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ORIGINAL RESEARCH

Attention control and its emotion-specific association with cognitive emotion regulation in depression

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Abstract

Individuals with major depression show impaired control of attention and emotions. Both processes are conceptually similar and might share common mechanisms. The current study aims to examine attention control and its association with cognitive emotion regulation in depression. 26 patients with a history of major depression (14 females) and 26 healthy controls (14 females) performed an emotional face-word Stroop task and a cognitive emotion regulation task while undergoing fMRI. Patients and controls showed a similar behavioral performance in both tasks. Across groups, participants who were less distracted from happy faces by the incongruent word "sadness" (Stroop task) were better at regulating their happiness (emotion regulation task). Notably, both the Stroop and emotion regulation task recruited the left supramarginal gyrus. Additionally, only patients showed a relative attentional disengagement from positive compared to negative stimuli in the Stroop task. Attention control and cognitive emotion regulation capabilities appear to be linked at both the behavioral and neural level. Shared mechanisms suggest that emotional disturbances in depression may be improved by interventions that target attention control, particularly regarding the processing of positive stimuli.

Keywords Stroop · Attention control · Interference processing · Cognitive emotion regulation · Reappraisal · Depression · fMRI

Introduction

Individuals suffering from major depression (MDD) show various cognitive biases such as an attentional bias favoring negative stimuli and neglecting positive stimuli (Joormann and Vanderlind 2014; Peckham et al. 2010). Moreover, depressed patients tend to interpret emotional situations in a more negative way than non-depressed individuals do (Beck 2008). These biases significantly contribute to the disorder's development and maintenance (Beck 2008; Gross 1998; Ochsner and Gross 2005). Emotions, particularly distressing ones, might be changed by i) altering the focus of attention (e.g. away from distressing to more favorable information) or ii) changing how one thinks about a situation (Gross 1998),

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which is often referred to cognitive emotion regulation. These two strategies are conceptually similar and both require the ability to detect problematic occurrences through self-monitoring. Furthermore, the ability to exert top-down cognitive control on either attention or emotion is performed by the executive system, which implements corrective changes by promoting goal-relevant and inhibiting incompatible responses (Inzlicht et al. 2015). Therefore, attention control and cognitive emotion regulation might share common mechanisms.

A valuable measure of attention control to certain emotional stimuli without getting distracted by irrelevant emotional information is the emotional face-word Stroop task (Phillips et al. 2008). Similar to the classical version, the emotional face-word Stroop task creates an attentional conflict between target and distractor stimuli. Specifically, participants are asked to name the emotion expressed by a face while ignoring an overlaying emotional word. Emotional faces communicate essential social and self-relevant information and therefore offer the opportunity to assess attention control to specific emotional information in social interactions. While the classical Stroop task measures how well a person can suppress a habitual (reading) response, the emotional face-word Stroop task examines a person's ability to attend to specific emotional information (facial emotion) without getting distracted by emotional distractors (emotional words). Resolving such emotional conflict requires the ability to overcome interference from emotional distractors and to direct attention on the relevant stimuli, which relies on the frontal cortex (especially superior and inferior frontal gyrus), cingulate cortex, insula, as well as parietal, temporal, and extrastriatal brain regions (e.g. Chechko et al. 2013; Krebs et al. 2015; Xu et al. 2016). Furthermore, brain regions related to emotional processing are engaged. MDD patients compared to healthy controls (HC) show hypoactivation in prefrontal and insular regions (Chechko et al. 2013), possibly explaining attentional biases related to depression. However, imaging research on the emotional-face word Stroop task in clinical samples is rare. A different task version, namely the emotional Stroop task, has been extensively researched, both in healthy individuals and people with mental disorders such as depression. In this task, individuals usually have to name the ink color of words which are either emotional or neutral. Several meta-analyses (Epp et al. 2012; Joyal et al. 2019; Peckham et al. 2010) revealed marginally significant to large depression-related Stroop effects. Interestingly, such group differences increased with increasing depression severity (Epp et al. 2012). In a recent meta-analysis on the emotional Stroop task, Feng et al. (2018) identified hyper-activation in patients compared to controls in the dorsolateral prefrontal cortex, ventrolateral prefrontal cortex, dorsomedial prefrontal cortex, dorsal anterior cingulate cortex, inferior parietal lobule, and posterior cingulate cortex. When combining clinical and subclinical populations, there was exaggerated recruitment of the ventrolateral prefrontal cortex (Feng et al. 2018). The emotional Stroop task and the emotional face-word Stroop task differ, however, as the former lacks a semantic conflict between target (ink color) and distractor (emotional words). By creating a conflict between an emotional label and emotional facial expression, the emotional face-word Stroop task therefore offers the unique possibility to examine attention control to specific emotional information.

Meta-analyses on cognitive emotion regulation revealed a network including lateral prefrontal cortices, temporal and parietal regions as well as the (pre-)supplementary motor area (SMA) and the cingulate cortex (Buhle et al. 2014; Kohn et al. 2014; Morawetz et al. 2017). Patients suffering from depression, compared to healthy controls, show changes in the recruitment of several of these regions during cognitive emotion regulation. Beauregard et al. (2006), for instance, identified increased activation in the dorsal anterior cingulate cortex, anterior temporal pole, amygdala, and insula in unmedicated, acutely depressed patients during the voluntary down-regulation of sadness. Similarly, acutely depressed patients exhibited increased activation in the middle frontal gyrus when down-regulating negative emotions (Johnstone et al. 2007). However, emotion (down-) regulation in depression does not only involve neural hyperactivation. Radke et al. (2018) recently revealed reduced activation in the insula, amygdala, and putamen in acutely and remitted depressed patients compared to non-depressed controls during the down-regulation of negative emotions.

Overlapping networks of attention control, as measured with the Stroop task, and cognitive emotion regulation, as measured with an emotion regulation task, support the notion of shared underlying mechanisms (also see the meta-analysis by Feng et al. (2018)). Research has also begun to investigate more directly the possibility of common mechanisms. In healthy individuals, performance in the classical color-word Stroop task is associated with successful emotion regulation in daily life (Compton et al. 2008). Similarly, recent research revealed a positive link between the daily use of cognitive emotion regulation strategies and the ability to resolve interference in a cued emotional conflict task, both on a behavioral and a neural level (i.e. dorsolateral prefrontal cortex, dorsal anterior cingulate cortex; Vanderhasselt et al. 2013). However, to our knowledge, imaging research directly investigating attention control to specific emotional stimuli and its association with cognitive emotion regulation in MDD is lacking. The current study therefore examined such a link in patients with a history of depression and a healthy comparison sample using two experimental paradigms: an emotional face-word Stroop task and a cognitive emotion regulation task. We predicted that less attentional interference in the emotional face-word Stroop task, indicating a better ability to attend to specific emotional stimuli without getting distracted by competing emotional information (or in

other words: less attentional bias for the distracting stimuli), would be correlated with subjective cognitive emotion regulation success (i.e. regulation compared to no regulation). Furthermore, we expected that brain areas involved in attention control would be also recruited by cognitive emotion regulation, namely frontal cortices such as the superior and inferior frontal gyri, insula, cingulate cortices, and parietal brain regions (e.g. intraparietal lobule). Finally, we expected that depressed individuals would show impaired attention control and cognitive emotion regulation compared to healthy controls. Impaired attention control is thereby indicated by increased reaction times and altered brain activation in aforementioned cognitive control regions (Feng et al. 2018) during interference processing (Stroop task). Based on findings of an attentional bias for negative information in depression, we expected that impaired attention control is particularly prominent when positive target stimuli and negative distractors are presented. Disturbed cognitive emotion regulation is characterized by a reduced difference in emotion ratings as well as altered brain activation in the mentioned control regions during emotion regulation compared to no regulation.

Methods and materials

Participants

The final sample comprised 26 patients meeting the criteria of a current ($n = 10$) or (partially) remitted ($n = 16$) MDD according to the DSM-IV, and 26 healthy controls (HC) who were individually matched for age (± 2 years) and sex (Table 1). Further results on this sample are reported in Loeffler et al. (2018), which focuses on a different research question. Four participants (HC) were excluded from the initial sample due to massive head movement during scanning ($n = 1$), technical problems ($n = 1$), and non-compliance with task instructions ($n = 2$). All participants were Caucasian.

Patients were recruited from the Department of Psychiatry, Psychotherapy and Psychosomatics of the RWTH Aachen University. Diagnoses were confirmed by the Structured Clinical Interview for DSM-IV (Wittchen et al. 1997). Exclusion criteria for patients were current substance dependency, previous/current psychotic and (hypo-)manic symptoms, treatment for other psychiatric disorders than depression, and personality disorders. Twenty-two patients received antidepressant treatment (Table 1). HC were excluded when meeting criteria for current/lifetime axis I psychiatric disorders or having first-degree relatives with psychotic or bipolar disorder. Exclusion criteria for both groups were age < 18 or > 55 years, neurological diseases, left-handedness, and contraindications for MRI.

Informed consent was obtained from all individuals included in the study. Participants received financial compensation (30 €). This study was approved by the local ethics committee of the Medical Faculty of the RWTH Aachen University and was conducted according to the Declaration of Helsinki.

Clinical assessment

To specify the current clinical state, we included measures of depressive symptoms (Beck Depression Inventory II, BDI-II; Hautzinger et al. 1995; Hamilton Rating Scale of Depression 17-items, HRSD; Williams 1988; Mood and Anxiety Symptom Questionnaire anhedonia subscale, MASQ-Anhedonia; Watson and Clark 1991), and anxiety symptoms (State Trait Anxiety Inventory, STAI; Laux et al. 1981). In addition, participants underwent neuropsychological testing tapping executive functioning (Trail Making Test-A/B, TMT-A/B; Army Individual Test Battery 1944) and verbal intelligence ("Wortschatztest", WST; Schmidt and Metzler 1992) to compare groups on a general level of functioning.

Attention control - emotional face-word Stroop task

Pictures of 42 sad and 42 happy Caucasian faces (balanced for age and sex) from the FACES database (Ebner et al. 2010) were presented twice. Either "Trauer" (sadness) or "Freude" (happiness) was printed in red letters on the faces. The pictures were edited in such a way that the nose of the faces was centered and the emotional label was printed on the nose in all images without covering the eye or the mouth region. In congruent trials (84 trials), these labels matched the facial emotion, whereas in incongruent trials (84 trials), the labels did not match the facial emotion (Fig. 1a). Participants should indicate the facial emotion as fast and correctly as possible by button press while ignoring the labels. Throughout the article, attention control refers to the ability to attend to relevant emotional stimuli (i.e. emotional faces) while ignoring irrelevant emotional distractors (i.e. emotion labels). Difficulties to attend to target stimuli indicate an attentional bias for the distracting information (Peckham et al. 2010). To assess attention control, reaction times and brain activation during the processing of incongruent compared to congruent trials were analyzed (Phillips et al. 2008; Rive et al. 2013).

Faces were presented for 1 s, followed by an inter-stimulus-interval of 2–4 s. Answers were possible until the next trial started. A 400 ms fixation cross primed the participants for the next face. Trials were presented in a random order. Prior to the experiment, all participants performed several practice trials to ensure full comprehension of the task. The paradigm took approximately 12 min. A similar design has been successfully implemented in previous studies (Chechko et al. 2013; Egner and Hirsch 2005; Etkin et al. 2006; Hornung et al. 2018; Stickel et al. 2019).

Table 1 Sociodemographic and clinical characteristics of study participants (indicated as n or mean with SD in parentheses; Loeffler et al. (2018))

	HC ($n = 26$)	Range	MDD ($n = 26$)	Range	p-values
Sex (M/F)	12/14		12/14		
Age (in years)	35.31 (11.23)	22–54	35.27 (11.03)	22–55	.956
Education (in years)	13.62 (3.03)	9–18	13.92 (3.31)	9–21	.779
TMT-A (in seconds)	22.22 (5.81)	11–34	18.77 (4.67)	13–30	.322
TMT-B (in seconds)	39.50 (10.06)	25–66	39.12 (15.09)	18–76	.914
WST	31.96 (3.54)	21–36	33.42 (3.48)	24–42	.184
MASQ-Anhedonia	43.92 (9.93)	26–63	67.96 (17.80)	34–101	<.001***
BDI-II	2.42 (3.20)	0–11	17.62 (10.33)	2–37	<.001***
HRSD	–	–	10.6 (7.70)	0–23	–
STAI-State	32.04 (5.42)	24–49	40.23 (7.38)	26–60	<.001***
STAI-Trait	33.42 (7.15)	23–58	52.35 (9.93)	33–65	<.001***
Clinical state (acute/remitted)			10/16		
Time since last episode (in months)			7.15 (10.34)	0–31	
Age at onset (in years)			26.35 (9.67)	13–47	
Time since first episode (in years)			9.59 (8.54)	0.5–35	
Number of episodes			3.32 (3.30)	1–13	
Duration of episodes (in months)			6.20 (4.37)	0.75–18	
Patients with recurrent MDE			18		
SSRI only			5		
Tricyclic antidepressant only			4		
SSRI + NaSSA			3		
SSNRI only			3		
Melatonergic antidepressant only			2		
Atypical antidepressant only			1		
SSNRI + Anticonvulsant			1		
SSNRI + Atypical antipsychotic			1		
SSNRI +Tricyclic antidepressant			1		
NaSSA + Tricyclic antidepressant			1		

Abbreviations: *BDI-II* Beck depression inventory-II, *MDD* Patients with lifetime major depressive disorder, *HC* Healthy controls, *HRSD* Hamilton rating scale of depression, *MASQ* Mood and anxiety symptom scale, *MDE* Major depressive episode, *NaSSA* Noradrenergic and specific serotonergic antidepressant, *SSNRI* Selective serotonin noradrenalin reuptake inhibitor, *SSRI* Selective serotonin reuptake inhibitor, *STAI* State trait anxiety inventory, *TMT-A/B* Trail making test-A/B, *WST* "Wortschatztest" (verbal intelligence). Group differences are indicated by p-values. The following significance levels are applied: *$p < .05$, **$p < .01$, ***$p < .001$

Cognitive emotion regulation - emotion regulation task

A detailed description of the emotion regulation task and its results has been reported elsewhere (Loeffler et al. 2018). Pictures of 60 sad and 60 happy Caucasian faces from the FACES database (Ebner et al. 2010), which were not used in the Stroop task, were presented for 4 s. Subsequently (max. 5 s), participants indicated via button press how sad (regarding sad faces) and how happy (regarding happy faces) they felt on a scale ranging from 1 (*not at all*) to 8 (*very*; Fig. 2). In the *view* condition, no regulation was applied. In the experimental conditions *increase* and *decrease*, participants applied cognitive emotion regulation strategies in order to regulate their emotions. Cognitive emotion regulation thereby refers to the ability to change the own emotional experience by changing the interpretation of the situation. In more detail, participants were asked to imagine a closely related person being depicted on the picture in order to enhance personal relevance. In the increase condition, participants were additionally instructed to imagine that the person in the picture was sad/happy because of them whereas in the decrease condition they should imagine that they had nothing to do with the emotional state of the person. Prior to the experiment, all participants performed several practice trials to ensure full comprehension of the task. The paradigm took approximately 24 min.

Participants first performed the emotion regulation task and then the emotional face-word Stroop task as the former task is

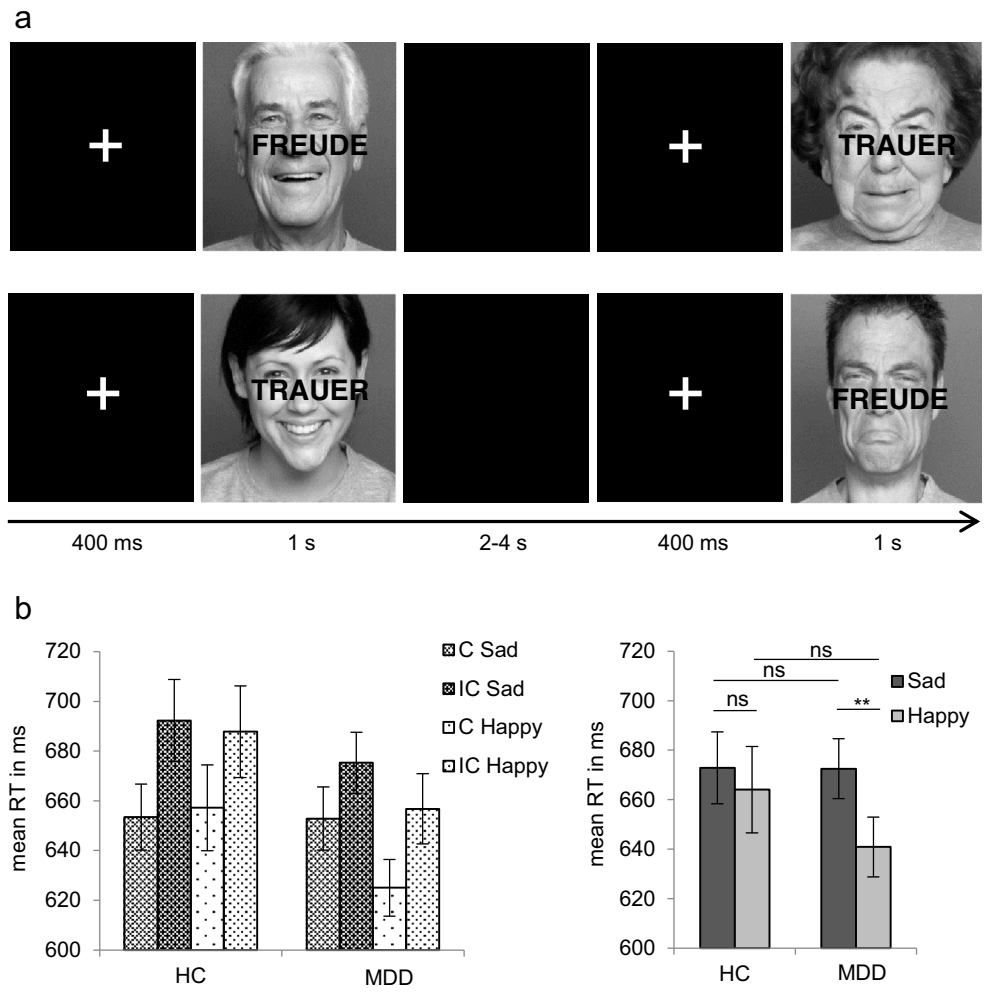

Fig. 1 Emotional face-word Stroop task. **a**. Participants are asked to indicate the facial emotion as fast and precisely as possible while ignoring the superimposed emotion label. Faces are presented for 1 s, followed by an inter-stimulus-interval of 2–4 s. A 400 ms fixation cross primes the participant for the next face. In congruent trials the German word for sadness ("Trauer") and happiness ("Freude") matches the facial expression whereas in incongruent trials the word does not match the facial expression. **b.** Mean reaction times (RT) in milliseconds (ms). Left panel: Participants show longer RTs in response to incongruent (IC) compared to congruent (C) trials (main effect congruency: $p < .001$) and shorter RTs in response to happy faces compared to sad faces (main effect emotion: $p = .026$; p-values not graphically indicated for visual purposes). Right panel: Following up a trend for a group x emotion interaction ($p = .054$) reveals that only MDD respond faster to happy compared to sad faces ($p = .003$) but not HC ($p = .829$). Ns = not significant, $^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$

more strenuous. In this way, it should be ensured that participants were sufficiently motivated and capable to put the necessary effort in the emotion regulation task. A post-experimental survey indeed showed that using this approach, participants put equal effort in both tasks ($p = .120$). Stimuli were presented by Presentation Software (Neurobehavioral Systems, Albany, CA) and viewed on a screen at the end of the MR scanner through a mirror mounted on the head coil.

Image acquisition and preprocessing

MRI data were acquired on a 3 T Siemens PRISMA scanner using a 24-channel head coil. Functional data were obtained with a T2*-weighted echo-planar sequence (TR: 2000 ms, TE: 30 ms, FoV: 210 mm, 36 slices (ACPC), voxel size: 3.3 × 3.3 × 3.0 mm, flip angle: 77°, distance factor: 20% (= 0.6 mm)). An anatomical reference image was acquired with a sagittal T_1-weighted 3D magnetization-prepared rapid gradient-echo (MPRAGE) sequence at the end of the scanning session (TR: 2300 ms, TE: 2.98 ms, FoV: 256x256mm, voxel size: 1x1x1mm, flip angle: 9%, distance factor: 50%).

For preprocessing, statistical parametric mapping (SPM12, Wellcome Department of Imaging Neuroscience, London) was used. To allow for magnetic field saturation, dummy volumes at the beginning of the tasks were discarded. The remaining images were realigned to the mean functional image and slice-time corrected. Subsequently, the mean functional image was coregistered to the anatomical image and all images were normalized to MNI space and spatially smoothed using a 6 mm full-width-at-half-maximum Gaussian kernel.

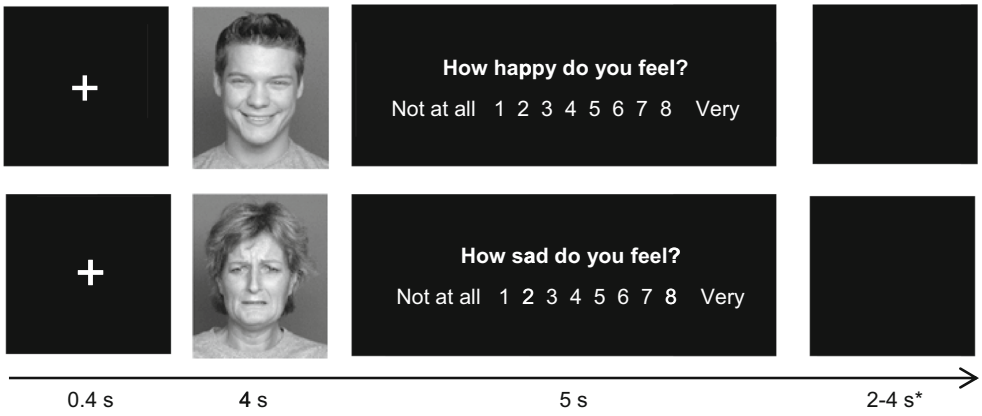

Fig. 2 Emotion regulation task. Faces are presented for 4 s, followed by a rating phase of maximum 5 s. A 400 ms fixation cross primes the participant for the next face. Participants should indicate on a scale ranging from 1 (not at all) to 8 (very) how sad (regarding sad faces) or happy (regarding happy faces) they feel. In a *view* condition, no emotion regulation strategy should be applied. In two regulation conditions (*increase, decrease*), participants are asked to imagine a closely related person being depicted in order to increase personal relevance. In the *increase* condition, participants are additionally instructed to imagine that the person in the picture is sad/happy because of them whereas in the *decrease* condition, they should imagine that they have nothing to do with the emotional state of the person. All participants completed all three conditions in a counterbalanced order. *The inter-stimulus interval amounts to 2–4 s and is extended to 9–11 s after each mini-block, containing 5 faces of the same emotions

Behavioral data analysis

Two HC have entered their responses incorrectly during the emotional face-word Stroop task and were excluded from further analyses of the Stroop data. Error trials (incorrect answers, no responses, double button presses) and trials with reaction times (RTs) faster than 200 ms were excluded. Subsequently, we defined outliers on a subject level as deviating two standard deviations (SD) from the mean RT of each condition. In total, 10.4 % of the trials were excluded of which 6.1 % were error trials and 4.3 % outliers. Groups did not differ in the number of error trials ($p = .112$) or outliers ($p = .353$). RTs of button presses during the emotional face-word Stroop task were averaged per condition to investigate attention control to emotional information. In more detail, we were interested how well participants could focus/control attention on positive or negative information without getting distracted by distractor words (i.e. interference processing: RT incongruent minus RT congruent). To investigate subjective emotion regulation, mean sadness/happiness ratings of the emotion regulation task were analyzed. Specifically, we compared emotion ratings in the increase and decrease condition [increase + decrease] to the no regulation condition [view] to obtain a general index of emotion regulation ability (Morawetz et al. 2016). To ensure normal distribution of the data, RTs (Stroop task) and emotion ratings (regulation task) were normalized using a logarithmic transformation (y = log10[x]).

Two mixed-model ANOVAs with group (HC, MDD) as a between-subjects factor and condition (Stroop task: congruent, incongruent; regulation task: view, increase, decrease) and emotion (sad, happy) as within-subject factors were conducted. To describe the relationship between depression severity (BDI-II, HRSD, MASQ-Anhedonia) and attention control (Stroop task) and cognitive emotion regulation (emotion regulation task), respectively, spearman correlations were computed per group since data was not normally distributed. Questionnaire data was compared between groups using independent t-tests or Mann-Whitney-U tests in case the assumption of normal distribution was not met to assess group differences in symptom severity and general functioning.

Besides effects of the experimental tasks, we were interested in the relationship between attention control and cognitive emotion regulation. Task-specific analyses revealed no group differences in attention control. For this reason, shared mechanisms were examined across groups. Since this study is characterized by a distinction between positive and negative emotions, overlapping mechanisms were analyzed separately for happiness and sadness. Emotion ratings (regulation task) in the increase and decrease condition relative to emotion ratings in the no regulation condition [increase + decrease > view] served as index of general emotion regulation ability (Morawetz et al. 2016), while mean reaction times (Stroop task) during interference processing (incongruent > congruent) provided a measure of attention control (Phillips et al. 2008). Spearman correlations were conducted to examine the relationship between these measures. Statistical testing was performed with SPSS 22.0 applying an α-level of $p < .05$ and partial eta squared as estimate of effect sizes.

fMRI data analysis

Using two event-related GLM models, events of interest were isolated by convolving vectors of stimulus onset times and stimulus duration (Stroop task: 1 s; regulation task: 4 s) with the canonical hemodynamic response function. For the emotional face-word Stroop task, a first-level model was estimated with 4 regressors of interest (2 levels of condition [congruent, incongruent] by 2 levels of emotion [sad, happy]) and 2 regressors of no interest (instruction, error trials). For the emotion regulation task, a first-level model was estimated with 6 regressors of interest (3 levels of condition [view, increase, decrease] by 2 levels of emotion [sad, happy]) and 1 regressor of no interest (rating phase). Additionally, six movement parameters were modeled as regressors of no interest for both tasks. Images were high-pass filtered at 128 s and an autoregressive AR(1) model was used to account for temporal autocorrelations.

On group level, full factorial GLM analyses with the between-subjects factor group (HC, MDD) and the within-subject factors condition (Stroop task: congruent, incongruent; regulation task: view, increase, decrease) and emotion (sad, happy) were applied. Whole-brain analyses were corrected for multiple comparisons using a Monte-Carlo correction (Forman et al. 1995) implemented in AFNI's 3dClustSim (voxel-level threshold $p < .001$, cluster-level threshold:$p < .05$, smoothness [Stroop task: $9.2 \times 9.2 \times 9.0$ mm, regulation task: $9.0 \times 9.0 \times 8.8$ mm], 10,000 iterations). This revealed an extended threshold of 95 voxel (Stroop task) and 91 voxel (regulation task) for one-sided tests and 83 voxel (Stroop task) and 79 voxel (regulation task) for two-sided test. Identified regions were labeled according to the SPM Anatomy Toolbox 2.2c (Eickhoff et al. 2005).

Next, we tested whether cognitive emotion regulation relies on similar brain regions as attention control. Due to the temporal course of emotion generation, in which attention processes take place before the interpretation of emotional stimuli (see modal model; Gross and Thompson 2007), we decided to first identify brain regions that are involved in attention processes and then investigate whether the identified regions are also involved in the later (re)interpretation of the stimuli. For this purpose, we first identified whole-brain activations linked to interference processing in the emotional face-word Stroop task (incongruent > congruent). Subsequently, we created spheres (10 mm) around peak activations of identified clusters using the WFU Pickatlas tool in SPM12 (see Table 2 for the identified brain regions) to determine whether the same brain areas are also involved in cognitive emotion regulation. These spheres were then used as mask images in a region of interest analysis of the emotion regulation functional data ([increase + decrease] > view). In this way we could examine whether brain regions involved in attention control are also recruited by cognitive emotion regulation. Results of the region of interest analysis were thresholded with $p < .001$ and small-volume corrected ($p < .05$). Similar to behavioral findings, task-specific analyses revealed no group differences in the emotional face-word Stroop task. Hence, we examined shared neural mechanisms between attention control and cognitive emotional regulation across groups. As mentioned above, a particular strength of this study is the distinction between positive and negative emotions. Therefore we have analyzed overlapping brain regions separately for happiness and sadness.

Table 2 Whole-brain, emotion-specific interference effects (incongruent > congruent) across patients and controls in the emotional face-word Stroop task

	k	L/R	MNI			t-value
			x	y	z	
Emotion-specific interference effects						
Incongruent > Congruent						
Sad						
Posterior-Medial Frontal	188	L	−2	16	52	4.35
Middle Frontal Gyrus	98	L	−46	14	48	3.76
Happy						
Inferior Frontal Gyrus	258	L	−42	24	0	4.97
Precentral Gyrus	1099	L	−38	2	42	4.82
Inferior Parietal Lobule	274	L	−28	−52	44	4.59
Cerebellum	175	R	24	−72	−28	4.49
Inferior Frontal Gyrus	328	R	46	16	32	4.45
SupraMarginal Gyrus	110	L	−54	−52	28	4.36
Posterior-Medial Frontal	704	L	−4	4	64	4.29
Precuneus	116	L	−4	−70	46	3.77

L Left, *R* Right. Spheres (10 mm) were created around peak activations of these clusters and subsequently used as mask images in the analysis of functional data of the emotion regulation task. Results are Monte-Carlo corrected and cluster size (k), hemisphere, MNI coordinates and t-values are given

Results

Questionnaires

MDD were more depressed (BDI-II: $U = 39.50$, $z = 5.50$, $p < .001$; MASQ-Anhedonia: $t(50) = 6.02$, $p < .001$) and anxious (STAI-State: $U = 96.00$, $z = 4.44$, $p < .001$; STAI-Trait: $U = 45.00$, $z = 5.37$, $p < .001$) than HC. All other group comparisons were not significant (all $p \geq .184$, see Table 1).

Attention control - emotional face-word Stroop task

As expected, participants responded significantly slower in response to incongruent compared to congruent trials

Table 3 Mean reaction times (RTs) of the emotional face-word Stroop task

Condition	Group	Mean RT (ms)	SD	Range
C Sad	HC	653.43	64.95	510.78–778.58
	MDD	652.87	64.57	530.72–805.63
	Total	653.15	64.09	510.78–805.63
C Happy	HC	657.19	84.34	526.90–865.58
	MDD	625.04	58.02	538.33–761.46
	Total	640.47	72.93	526.90–865.58
IC Sad	HC	692.31	80.89	533.58–883.36
	MDD	675.31	62.63	565.47–811.00
	Total	683.47	71.74	533.58–883.36
IC Happy	HC	687.80	90.49	553.76–909.79
	MDD	656.75	71.93	513.16–905.95
	Total	671.65	82.03	513.16–909.79

C congruent, *HC* Healthy controls, *IC* Incongruent, *MDD* Patients with a lifetime major depressive disorder, *RT* Reaction time, *SD* Standard deviation

($F(1,48) = 71.02$, $p < .001$, $\eta_p^2 = .58$), confirming an interference effect (Fig. 1b, left panel; see Table 3 for mean RTs). This interference effect was reflected in increased activation in the left precentral gyrus, left posterior-medial frontal, right inferior frontal gyrus, right mid cingulate cortex, bilateral insula, left superior parietal lobule, left middle temporal gyrus, and left precuneus (Table 4, Fig. 3). The opposite contrast (congruent > incongruent) yielded no suprathreshold activation.

Interestingly, there were no group differences in either RT ($p = .322$) or neural activation during the emotional face-word Stroop task. However, emotion-specific effects emerged: Generally, participants responded faster in response to happy faces than to sad faces ($F(1,48) = 5.23$, $p = .026$, $\eta_p^2 = .10$), irrespective of condition (interaction emotion by condition: $p = .899$). There was also a trend for a group by emotion interaction ($F(1,48) = 3.90$, $p = .054$, $\eta_p^2 = .08$). Follow-up analyses of this trend revealed that only MDD, but not HC, responded significantly faster in response to happy compared to sad faces

Table 4 Whole-brain effects of the emotional face-word Stroop task

	k	L/R	MNI			t-value
			x	y	z	
Condition effect						
HC + MDD						
Incongruent > Congruent						
Posterior-Medial Frontal	1414	L	−6	4	66	5.66
Precentral Gyrus	1551	L	−42	0	48	5.29
Insula	372	L	−30	18	−10	5.18
Mid Cingulate Cortex	412	R	4	−18	32	5.11
Insula	199	R	34	24	−6	4.71
Middle Temporal Gyrus	205	L	−52	−52	0	4.62
Inferior Frontal Gyrus	489	R	48	18	22	4.49
Superior Parietal Lobule	293	L	−24	−52	44	4.41
Precuneus	138	L	0	−60	40	3.81
Congruent > Incongruent		–				
Group by emotion interaction						
HC vs. MDD						
Sad		–				
Happy		–				
HC						
Sad vs. Happy		–				
MDD						
Sad>Happy						
Posterior-Medial Frontal	121	R	8	22	62	4.65
Happy>Sad		–				

HC Healthy controls, *MDD* Patients with lifetime major depressive disorder, *L* Left, *R* Right. Results are Monte-Carlo corrected and cluster size (k), hemisphere, MNI coordinates and t-values are given. This table only shows follow-up analyses (t-contrasts) of a significant main effect of condition (F-contrast) and a significant group by emotion interaction (F-contrast). There was no significant main effect of group or emotion or any other interaction (F-contrasts) for which reason no follow-up analyses (t-contrasts) have been conducted.

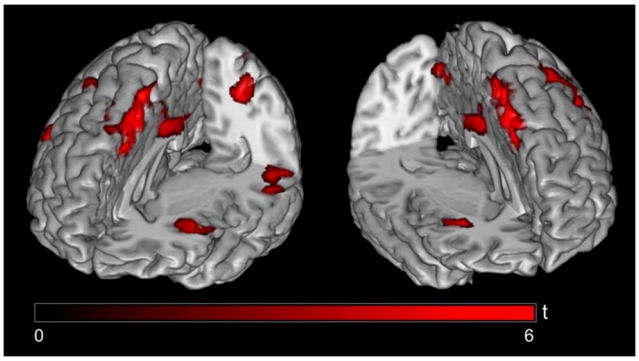

Fig. 3 Across groups, incongruent compared to congruent trials in the emotional face-word Stroop task activated the left posterior medial frontal cortex, left precentral gyrus, bilateral insula, right mid cingulate cortex, left middle temporal gyrus, right inferior frontal gyrus, left superior parietal lobule, and left precuneus. Results are Monte-Carlo corrected for multiple comparisons (voxel-level threshold: $p < .001$, cluster-level threshold: $p < .05$)

(MDD: $p = .003$; HC: $p = .829$). However, groups did not differ in RTs in response to either happy ($p = .152$) or sad faces ($p = .680$). A similar pattern was also reflected on a neural level: Follow-up analyses of a significant group by emotion interaction revealed increased activation in the right posterior-medial frontal cortex (Table 4) in response to sad compared to happy faces in MDD, while no suprathreshold activation emerged in HC for this contrast (sad>happy). Alike the behavioral findings, groups did not differ significantly in neural response to either sad or happy faces.

There were no significant correlations between depression severity (BDI-II, MASQ-Anhedonia, HAMD) and attention control (incongruent > congruent), either on a behavioral (all $p's \geq .179$) or on a neural level (all $p's \geq .093$).

Table 5 Whole-brain effects of the emotion regulation task (Loeffler et al. 2018)

	k	L/R	MNI			t-value
			x	y	z	
HC + MDD						
Regulation > View						
Precuneus	302	L	−6	−56	32	4.44
Angular Gyrus / IPL	142	L	−48	−64	28	4.09
Regulation Happy > View Happy						
Angular Gyrus / IPL	102	L	−56	−60	24	4.01
Regulation Sad > View Sad						
Precuneus	140	L	−6	−56	34	4.32

HC Healthy controls, *MDD* Patients with lifetime major depressive disorder, *L* Left, *R* Right. Results are Monte-Carlo corrected and cluster size (k), hemisphere, MNI coordinates and t-values are given. This table only shows t-contrasts relevant to the research question

Cognitive emotion regulation - emotion regulation task

A detailed description of cognitive emotion regulation effects is provided elsewhere and not the focus of the current article (Loeffler et al. 2018). Behaviorally, subjective emotion ratings differed between conditions ($F(2,100) = 53.63$, $p < .001$, $\eta_p^2 = .52$), confirming that the application of cognitive emotion regulation strategies successfully regulated emotions. There was no significant main effect of group ($p = .322$) or group by condition interaction ($p = .392$). However, a significant group by emotion interaction ($F(1,50) = 6.98$, $p = .011$, $\eta_p^2 = .12$) pointed to a reduced emotional reactivity in response to happy faces in MDD compared to HC ($p = .017$). There was no significant correlation between subjective emotion regulation and depression symptoms (all $p \geq .619$).

On a neural level, cognitive emotion regulation compared to no regulation (view) yielded suprathreshold activation in the left precuneus and left angular gyrus / intraparietal lobule (IPL; Loeffler et al. 2018). The regulation of positive emotions recruited the left angular gyrus / IPL while negative emotion regulation relied on the left precuneus (see Table 5).

Association between attention control and cognitive emotion regulation across patients and controls

First, we were interested whether attention control to positive/negative information (Stroop task) correlates with cognitive emotion regulation (regulation task) on a behavioral level. Such an association was indeed found, but only for happiness ($r = -.392$, $p = .005$) and not for sadness ($r = .040$, $p = .783$): participants with a greater ability to focus attention on happy faces without getting distracted by the distractor word in the emotional face-word Stroop task (indicated by less interference), were also better at regulating happiness in the emotion regulation task (indicated by subjective emotion ratings). For sad faces no such association was found (Fig. 4).

Next, we were interested whether cognitive emotion regulation recruits the same brain regions as attention control. Results point to such an overlap, but again, only for happiness and not for sadness: activation in the left supramarginal gyrus, as identified during attention control to happy faces (incongruent happy > congruent happy), was also involved in the regulation of happiness ([increase happy + decrease happy] > view happy). Controlling attention to happy faces and regulating happiness both relied on this particular region in patients and controls. No other brain region identified in the emotional face-word Stroop task was recruited in the emotion regulation task.

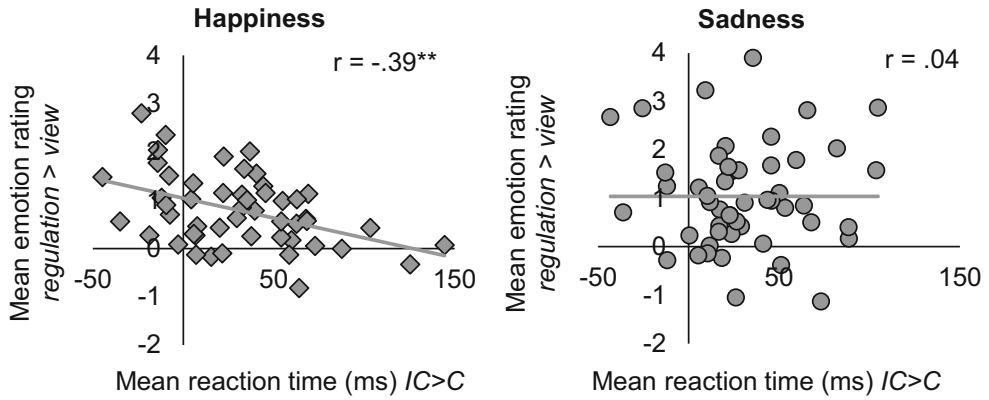

Fig. 4 Emotion-specific Spearman correlations between mean emotion ratings during the emotion regulation task (emotion regulation compared to no regulation (*view*)) and mean reaction times (RTs) of interference processing (incongruent (IC) > congruent (C)) during the emotional face-word Stroop task. Better attention control to positive stimuli (indicated by less interference) correlates with a better ability to regulate positive emotions across the whole sample (left graph). No such correlation is found for negative emotions (right graph). * $p < .05$, ** $p < .01$, *** $p < .001$

Discussion

This fMRI study investigated the neural correlates of attention control and its association with cognitive emotion regulation in patients with a history of major depression and healthy controls. Contrary to our expectations, we did not find significant group differences in attention control to emotional stimuli in an emotional face-word Stroop task or in the ability to regulate emotions in an emotion regulation task. Across patients and controls, better control of attention to positive stimuli was associated with a better ability to regulate own positive emotions. On a neural level, both processes recruited the left supramarginal gyrus, implying shared underlying mechanisms. Besides common mechanisms of attention control and cognitive emotion regulation across groups, depression was linked to altered processing of positive compared to negative stimuli. However, there were no group differences in reaction times or neural response to happy or sad stimuli between patients and controls.

Attention control is associated with cognitive emotion regulation across patients and controls

Attention control to emotional information, estimated by interference processing (incongruent compared to congruent trials) in an emotional face-word Stroop task, generally recruited the posterior medial frontal, dorsolateral and ventrolateral prefrontal cortices, temporal and parietal regions as well as the midcingulate cortex. Our findings closely correspond to previous findings using this task (Chechko et al. 2013; Krebs et al. 2015), verifying a successful task manipulation. Unlike previous studies (Armstrong and Olatunji 2012; Chechko et al. 2013; Epp et al. 2012; Hu et al. 2012; Peckham et al. 2010) and against our expectation, individuals with a history of depression did not differ significantly from healthy controls in attention control to either positive or negative stimuli, both on a behavioral and on a neural level. The absence of group differences might be due to a substantial proportion of our depressed patients being remitted. However, exploratory analyses comparing only acutely depressed patients and healthy controls did not reveal group differences either (see Online Resource), making this explanation less likely. Exploratory comparisons between acute and remitted depressed patients did not reveal group differences either. However, a significant group-by-condition-by-emotion interaction in the right middle temporal gyrus pointed to stronger emotion-specific effects within acutely depressed patients during congruent compared to incongruent trials. But direct group comparisons (i.e. remitted vs. acute: congruent sad, congruent happy, incongruent sad, incongruent happy) did not yield suprathreshold activation. From these results, we concluded that the two groups are homogenous enough to be combined into a single patient group. Moreover, symptoms of acute depression (BDI-II, HRSD, MASQ-Anhedonia) were not associated with attention control.

In line with our expectation, we revealed an association between the ability to control attention to positive stimuli and the ability to regulate positive emotions across patients and controls. The more participants were able to focus attention on positive facial expressions without getting distracted by emotional words (as indicated by reaction time), the better they could regulate their own positive emotions (as indicated by subjective regulation success). This is in line with previous findings from undergraduate students (Compton et al. 2008), which revealed a close link between attention control in a Stroop task and emotional coping. The current study extends these findings by showing that this association was only given for positive emotions.

On a neural level, both attention control and cognitive emotion regulation involved the supramarginal gyrus, confirming our hypothesis of shared neural mechanisms. Similar to the behavioral findings, this only occurred for positive and not for negative emotions. The supramarginal gyrus has been generally implicated in attention orientation (Corbetta and Shulman 2002) and verbal working memory (Deschamps et al. 2014). Previous research supports the relevance of the supramarginal gyrus in both attention control to emotional information (Chechko et al. 2013; Krebs et al. 2015) and cognitive emotion regulation (Morawetz et al. 2017; Ochsner et al. 2012). Together with dorsolateral and posterior prefrontal regions, the supramarginal gyrus might direct attention to relevant stimuli and maintain goal-relevant information in mind (Ochsner et al. 2012). Cingulate regions are implicated in performance monitoring and might therefore detect conflicts with desired goals and keep track whether goals have been met (Botvinick 2007; Kerns et al. 2004). The ventrolateral prefrontal cortex is involved in the selection of goal-appropriate and the inhibition of goal-inappropriate responses (Ochsner et al. 2012). These neural systems both subserve attention control and cognitive emotion regulation (Buhle et al. 2014; Chechko et al. 2013; Kohn et al. 2014; Krebs et al. 2015; C Morawetz et al. 2017). Surprisingly, the current study identified only the supramarginal gyrus as a brain region recruited by both processes. This is very likely to be attributed to properties of the emotion regulation paradigm. In contrast to previous research (e.g. Kanske et al. 2011), the current study applied emotion regulation strategies which required more self-related processing, which may more strongly rely on medial brain structures (Northoff et al. 2006; Ochsner et al. 2012). Furthermore, emotions have been evoked by facial expressions instead of complex scenes (i.e. IAPS pictures). These facial expressions might have communicated more self-relevant information, thereby recruiting more medial brain regions. Whole-brain analyses of brain regions linked to cognitive emotion regulation indeed showed a different activation pattern than conventional emotion regulation studies: Positive emotion regulation recruited the left angular gyrus / intraparietal lobule, while negative emotion regulation (compared to view) relied on left precuneus. Future research may want to elucidate shared neural mechanisms when using a more classical emotion regulation task.

Depressed patients, but not controls, show an attentional disengagement from positive compared to negative stimuli

Even though groups did not differ significantly in reaction times to either positive or negative stimuli, patients responded significantly faster in response to happy compared to sad faces (Stroop task), suggesting a relative disengagement from positive stimuli, whereas healthy controls did not show such an emotion-specific effect. In line with this finding, depressed patients displayed increased attention to negative and reduced attention to positive stimuli in previous emotional Stroop and dot probe experiments (Peckham et al. 2010). Likewise, eye-tracking studies revealed a reduced orientation to and maintenance of gaze on positive stimuli and an increased maintenance of gaze on dysphoric stimuli in depressed individuals compared to controls (Armstrong and Olatunji 2012). The authors speculated that depressed patients are less sensitive to reward and thus, rewarding stimuli fail to capture their attention. Depressed individuals might also lack the motivation to sustain attention on positive stimuli because they are less sensitive to their pleasantness (Armstrong and Olatunji 2012). However, in contrast to previous research, the current study did not identify group differences in reaction times to either positive or negative stimuli, but only indicates an attentional disengagement from positive compared to negative stimuli within depressed patients. Altered emotional processing, i.e. increased processing of negative stimuli relative to positive stimuli, within depressed patients was further reflected in the brain. Negative stimuli generally activated the left posterior medial frontal cortex to a stronger extent than positive stimuli. The activated cluster corresponds to the anterior portion of the preSMA (Zhang et al. 2012) and is essential for cognitive control processes (Nachev et al. 2008) such as the inhibition of responses (Li et al. 2006, 2009). Resting-state findings in healthy individuals revealed functional connections between the anterior preSMA and prefrontal regions such as the insula and other cognitive control regions (Zhang et al. 2012). Accordingly, negative stimuli might have required more inhibitory control than positive stimuli. This interpretation is supported by shorter reaction times in response to happy compared to sad faces. Possibly, sad faces captured patients' attention to a greater extent than happy faces did, with disengagement requiring more cognitive control. Previous studies indeed revealed difficulties in disengaging attention from negative stimuli in depression (Joormann and Vanderlind 2014). But again, it must be pointed out that patients and controls did not differ in their neural responses to either positive or negative stimuli. Emotion-specific effects only occurred within the patients.

Despite lacking group differences, a relative disengagement from positive compared to negative stimuli within patients offers a promising treatment target. Such a bias may reduce memory for positive events but increases memory for negative events, eventually leading to a negatively biased view of the world (Armstrong and Olatunji 2012). Complementing conventional psychotherapy with attentional training might prevent this effect. Such training has indeed been proven to successfully reduce depression symptoms (Browning et al. 2010; Wells et al. 2010) and might be therefore considered a valuable augmentation approach for depression treatment.

Limitations

In order to represent a broad spectrum of depression, acutely depressed and (partially) remitted depressed patients were included, which possibly accounts for the lack of group differences. Research suggests, however, that an affective processing bias is a trait characteristic of depression rather than a state marker (Van Oostrom et al. 2013). For example, never-depressed females with a family history of depression have been reported to show biased affective processing in an emotional Stroop task when compared to never-depressed women without family history (Van Oostrom et al. 2013). In line with these findings, the current study revealed no association between symptoms of acute depression and attention control and cognitive emotion regulation. Likewise, exploratory analyses did not reveal differences between acutely depressed patients and healthy controls.

Additionally, the current study was not designed to evaluate medication or psychotherapeutic effects. Previous treatment might have contributed to the lack of group differences. Future research should therefore examine cognitive control in treated compared to untreated patients.

Implications

Despite these limitations, the current study provides valuable insights into behavioral and neural correlates of attention control and its association with cognitive emotion regulation. Individuals with a lifetime major depression did not differ from healthy controls in attention control and cognitive emotion regulation, but displayed an attentional bias, favoring negative over positive information. Since attention control to positive information was associated with the regulation of positive emotions in patients and controls, training attentional control might indirectly improve patients' emotion regulation abilities, thereby reducing emotional disturbances as well as depressive symptoms. Specifically, disturbances of positive emotion processing might be addressed by attention modifications. Future research should examine possible applications in depression treatment.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical standards All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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