., 2014). For example, regarding the polarity and intensity of the variable outcomes of tDCS, a study of Batsikadze et al. demonstrated that cathodal tDCS with 2 mA applied to the motor cortex significantly increased Motor Evoked Potentials (MEP) amplitudes, while 1 mA of cathodal tDCS decreased cortico-spinal excitability. They suggested that low-intensity cathodal tDCS induces low postsynaptic calcium enhancement and leads to long-term depression, while higher intensity cathodal tDCS induces a large calcium increase, resulting in long-term potentiation (Batsikadze et al., 2013). However, the effects of tDCS on the motor system cannot be directly transferred to effects on higher cognitive functions as already mentioned.

Nevertheless, the limitations listed here may explain the different effects of tDCS on the performance in emotion recognition and their correlations. While cathodal stimulation of the left IFG during the tDCS session led to a better performance only according to a better reaction time, the main finding of this study (stronger emotion-specific NIRS IFG activation was associated with a more pronounced reduction of performance in the RME test under cathodal stimulation) was based on the reduction

of errors as another aspect of task performance. Furthermore, the correlation between NIRS activity and the different task conditions during the NIRS session was based on the reaction time again.
The different variety of modulating effects depending on interindividual characteristics could also provoke the differing correlations between different calculated emotion-specific NIRS activation (task A-B in the NIRS session or task A-C in the correlation of NIRS activation and cathodal tDCS effects) or the missing effects of anodal tDCS.
Nonetheless, this study could show a causal relationship between interindividual brain activation and tDCS effects on cognitive functions like emotion recognition. It is one of the first studies to allow a prediction of tDCS effects from brain imaging data and thus contributes to a better understanding of the effects of non-invasive brain stimulation methods like tDCS on higher cognitive functions.
Further research is necessary to examine the relationship between tDCS and emotion recognition in more detail. For a more precise statement regarding the influences of brain activation on tDCS effects, brain imaging, for example, could be conducted with fMRI. As using a more dynamic or interactive test to measure emotion recognition a better link to everyday situations could be done. High-definition tDCS could be applied to allow more precise targeting of cortical structures. Furthermore, clinical studies of patients with impaired emotion recognition like schizophrenic or autistic patients are necessary especially because the effort of non-invasive brain stimulation should be and already is the improvement of impaired cognitive functions.

4.6 Conclusion

This study shows the activity-dependent effects of tDCS on emotion recognition. As hypothesized, a significant correlation between the emotion-specific activity (activity difference between task A and task C under NIRS) and the improvement of emotion recognition under cathodal tDCS compared to sham stimulation was found. The participants' preactivation of the left IFG is of central significance for the interpretation of the tDCS effects on emotion recognition. The interindividual differences in this preactivation could explain the missing effects of tDCS on emotion recognition in previous studies. According to what is known, this is first evidence for a beneficial, state-dependent effect of excitability-decreasing cathodal tDCS on emotion recognition. The correlation with individual imaging data supports the concept of a focusing effect of cathodal tDCS reducing neural noise and facilitating signal detection.

5 Abstract

Facial emotion recognition is a prerequisite of successful social cognition and interaction (Haxby et al., 2002). The left inferior frontal gyrus (IFG) is critically involved in the neuronal network subserving emotion recognition (Dal Monte et al., 2014). Transcranial direct current stimulation (tDCS) can be used to modulate cortical excitability and associated behavioral functions in a polarity-specific and activity-dependent manner (Dayan et al., 2013; Wolkenstein and Plewnia, 2013; Wolkenstein et al., 2014; Zwissler et al., 2014). In a sham-controlled crossover design, excitability enhancing anodal and excitability decreasing cathodal tDCS of 2mA were applied to the left IFG in 32 healthy subjects performing the 'Reading the Mind in the Eyes' (RME) test. The RME is widely used to measure emotion recognition in healthy subjects and psychiatric disorders (Baron-Cohen et al., 2001). Prior to the two (verum/sham) stimulation sessions, near-infrared spectroscopy (NIRS) was applied to measure brain activity in the IFG during RME performance (Ehlis et al., 2014). NIRS indicated a deactivation in the IFG during emotion recognition that was associated with faster responses. Consistently, cathodal, inhibitory tDCS of 2mA clearly accelerated emotion recognition in the RME test. Moreover, the change in response correctness induced by cathodal tDCS was significantly correlated with the emotion-specific IFG activity measured with NIRS during RME performance. This is first evidence for a beneficial, state-dependent effect of excitability-decreasing cathodal tDCS on emotion recognition. The correlation with individual imaging data supports the concept of a focusing effect of cathodal tDCS that reduces neural noise facilitating signal detection (Antal et al., 2004; Dockery et al., 2009; Miniussi et al., 2013).

6 Zusammenfassung

Die korrekte Wahrnehmung des emotionalen Gesichtsausdruckes ist eine Grundvorraussetzung für eine erfolgreiche soziale Kognition und Interaktion (Haxby et al., 2002). Der linke inferiore frontale Gyrus (IFG) ist wesentlich in das neuronale Netzwerk der emotionalen Wahrnehmungsfähigkeit involviert (Dal Monte et al., 2014). Mithilfe der transkraniellen direkten Gleichstromstimulation (tDCS) können die kortikale Erregbarkeit und damit einhergehende Verhaltensfunktionen in einer polaritäts-spezifischen und aktivitätsabhängigen Art und Weise moduliert werden (Dayan et al., 2013; Wolkenstein and Plewnia, 2013; Wolkenstein et al., 2014; Zwissler et al., 2014). Erregungssteigernde anodale tDCS und -reduzierende kathodale tDCS mit einer Stromstärke von 2 mA wurden in einem sham-kontrollierten Crossover-Design über dem linken IFG von 32 gesunden Probanden appliziert, während diese den 'Reading the Mind in the Eyes' (RME) Test durchführten. Der RME Test ist ein weitverbreitet angewandter Test, um die emotionale Wahrnehmungsfähigkeit in gesunden Probanden oder psychiatrischen Patienten zu testen (Baron-Cohen et al., 2001). Vor den zwei (Sham und Verum) Stimulationssitzungen wurde die Gehirnaktivität des linken IFG während der Durchführung des RME Tests mittels Nahinfrarotspektroskopie (NIRS) gemessen (Ehlis et al., 2014). NIRS zeigte eine Deaktivierung des linken IFG, welche mit einer schnelleren Reaktionszeit während des RME-Tests assoziiert war. Im Einklang damit zeigte sich eine signifikant schnellere emotionale Wahrnehmungsfähigkeit durch kathodale, inhibitorische tDCS mit 2mA. Darüber hinaus zeigte die durch kathodale tDCS verursachte Veränderung der korrekt gegebenen Antworten eine signifikante Korrelation mit der durch NIRS gemessenen emotionsspezifischen Aktivierung des linken IFG während der Durchführung des RME-Tests. Dies sind erste Hinweise für einen vorteilhaften zustandsabhängigen Effekt von erregungsreduzierender, kathodaler tDCS auf die emotionale Wahrnehmungsfähigkeit. Die Korrelation mit den individuellen Bildgebungsdaten unterstützt das Konzept eines fokussierenden Effektes von kathodaler tDCS, welche neuronales Rauschen reduziert, um eine Signalerkennung zu erleichtern (Antal et al., 2004; Dockery et al., 2009; Miniussi et al., 2013).

7 References

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8 Erklärungen zum Eigenanteil

Die Arbeit wurde in der Klinik für Psychiatrie und Psychotherapie unter Betreuung von Prof. Dr. med. Christian Plewnia durchgeführt.

Die Konzeption der Studie erfolgte in Zusammenarbeit mit Prof. Dr. med. Christian Plewnia und Dr. phil. Ann-Christine Ehlis.

Sämtliche Versuche wurden nach Einarbeitung durch Mitglieder der Arbeitsgruppen (Fabienne Große Wentrup und Ramona Täglich) von mir durchgeführt.

Die statistische Auswertung der NIRS-Aktivierung erfolgte in Zusammenarbeit mit Dr. phil. Ann-Christine Ehlis und Dr. rer. nat. Florian Häußinger. Die statistische Auswertung der tDCS Daten und der Korrelationen mit der NIRS-Aktivierung erfolgte nach Anleitung durch Prof. Dr. med. Christian Plewnia durch mich.

Ich versichere, das Manuskript selbständig verfasst zu haben und keine weiteren als die von mir angegebenen Quellen verwendet zu haben.

Hamburg, den 12.11.2018

9 Veröffentlichungen

Ergebnisse aus der vorliegenden Dissertationsschrift wurden bereits in folgenden Publikationen veröffentlicht:

Klimm, N. *et al.* (2015) ‘P 163. Reduction of excitability in the left inferior frontal gyrus by cathodal tDCS facilitates emotion recognition’, *Clinical Neurophysiology, 126*: e142.

Klimm, N. *et al.* (2016) ‘EP 26. Reduction of excitability in the left inferior frontal gyrus by cathodal tDCS facilitates emotion recognition’, *Clinical Neurophysiology, 127*: e244-245.