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Major Depression and the Perception of Affective Instrumental and Expressive Gestures: An fMRI Investigation

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ABSTRACT

Major depressive disorder (MDD) is associated with biased perception of human movement. Gesture is important for communication and in this study we investigated neural correlates of gesture perception in MDD. We hypothesised different neural activity between individuals with MDD and typical individuals when viewing instrumental and expressive gestures that were negatively or positively valenced. Differences were expected in brain areas associated with gesture perception, including superior temporal, frontal, and emotion processing regions. We recruited 12 individuals with MDD and 12 typical controls matched on age, gender, and handedness. They viewed gestures displayed by stick figures while functional magnetic resonance imaging (fMRI) was performed. Results of a random effects three-way mixed ANOVA indicated that individuals with MDD had greater activity in the right claustrum compared to controls, regardless of gesture type or valence. Additionally, we observed main effects of gesture type and valence, regardless of group. Perceiving instrumental compared to expressive gestures was associated with greater activity in the left cuneus and left superior temporal gyrus, while perceiving negative compared to positive gestures was associated with greater activity in the right precuneus and right lingual gyrus. We also observed a two-way interaction between gesture type and valence in various brain regions.

1. Introduction

Major depressive disorder (MDD) is a common mental disorder characterised by depressed mood (American Psychiatric Association, 2013). According to Beck's cognitive model of depression (Beck, 2008, 1976; Beck and Haigh, 2014), interactions between cognitive processes and adverse environmental factors can create negative schemata that guide the development of cognitive biases. Individuals with MDD frequently experience biased social and emotional processing, meaning they are more aware of the negative aspects of their social environment (Disner et al., 2011; Weightman et al., 2014). Interpretation biases are also common; individuals with MDD construct more negative than positive mental representations to resolve ambiguous information, such as emotions (Everaert et al., 2017; Lee et al., 2016; Nieto et al., 2020). These cognitive biases contribute to problems with communication and social functioning (Kessler and Bromet, 2013; Kupferberg et al., 2016; Weightman et al., 2014) and they contribute to the maintenance and recurrence of MDD (Everaert et al., 2014; Orchard and Reynolds, 2018). Therefore, a comprehensive understanding of cognitive biases in MDD is important to inform assessment and treatment (e.g., Kupferberg et al., 2016).

Behavioural studies that investigate cognitive biases in MDD have predominantly examined how social information (e.g., emotion) is processed from static facial expressions (Loi et al., 2013). Their findings commonly indicate impairments in emotion recognition and mood-congruent biases, meaning that perception is influenced by one's emotional state (Dalili et al., 2015; Joormann and Gotlib, 2006; Penton-Voak et al., 2017). Although there are investigations of gesture

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production in MDD (Pavlidou et al., 2021), the processing of human movement is less frequently investigated in MDD (Okruszek, 2018). Human movement, also referred to as biological motion (BM), is fundamental for effective communication of social intentions and emotions (Jaywant et al., 2016; Miller and Saygin, 2013; Pavlova, 2012). The importance of BM for human communication is illustrated by the ability of typical individuals to extract BM information from sparse visual point-light displays (PLDs), that portray human movement using a few light points located at major joints (Bachmann et al., 2021; Johansson, 1973).

1.1. BM Perception in MDD and Other Disorders

Individuals with MDD, however, present biased BM perception (Okruszek, 2018). Loi et al. (2013) instructed participants with MDD, participants with a history of MDD in remission, and typical control participants to recognise emotions (i.e., happiness, sadness, fear or anger) or a neutral state from BM stimuli depicted by PLDs. Individuals with MDD had a reduced ability to recognise happiness compared to the other groups. Similarly, Kaletsch et al. (2014) instructed participants with MDD and typical control participants to observe videos illustrating positive (i.e., expressing joy or love) or negative (i.e., expressing anger or sadness) human interaction depicted by PLDs. Compared to control participants, participants with MDD rated the interactions more negatively, gave negative emotions more intense ratings and were more confident in these ratings. Thus, there is behavioural evidence for cognitive biases in BM perception in MDD.

However, this field of research is in its early stages compared to the study of BM perception in other disorders associated with social processing biases or impairments (Okruszek, 2018; Okruszek and Pilecka, 2017; Pavlova, 2012; Todorova et al., 2019). In their meta-analysis, Todorova et al. (2019) indicated that individuals with autism spectrum disorder frequently have difficulties with BM perception and interpretation, particularly when the BM stimuli convey higher order, complex information (e.g., emotion). Additionally, typical individuals show greater activity in brain regions associated with human motion and action observation (e.g., superior temporal gyrus; STG) during BM perception than individuals with autism. Individuals with schizophrenia spectrum disorder also experience difficulties with BM perception, associated with the functioning of the superior temporal sulcus (STS) (Okruszek and Pilecka, 2017), which is a region frequently implicated in BM perception (Grosbras et al., 2012; Pavlova, 2012). Thus, there is evidence for altered neural activity during BM perception in disorders other than MDD that are characterised by social processing biases or impairments.

1.2. Gesture

Gestures, a subtype of BM involving arm and hand movements, are particularly important for the communication of social information (Bachmann et al., 2020; Fourie et al., 2020; Yang et al., 2015). Intransitive gestures are non-object related and directed towards an observer for the purpose of communication (Balconi et al., 2021; Bartolo et al., 2019). There are multiple subtypes of intransitive gestures, including instrumental gestures that indicate instructions (e.g., “Come here”) and expressive gestures that indicate an individual’s inner state (e.g., “I am angry”) (Gallagher and Frith, 2004). Importantly, in this study we only focus on gestures not accompanied by speech or writing.

1.3. Neural Correlates of Gesture Perception

Generally, gesture perception in typical individuals is associated with neural activity in temporal regions, including the STS and STG (Yang et al., 2015). More specifically, a study by Gallagher and Frith (2004) indicated that the perception of instrumental gestures was associated with activity in the left inferior and middle frontal cortex, which are areas implicated in the left lateralised language and mirror neuron network. Perceiving expressive gestures was associated with activity in areas involved in social cognitive processing, including the anterior paracingulate cortex, amygdala, bilateral temporal poles, and right STS. These results suggest different neural networks are involved in the processing of instrumental and expressive gestures.

An important point to consider about gesture is its affective valence. In real-world settings, instrumental or expressive gestures often have an associated valence that influences perception (de Gelder, 2006; Flaisch et al., 2009; Yang et al., 2015). In typical individuals, perceiving meaningful, valenced gestures is associated with activity in the inferior frontal gyrus, insula and putamen (Yang et al., 2015). Lotze et al. (2006) investigated the processing of positive and negative gestures in typical participants. Valence ratings for negative intransitive gestures (e.g., threatening with the fist) were positively associated with right STS activity. Overall, valence ratings were positively associated with left ventrolateral prefrontal cortex (vlPFC) activity, a region involved in emotion perception and stimulus selection (Disner et al., 2011). In contrast to Lotze et al. (2006), Flaisch et al. (2009) investigated valenced gesture perception using gesture stimuli without facial expressions. Perceiving positively or negatively valenced gestures (i.e., up-raised thumb or up-raised middle finger, respectively) compared to neutral gestures (i.e., forefinger pointing horizontally) was associated with activity in striate and extrastriate areas, including the cuneus and middle occipital gyrus. This implies that valenced gestures capture visual attention.

The aforementioned brain regions associated with BM and gesture perception show aberrant activity in individuals with MDD during exposure to valenced social stimuli or cognitive tasks (see meta-analyses by Fitzgerald et al., 2008; Gray et al., 2020; Groenewold et al., 2013; Palmer et al., 2015; Pozzi et al., 2021). Processes required during these tasks, such as visual attention, are also required during gesture perception (e.g., Flaisch et al., 2009; Groenewold et al., 2013; Keller et al., 2019). Given behavioural evidence that perception of BM is affected by MDD it is important to examine how the neural correlates of gesture perception might differ between individuals with MDD and typical individuals.

While there is limited research into the neural correlates of gesture perception in MDD, Suffel et al. (2020) examined the processing of gestures in MDD. Participants watched videos of a speaking actor from different viewpoints, and the speech was sometimes accompanied by gesture. The activity in the anterior cingulate, bilateral superior/middle frontal cortex and the right angular gyrus was greater in individuals with MDD compared to a control group when they viewed the actor from the front compared to the side. From this data they concluded that processing gesture and body orientation requires greater neural resources for individuals with MDD. However, all stimuli used by Suffel et al. (2020) included gesture with speech, raising the important question of how neural correlates of perceiving gesture alone might be affected by MDD.

2. Current Study

Here, we investigated the neural correlates of gesture perception, independent of speech, in individuals diagnosed with MDD and typical individuals. This work could complement behaviour findings of Loi et al. (2013) and Kaletsch et al. (2014) and enhance an understanding of how social communication and social processing is affected in MDD. Aside from its theoretical importance, this knowledge could inform the development of diagnostic tools and treatments that include assessments of, and strategies to improve, social functioning in MDD (Kaletsch et al., 2014; Kubon et al., 2021; Kupferberg et al., 2016; Pandya et al., 2012; Weightman et al., 2014).

Specifically, we examined effects of group, gesture type, gesture valence and their interactions on the blood-oxygen-level-dependent (BOLD) signal using a whole brain analysis of functional magnetic

Table 1
Demographic characteristics of the groups. HRDS = Hamilton Rating Depression Scale; EHI = Edinburgh Handedness Index; NART = National Adult Reading Test; MDD = Major Depressive Disorder.

	Group		
	MDD Mean (*SD*)	Control Mean (*SD*)	Comparison Statistic
Gender	Eight women, four men	Eight women, four men	-
Age: Women	31.13 (9.66)	31.88 (9.49)	$t(14) = 0.16, p = .88$
Age: Men	36.75 (7.14)	37.75 (7.59)	$t(6) = 0.19, p = .85$
NART	117.5 (6.71)	120.75 (4.81)	$t(22) = 1.36, p = .19$
EHI	34.92 (1.44)	35.08 (1.56)	$t(22) = 0.27, p = .79$
HRDS	23.00 (5.72)	1.42 (1.73)	$t(22) = 12.51, p < .000001$

resonance imaging (fMRI) data. The effects of gesture type and valence were chosen because there is evidence that instrumental and expressive gesture type, as well as gesture valence, can modulate neural response in typical individuals (Flaisch et al., 2009; Gallagher and Frith, 2004; Lotze et al., 2006), but there is a lack of studies that consider the effects of both instrumental and expressive gesture type and valence. By including these factors, we advance understanding and methods for future studies of gesture processing and contribute to setting the groundwork for future studies to study the processing of gesture in greater detail. Furthermore, presenting individuals with MDD and typical individuals with displays of gestures of various types and valences allows for a holistic assessment of the neural correlates of gesture perception. Based on the presented behavioural and neuroscientific evidence, we expected a difference between neural activity of individuals with MDD and typical individuals when perceiving stimuli of negatively or positively valenced instrumental and expressive gestures. This could manifest in brain regions associated with gesture perception including the STS, STG, striate and extrastriate cortex, inferior and middle frontal cortex, amygdala, and insula.

3. Method

3.1. Participants

Twenty-eight English speaking individuals with a history of MDD were recruited via word-of-mouth and social media. The Structured Interview for Diagnosis DSM-IV (American Psychiatric Association, 1994) and the 21-item Hamilton Rating Scale for Depression (HRDS; Hamilton, 1960) were used to confirm their MDD diagnosis. Verbal IQ was measured using the National Adult Reading Test (NART; Nelson, 1982) and right-handedness was confirmed using the Edinburgh Handedness Inventory (EHI; Oldfield, 1971). Subsequently, 12 participants (M age = 33.00 years; $SD = 8.99$; range = 22–46) diagnosed with unipolar MDD and no comorbid disorders were invited to participate in the study, consisting of eight women (M age = 31.13 years; $SD = 9.66$) and four men (M age = 36.75 years; $SD = 7.14$). Of the excluded individuals, three were eliminated due to comorbid disorders, one currently did not have depression, three had contraindications for scanning, three had significant health issues, three were left-handed, two were non-native speakers and one failed to attend multiple scanning appointments. Seven participants were taking selective serotonin reuptake inhibitors, one participant was taking a tricyclic antidepressant and four participants were taking no MDD medication. Due to variability in the self-report of dosage and the small sample size we did not estimate a medication load index to use as a covariate (Enneking et al., 2019; Redlich et al., 2014). Using the same screening procedures, 12 control participants matched for age, gender, and handedness were recruited, consisting of eight women (M age = 31.88 years; $SD = 9.49$) and four men (M age = 37.75 years; $SD = 7.59$). See Table 1 for a summary of participant demographics.

The HRDS scores of the MDD group ranged from 15 to 32 ($M = 23.00$; $SD = 5.72$), with one participant scoring less than 17, six participants scoring between 17 and 23, and the remaining five participants scoring greater than 23. The scores in the control group ranged from 0 to 5 ($M = 1.42$; $SD = 1.73$). Independent t-tests on the means indicated no significant mean group differences in NART scores ($t(22) = 1.36$, $p = .19$) or EHI scores ($t(22) = 0.27$, $p = .79$), indicating that the participant groups were appropriately matched.

3.2. Ethics

The study was approved by the National Research Ethics Service and the Local Research Ethics Committee of the South Glasgow University Hospitals NHS Trust Ethics Committee. All participants provided written informed consent prior to commencing the study. A data-sharing agreement was arranged with the National Research Ethics Service and the South Glasgow University Hospitals NHS Trust Ethics Committee to accommodate transference and analysis of the data.

3.3. Paradigm

The study's paradigm was adapted from Gallagher and Frith (2004), but the stimulus type was changed. The stimuli used by Gallagher and Frith (2004) were short videos of actors depicted by full-light displays. Instead, the stimuli of this study were 3s animations of stick figures (i.e., PLDs with connected points) (Fig. 1), depicting a single actor miming an expressive or instrumental gesture that was positively, negatively, or neutrally valenced. Stick figures were used to minimize differences in

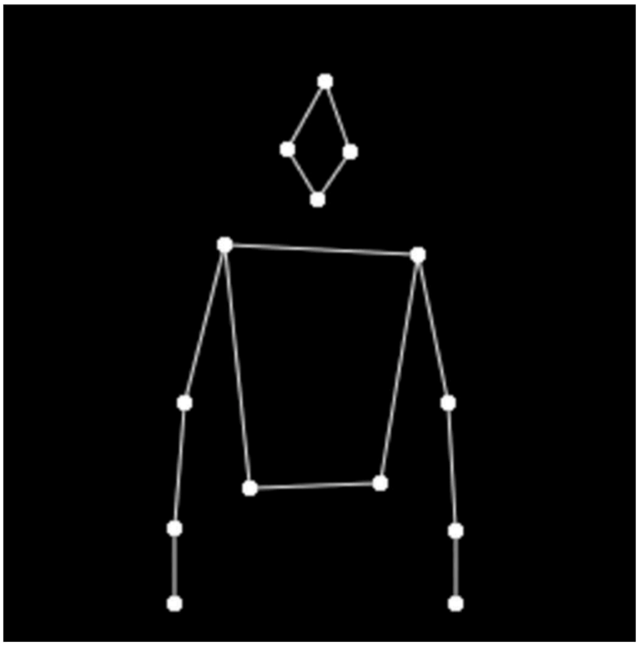

Fig. 1. Example of a still from a gesture animation depicted by a stick figure

luminosity and movement velocity across gesture displays and to control for non-kinematic and distracting social information (e.g., facial expressions and body shape) from influencing brain activity (Johansson, 1973; Kaletsch et al., 2014; Okruszek, 2018). The rationale being that by eliminating variability due to the processing of person surface properties in full-light displays we would have a more clear view of brain activity related to processing of affective body motion. To obtain the stimuli, 14 markers were placed on the bodies of two actors at their main joints. The recordings were obtained using a Qualysis infra-red motion capture system, which separately recorded each actor's body movements. Each gesture was repeated with the actor's right hand lifted higher, the left hand higher and with both hands at the same height. After pre-processing, pilot testing and further analysis of motion properties, the final 40 stimuli per gesture type were selected. Half were positively and half were negatively valenced (see Table 2 for examples). Control stimuli were scrambled stick figures that did not resemble human movement and only conveyed motion information. The participants viewed the stimuli in two experimental conditions, being "observe only" or "observe and recognise". Hence, a 2 (MDD vs. control) x 2 (expressive vs. instrumental) x 2 (negative vs. positive) x 2 (observe vs. observe and recognise) mixed design was originally employed.

3.4. Data Acquisition

A GE Signa 3 Tesla MRI system was used to acquire T1 weighted anatomical and echo-planar T2* weighted image volumes with BOLD contrast. The study used a hybrid short epoch/ event related design. Three 12-minute image runs were used to acquire the functional images (TR = 2700 ms, TE = 30 ms, each image volume contained 30 4.5 mm axial slices, and in-plane resolution = 3.75 mm x 3.75 mm of the whole brain). Each run consisted of 20 task blocks containing six stick figure animations. Hence, a total of 120 animations were presented in each run, consisting of 40 expressive gestures, 40 instrumental gestures and 40 control animations. The first four volumes of each run were discarded to allow for T1 saturation effects, leaving 768 volumes for analysis. The whole-brain anatomical data were acquired using a three-dimensional inversion-recovery-prepared fast-spoiled gradient sequence (IR-FSPGR; 160 slices, voxel size = 0.5078 mm x 0.5078 mm x 1.00 mm).

3.5. Procedure

Stimuli were presented on a translucent screen placed behind the fMRI scanner using an LCD projector linked to a computer. Participants viewed the screen via a 45-degree angled mirror that was positioned on the superior surface of the head coil. A test image was presented prior to the main scanning session to ensure that the image was in focus. The mirror was adjusted if necessary.

Prior to each task block, "Get Ready" was displayed on the screen for 1s, followed by either the question "Which hand is higher?" or "Is the gesture positive?". These questions defined the experimental conditions "observe only" and "observe and recognise", respectively. Subsequently, six gesture stimuli were displayed, each followed by a 2s display of a fixation cross. During the presentation of the fixation cross, participants used a two-button finger press box to indicate their answer to the previously displayed question. The right button represented the answer "right hand" or "positive gesture" and the left button "left hand" or "negative gesture". The order of stimuli presentation was counterbalanced per image run, and the order of each run was randomised across participants. Each scanning session took approximately one hour.

Table 2
Examples of gesture titles per stimulus category

Negative Instrumental	Positive Instrumental	Negative Expressive	Positive Expressive
No, you are wrong	Come over here	I am angry	I am blowing kisses
Do not do that	Fly away	I am cold	I feel full
Put it there	Kiss my cheek	I do not know	I salute you
What time do you call this?	Stand up	I am scared	I am touched
That is enough	Turn around	I am pleading	I want a hug

3.6. Data Pre-Processing

BrainVoyager QX [Version 2.3] (Brain Innovation, Maastricht, The Netherlands; Goebel et al., 2006) was used to pre-process the data using a standard pipeline. The anatomical data of each participant were transformed using iso-voxel scaling and corrected for spatial intensity inhomogeneities. This procedure also removed the skull. Anatomical data were aligned with the anterior commissure – posterior commissure (AC-PC) plane and subsequently transformed into Talairach standard space (Talairach and Tournoux, 1988) to facilitate intersession and intersubject comparisons. The transformed anatomical data for all participants were combined for an average template of the participants' anatomical data.

Sinc-interpolated three-dimensional motion correction was applied to the functional data to correct for small head movements and scans were discarded if a participant moved > 3 mm along any dimension (x, y, or z). Slice-scan time correction using sinc-interpolation was applied to correct for different slice scan timings. High-pass filtering using fast fourier transform (three cycles) removed low frequencies (i.e., signal drifts) to improve the statistical power. Functional and anatomical data were co-registered using a two-stage co-registration process, consisting of initial rough co-registration of the data followed by further translations and rotations for final refinements. Subsequently, four-dimensional functional volume time course data files were created with a resulting voxel resolution of 3×3×3 mm. To account for intersubject variability, these functional data were smoothed with a Gaussian filter (FWHM = 6 mm). Functional data of one run of a participant in the MDD group were excluded prior to the analysis due to data corruption during data collection.

3.7. Statistical Analysis

After pre-processing, BrainVoyager [Version 21.4.5] (Brain Innovation, Maastricht, The Netherlands; Goebel et al., 2006) was used for further statistical analyses of the fMRI data. Data were collapsed across experimental condition ("observe only" and "observe and recognise"), because preliminary analyses of the data did not indicate an effect of this factor.

A first level analysis was performed on data from the multiple runs of the individual participants. For each run, the time course of stimulus presentation was used in a multiple linear regression of the blood oxygenation level dependent (BOLD)-response time course in each voxel, using the four predictors of gesture type and valence (Negative Instrumental, Positive Instrumental, Negative Expressive, Positive Expressive). Predictors' time courses were adjusted for the haemodynamic response delay by convolution with a haemodynamic response function. The resulting analysis resulted in statistical maps that contained the beta values (i.e., effect estimates) for each participant for each stimulus category.

For the second level analysis a random effects three-way mixed ANOVA was conducted on the beta values to examine the effect of group (MDD vs. control), gesture type (instrumental vs. expressive), gesture valence (negative vs. positive) and their interactions. Results were overlaid on the average anatomical data of all participants. The uncorrected voxel-level threshold was set at $p < .0005$ and cluster thresholding was applied to correct for multiple comparisons (see Müller et al., 2017; Woo et al., 2014). Cluster thresholding rests on the assumption that brain activity relates to BOLD signal changes over adjacent clusters of voxels rather than isolated voxels (Forman et al., 1995; Goebel et al., 2006; Woo et al., 2014). Cluster-level false-positive rates were estimated using Monte Carlo simulations (1000 iterations). The statistical maps were thresholded using the minimum cluster size that generated a cluster-level false positive rate of 5%, and were arranged and saved in volume map files. The clusters of the statistical maps were converted to regions of interest. Beta values for each stimulus category were extracted and visually inspected using R [Version 4.0.2] (R Core Team, 2020) with RStudio [Version 1.3.1093] (RStudio Team, 2020) package tidyverse (Wickham et al., 2019) to determine the directionality of the results.

4. Results

The whole brain analysis results from the random effects 2 (group: MDD vs. control) x 2 (gesture type: instrumental vs. expressive) x 2 (gesture valence: negative vs. positive) mixed ANOVA conducted on the beta values are shown in Table 3.

4.1. Main Effect of Group

The mixed ANOVA demonstrated a main effect of group for the right claustrum (Table 3; Fig. 2). Inspection of the beta values indicated greater activity for participants with MDD compared to control participants, suggesting that participants with MDD had greater activity in the right claustrum when perceiving gesture stimuli depicted by stick figures, regardless of gesture type or valence. The ANOVA results supported no other effects involving group differences or interactions.

4.2. Other Main Effects and Interactions

Furthermore, the ANOVA results supported main effects of, and a two-way interaction between, gesture type and gesture valence.

4.2.1. Main Effect of Gesture Type

The mixed ANOVA indicated a main effect of gesture type (Table 3; Fig. 3). Visual inspection of the beta values showed greater activity in the left cuneus and left STG when the participants viewed instrumental compared to expressive gestures.

4.2.2. Main Effect of Gesture Valence

Additionally, the mixed ANOVA supported a main effect of gesture valence (Table 3; Fig. 4). Visual inspection of the beta values indicated greater activity in the right precuneus and right lingual gyrus when the participants viewed negative compared to positive gestures.

4.2.3. Interaction Between Gesture Type and Gesture Valence

Lastly, the mixed ANOVA demonstrated a two-way interaction between gesture type and gesture valence for the right precuneus, right lingual gyrus, right paracentral lobule, left cingulate gyrus, right brainstem and left declive (Table 3; Fig. 5). Visual inspection indicated greater activity in these areas when the participants viewed negative instrumental gestures compared to positive instrumental gestures, while those differences appeared less pronounced between negative expressive and positive expressive gestures (Fig. 6). The results of the mixed ANOVA supported no other interactions.

5. Discussion

This study investigated the neural activity of individuals with MDD and typical individuals during the perception of negatively or positively valenced instrumental and expressive gestures. As hypothesised, the mixed ANOVA results indicated a difference between the neural activity of individuals with MDD and typical individuals. This result was in line with behavioural evidence from existing research indicating differences in BM perception between individuals with MDD and typical individuals (Kaletsch et al., 2014; Loi et al., 2013). However, those behavioural findings were related to stimulus valence; individuals with MDD showed a reduced ability to recognise happiness from BM stimuli (Loi et al., 2013), and tended to rate negative emotions from BM stimuli more negatively (Kaletsch et al., 2014). These valence-related results were not corroborated by the current study, as no interaction effect between group and gesture valence was found. As will be discussed later, this might be related to the study's small sample size. Overall, no interactions involving group effects were identified.

We expected that a group effect might manifest in a brain area associated with gesture perception, such as the STS, STG, striate and extrastriate cortex, inferior and middle frontal cortex, amygdala, or insula. However, the identified group effect was not associated with those proposed areas, but with a region adjacent to the insula, the right claustrum. The right lateralisation of this activity was consistent with the right hemisphere superiority in biological motion perception (Pavlova, 2012; Servos et al., 2002) and visuospatial attention (Rosch et al., 2012; Sanefuji et al., 2018; Spagna et al., 2020; Zago et al., 2017). However, to the best of our knowledge, there are no studies investigating the function of the claustrum in gesture perception or MDD. Therefore, we outline two main functions of the claustrum and propose its role in gesture perception and MDD.

Table 3
Main and interaction effects. BA = Brodmann Area; R = right; L = left.

Brain Area	Peak Talairach Co-ordinates (mm)			BA	Cluster Size	F(1, 22)	p-value
	x	y	z		(n Voxels)		
Group							
MDD > Control							
R Claustrum	30	-16	19		358	30.961	0.000014
Gesture Type							
Instrumental > Expressive							
L Cuneus	-15	-88	7	17	9225	54.342	<0.000001
L Superior Temporal Gyrus	-45	-28	1	22	364	28.616	0.000023
Gesture Valence							
Negative > Positive							
R Precuneus	12	-67	19	31	1364	38.900	0.000003
R Lingual Gyrus	12	-76	-5	18	1654	31.153	0.000013
Type x Valence							
R Precuneus	18	-70	22	31	538	26.393	0.000038
R Lingual Gyrus	18	-82	-11	18	467	24.637	0.000058
R Paracentral Lobule	9	-25	49	6	408	28.625	0.000023
L Cingulate Gyrus	-6	-37	37	31	973	30.973	0.000014
R Brainstem	3	-31	-11		472	26.122	0.000040
L Declive	-24	-88	-20		513	35.183	0.000006

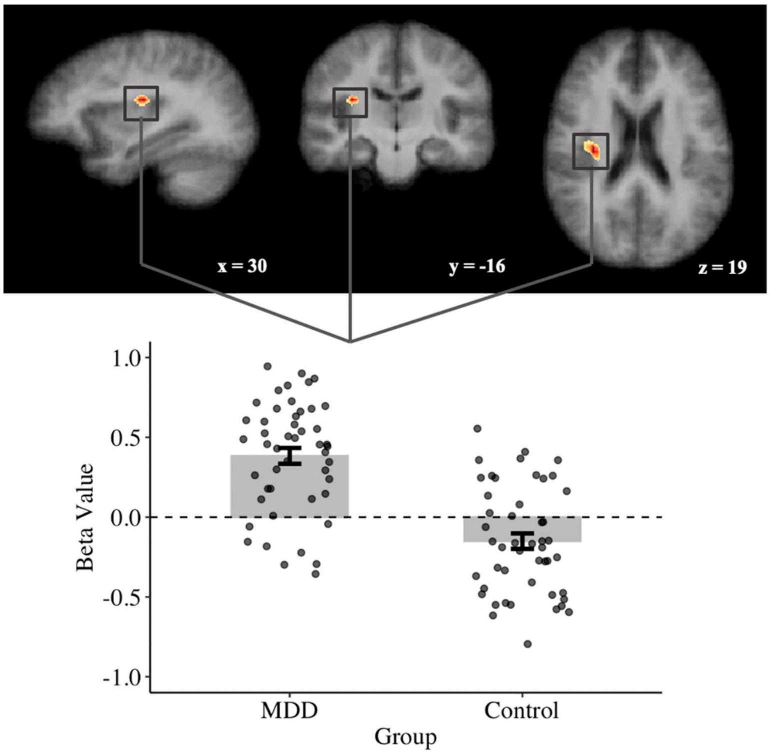

Fig. 2. Main effect of group (MDD vs. control). Top: Sagittal, coronal, and transverse slices in radiological convention (left hemisphere on the right) depicting significant activation in the right claustrum ($p < .0005$ uncorrected, $p < .05$ cluster-threshold corrected), associated with the main effect of group. Data are shown on the average template of the participants' anatomical data. Bottom: Bar plot indicating the mean beta value associated with the right claustrum per group with scatter depicting the individual participant beta values collated over gesture type and valence, with error bars depicting the standard error of the mean (*SEM*).

5.1. *Claustrum as a Connectivity Hub*

The claustrum is a thin, subcortical structure located between the insula and putamen, occupying 0.25% of the cerebral cortex volume (Benarroch, 2021; Smith et al., 2019). It has reciprocal functional connections with sensorimotor, associative and frontal areas, particularly the cingulate gyrus (Benarroch, 2021; Chia et al., 2020; Smith et al., 2020). Additionally, the claustrum receives input from limbic and subcortical structures, including the insula, basolateral amygdala, hippocampus and thalamus (Benarroch, 2021; Chia et al., 2020; Smith et al., 2020). Hence, the claustrum can be considered a connectivity hub, potentially supporting the association of sensory, motor and limbic information, or directing attention during gesture perception (Goll et al., 2015; Smith et al., 2019).

5.1.1. *Associating Sensory, Motor and Limbic Information*

The claustrum appears involved in associating sensory, motor and limbic information, which might be relevant for gesture perception (Benarroch, 2021; Bernstein et al., 2016; Crick & Koch, 2005; Koubeissi et al., 2014; Mathur, 2014; Smith et al., 2020; Stiefel et al., 2014). The claustrum expresses feedforward inhibitory control over the cortex, limiting activity in cortical regions and synchronising spike timings, which facilitates interareal brain communication and integration of cortical activity (Benarroch, 2021; Chia et al., 2020; Jackson et al., 2020, 2018). Subcortical input could enhance or suppress the claustral inhibitory output (Smith et al., 2020). Altogether, this supports the conjecture that the claustrum functions as a conductor of various cortical areas (Crick and Koch, 2005).

The greater claustrum activity we found for participants with MDD compared to control participants could reflect a greater effort to associate sensory, motor and limbic information during gesture perception, such as visual form, motion and valence information. This is in line with recent behavioural evidence that face recognition is associated with visual perceptual organisation in individuals with MDD, while face recognition is associated with top-down social cognition in typical individuals (Kubon et al., 2021). Considering that social processing biases and interpretation biases are well-established characteristics of MDD (Disner et al., 2011; Everaert et al., 2017; Weightman et al., 2014), the greater claustrum activity might represent an additional, or potentially compensatory, mechanism supporting the processing of the valenced expressive and instrumental gestures into one conscious percept.

5.1.2. *Salience Processing and Attention*

Recent evidence also emphasises the involvement of the claustrum in bottom-up salience processing and top-down attention, which are functions closely related to the integration of sensory, motor and limbic information, and functions necessary for gesture perception (Benarroch, 2021; Smith et al., 2020). The cingulate cortex and insula form the salience network, which directs bottom-up attention towards the most relevant (i.e., salient) sensory input (Goll et al., 2015; Seeley et al., 2007; Smith et al., 2019). Recent evidence, however, suggests that the claustrum is connected to the cingulate cortex and is part of the salience network, but that the claustrum also directs top-down attention (Arrigo et al., 2019; Atlan et al., 2018; Goll et al., 2015; Smith et al., 2020; White et al., 2018). Specifically, frontal cortical regions send top-down 'attentional strategies' to the claustrum, modulating inhibitory claustral projections to cortical regions (Benarroch, 2021; Goll et al., 2015; Smith et al., 2020). Salient sensory input to the claustrum from sensory, limbic and subcortical regions could override attentional strategies, relocating attention to novel, salient information (Goll et al., 2015).

Biased salience processing of negative stimuli is an established characteristic of MDD (Kaletsch et al., 2014; Keller et al., 2019; Loi et al., 2013; Menon, 2011). However, this negativity bias does not explain the lack of a modulatory effect of gesture valence in the group results. Instead, the greater claustrum activity could reflect a general attention bias in MDD (see Keller et al., 2019). For instance, individuals with MDD

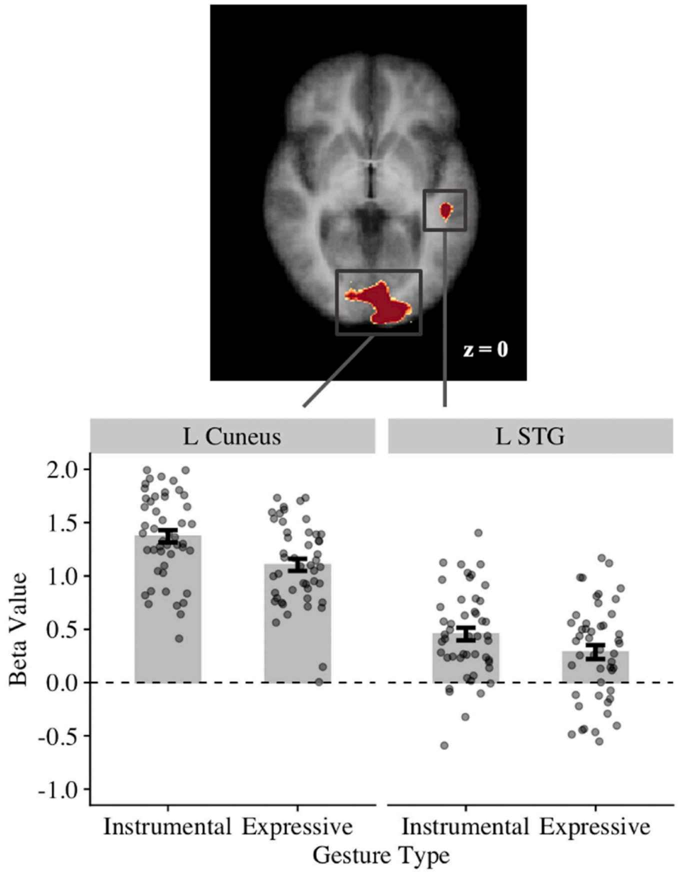

Fig. 3. Main effect of gesture type (instrumental vs. expressive). Top: Transverse slice in radiological convention depicting significant activation in the left cuneus and left STG (all $p < .0005$ uncorrected, $p < .05$ cluster-threshold corrected), associated with the main effect of gesture type. Data are shown on the average template of the participants' anatomical data. Bottom: Bar plots indicating the mean beta values associated with the left cuneus and left STG per gesture type with scatter depicting the individual participant beta values collated over group and gesture valence, with error bars depicting the *SEM*. L = left.

have impaired performance on tasks requiring selective attention for task-relevant information such as colour, while ignoring task-distracting information such as semantic meaning (Cataldo et al., 2005; Holmes and Pizzagalli, 2008; Keller et al., 2020; Kertzman et al., 2010). The greater claustrum activity in MDD might reflect the recruitment of additional resources to attend to and perceive the different gesture stimuli.

In summary, the greater claustrum activity in individuals with MDD might reflect a greater effort to associate sensory, motor, and limbic information, or might reflect altered attention during gesture perception. These functions could be related, as the integration of information is needed to direct and sustain attention (Smith et al., 2020). Future studies are encouraged to test these hypotheses, and to further investigate the role of the claustrum in gesture perception.

5.2. Further Findings

We also identified main effects of, and an interaction between, gesture type and gesture valence, not involving group effects. While this study was primarily focused on the differences between the neural activity of individuals with MDD and typical individuals, these additional findings might contribute to an understanding of the neural bases of gesture perception.

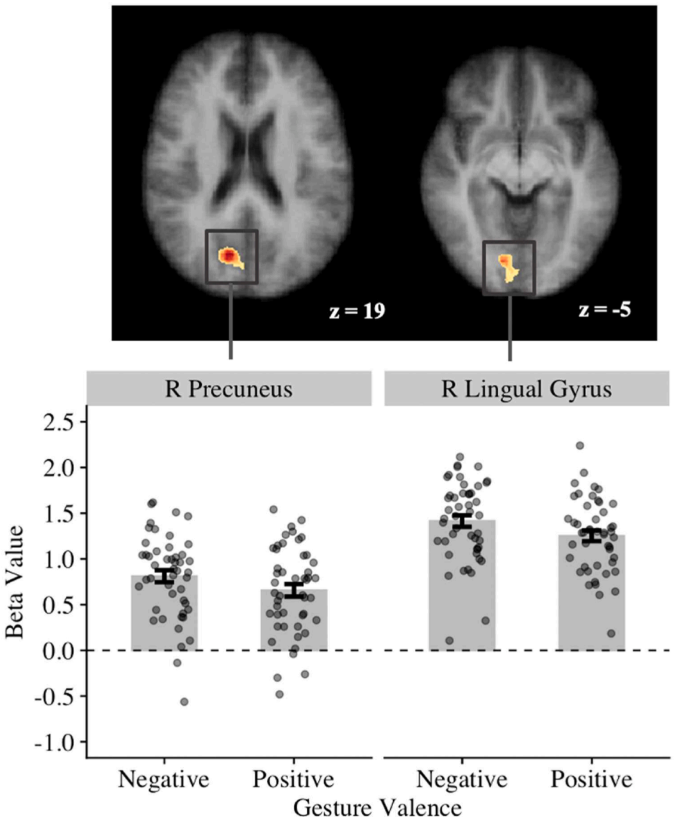

Fig. 4. Main effect of gesture valence (negative vs. positive). Top: Transverse slices in radiological convention depicting significant activation in the right precuneus and right lingual gyrus ($p < .0005$ uncorrected, $p < .05$ cluster-threshold corrected), associated with the main effect of gesture valence. Data are shown on the average template of the participants' anatomical data. Bottom: Bar plots indicating the mean beta values associated with the right precuneus and right lingual gyrus per gesture valence with scatter depicting the individual participant beta values collated over group and gesture type, with error bars depicting the *SEM*. R = right.

5.2.1. Gesture Type and Self-Preference

Perceiving instrumental compared to expressive gestures was associated with greater activity in the left cuneus and left STG. These results did not corroborate previous findings obtained by Gallagher and Frith (2004), who argued that perceiving instrumental gestures was associated with frontal activity. This difference might be related to the stimulus type used. Gallagher and Frith (2004) used full-light videos of actors preforming gestures. While these can enhance ecological validity, non-kinematic and distracting social information (e.g., body shape) might have influenced brain activity (Johansson, 1973; Kaletsch et al., 2014; Okruszek, 2018). The current study used stick figures to control for such influences.

Instrumental gestures explicitly address an observer, while expressive gestures indicate an actor's state. People process self-relevant stimuli in a preferential manner, suggesting that the instrumental gestures captured more attention (Hudson et al., 2020; Nijhof et al., 2020; Zhang et al., 2016). Consistent with this theory, Zhang et al. (2016) found increased activity in the left cuneus and left STG after participants received performance feedback from another person on a gesture imitation task. Thus, the greater activity in the left cuneus and left STG during instrumental compared to expressive gesture perception might be related to self-preferential biases.

5.2.3. Gesture Valence and Negativity Bias

Perceiving negative compared to positive gestures was associated with greater activity in the right precuneus and right lingual gyrus. The

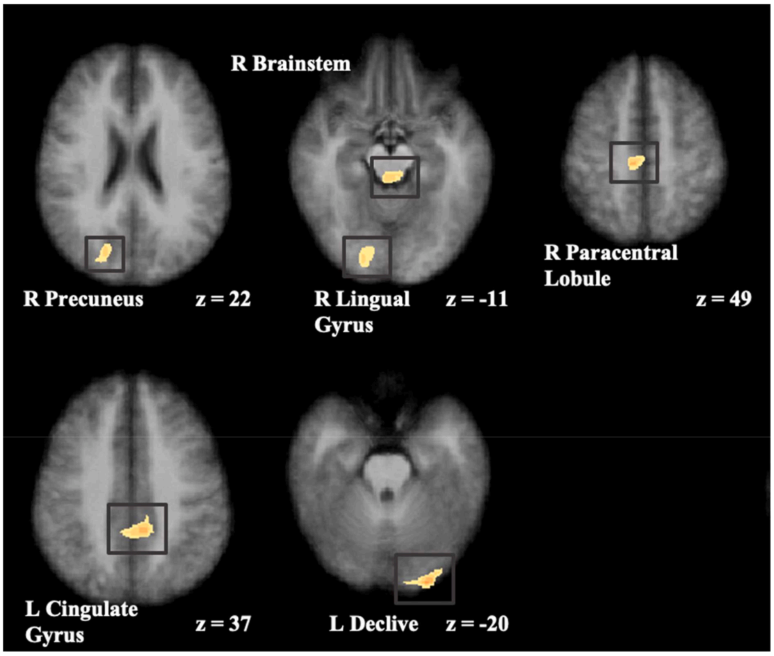

Fig. 5. Two-way interaction between gesture type and gesture valence. Transverse slices in radiological convention depicting significant activation in the right precuneus, right lingual gyrus, right brainstem, right paracentral lobule, left cingulate gyrus and left declive (all $p < .0005$ uncorrected, $p < .05$ cluster-threshold corrected), associated with the interaction between gesture type and gesture valence. Data are shown on the average template of the participants' anatomical data. R = right; L = left.

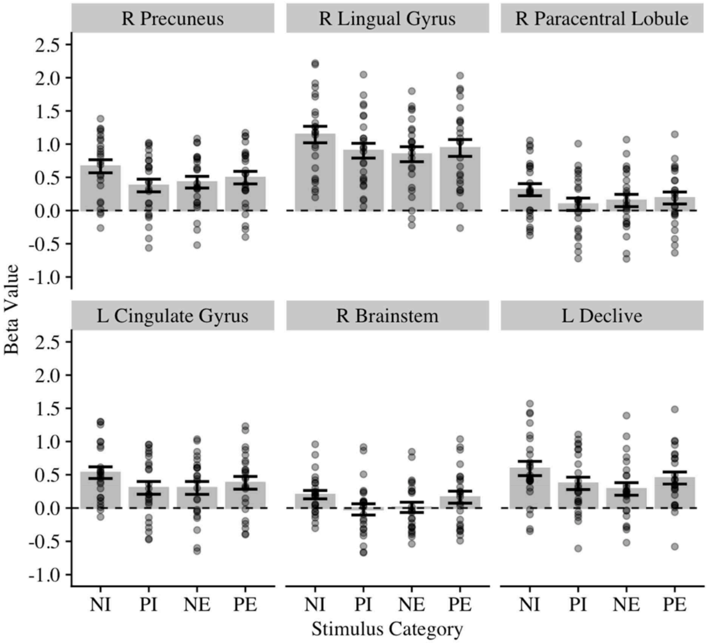

Fig. 6. Graphical representation of the two-way interaction between gesture type and gesture valence. Bar plots indicating the mean beta values associated with the right precuneus, right lingual gyrus, right paracentral lobule, left cingulate gyrus, right brainstem and left declive per stimulus category with scatter depicting the individual participant beta values collated over group, with error bars depicting the *SEM*. NI = negative instrumental; PI = positive instrumental; NE = negative expressive; PE = positive expressive; R = right; L = left.

right precuneus is implicated in gesture perception (Flaisch et al., 2009; Villarreal et al., 2008; Yang et al., 2015). Likewise, the right lingual gyrus is implicated in BM and gesture perception (Cignetti et al., 2017; Lotze et al., 2006; Servos et al., 2002; Vaina et al., 2001). However, previous studies did not associate these brain areas with negative gesture perception, which might again be related to their use of full-light gesture stimuli (e.g., Flaisch et al., 2009; Lotze et al., 2006).

The right precuneus and right lingual gyrus activity could potentially be explained by a negativity bias, which is a bias present in the general population (Norris, 2021; Smith et al., 2003). In support of this theory, processing negatively valenced words and facial expressions is associated with increased activity in these regions (Fusar-Poli et al., 2009; Richter et al., 2010; Zhao et al., 2017).

5.3.4. Negative Instrumental Gesture Perception

The interaction between gesture type and gesture valence was associated with activity in the right precuneus, right lingual gyrus, right paracentral lobule, left cingulate gyrus, right brain stem and left declive. These brain areas are associated with affective and social processing, or BM perception (Benito-León et al., 2019; Fusar-Poli et al., 2009; Gallagher and Frith, 2004; Goll et al., 2015; Grèzes et al., 2001; Jing et al., 2020; Li et al., 2020; Richter et al., 2010; Ruder et al., 2021; Van Overwalle et al., 2015, 2014; Zhao et al., 2017; Zinchenko et al., 2018). Across all regions identified by the two-way interaction of gesture type and valence, we observed most activity during negative instrumental gesture perception, potentially reflecting a self-preferential and negativity bias (Hudson et al., 2020; Nijhof et al., 2020; Norris, 2021; Zhang et al., 2016). In effect, for the MDD group these regions would activate particularly for negative instrumental gestures such as 'No, you are wrong', 'Do not do that', 'What time do you call this?' where there is the potential for an observer to subjectively feel scolded by the stick-figure animation. Such a subjective interpretation is not readily available for either the positive or negative expressive gestures or the positive instrumental gestures. Although our design focused on group effects and this limited statistical power for finding an interaction of gesture type and valence, the pattern of increased activity for negative instrumental gestures suggests the importance of future research to explore these gestures in greater detail.

5.4. Considerations and Future Directions

The present study did not identify a group effect in the brain regions commonly associated with gesture perception and social processing, such as the insula. Yet similar to the claustrum, the insula is involved in sensory and limbic information integration and attention (Namkung et al., 2017; Uddin et al., 2017). Additionally, no interactions involving group effects were identified. These phenomena could be related to the study's relatively low sample size (i.e., 12 individuals with MDD and 12 control individuals), making false positive findings more probable but also hindering the detection of potentially true effects of, and interactions between group, gesture type and gesture valence on the BOLD signal (Button et al., 2013). However, there is some debate on appropriate sample sizes in fMRI studies. While some recommend large samples ($n = 100$; Turner et al., 2018), others argue that smaller sample sizes ($n = 16$) could be sufficient if there are enough individual-level data recorded, for instance through multiple imaging runs (Nee, 2019). In light of this latter perspective, this study provided initial insights into the neural correlates of gesture perception in MDD. To extend these initial findings, replications with larger samples and more imaging runs are recommended. Another point to consider in the present study was the self-reported variability in medication types and dosages that were obtained. This limited the ability to account for possible variations in brain activity due to medication, and can be addressed in future studies.

A strength of the current study was the inclusion of gestures of different types and valences. Within these gesture categories, however, the variation space is large, as various parameters such as gesture velocity and size influence whether the message of a gesture is correctly interpreted, for instance during simultaneous speech (Ferstl et al., 2020). Related to the space of possible gestures it is important to note that while our animated displays allowed control of extraneous visual properties, they did omit motion of the hand and fingers. Hand and finger motion can provide essential information in gesture (Cartmill et al., 2012; Kang and Tversky, 2016), and their omission might have affected the neural response. Additionally, gesturing is universal amongst humans, but specific gestures are idiosyncratic; they differ between and within an actor (Ferstl et al., 2020; Mechraoui and Noor, 2017). Hence, variables related to the actor (e.g., gesture velocity) and observer (e.g., gesture familiarity) might influence the observer's neural activity (e.g., Balconi et al., 2021). Future studies are encouraged to further explore these phenomena for comprehensive conclusions about the neural correlates of gesture perception in MDD and the general population.

The data in the present study were obtained using a common 'one-person approach', meaning that the neural activity of a single participant was measured when viewing gesture stimuli (Yang et al., 2015). While this approach provides valuable insights into gesture perception, it has relatively low ecological validity (Balconi et al., 2021). Balconi et al. (2021) recently investigated the neural correlates of gesture perception using near-infrared spectroscopy and a 'two-person approach', where one participant performed gestures that were observed by the other participant. Future studies could adopt this approach to complement the initial findings in order to form a holistic insight into the differences between the neural activity of individuals with MDD and typical individuals during gesture perception.

6. Conclusion

This study provided initial support of a difference between the neural correlates underlying gesture perception for individuals with MDD and typical individuals. Specifically, individuals with MDD had greater activity in the right claustrum during gesture perception, irrespective of gesture type and valence, potentially reflecting altered attention, or a greater effort to associate sensory, motor, and limbic information. Irrespective of group effects, different brain regions appear to underly the perception of gestures of different types and valences, potentially reflecting self-preferential and negativity biases, but these results need to be interpreted with caution and future investigations are encouraged. Generally, replications with larger samples are recommended to extend the initial findings for a comprehensive understanding of gesture perception in MDD.

Author statement

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Declaration of Competing Interest

The authors have no disclosures of interest to state and did not use generative AI in their writing.

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