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Spectral fingerprints of facial affect processing bias in major depression disorder

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Abstract

In major depressive disorder (MDD), processing of facial affect is thought to reflect a perceptual bias (toward negative emotion, away from positive emotion, and interpretation of neutral as emotional). However, it is unclear to what extent and which specific perceptual bias is represented in MDD at the behavior and neuronal level. The present report examined 48 medication naive MDD patients and 41 healthy controls (HCs) performing a facial affect judgment task while magnetoencephalography was recorded. MDD patients were characterized by overall slower response times and lower perceptual judgment accuracies. In comparison with HC, MDD patients exhibited less somatosensory beta activity (20–30 Hz) suppression, more visual gamma activity (40–80 Hz) modulation and somatosensory beta and visual gamma interaction deficit. Moreover, frontal gamma activity during positive facial expression judgment was found to be negatively correlated with depression severity. Present findings suggest that perceptual bias in MDD is associated with distinct spatio-spectral manifestations on the neural level, which potentially establishes aberrant pathways during facial emotion processing and contributes to MDD pathology.

Key words: major depressive disorder (MDD); magnetoencephalography (MEG); perceptual bias; beta activity; gamma activity

Introduction

Meta-analyses of hemodynamic literature on facial emotion processing highlight the presence of mood-congruent processing bias in major depressive disorder (MDD) (Stuhrmann *et al*., 2011; Dalili *et al*., 2015). MDD patients exhibit difficulties in recognition of facial affect for all basic emotions with low to medium effect sizes. Specifically, MDD patients show an attentional bias toward negative emotional expressions (e.g. sad faces), an attentional bias away from positive emotional expressions (e.g. happy faces), and interpret neutral expressions as emotional expressions (Leppanen, 2006; Stuhrmann *et al*., 2011). Based on functional magnetic resonance imaging meta-analysis, the largest group

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differences have been reported to reflect 'hyperactivation' to negative and 'hypoactivation' to positive stimuli particularly in the amygdala, insula, parahippocampal gyrus, fusiform face area and putamen, indicative of a behaviorally relevant processing bias toward negative hedonic content (Stuhrmann *et al.*, 2011). It has been concluded that despite their presence, the effect size of behavioral abnormalities in response to affective faces is small and would require a substantial increase in sample size to be detected (Dalili *et al.*, 2015). However, processing of facial expression constitutes a rapid and dynamic process (Wood *et al.*, 2016), the manifestation of which could be of higher penetrance on the neural level, particularly when utilizing imaging modality operating on a faster temporal scale such as electroencephalography (EEG) and magnetoencephalography (MEG).

Neuroelectric and neuromagnetic evidence suggest the involvement of neuronal oscillatory activity across a variety of frequency bands mainly in the alpha/beta (8–30 Hz) and gamma (>30 Hz) frequency range (Basar *et al.*, 2006; Tuladhar *et al.*, 2007; Zion-Golumbic and Bentin, 2007; Basar *et al.*, 2008; Maratos *et al.*, 2009; Gao *et al.*, 2013; Furl *et al.*, 2014; Popov *et al.*, 2014; Sato *et al.*, 2014; Kang *et al.*, 2015; Matsuzaki *et al.*, 2015; Chand *et al.*, 2016; Jiang *et al.*, 2016; Dikker *et al.*, 2017; Furl *et al.*, 2017; Sato *et al.*, 2017; Liu *et al.*, 2018). It is generally accepted that power increases in the gamma frequency range, typically accompanied by power decrease in the alpha/beta bands indicate active neural engagement in task processing (Pfurtscheller and Aranibar, 1977; Pfurtscheller and Andrew, 1999; Pfurtscheller and Lopes da Silva, 1999; Klimesch *et al.*, 2007; Jensen and Mazaheri, 2010; Hanslmayr *et al.*, 2012; Fries, 2015) and correlate with the blood–oxygen level-dependent signal (positive correlation with gamma and negative correlation with alpha/beta) (Logothetis *et al.*, 2001; Scheeringa *et al.*, 2011; Scheeringa *et al.*, 2016; Hermes *et al.*, 2017). In the context of facial processing tasks, both alpha/beta and gamma band activity have been related to the processing of affective expressions (Luo *et al.*, 2007; Popov *et al.*, 2013), strengthening the possibility that rapid and dynamic processes related to mood-congruent bias in depression can be addressed by examining neuronal oscillatory activity. Especially, beta band activity plays an essential role in facilitating multimodal integration related to later stages of emotional processing including the generation of affective states, sensorimotor responses and conscious emotional feelings (Huebl *et al.*, 2016). Gamma band activity, on the other hand, has been suggested to be modulated by the valence of emotional face expression (Balconi and Pozzoli, 2009). Complementing the existent hemodynamic literature, EEG and MEG studies highlight the particular relevance of gamma oscillatory activity in feature binding in general (Tallon *et al.*, 1995; Tallon-Baudry *et al.*, 1997; Tallon-Baudry and Bertrand, 1999) and perceptual closure of face processing in particular (Grutzner *et al.*, 2010; Grutzner *et al.*, 2013; Castelhano *et al.*, 2014; Brodski *et al.*, 2015). It is conceivable that variations of facial features (e.g. eyes and eyebrows, gaze and mouth position) and their 'binding' into a coherent percept are fostered by neuronal activity in the gamma frequency range in early visual areas. Accordingly, abnormal facial emotion processing in MDD could be reflected by disrupted visual gamma modulations.

On a behavioral level and compared to healthy control (HC), MDD patients tend to recognize neutral faces less accurately than happy or sad expressions, paralleled by an increase in RT particularly in the neutral condition (Leppanen *et al.*, 2004). Besides, a negative perceptual bias has also been reported. Munkler *et al.* assessed the perceptual judgment of patients watching morphed stimuli that transitioned from sad to neutral to happy expressions (Munkler *et al.*, 2015). MDD patients exhibited a perceptual shift in the differentiation between sad and happy expression, in that greater intensity of the happy expression was needed to classify an expression as happy. That is, 'patients with MDD judged morphed facial expressions with neutral or near-neutral emotional expression more frequently as sad' (Munkler *et al.*, 2015). This is somewhat at odds with a considerable amount of literature demonstrating that MDD patients significantly differ in discrimination accuracy for sad and, to a lesser extent, happy expression compared to controls (Surguladze *et al.*, 2004; Carl *et al.*, 2013; Joormann and Quinn, 2014). Moreover, to what extent such perceptual biases are reflected in compromised neuronal oscillations awaits demonstration.

Table 1. Demographic and clinical information of participants

	MDD ($n = 48$)	HC ($n = 41$)	P-value
Gender (M/F)	25/23	21/20	0.99[a]
Age (years)	32.4 ± 9.1	30.8 ± 7.11	0.35[b]
HAMD	25.8 ± 5.2	N/A	N/A
Total illness duration (months)	32.6 ± 52.2	N/A	N/A
Number of episodes	1.7 ± 1.2	N/A	N/A
Comorbidity with anxiety disorder	19 (39.6%)	N/A	N/A

[a]Sex difference between the two groups statistic was assessed by two-tailed chi-square t-test.
[b]Age differences between two groups were evaluated by two-sample two-tailed t-test.

The present report examines neuromagnetic activity in a population of MDD patients and HC performing a dynamic facial expression task with the following hypotheses:

(i) MDD patients are expected to exhibit overall slower response times and lower facial recognition accuracies compared to HC.
(ii) This perceptual bias is associated with abnormal beta and gamma modulations.

Moreover, exploratory analyses will examine the clinical relevance of oscillatory disruptions by computing the association with symptom severity as measured by the Hamilton Depression Rating Scale (HAM-D).

Methods

Participants

All participants were screened by Mini International Neuropsychiatric Interview (MINI) prior to participation, ensuring the absence of MDD in the HC group. In total, 48 medication-free MDD patients and 41 gender- and age-matched HC were recruited in the study (Table 1). Furthermore, the depression severity of MDD patients was assessed by professional psychiatrists at Nanjing Brain Hospital based on the HAM-D and the Diagnostic and Statistical Manual of Mental Disorders, fourth edition. Other inclusion criteria were no brain injury, cardiovascular disease and alcohol or drug abuse. All participants were right-handed (Li, 1983) and provided written informed consent prior to participation. The study was approved by the local ethics committee at Nanjing Medical University, affiliated Nanjing Brain Hospital, and was in line with the Declaration of Helsinki.

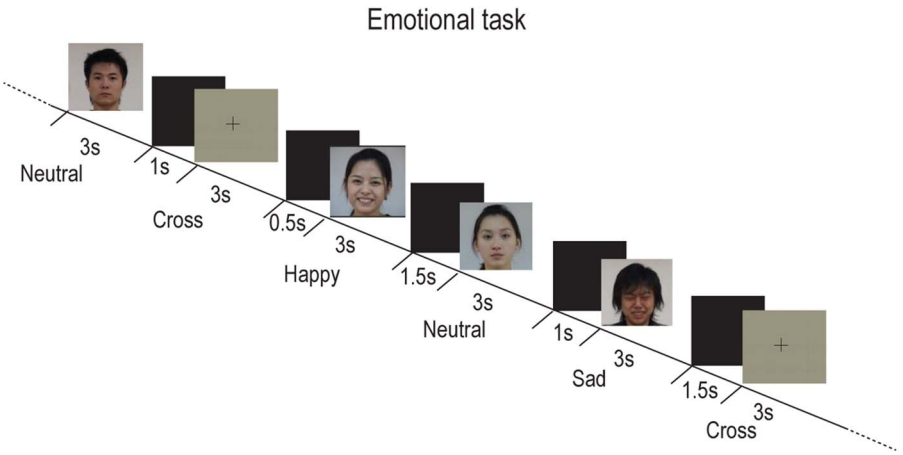

Fig. 1. Emotional task paradigm. Participants were presented with 3 s happy, sad or neutral facial emotion movie clips and instructed to indicate whether the presented stimulus was emotional or not.

Stimuli and task

Participants were engaged in a facial affect recognition task (Figure 1). Sad, happy and neutral facial expressions were selected from the Chinese Facial Expression Video System (Du *et al.*, 2007; Qing *et al.*, 2010; Lu *et al.*, 2013; Lu *et al.*, 2014). A representative video stimulus of 3 s displayed an actor performing a facial expression (sad, happy or neutral). There was also a rest condition during which a fixation cross was present. A representative trial began with an inter-trial interval of 1 ± 0.5 s followed by a 3 s facial expression video. Participants needed to indicate whether the presented expression was emotional (right-hand response) or not (left-hand response). Video stimuli were randomly presented with 20 trials per category.

Data acquisition

Data were recorded with a CTF275 MEG system (VSM MedTech, Coquitlam, BC, Canada) with a 1200 Hz sampling rate. Participants were examined in a seated position. Head motion tracking was used based on marker coils placed at nasion and left and right ear canal. If the head motion exceeded 5 mm compared to the starting point, subjects were instructed to adjust their head positions. Structural T1 MRI images were acquired by a 1.5 T GE system 3D gradient-echo pulse sequence. To allow offline MRI and MEG data co-registration, earplugs containing vitamin E were placed in the ear canals during MRI acquisition.

Data pre-processing and spectral analysis

All offline aspects of data analyses were performed using the MATLAB-based FieldTrip toolbox (Oostenveld *et al.*, 2011). First, 50 Hz power line noise was removed via notch filter following by removing non-zero DC components and compensating for low-frequency drifts. Trials dominated by increased variance due to channel jumps and movement were excluded by visual inspection. There was no significant difference in the number of rejected trials between two groups (MDD: 5.6 ± 4.1; HC: 4.7 ± 2.1). Subsequently, an independent component analysis (ICA) (Jung *et al.*, 2001) was performed and decomposed the data into 275 ICA components, which was equal to the number of MEG sensors. ICA components associated with eye movement and cardiac activity were rejected, and the number of rejected ICA components (MDD: 1.9 ± 1.0; HC: 2.0 ± 1.0) did not differ between groups. The time–frequency representation of power (TFR) was calculated for each trial and condition using fast Fourier transform. For frequencies below 40 Hz, an adaptive time window of 4 cycles per frequency (i.e. $\Delta T = 4/f$) multiplied by a Hanning taper was used. Power analyses of frequency above 40 Hz were estimated using three orthogonal Slepian tapers with a 200 ms fixed sliding window, resulting in a spectral smoothing of ~10 Hz.

Source analysis

Source estimates of oscillatory activity were performed utilizing dynamic imaging of coherent source beamforming technique (Gross *et al.*, 2001). A realistic single-shell head model was constructed based on individual anatomical MRI. An equidistant source model spanning the entire brain volume was constructed with a grid point resolution of 6 mm. Fostering group analyses such as grand averaging and statistical evaluation, individual source models were warped to a common Montreal Neurological Institute space. Subsequently, lead fields were computed for each grid point. Sensor-level cross-spectral density matrices and leadfields were used to construct spatial filers optimized for a given frequency band at a given location. Source activity was estimated by multiplying spatial filters with Fourier-transformed sensor-level data at each source location.

Statistical analysis

Non-parametric cluster permutation tests were performed at both sensor and source levels for the neural data (Maris and Oostenveld, 2007). Instead of treating each time, frequency and sensor/voxel index independently, this procedure forms clusters of neighboring time points, frequencies and sensors/voxels, thus effectively controlling for multiple comparison testing. Since there were group differences in RT, the RT was included as the covariate in the two-way analysis of covariance with factors group (MDD/HC) and valence (sad/happy/neutral). The *t*-statistic (e.g. MDD *vs* HC) or *F*-statistic (e.g. sad *vs* happy *vs* neutral) depending on the effects of interest was used as the test statistic, with a pre-defined threshold of $P < 0.05$. The sum of the *t* or

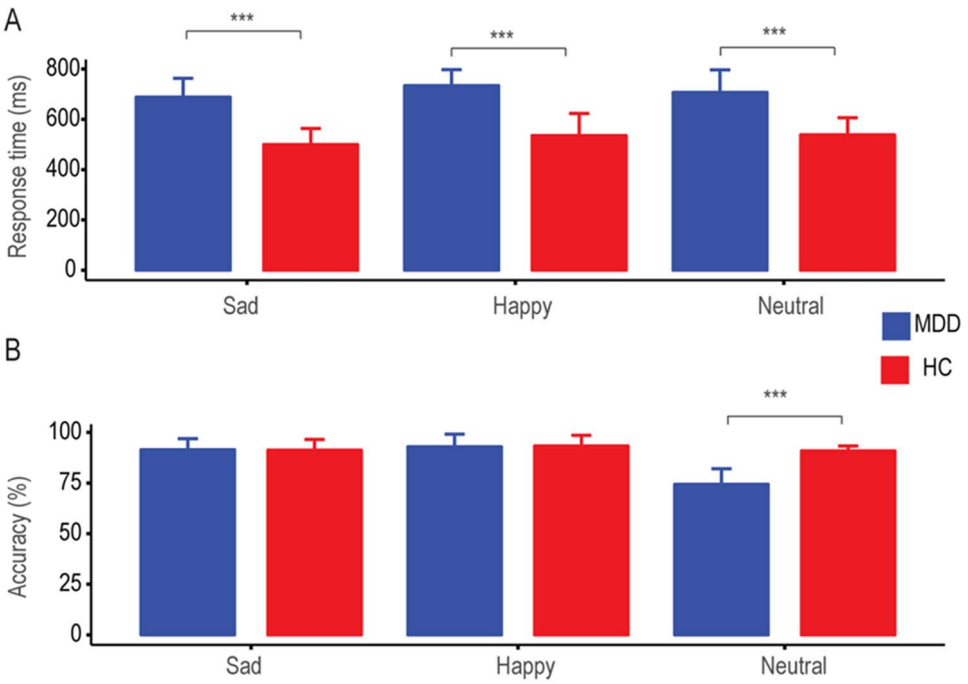

Fig. 2. Emotion task behavior results. (A) Response time. (B) Accuracy. Error bars indicate s.d. ***$P < 0.005$.

F values within a given cluster were defined as the cluster-level statistic. To obtain the reference cluster distribution, group labels were randomly shuffled 1000 times. For each shuffling, the clusters with maximum t or F values were used to create the reference distribution. Observed cluster statistic values exceeding the 95th percentile of the reference cluster distribution were considered as significant ($P < 0.05$). Examination of the relationship between power estimates and depression severity followed a similar procedure. The only difference herein was that the Spearman correlation coefficient was used as the test statistic. During each permutation, HAM-D values across MDD patients were shuffled.

Results

Increased RT and decreased accuracy judgment in MDD patients

Behavioral results during the emotional recognition task are illustrated in Figure 2. A 2×3 repeated measures analysis of variance with the factors group (MDD/HC) and valence (sad/happy/neutral), and response time as the dependent variable, revealed significant main effects for group ($F(1,261) = 397.9$, $P < 0.001$) and valence ($F(2,261) = 6.8$, $P < 0.01$). There was no group $\times$ valence interaction ($F(2,261) = 0.9$). Patients' reaction times were slower (neutral: 706.8 ± 89.8 ms; sad: 688.3 ± 75.1 ms; happy: 734.0 ± 64.0 ms) as compared to HC (neutral: 538.0 ± 68.4 ms, $t(87) = 9.8$, $P < 0.001$, $d = 2.1$; sad: 499.6 ± 63.9 ms, $t(87) = 12.6$, $P < 0.001$, $d = 2.7$; happy: 535.5 ± 87.8 ms, $t(87) = 12.3$, $P < 0.001$, $d = 2.6$) (Figure 2A). In terms of accuracy, there were significant main effects for group ($F(1,261) = 62.6$, $P < 0.001$), valence ($F(2,261) = 98.0$, $P < 0.001$) and group $\times$ valence interaction effect ($F(2,261) = 61.1$, $P < 0.001$) (Figure 2B). Specifically, MDD patients made more mistakes in their judgment of neutral stimuli ($74.4 \pm 7.7\%$) as compared to HC ($90.8 \pm 2.5\%$). As per hypothesis 1, MDD patients showed overall slower response times and lower facial recognition accuracies compared to HC.

Less sensorimotor beta suppression and more visual gamma modulations in MDD patients independent of facial expressions

At the neuronal level, there was a significant main group effect, but no main valence or group $\times$ valence interaction effects. Figure 3A and B illustrates the TFRs per group averaged across all conditions in the frequency range from 5 to 30 Hz. The power decrease of alpha/beta activity is apparent, starting around 0.3 s post-stimulus presentation in both groups. The non-parametric cluster permutation test revealed significant group differences in the beta band (20–30 Hz), predominantly over central–parietal sensors (Figure 3C and D, $P = 0.004$, non-parametric cluster approach). Source analysis confirmed the origin of this effect in the bilateral sensorimotor cortices (Figure 3E). In line with the RT results, MDD patients exhibited overall less beta activity suppression.

In the high-frequency range (40–150 Hz), the sustained increase of gamma band activity (40–80 Hz) was observed initiating around 0.25 s after stimulus presentation in both groups (Figure 4A and B). This increase was stronger in MDD as compared to HC participants, most prominently over occipital sensors (Figure 4C and D, $P = 0.002$, non-parametric cluster approach). Source analysis confirmed the primary generators within visual areas (Figure 4E). MDD patients were characterized by a general increase in the visual gamma band activity, independent of emotional valence.

Overall, MDD patients exhibited a general deficit with less beta suppression and stronger gamma power increase independent of the emotional valence. These power modulations had different spatial profiles, the former originating predominantly from sensorimotor regions and the latter mainly confined to visual regions. Evidence suggests that power–power modulations of oscillatory activity at different frequencies may, in fact, provide a mechanism of inter-areal communication. Thus, an exploratory analysis has been performed next to determine possible relationships in the context of the present task.

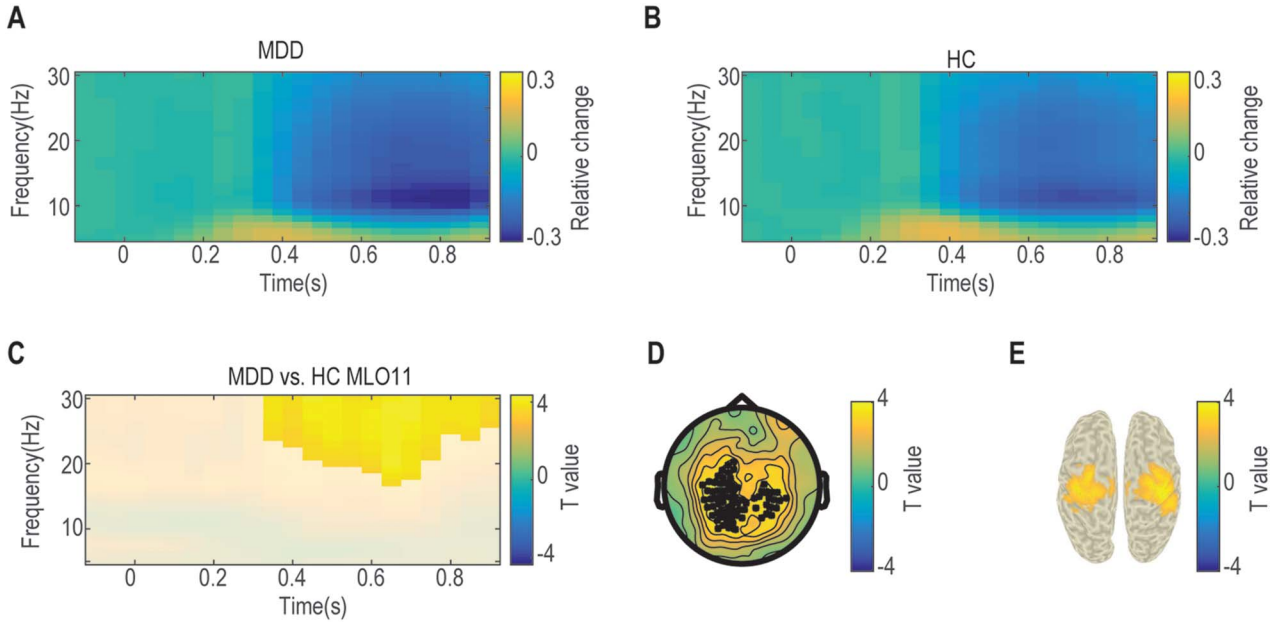

Fig. 3. Beta modulation (20–30 Hz) during facial affect processing. (A) Mean TFR of power over the marked sensors in the scalp topography across all conditions (sad/neutral/happy) for MDD. (B) The same as (A) but for HC. (C) Significant TFR group difference in the representative MLO11 sensor. (D) Scalp topography of the group differences in the beta band. The dots mark sensors belonging to the cluster identified by the cluster-based permutation test. (E) Source localization of the group difference in the beta band.

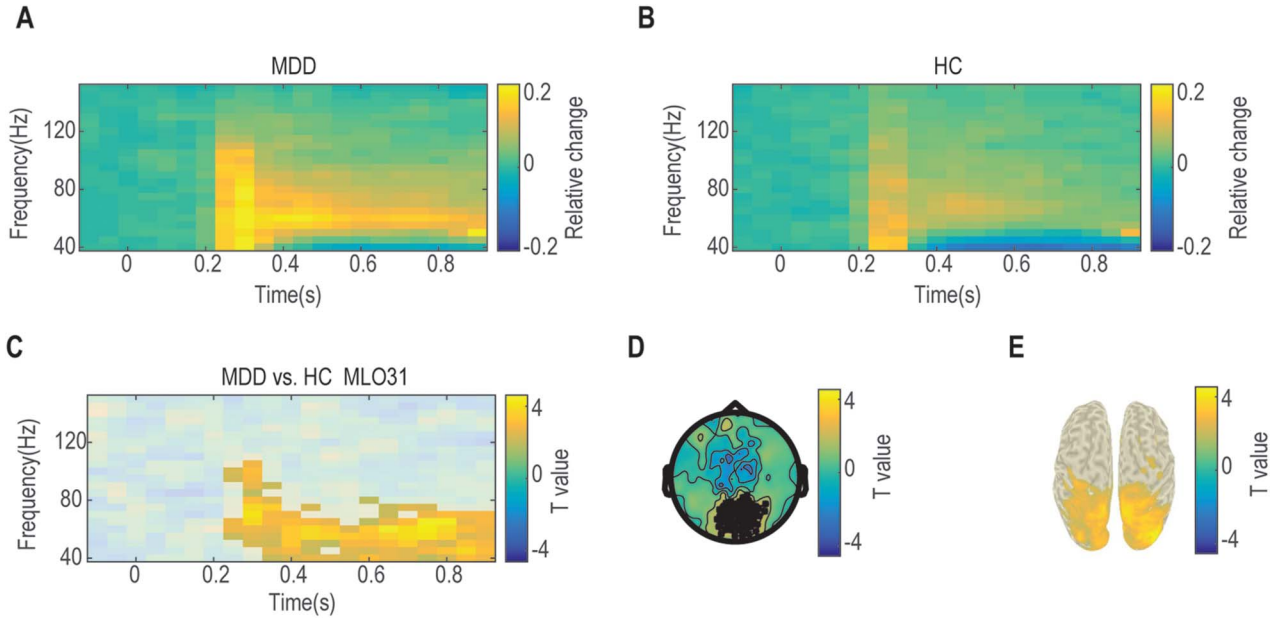

Fig. 4. Gamma modulation during facial affect processing. (A) Mean TFR of power over the marked sensors in the scalp topography across all conditions (sad/neutral/happy) for MDD. (B) The same as (A) but for HC. (C) Significant TFR group difference in the representative MLO31 sensor. (D) Scalp topography of the group differences in the gamma band. The dots mark sensors belonging to the cluster identified by the cluster-based permutation test. (E) Source localization of the group difference in the gamma band.

Sensorimotor beta and visual gamma activity are related between and within trials in HC but not in MDD patients

The beta–gamma Spearman correlations for MDD and HC at the group level are shown in Figure 5A. For each subject, relative changes of 20–30 Hz beta and 40–80 Hz gamma activity within the 0.3–0.8 s time window were averaged across all trials over the marked sensors in Figure 3D and Figure 4D, respectively. In the HC group, significant positive beta–gamma correlation ($r = 0.34$, $P = 0.03$) was found, while this was not the case in the MDD group ($r = -0.025$, $P = 0.82$) (Figure 5B). Homogeneity of the regression test confirmed the specificity of this relationship for the HC group. Examining trial-by-trial correlations between beta and gamma activity within each participant confirmed a significant group difference, as illustrated in Figure 5C (MDD: 0.06 ± 0.18; HC: 0.12 ± 0.17; $t(87) = -1.91$, $P < 0.05$). More precisely, 18.7%

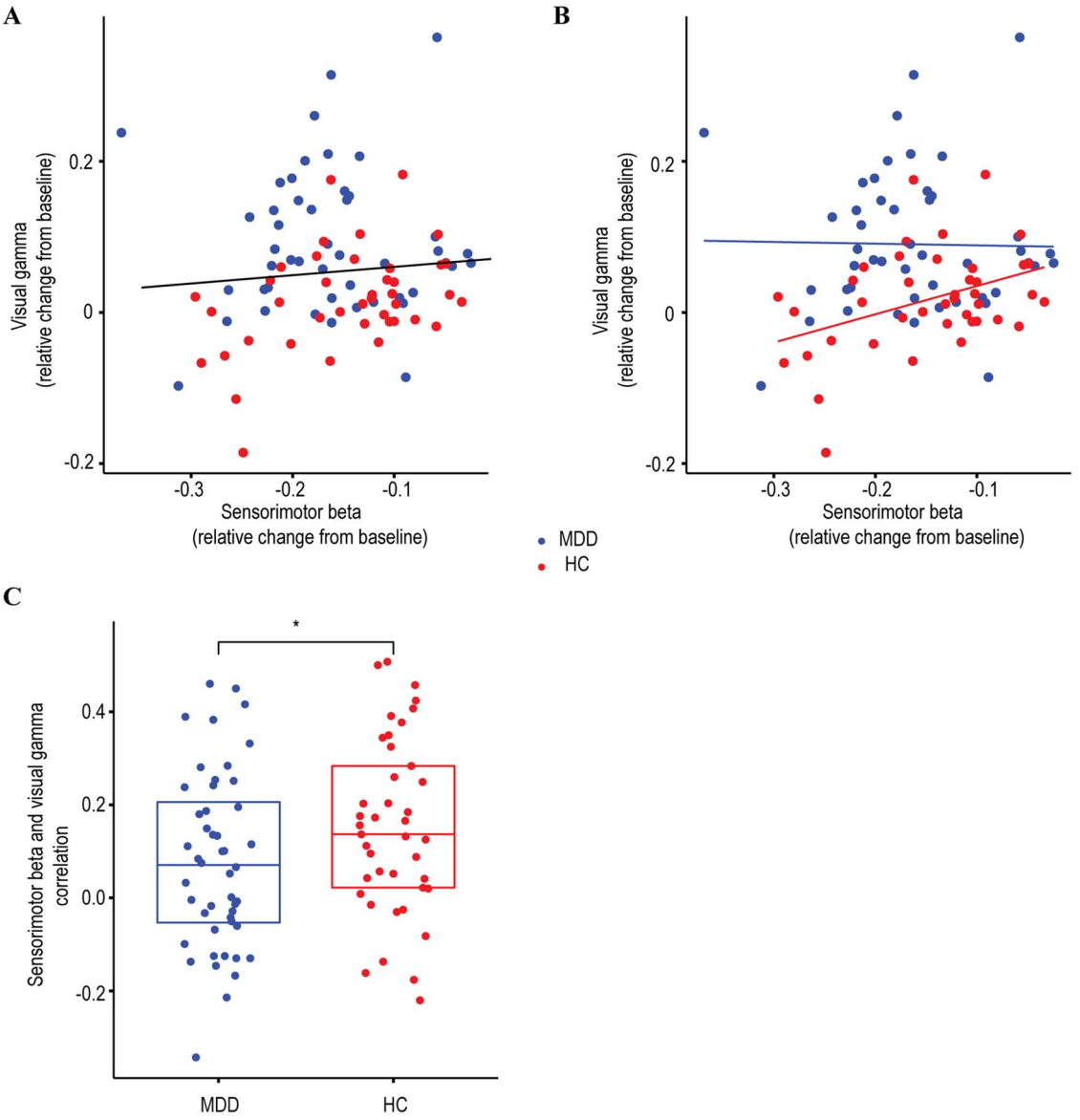

Fig. 5. Beta–gamma correlation. (A) Beta–gamma correlation across subjects for both MDD and HC groups ($r = 0.08$, $P = 0.4$). The relative changes from the pre-stimulus baseline of sensorimotor beta and visual gamma activity were averaged over the marked sensors in Figures 3D and 4D, respectively. (B) Beta–gamma correlation for MDD and HC group respectively (MDD: $r = -0.025$, $P = 0.82$; HC: $r = 0.34$, $P = 0.03$). (C) Within-subject beta–gamma correlation for MDD and HC, respectively. The middle line within the box indicates the mean and the boundary represented one s.d. $^*P < 0.05$.

(9 out of 48) of MDD patients had significant positive beta–gamma correlations, while 29.2% (12 out of 41) were found to display this correlation in HC participants.

Sensorimotor beta activity is related to response speed in HC but not in MDD patients

MDD patients showed overall slower RT on the behavior level accompanied by less sensorimotor beta suppression and more visual gamma modulations on the neural level. The relationship between RT and compromised power modulations was examined next (Figure 6A and B). Sensorimotor beta and visual gamma modulations were extracted in the same way as described above, and RT was pooled across sad, happy and neutral conditions. Significant negative sensorimotor beta RT correlation was found in HC ($r = -0.59$, $P < 0.001$) but not in MDD groups ($r = -0.21$, $P = 0.14$) (Figure 6C). This beta RT relationship was specific to the HC group, confirmed by the homogeneity of regression test. A positive gamma RT correlation was observed when pooling all participants together ($r = 0.38$, $P < 0.001$). Yet, this relationship could not be confirmed within the individual groups (Figure 6D).

Reduced frontal gamma activity relates to higher depression severity under positive facial expression

Finally, relationships between differentiated oscillatory changes (beta/gamma) over valence (sad/happy/neutral) and depression severity, as measured by the HAM-D score, were explored. There was no significant correlation identified in the beta band across all conditions. However, a significant negative correlation was found in the 40–80 Hz gamma range within 0.3–0.8 s time

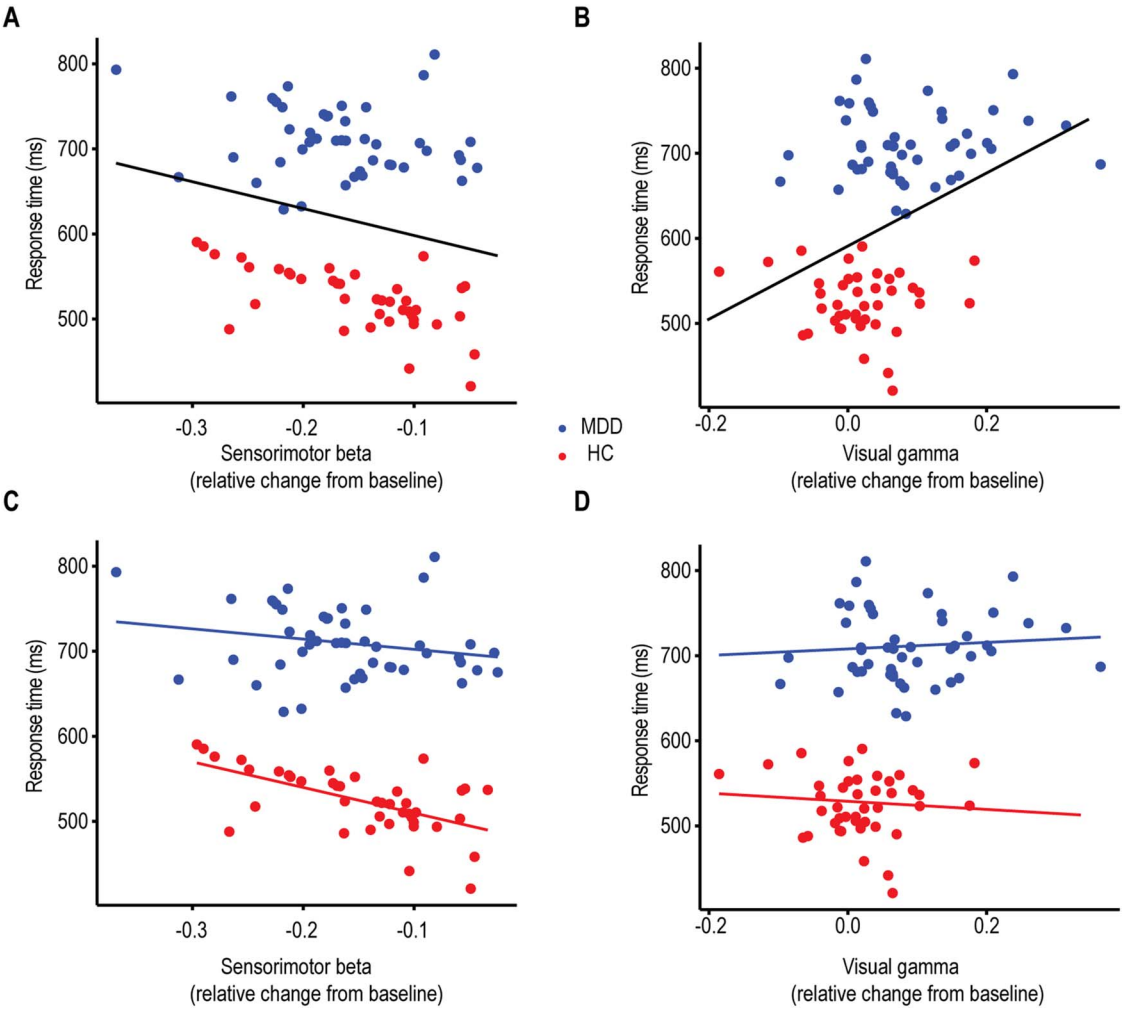

Fig. 6. Correlation between sensorimotor beta/visual gamma activity and response time. (A) Correlation between sensorimotor beta activity and response time for both MDD and HC groups ($r = -0.228$, $P = 0.031$). (B) Correlation between visual gamma activity and response time for both MDD and HC groups ($r = -0.38$, $P < 0.001$). (C) Correlation between sensorimotor beta activity and response time for MDD and HC groups, respectively (MDD: $r = -0.21$, $P = 0.14$; HC: $r = -0.59$, $P < 0.001$). (D) Correlation between visual gamma activity and response time for MDD and HC groups, respectively (MDD: $r = -0.08$, $P = 0.55$; HC: $r = -0.08$, $P = 0.58$).

window after stimulus onset under the happy facial expression condition ($r = -0.52$, $P < 0.001$). Note that the significance remains after Bonferroni correction with the number of frequency bands and emotional valence. This correlation effect was predominantly observed over frontocentral regions (Figure 7A). Moreover, no relationships were found under sad or neutral facial expression conditions (sad: $r = 0.068$, $P = 0.645$; neutral: $r = 0.002$, $P = 0.98$), indicating the effect was specific to the happy facial expression condition in the gamma band (Figure 7B).

Discussion

The present report examined oscillatory neural patterns related to mood-congruent perceptual bias in a sample of 48 patients diagnosed with MDD and 41 HCs. During the random presentation of video stimuli displaying actors expressing sad, happy and neutral facial expressions, participants had to identify the particular expression via button press. Relative to HC, MDD patients were characterized by an overall slowing in response times and an accuracy decrease in facial expression judgments. Independent of the emotional condition, perception of facial affect was associated with increased visual gamma band activity and less sensorimotor beta suppression. Power modulations of beta and gamma activity were found related across and on a trial-by-trial basis in HC but not in MDD patients. Moreover, the frontal gamma activity under positive emotional stimuli correlated inversely with depression symptom severity.

The present behavioral results are in line with the robust observation portraying a general reaction time decrease of patients diagnosed with MDD (Azorin *et al.*, 1995; Gorwood *et al.*, 2014). Besides, present neuromagnetic findings suggest that these behavioral deficits are preceded by a compromised ability to modulate sensorimotor beta activity. It is well-established that sensorimotor beta modulation parametrically relates to response speed (Senkowski *et al.*, 2006; van Ede *et al.*, 2011; Popov *et al.*, 2018a; Popov *et al.*, 2018b). It is conceivable that maladaptive changes in cerebral organization manifest into a compromised ability to modulate sensorimotor beta rhythm. Consequently, the correlation between RT and sensorimotor beta modulation was impaired in the MDD group while it was intact in the HC group. Therefore, less sensorimotor beta suppression in MDD may indicate patients' compromised ability to facilitate perception. In relation to emotion processing,

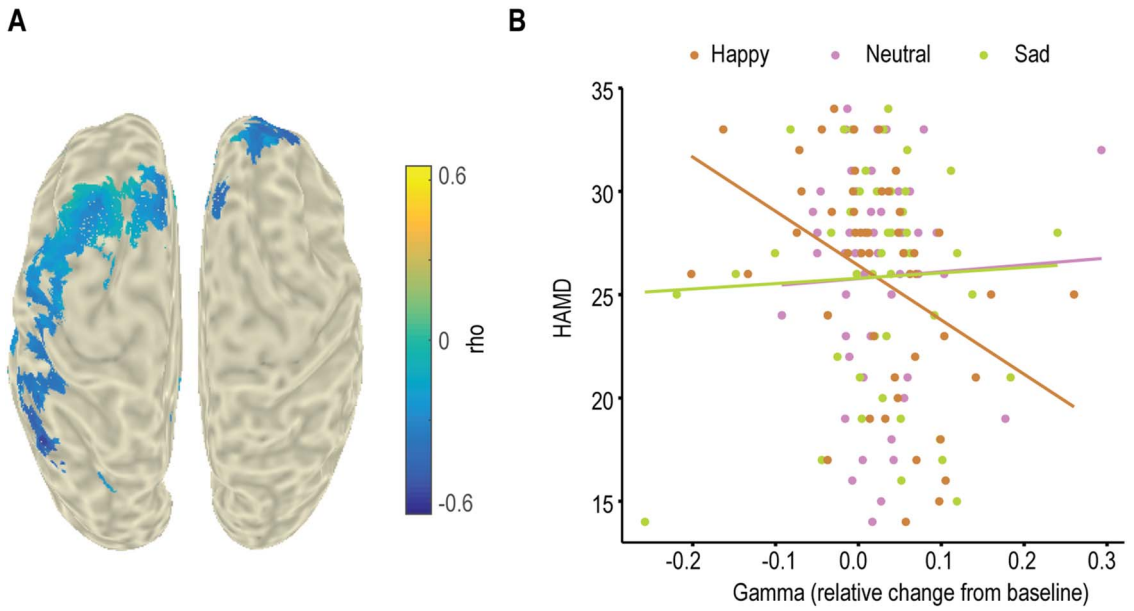

Fig. 7. Correlation between 40–80 Hz gamma activity and HAMD scores within the 0.3–0.8 s time window after stimulus presentation. (A) Regions characterized by a significant negative correlation during the happy condition. (B) Scatterplot of the relationship for each individual condition: sad ($r = 0.068$, $P = 0.645$), happy ($r = -0.52$, $P < 0.001$) and neutral ($r = 0.002$, $P = 0.98$) conditions. Gamma activity was averaged across regions identified in (A).

it has been shown that processing of emotional stimuli is associated with decreased beta band and increased gamma band activity in MDD patients, with a main effect of valence for event-related desynchronization in the beta frequency range (Huebl *et al.*, 2016; Merkl *et al.*, 2016). Reductions in M/EEG beta power are commonly interpreted as the result of desynchronized underlying neuronal activity (Pfurtscheller and Lopes da Silva, 1999), allowing for sensory input processing. It has also been suggested that beta power decreases reflect the degree of information that needs to be encoded (Hanslmayr *et al.*, 2012). Thus, less sensorimotor beta suppression in MDD might lead to compromised information encoding, resulting in disruption of multimodal integration critical for emotional processing.

Gamma activity has been suggested to be critical in feature binding and perceptual closure processes (Tallon *et al.*, 1995; Grutzner *et al.*, 2010). In line with this, the exaggerated visual gamma activity in MDD independent of emotional conditions may reflect bottom-up overcompensation deficit, manifesting in overextrapolation and binding of elementary facial features into a coherent percept. Besides, increased gamma power following emotional stimuli has been demonstrated in MDD patients (Siegle *et al.*, 2010; Yamamoto *et al.*, 2018), potentially related to higher arousal and cognitive reactivity. It is conceivable that an excess of visual gamma activity might reflect a hyperarousal in MDD patients when confronted with emotional stimuli. Furthermore, present exploratory analyses suggest a potential clinical relevance of gamma activity reflected in the negative correlation between frontal–central gamma activity of positive emotional processing and depression severity in MDD. Systematic reviews indicate a 'hyperactivation' to negative and 'hypoactivation' to positive stimuli in MDD (Stuhrmann *et al.*, 2011). Thus, less frontal gamma activity might represent diminished pre-frontal control processes such that the existing negative relationship with psychopathology may reflect the manifestation of the hypothesized 'hypoactivation'. Moreover, it should be noted that HCs were not screened with HAM-D after using MINI examination to ensure that they were not depression patients. Nonetheless, it is possible that some depression symptoms could still be evident in the HC group. Thus, future research should address the specificity of the present relationship between frontal–central gamma connectivity and depression severity in the HC group as well.

A growing body of literature highlights that slow and fast oscillations are not independent but interacting: a phenomenon termed cross-frequency coupling (Jensen and Colgin, 2007; Jiang *et al.*, 2015; Park *et al.*, 2016). This phenomenon is considered a fundamental mechanism facilitating functional interactions both within and across cortical networks. Several studies have reported stimulus-induced gamma activity increase accompanied by alpha/beta activity decrease (Bauer *et al.*, 2014; Michalareas *et al.*, 2016; Popov *et al.*, 2018a), reflecting the overall involvement level of task-relevant cortical areas. In the present report, Spearmen correlations between averaged sensorimotor beta suppression and visual gamma modulations were calculated. This relationship was evident in HC but missing in MDD both across and between trials, suggesting that inter-areal communication between sensorimotor and visual areas might constitute a compromised connectivity pattern manifesting in patients during the facial affect judgments.

In conclusion, present findings demonstrate that perceptual biases in MDD are related to distinct spatial and spectral disruptions, including sensorimotor beta and visual gamma band responses. Exploratory analyses revealed candidate spectral markers of compromised valence processing in addition to a robust relationship to disease severity. Future work is needed to confirm these exploratory findings and potentially extend them toward an integrated connectivity framework (Jiang *et al.*, 2019), accounting for abnormal facial affect processing in affective disorders.

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Conflict of interest. None declared.

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