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Research paper

Hand gesture performance is impaired in major depressive disorder: A matter of working memory performance?

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ABSTRACT

Objective: Individuals with depression exhibit numerous interpersonal deficits. As effective use of gestures is critical for social communication, it is possible that depressed individuals' interpersonal deficits may be due to deficits in gesture performance. The present study thus compared gesture performance of depressed patients and controls and examined whether these deficits relate to cognitive and other domains of dysfunction.
Methods: Gesture performance was evaluated in 30 depressed patients and 30 controls using the Test of Upper Limb Apraxia (TULIA). Clinical rating scales were assessed to determine if gesture deficits were associated with motor, cognitive or functional outcomes.
Results: Compared to controls, depressed patients exhibited impaired gesture performance with 2/3 of the patients demonstrating gesture deficits. Within depressed patients, gesture performance was highly correlated with working memory abilities. In contrast, no association between gesture performance and gestural knowledge, psychomotor retardation, depression severity, or frontal dysfunction was observed in patients.
Limitations: This is a cross-sectional study and a larger size would have allowed for confident detection of more subtle, but potentially relevant effects.
Conclusion: Gesture performance is impaired in depressed patients, and appears to be related to poor working memory abilities, suggesting a disruption in the retrieval of gestural cues indicative of a distinct clinical phenomenon that might be related to social functioning.

1. Introduction

Depression is a severe, recurrent and prevalent mental health disorder that has a negative impact on subjects' cognitive and emotional state. Depression is characterized by low mood and apathy and is associated with poor concentration, memory and executive functioning (Marazziti *et al.*, 2010;Snyder, 2013). Depressed patients report less enjoyment during social situations resulting in fewer social interactions and inadequate interpersonal relationships (Weightman *et al.*, 2014; Bora and Berk, 2016;Weightman *et al.*, 2019).

Interpersonal relationships involve both verbal and non-verbal communication. In particular, non-verbal communication encompasses a wide range of communicative behaviors that include facial expressions and gestures that are difficult to consciously control (Vrij *et al.*, 2000). Non-verbal communication is often delivered unconsciously and greatly contributes to the development of meaningful relationships and interactions (Roter *et al.*, 2006). Several studies report numerous abnormalities in non-verbal communication in depressed individuals. For example, depressed patients process positive and neutral facial expressions abnormally (Weightman *et al.*, 2014;Weightman *et al.*, 2019) and exhibit higher levels of negative non-verbal behaviors such as frowning (Fiquer *et al.*, 2018). Furthermore, depressed patients tend to maintain less eye contact and perform fewer gestures and movements during interpersonal interactions (Hinchliffe *et al.*, 1975;Hinchliffe, 1975;Fossi

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et al., 1984;Dimic et al., 2010).

Gesture performance occurs in the context of spoken language and involves movements that accompany speech, facilitating communication, understanding, and learning during social interactions (Cook et al., 2008;Kelly et al., 2010). Gesture performance can be quantified in two domains; imitation (performance after demonstration) and pantomime (performance following verbal command), and can either be meaningful or meaningless in nature (Vanbellingen et al., 2010). Gestures predominantly engage the left frontal-parietal networks of the brain (Fridman et al., 2006;Bohlhalter et al., 2009;Lesourd et al., 2018). In recent years, studies in schizophrenia patients reveal the importance of assessing gesture deficits in mental health conditions. These studies have shown that gesture deficits are prevalent across all stages of the disease, present in both medicated and non-medicated patients with schizophrenia (Mittal et al., 2006;Walther et al., 2015), and are directly associated with poor social functioning, motor abnormalities, frontal lobe dysfunction, working memory abilities and gestural knowledge (Walther et al., 2013a;Walther et al., 2015;Walther et al., 2016;Walther et al., 2020a). Neuroimaging studies have also shown that poor gesture performance is directly related with reduced structural connectivity and cortical thickness, as well as, hypoactivation and altered resting-state functional connectivity within the left frontal-parietal-temporal network in patients with schizophrenia (Stegmayer et al., 2016a;Stegmayer et al., 2018;Viher et al., 2018;Wuthrich et al., 2020).

Schizophrenia and depression share some core phenotyping similarities in the affective domain (Annen et al., 2012;Olsen et al., 2015; Steinau et al., 2017) and both may present a generalized slowing of physical activity known as psychomotor retardation, which affects fine and gross motor behavior, as well as, motor speed and velocity, facial expressions and speech production (Nelson and Charney, 1981;Hoffmann et al., 1985;Lemke et al., 1997;Lemke et al., 2000;Morrens et al., 2007;Bennabi et al., 2013;Walther et al., 2019). Although psychomotor retardation has long been associated with severity of depressive symptoms, the performance of hand gestures has been greatly overlooked in depression.

In this study, we aim to explore gesture deficits in patients with depression and their relation to psychomotor retardation and cognitive processes. We hypothesize that a significant percentage of depressed patients are impaired in gesturing and that these deficits are associated with cognitive and functioning outcomes.

2. Materials and methods

2.1. Participants

The current study included 30 patients (17 females) and 30 controls (16 females) matched for age, gender and education. All participants were right-handed in accordance to the Edinburgh Handedness Inventory (Oldfield, 1971), were native German speakers, and had grown up in Switzerland. Demographic and clinical characteristics of patients and controls are presented in Table 1. Written informed consent was attained from all participants and the study was approved by the local ethics committee (2018–01188), and thus complies with the tenants of the Declaration of Helsinki.

Patients were recruited from the inpatient and outpatient departments at the University Hospital of Psychiatry in Bern Switzerland, and diagnosed with current major depressive disorder in accordance to the Mini International Neuropsychiatric Interview (MINI) and DSM-5 criteria. Most patients ($n = 28$) were on stable antidepressant medication at the time of testing that fall under 8 classes: selective serotonin reuptake inhibitors (SSRI's; $n = 10$), selective serotonin and norepinephrine reuptake inhibitors (SSNRI's; $n = 8$), tricyclic antidepressants (TCA; $n = 5$), tetracyclic antidepressants (TeCa's; $n = 5$), norepinephrine and dopamine reuptake inhibitors (NRDI's; $n = 2$), monoamine oxidase inhibitors (MAOI's; $n = 2$) and Lithium ($n = 4$). Some patients ($n = 10$) were taking more than one class of antidepressant medication, while two

Table 1
Demographic and clinical characteristics.

	Patients (n = 30)	Controls (n = 30)	t- test
Demographic			
Age (years)	37.3 ± 12.5	37.4 ± 12.7	t = -0.02; p = 0.98
Gender (females %)	56.6 %	53.3 %	t = -0.25; p = 0.79
Education (years)	14.6 ± 3.5	14.6 ± 2.4	t = 0.02; p = 0.98
Assessments			
PKT [b]	24.8 ± 3.4		
BAG	31.3 ± 2.7	31.6 ± 6.0[a]	t = -0.23; p = 0.81
CRT	11.4 ± 3.89	14.3 ± 2.6	t = -3.32; p = 0.001***
SRRS [b]	21.4 ± 9.2		
MADRS [b]	26.9 ± 10.5		
SOFAS [b]	55.3 ± 14.9		
FAB	16.3 ± 2.7	16.7 ± 1.4	t = -0.79; p = 0.43
DSB	4.6 ± 0.9	5.1 ± 0.9	W= 319; p = 0.043*

Values represent the mean ± SD for each group. BAG: Brief Assessments of Gestures; CRT: Coin Rotation Task; DSB: Digit Span Backwards; FAB: Frontal Assessment Battery; MADRS: Montgomery-Åsberg Depression Rating Scale; PKT: Postural Knowledge Task; SOFAS: Social and Occupational Functioning Assessment Scale; SRRS: Salpêtrière Retardation Rating Scale; TULIA: Test for Upper Limb Apraxia. [a] 3 controls did not complete BAG
[b] was not assessed in controls * and *** Denotes a significant difference between patient and control group.

patients were not on any antidepressant medication at the time of testing. Details of the type and dosage taken by each patient can be found in Supplementary Table 1. Controls were enrolled from a database of 84 healthy subjects, who participated in other studies using the TULIA and coin rotation performances (Walther et al., 2015;Walther et al., 2020b;Transcranial Direct Current Stimulation (tDCS) to Improve Gesture Control (GesttDCS); NCT03463902). Matching between patients and controls was based only on age, gender and education while remaining blind to all other assessments, including the TULIA and CRT performances. Exclusion criteria for both groups included substance abuse (excluding nicotine use), any history of current psychiatric or neurological disorders associated with movement impairments, and any first-degree relatives with psychosis.

2.2. Clinical symptom and functional outcome assessments

In patients, we assessed the severity of current depression using the Montgomery-Åsberg Depression Rating Scale (MADRS; (Montgomery and Asberg, 1979)), and used the Social and Occupational Functioning Assessment Scale (SOFAS; (Goldman et al., 1992)) to evaluate each patient's individual level of social and occupational functioning.

2.3. Gesture

Test of Upper LImb Apraxia (TULIA) measures hand and finger performance, based on 48 items in two different domains (Vanbellingen et al., 2010); imitation (24 items) and pantomime (24 items). During imitation trials, participants perform gestures following demonstration from the examiner. During pantomime, participants perform gestures only following verbal instruction. Within the two domains three semantic categories of gestures exist (8 items each); meaningless (novel gestures without semantic content), intransitive (communicative gestures) and transitive (gestures that are tool/object related). The TULIA was video recorded and later scored by two independent experts blind to group according to the manual. Raters were trained by the senior investigator to achieve interrater reliabilities of $\kappa > 0.80$. Scores for each item range from 0 to 5. For the lower score range (0–2), content errors, as well as, temporal and spatial errors that affect the meaning and/or trajectory of the gesture are included, while the 3–4 score range includes minimal temporal and spatial errors that are either corrected or don't affect the overall trajectory of the performed gesture. In contrast, a 5 score is given for entirely correct gesture performance. The maximum total score for TULIA is 240 (120 per domain) with higher scores indicating better performance. The cut-off score for total apraxia is 194/240; 95 for the imitation domain and 92 for the pantomime domain (Vanbellingen *et al.*, 2010), while the cut-off score for gesture deficits is 210/240; 104 for the imitation domain and 103 for the pantomime domain (Walther *et al.*, 2013a).

Postural Knowledge Task (PKT). In patients, we further evaluated gesture recognition performance using a modified version of the PKT (Mozaz *et al.*, 2002). Drawings of people carrying out 10 transitive and 10 intransitive gestures were shown with the distal parts of the executing limbs performing the gesture missing. Below each drawing, 3 images of different limb positions were shown and patients were asked to choose the image that illustrates the correct limb position. Furthermore, 10 tool/object based images were also shown, and patients were asked to choose the correct grip required to hold the tool/object by choosing one of the 3 choice images provided. The score for PKT ranges from 0–30.

Brief Assessment of Gestures (BAG). All participants completed a gesture questionnaire covering 12 statements on how comfortable and successful subjects are with co-speech gesture perception and production in various situations (Nagels *et al.*, 2015). These statements included situations, in which communication was either hindered (i.e. noisy places) or not hindered (e.g. everyday discussions), while statements were phrased with either a positive or negative manner (Nagels *et al.*, 2015).

2.4. Fine motor and motor slowing

Coin Rotation task (CRT). The CRT measures fine motor performance (Mendoza *et al.*, 2009) and requires the participants to rotate a ½ Swiss franc coin through uninterrupted 180° turns using only their thumb, index and middle fingers. Participants were instructed to rotate the coin as quickly and as accurately as possible. Three trials of 10 seconds were completed for each hand. Similarly to TULIA, the test was video recorded and later quantified by a blind, independent examiner. Deficits in the CRT task are designated by a reduced number of 180° turns, as well as, the number of coin drops per trial. The first trial for each hand was used to familiarize the participant with the task procedure and thus was not included in the final CR score. The CR scores for trials 2 and 3 were calculated separately using the formula: CR score = number of 180° turns – [(number of coin drops x 0.1) x number of 180° turns](Walther *et al.*, 2013b) . Since all our patients and controls were dominantly right-handed, the mean CR score of trials 2 and 3 for the right hand was used for further analyses.

The Salpêtrière Retardation Rating Scale (SRRS; (Dantchev and Widlocher, 1998)) was used to quantify psychomotor retardation. SRRS includes items that measure the quality of the patients' movements, speech flow and tone, cognition, fatigue, concentration, memory, perception of time and level of interest. Each item score ranges from 0 (absent) to 4 (severe). The SRRS score ranges from 0–60.

2.5. Cognition

In addition, the Frontal Assessment Battery (FAB) was applied to assess the presence and severity of a dysexecutive condition affecting both motor and cognitive behavior (Dubois *et al.*, 2000). The Digit Span Backwards (DSB) from the Wechsler Memory Scalle III (Wechsler, 1997) was used to assess working memory abilities and tests the capacity to retain information in short-term memory and the ability to manipulate the information to produce a novel result. FAB and DSB were assessed in both patients and controls.

2.6. Data Analyses

Mean total TULIA scores, as well as, mean TULIA scores for each domain (imitation and pantomime) and category (meaningless, intransitive, and transitive) were calculated using scripts written in R (version 3.6.3). Demographic and clinical data available for both patients and controls, as well as, performance in the CRT were compared using two sample t-tests. Performance score of the DSB was reported using the maximal span of each participant and differences between patients and controls was assessed using the Wilcoxon rank sum test for continuity correction since scores ranged from 3–6 (Leon, 1998). To assess whether age affected gesture performance, we ran a correlation between TULIA and age for both the patient (rho=0.002, *p*-value =0.98) and control group (rho = 0.01, *p-value* = 0.94), and found no significant association between the two, thus age was not used as a covariate in our statistical analyses. Analysis of the mean TULIA was carried out using ANOVAs with CR added as a covariate to control for any medication-induced slowing. Spearman correlations were used to explore within-group associations between gesture performance and clinical parameters.

3. Results

3.1. Demographic and clinical data

Overall, patients and controls did not differ in age, gender or education. However, there was a positive association between education and gesture performance for patients' (rho = 0.53; *p-value* = 0.003) but not controls (rho = 0.11; *p-value* = 0.54). In addition, controls demonstrated superior performance compared to patients in working memory (DSB) and fine motor performance (CRT) (Table 1). Patients had moderate to severe depression, and no differences in performance across measures was observed as a factor of gender (all F<1.7, all *p-values* >0.201).

3.2. Gesture domains

3.2.1. Hand gesture performance

TULIA revealed a high proportion (66.6%) of depressed patients with gesture deficits. This deficit was more pronounced in the pantomime (70%) than the imitation (53.3%) domain. A between group ANOVA found overall better performance in controls compared to patients for the total TULIA scores ($F_{1,\ 57} = 38.1$; $p < 0.0001$; Fig. 1A). No effect of fine motor slowing as measured by the CRT was observed on gesture performance ($F_{1,\ 57} = 1.6$; $p = 0.2$). In addition, a 2 (group) x 2 (domain) ANOVA revealed a significant main effect of group ($F_{1,\ 116} = 42.5$; $p <$ 0.0001) and domain ($F_{1,\ 116} = 10.4$; $p < 0.01$), with controls performing better in each domain and imitation was better than pantomime across both groups (Fig. 1B). However, we found no interaction between group and domain ($F_{1,\ 116} = 1.24$; $p = 0.266$).

Moreover, a 2 (group) x 2 (domain) x 3 (category) ANOVA revealed a 2-way interaction between group and categories ($F_{2,\ 348} = 4.95$; $p <$ 0.01), while the interaction between domains and categories was at trend level ($F_{2,\ 348} = 2.37$; $p= 0.094$). In contrast, there was no group x domain interaction ($F_{1,\ 348} = 2.07$; $p= 0.158$). Significant main effects were also observed for group, domain and category (all $F_{1,\ 348} > 14.65$; $p < 0.001$).

Importantly, we detected a significant 3-way interaction ($F_{2,\ 348} =$ 3.62; $p < 0.05$; Fig. 1C) between group x domain x category. Post-hoc analysis using the Benjamini-Hochberg method indicated significant between-group differences across all categories of the imitation (all *p-values* < 0.01) and pantomime domain (*p-values* < 0.0001) with controls outperforming patients with the exception of the pantomime meaningless gestures (*p-value* = 0.661). Across domains, patients performed significantly better in the imitation intransitive than the pantomime intransitive category (*p-value* < 0.01), while no significant differences were observed for the transitive (*p-value* = 0.103) and meaningless (*p-*

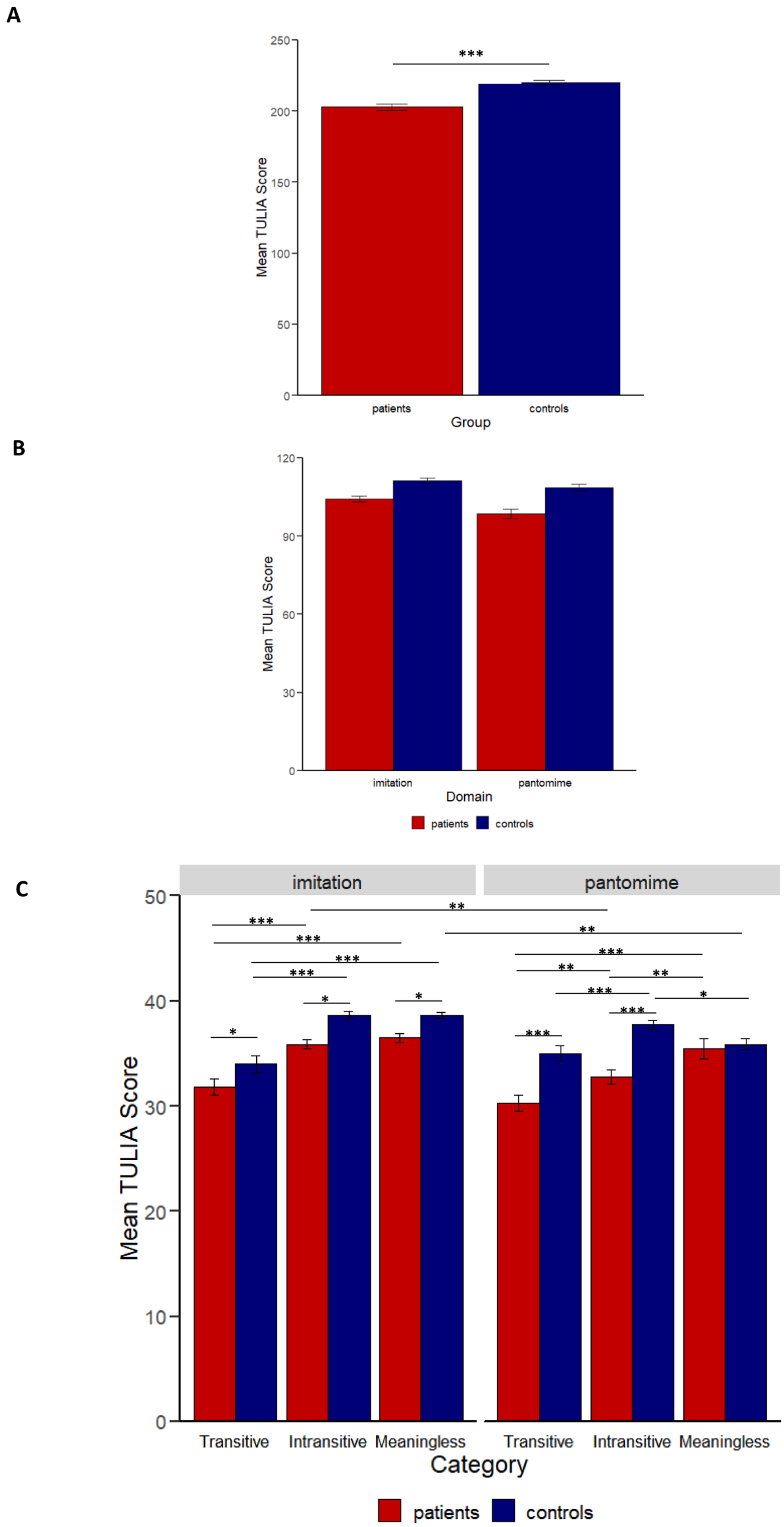

Fig. 1. TULIA scores. A) Bar plot represents mean total TULIA scores for patients (red) and controls (blue). *** denotes a significant difference between patients and controls. Vertical bars represent the standard error of mean. **B)** Bar plot represents mean TULIA scores for patients and controls for each domain (imitation and pantomime). Vertical bars represent the standard error of mean. **C)** Bar plot represents mean TULIA scores for patients and controls in each category (transitive, intransitive and meaningless) across the two domains. * denotes a significant difference < 0.05, ** denotes a significant difference < 0.01, and *** denotes a significant difference <0.001. Vertical bars represent the standard error of mean.

value = = 0.304) categories. In contrast, controls performed significantly better during the imitation meaningless than the pantomime meaningless category (*p-value* < 0.01), while no significant difference was observed for the transitive (*p-value* = 0.302) and intransitive (*p-value* = 0.355) categories. Importantly, patients displayed superior performance in the meaningless category (*p-values* < 0.01), compared to the transitive and intransitive categories in the pantomime domain, while controls performed significantly better in the intransitive category (*p-values* < 0.05). On the other hand, in the imitation domain both groups performed better during intransitive and meaningless gestures (*p-values* < 0.0001) compared to transitive.

3.2.2. Hand gesture knowledge

Although gesture recognition performance was not assessed in controls in this study, the mean score (mean ± SD; 24.8 ± 3.4) of our depressed patients is similar to that reported in patients with schizophrenia (24.4 ± 4.3; Walther *et al.*, 2015). In addition, Walther and colleagues reported patients were worse than controls at recognizing gestures(27.3 ± 1.4). However, in our study we found no association between gesture recognition and gesture performance (TULIA-PKT rho = -0.06, *p-value* = 0.727; Table 2).

3.2.3. Gesture self-report

No differences between patients and controls were observed on self-reported gesture production and processing (Table 1). In addition, no association between subjective preferences and actual gesture performance was observed (TULIA-BAG rho = -0.07, *p-value* = 0.727; Table 2).

3.3. Gesture domains and motor behavior

No significant associations between any of the three gesture domains and fine motor performance or psychomotor slowing were observed for patients (all rho ≤ .327, *p-values* ≥ .527; Table 2).

3.4. Gesture domains and clinical parameters

Performance in all three gesture domains was not associated with depression severity (all rho ≤ .251, *p-values* ≥ .650). In addition, no significant associations were observed between gesture recognition performance and functional outcome (all rho ≤ .372, *p-values* ≥ .213; Table 2), although a weak association was observed between TULIA performance and social functioning that did not reach significance following multiple comparison correction (TULIA – SOFAS rho = 0.372, *p-value* = 0.213 (uncorrected 0.043); Table 2).

3.5. Gesture domains and cognition.

Superior gesture performance in TULIA was strongly associated with working memory abilities in patients (TULIA-DSB rho = 0.651, *p-value* = 0.001). No other associations between gesture performance and working memory or executive dysfunction was observed for patients or controls (all rho ≤ .46, *p-value* ≥ .109; Table 2).

4. Discussion

Depression is a mood disorder whose severity is often associated with a reduction in gross and fine movements (psychomotor retardation) and poor social functioning (Schrijvers *et al.*, 2009;Bennabi *et al.*, 2013; Weightman *et al.*, 2014;Walther *et al.*, 2019). Social interactions depend on performing and understanding non-verbal cues that help facilitate communication and connection between two or more parties and gestures are an integral part of this form of communication (Goldin-Meadow and Alibali, 2013). Although, depressed patients have been reported to use fewer gestures during interpersonal interactions (Hinchliffe *et al.*, 1975;Hinchliffe, 1975), deficits in the performance of these gestures and how it relates to poor social and cognitive functioning remains elusive. This study examined gesture performance deficits in depressed patients and whether these deficits are directly associated with gestural knowledge, psychomotor retardation, depression severity, social functioning, working memory, or executive dysfunction. A strikingly high percentage of patients with depression (66.6%) exhibited gesture deficits as measured by TULIA, which is similar to that reported in schizophrenia (Walther *et al.*, 2013b). Patients with depression exhibited inferior gesture performance compared to controls across both

Table 2
Correlations for both patients and controls.

Patients					Controls				
Gesture domains					*Gesture domains*				
TULIA	PKT	-0.06	0.727	0.727	TULIA	BAG	-0.03	0.933	0.889
TULIA	BAG	-0.07	0.727	0.704					
Gesture domains and motor behavior					*Gesture domains and motor behavior*				
TULIA	CRT	0.13	0. 727	0.486	TULIA	CRT	0.26	0.617	0.165
TULIA	SRRS	-0.18	0.713	0.340	BAG	CRT	0.017	0.933	0.933
PKT	CRT	-0.08	0.727	0.727					
PKT	SRRS	0.33	0.559	0.077					
BAG	CRT	-0.18	0.727	0.707					
BAG	SRRS	-0.17	0.713	0.357					
Gesture domains and clinical parameters									
TULIA	MADRS	-0.08	0.783	0.643					
TULIA	SOFAS	0.37	0.213	0.043*					
PKT	MADRS	0.12	0.783	0.506					
PKT	SOFAS	-0.07	0.783	0.714					
BAG	MADRS	-0.25	0.605	0.182					
BAG	SOFAS	0.05	0.783	0.783					
Gesture domains and cognition					*Gesture domains and cognition*				
TULIA	DSB	0.65	0.001**	<0.001**					
TULIA	FAB	0.24	0.372	0.186	TULIA	DSB	0.46	0.109	0.011*
PKT	DSB	0.01	0.949	0.949	TULIA	FAB	0.219	0.617	0.244
PKT	FAB	0.25	0.372	0.181	BAG	DSB	0.17	0.809	0.405
BAG	DSB	-0.31	0.37	0.090	BAG	FAB	0.058	0.933	0.775
BAG	FAB	-0.07	0.808	0.714					

BAG: Brief Assessments of Gestures; CRT: Coin Rotation Task; DSB: Digit Span Backwards; FAB: Frontal Assessment Battery; MADRS: Montgomery-Åsberg Depression Rating Scale; PKT: Postural Knowledge Task; SOFAS: Social and Occupational Functioning Assessment Scale; SRRS: Salpêtrière Retardation Rating Scale; TULIA: Test for Upper Limb Apraxia. * Denotes a significant correlation *p-value* < .05; ** Denotes a significant correlation *p-value* < .01; All p-values are corrected using the Benjamini-Hochberg method.

domains (imitation and pantomime), and categories of gestures (transitive, intransitive, meaningless), with the exception of pantomime meaningless gestures. In addition, gestural knowledge or self-reported gesture behavior in social interactions was unrelated to actual gesture performance, suggesting that the gestural performance and knowledge are at least partially independent constructs. Likewise, neither aberrant motor behavior nor executive dysfunction were related to gesture deficits. However, these deficits were linked to impaired working memory abilities and poor social functioning (uncorrected). Performance across these measures was not different between genders.

When focusing on the compromised gesture categories in depression, patients performed worst when producing intransitive, i.e. symbolic, highly learned gestures. In contrast, patients' performance was superior in the novel, meaningless gesture category across domains, with the exception of meaningless pantomimes. This pattern of deficits is clearly different from that observed in two schizophrenia samples, where symbolic gestures are less compromised, while meaningless pantomimes are most affected (Walther *et al.*, 2013a;Stegmayer *et al.*, 2016b). In depression, performance of meaningless pantomime gestures remains preserved and comparable to that of controls. Pantomime meaningless gestures involves the production of novel movements where patients are unable to rely on visual cues otherwise provided by the examiner or on semantic-conceptual knowledge of the commanded gesture, making them particularly hard to perform (Vanbellingen *et al.*, 2010). It requires selecting, planning and retrieving details of the gesture and relies on the interaction between left inferior frontal gyrus (IFG) and left parietal lobe (IPL) (Goldenberg *et al.*, 2007;Goldenberg, 2009). Sufficient performance of this type of gestures, suggests that the interaction between left IFG and left IPL remains undisturbed in depression. Therefore, the distinct disruptions within the left premotor-parietal network appear to be different between schizophrenia and depression (Wuthrich *et al.*, 2020).

Adequate gesture performance relies on the multisensory integration of motor, sensory and speech cues, and depends on the retrieval of semantic and conceptual knowledge (Walther and Mittal, 2016). Poorer performance indicates dysfunction of one or more of these processes. We therefore explored potential contributing factors to impaired gesture performance in depression. For example, in schizophrenia poor gestural knowledge, motor slowing, frontal dysfunction, and poor working memory abilities have all been linked to impaired hand gesture performance (Walther *et al.*, 2013b;a;Walther *et al.*, 2015).

Gestural knowledge was not related to gesture performance in depression, even though patients had low scores on the gestural knowledge task (PKT). Conversely, in schizophrenia we detected similar PKT performance, but this was strongly correlated to poor gesture performance and cortical thinning within premotor-parietal-temporal network (Walther *et al.*, 2015;Viher *et al.*, 2018). In line with this observation, patients with depression seem to recruit more neural resources to correctly process information such as co-speech gestures and body orientation (Suffel *et al.*, 2020).

Self-reported gesture use was not different between patients and controls. Furthermore, self-report did not correlate with actual gesture performance. The only other study using the BAG questionnaire in depression found a trend level group difference (Suffel *et al.*, 2020).

Patients with depression demonstrated clear psychomotor retardation. However, both measures of psychomotor retardation were not associated with gesture performance. Indeed, psychomotor slowing is a common occurrence in both depression and schizophrenia, reflecting dysfunction within the frontal-striatal circuits (Morrens *et al.*, 2007; Liberg and Rahm, 2015;Walther and Mittal, 2017;Osborne *et al.*, 2020). Correct planning and execution of complex gestures can thus be compromised by motor slowing. For example, in schizophrenia such impairments have been linked to deficits in the production of complex gestures (Walther *et al.*, 2013b;Walther *et al.*, 2015). However, in depression the gesture deficit seems to occur despite psychomotor slowing.

In the present study, depression severity was not correlated with any of the gesture domains. This finding argues for a categorical association, i.e. a majority of patients have clear deficits, while there is no additional effect of the severity of the current episode. Poor nonverbal communication skills especially for communicating affective information are an established finding in depression and have been shown to negatively impact social interactions and increase social withdrawal (Bourke *et al.*, 2010;Weightman *et al.*, 2014;Weightman *et al.*, 2019). The current study extends these findings and suggests that depressed patients exhibit deficits in non-affective gestures as well. Patients with depression require more effort to process social information from gestures (Suffel *et al.*, 2020). In fact, we found poor gesture performance to be linked to lower social functioning (uncorrected *p-value* = 0.043). This study suggests that deficits in gesture performance in depressed patients may also be an indicator of poor social functioning and must not be ignored, however the causality between the two remains unclear.

Working memory is critical to perform gestures following demonstration by the examiner, i.e. imitation. In addition, performance of meaningful gestures following verbal instruction, i.e. pantomime, also requires retrieval of semantic or conceptual knowledge (Vanbellingen *et al.*, 2010). In this study, patients performed inferior to controls in all categories except the meaningless pantomimes, suggesting that they fail in situations with strong working memory load or retrieval of prior knowledge. This notion aligns with the observed association between gesture performance and educational achievement in patients with depression; but keeping in mind, that educational achievement has various influences. Previous studies suggest deficits in long-term memory in patients with depression (Williams *et al.*, 2007;Gorlin *et al.*, 2019), with one study in particular showing depressed patients had deficits in the retrieval of words during a letter fluency test (Douglas *et al.*, 2013). In line with previous reports, we found differences between patients with depression and controls in verbal working memory as measured by DSB with controls outperforming patients, while performance in TULIA for patients was associated with working memory abilities. This suggests working memory to be critical when understanding, planning and performing gestures that rely on previous knowledge.

Finally, patients with depression had intact executive function as measured by the FAB, suggesting that the effects of working memory may not reflect a broader executive functioning deficit and may be specific to working memory (Banich, 2009). Further, executive function was not correlated with gesture domains. This again is in strong contrast to schizophrenia, where we repeatedly found executive dysfunction to be associated with gesture impairments (Walther *et al.*, 2013a;Walther *et al.*, 2015;Walther *et al.*, 2020a).

Taken together, the current study shows that a significant number of depressed patients suffer from gesture deficits. These deficits seem to be directly related to a dysfunction in the retrieval mechanisms required to correctly plan and execute a gesture and may become a predictor of poor social functioning in depressed patients. In contrast to schizophrenia patients, the observed gesture deficits are not related to, gesture knowledge, psychomotor retardation or executive dysfunction. These findings argue for distinct mechanisms contributing to gesture deficits in depression or schizophrenia. Future studies can employ neuroimaging techniques to understand how these differences emerge in the brain. This will aid establishing therapeutic interventions to tackle gesture deficits specific to depression using neurostimulation (Lefebvre *et al.*, 2020) or cognitive remediation therapy.

Some considerations should be addressed regarding the current study. First, it is important to point out that this is a cross-sectional study with a relatively small number of patients with moderate to severe depression. Measuring gesture deficits at a specific state of the disorder offers very little information on the progression of these deficits. Longitudinal studies including a much larger population can shed light on how gesture deficits materialize in depression and how prevalent they are over time. In addition, our selection of cognitive tests (FAB and DSB) was done solely to compare their effect on gesture performance in depression to that previously observed in schizophrenia (Walther *et al.*, 2013b;Walther *et al.*, 2015). Considering a more comprehensive assessment of cognitive functioning in depression will be critical in the future. Moreover, it is worth noting that most of our patients were on antidepressants during the time of testing, which may impact gesture performance by introducing subtle fine motor disturbances. Evidence of such phenomenon are sparse, and seem unlikely as gesture deficits have also been observed in non-medicated patients with psychosis (Mittal *et al.*, 2006;Millman *et al.*, 2014). Prolonged use of antidepressive medication has been linked to improvements in affective impairments in depressed patients; their effect on gesture deficits however remains unclear. Additionally, psychomotor slowing was included as a covariate in the models, so any medication-induced slowing effects were accounted for in the models. Future studies can compare first-episode depressed patients, non-medicated patients diagnosed with depression, as well as, remitted patients to establish if gesture deficits are prevalent across all stages of depression (Shankman *et al.*, 2020), as characterized in schizophrenia patients.

In conclusion, depressed patients clearly display impaired gesture performance, with 2/3 patients exhibiting gesture deficits. These deficits were not associated with gestural knowledge, psychomotor retardation, depression severity, or executive dysfunction, but were linked to working memory abilities and poor social functioning. We suggest a dysfunction in the retrieval of gestural cues required to plan and execute gestures. Gesture deficits may represent a distinct treatment target in the care of patients with depression.

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CRediT authorship contribution statement

Anastasia Pavlidou: Formal analysis, Validation, Writing - original draft, Writing – review & editing. **Petra V. Viher:** Conceptualization. **Hanta Bachofner:** Data curation. **Florian Weiss:** Data curation. **Katharina Stegmayer:** Data curation. **Stewart A. Shankman:** Funding acquisition, Validation, Writing - original draft, Writing – review & editing. **Vijay A. Mittal:** Funding acquisition, Validation, Writing – review & editing. **Sebastian Walther:** Conceptualization, Funding acquisition, Validation, Writing – review & editing.

Declaration of Competing Interest

Dr. Walther received honoraria from Janssen, Lundbeck, and Sunovion. Dr. Stegmayer received honoraria from Lundbeck and Sunovion. All other authors confirm that they have no conflict of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2021.05.055.

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