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Observer-rated retardation but not agitation corresponds to objective motor measures in depression

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Abstract

Objective: To explore the correlations between observer ratings and instrumental parameters across domains of psychomotor functioning in depression. *Method:* In total, 73 patients with major depressive disorder underwent extensive psychomotor and clinical testing. Psychomotor functioning was assessed with (i) an observer-rated scale (the CORE measure) and also objectively with (ii) 24-h actigraphy, and (iii) a fine motor drawing task. *Results:* Observer ratings of retardation correlated with instrumental assessments of fine and gross motor functioning. In contrast, observer ratings of agitation did not correlate with observer ratings of retardation or with the instrumental measures. These associations were partly influenced by age and, to a lesser extent, by depression severity. *Conclusion:* Psychomotor disturbance is a complex concept with different manifestations in depressed patients. Although observer ratings of retardation correspond well with instrumental measures of the motor domains, objective measurement of agitation and other aspects of psychomotor disturbance require further research.

Significant outcomes

- Observer-rated retardation correlated with an instrumental assessment of motor functioning.
- Agitation did not correlate with objectively measured motor functioning.
- Associations found were partly influenced by age and depression severity.

Limitations

- Not all aspects of psychomotor functioning were captured by our measurement methods.
- Due to the complexity of the task, there was 23% dropout on the task of fine motor functioning.
- Our sample was heterogeneous, and we did not control for all factors with a potential influence on psychomotor functioning.

Introduction

According to the Diagnostic and Statistical Manual of Mental disorders 5th edition (DSM-5), psychomotor retardation and agitation are symptoms of major depressive disorders (MDD) and have significant diagnostic and therapeutic implications (1,2). Although psychomotor disturbance (PMD) in depression may include psychomotor retardation and agitation, their defining features remain unclear, including the motor and cognitive domains. Therefore, the combined application of psychomotor rating scales, instruments and experimental tasks covering motor and cognitive domains could help to clarify this issue (2).

Observer-based rating scales have been developed to quantify PMD. For example, the CORE measure of psychomotor functioning provides a global impression of psychomotor functioning in the domains retardation, agitation and non-interactiveness; the CORE was designed to distinguish between non-melancholic and melancholic depression (3,4). However, all clinical rating scales require training and are prone to observer bias. Therefore, in-depth objective instrumental testing is recommended to explore the various domains of PMD (1,2).

Short Communication

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The three domains that have received the most attention are speech, and gross and fine motor activity (2). Actigraphy allows continuous objective quantification of spontaneous gross motor activity (5). Similarly, computerised drawing tasks can assess cognitive and motor components of fine motor activity (6). However, reports of assessments across all psychomotor domains are scarce (2,7).

This study aimed to explore the association between observer ratings of psychomotor retardation and agitation, and objective measures of gross and fine motor functioning, in currently depressed subjects. We hypothesised that gross and fine motor functioning would be related (to varying extents) to expert observer ratings of psychomotor retardation and agitation.

Material and methods

Study population

This study included 73 patients (56 women, 17 men) with an MDD or a depressive episode in bipolar disorder (according to the DSM-IV-TR) recruited from the inpatient and outpatient department of Duffel Psychiatric Hospital (Belgium); their mean age was 58.8 (±15.1) years, and the (average) duration of a depressive episode was 14.3 (±18.1) months. These patients were awaiting treatment with electroconvulsive therapy (ECT) and are part of the PROTECT cohort (8). Diagnoses were confirmed by the MINI diagnostic interview version 6.0 and, at inclusion, patients had to score ≥ 17 on the Hamilton Depression Rating Scale-17 items (HDRS17) (9). Excluded were patients with a history of substance abuse (<6 months previously), or a primary psychotic or schizoaffective disorder.

All patients provided written informed consent before the study procedures were performed. The study protocol was in accordance with the Declaration of Helsinki and was approved by the local Medical Ethics committee.

Treatment

Most patients were treated with antidepressants: 37 were on tricyclic antidepressant monotherapy, 12 on selective serotonin reuptake inhibitors monotherapy and four were treated with another antidepressant. Five patients were not treated with antidepressants, and 15 used a combination of antidepressants. Of all patients, 79% used antipsychotics for agitation or concurrent psychotic symptoms, 26% received add-on mood stabilisers (mainly lithium) and 73% were treated with benzodiazepines (at a dose of, on average, 8.4 mg diazepam equivalents). The study procedures were scheduled before ECT.

Clinical assessment

Mood

The severity of the depressive disorder was assessed with the HDRS17 (9). To rule out double incorporation of psychomotor symptoms in our analyses, the depression severity score excluding the items on psychomotor functioning (8 – retardation and 9 – agitation) was calculated (HDRS15).

Psychomotor functioning

Psychomotor functioning was assessed as part of a larger test battery with an assessment of mood and cognitive functioning. Patients had therefore been observed for about 1 h before psychomotor functioning was assessed by the main researcher, an MD trained in psychiatry. For patients on two of the participating wards (~10% of measurements), psychomotor functioning was assessed by the psychomotor therapists of these wards that were trained to rate the CORE. All assessments were conducted in the week before ECT. Gross motor functioning was assessed within 2–3 days of the CORE ratings and fine motor measures.

Clinician rated The CORE measurement tool was used to assess observable psychomotor functioning (3,4). The clinician scores 18 observable clinical features on a 4-point scale based on severity ranging from 0 (absence of symptom) to 3 (severe). The CORE generates scores in three psychomotor categories: a central non-interactiveness scale capturing cognitive impairment, and two motoric scales capturing retardation and agitation. The Dutch version of the CORE has high inter-rater reliability and excellent validity (10).

Gross motor functioning Gross motor functioning was measured by means of the MotionWatch8 (MW) (CamNtech Ltd, Cambridge, UK) using accelerometry. Earlier studies support the use of accelerometry as an objective measure of spontaneous gross motor functioning (11) with reduced activity levels in depression (7,12–14).

Patients wore the actigraphy watch on the wrist of the non-dominant arm for 24 consecutive hours. Activity counts were stored in 2-s intervals. The approximated wake-up time and bedtime were set, and the software provided a daytime activity level (DAL) and nighttime activity level.

Fine motor performance Fine motor performance was measured with a digital Line Copying Task (LCT). On this task, significantly more psychomotor slowing has been demonstrated for melancholic versus non-melancholic depressive patients and patients with depression in general compared with controls (1,2,15,16). A full description of the set-up for this task is already published (17,18). In brief, patients sit at a table and are asked to copy lines presented on a computer screen. The use of a graphic tablet (WACOM Intuos Pro) and a pressure-sensitive pen, connected to a laptop, allows the calculation of variables such as initiation time (IT) and movement time (MT). IT mainly reflects the cognitive component of the performance and is defined as the time between the presentation of the stimulus and the start of the first drawing movement. MT reflects the motor component and is defined as the time from the start of the first drawing movement to the end of the last drawing movement.

The drawing tasks could not be performed by all patients as some of them were too agitated or severely depressed to follow instructions adequately ($N = 17$). Two patients had no baseline measurement of fine motor functioning because of planning issues, three measurements could not be used as a consequence of technical problems at the moment of testing.

Statistical analysis

Statistical analyses were performed with SPSS 24 and JMP 13.

Descriptive statistics are reported as a mean ± standard deviation. The normal distribution of the variables allowed the use of Pearson's correlation. Partial correlation coefficients were calculated using multiple linear regression models accounting for either age alone, or age and depression severity; these two latter

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variables are known to influence psychomotor performance (11,15,19). In case of missing data, patients were only excluded in the comparisons with missing data and not completely excluded from analyses. Because 21 comparisons were made, a Bonferroni-corrected p-value was calculated.

Differences in psychomotor functioning caused by potential confounders such as medication use, body mass index (BMI) (20) and smoking status (21) were assessed with analysis of variance (for medication use and smoking status) or correlational (for BMI) analyses.

Multiple regression models were calculated to further explore the relation between gross and fine motor functioning and the score on the CORE retardation subscale, including age, depression severity and smoking status as covariates. The relative contribution of the motor function to the prediction is expressed as the change in R^2 between a model including (i) solely age and depression severity, and a model including (ii) age, depression severity and motor function, as explanatory variables. Patients that had missing values in gross motor functioning or fine motor performance were excluded from the respective regression analyses.

Results

Out of the 73 patients, 33 had psychotic symptoms, 46 had melancholic depression and 13 had bipolar depression. The average HDRS17 score was 24.8 (±6.0), the average HDRS15 score was 22.3 (±5.5). The total CORE score was 10.6 (±7.9), consisting of an average CORE subscale rating of 5.4 (±4.1, retardation), 2.4 (±2.8, agitation) and 2.8 (±3.4, non-interactiveness). On instrumental measures of gross psychomotor functioning, patients ($n = 71$) had a DAL of 3.9 (±2.4) counts per 2 s. Fine motor functioning could be tested in 51 patients; LCT IT was 1.1 (±0.5) s, and LCT MT was 0.6 (±0.4) s. In total, 50 patients had all three assessments.

Table 1 presents the correlation matrix. Strong correlations were found between the CORE total and its subscales, as well as between the cognitive and motor components of the LCT.

Observer ratings of psychomotor retardation and agitation correlated with the total CORE score, but not with each other. Similarly, objective instrumental measures of both gross and fine motor functioning correlated with CORE total scores, but not with each other. In addition, there was no correlation between the CORE agitation subscale and either of the objective measures of psychomotor performance. Correcting for age decreased the correlation coefficients, whereas adding depression severity to the partial correlation analysis slightly increased the strength of the correlation.

There was no significant difference in psychomotor functioning between patients that used no antidepressants, those that were on monotherapy and those that were treated with a combination of antidepressants, nor did psychomotor functioning correlate with BMI (all p-values >0.05). Smokers ($N = 22$), however, had significantly lower CORE total ($F = 5.78$, $p = 0.0188$) and retardation subscale ($F = 10.72$, $p = 0.0016$) scores than the non-smokers. They were also somewhat faster on the motor component of the drawing task (LCT MT, $F = 8.51$, $p = 0.0053$).

To test whether information on motor functioning could improve the prediction of the CORE retardation scores, multiple regression models were fitted with gross (MW DAL) and fine motor (LCT MT) functioning as explanatory variables, in addition to age, smoking status and depression severity scores (Table 2).

The regression model with the MW activity level explained 45% of the variance ($F = 1347$, $p < 0.0001$) in the CORE retardation rating, whereas the model with MT of the copying task explained 36% of the variance ($F = 6.33$, $p = 0.0004$). The fraction of the explained variance contributed by gross and fine motor functioning was 19% and 10%, respectively. This represents the additional accuracy in predicting the CORE retardation score contributed by the information on gross and fine motor functioning, in addition to the information on age, smoking status and depression severity.

Discussion

The present study confirms the association between observer ratings of retardation and instrumental assessment of fine and gross motor functioning. However, observer ratings of agitation did not correlate with the instrumental measures; also, there was no clear correlation between fine and gross motor functioning. The associations were partly influenced by age and depression severity.

To our knowledge, this is the first study to directly compare three different measurement methods for psychomotor functioning in a relatively large, depressed patient population. Because a strict Bonferroni correction was used to correct for multiple comparisons, some relevant correlations may not be labelled as significant results.

Correlations between observer ratings of retardation and DALs were the most obvious. Correlations between the CORE retardation subscale and instrumental measures of fine motor functioning were also present; however, significance was lost after correction for age. Subtle cognitive and fine motor slowing might be a component of psychomotor functioning that is better detected by objective measurement than by observer-rated measurement. The more cognitive component genuinely escapes the clinician's eye. Therefore, the CORE retardation subscale might be a better reflection of gross than fine motor retardation. As some of the most severely depressed patients (often with high CORE scores) were unable to complete the drawing tasks because of the relative complexity, correlations with fine motor functioning have to be interpreted with care. The moderate to strong correlation between the CORE and DALs are in line with previous reports (11). Correlations between the CORE and results on the drawing tasks are similar to those between the scores on the Salpêtière Retardation Rating Scale and the results of drawing tasks found by Pier et al. (16). However, neither of these latter studies corrected for the effect of age or depression severity.

Moreover, worth discussing is the fact that observer-rated agitation does not correlate with either of the instrumental measures. This result is in contrast with the findings of Attu et al. (11) who reported correlations between CORE agitation and activity levels in the same direction as the correlation with CORE retardation, indicating that slower patients often experience retardation combined with periods of agitation. We suggest that the concept of CORE-defined agitation is a construct that is not adequately captured by actigraphy (as used here). Although being restless and moving around is an activity that is normally captured by the MW, agitation often appears alongside retardation, thereby compensating for the moments of increased activity with overall diminished activity levels. Besides that, agitation frequently appears more episodic and is not always present at the moment of observation, thereby impeding registration of this symptom. Moreover, since we monitored activity levels for only

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Table 1. Pearson correlations between the psychomotor symptoms

	CORE total score	CORE NI	CORE AG	CORE RET	MW DAL	LCT IT	LCT MT
CORE total score	1						
CORE NI							
Not corrected	0.920*	1					
Age corrected	0.910*						
Age and HDRS15 corrected	0.909*						
CORE AG							
Not corrected	0.476*	0.306	1				
Age corrected	0.381*	0.204					
Age and HDRS15 corrected	0.209	0.071					
CORE RET							
Not corrected	0.829*	0.725*	−0.020	1			
Age corrected	0.792*	0.675*	−0.176				
Age and HDRS15 corrected	0.801*	0.659*	−0.323				
MW DAL							
Not corrected	*−0.458**	*−0.406**	*0.010*	*−0.546**	1		
Age corrected	*−0.376**	*−0.331*	*0.120*	*−0.488**			
Age and HDRS15 corrected	*−0.398**	*−0.335*	*0.162*	*−0.490**			
LCT IT							
Not corrected	*0.427**	*0.369*	*−0.016*	*0.429**	*−0.293*	1	
Age corrected	*0.234*	*0.216*	*−0.228*	*0.285*	*−0.173*		
Age and HDRS15 corrected	*0.385*	*0.307*	*−0.129*	*0.348*	*−0.187*		
LCT MT							
Not corrected	*0.532**	*0.455**	*0.009*	*0.523**	*−0.315*	0.769*	1
Age corrected	*0.385*	*0.332*	*−0.184*	*0.410*	*−0.205*	0.693*	
Age and HDRS15 corrected	*0.503**	*0.396*	*−0.129*	*0.452**	*−0.213*	0.685*	

AG, agitation subscale; HDRS15, Hamilton Depression Rating Scale, excluding 2 items on psychomotor functioning; IT, initiation time; LCT, Line Copying Task; MT, movement time; MW DAL, MotionWatch daytime activity level; NI, non-interactiveness subscale; RET, retardation subscale.
Correlations of interest are presented in italics.
*$p < 0.00239$.

24 consecutive hours, a non-parametric circadian rhythm analysis could not be carried out. One might expect that the stability of the activity-rest patterns could be more informative about agitation than the DAL. Moreover, calculation of immobility parameters could have been valuable (22). Besides motor agitation, the CORE agitation items are facial anxiety and agitation, verbal stereotypy and stereotype movements. Thus, four of the five CORE agitation items are unlikely to be captured by actigraphy, which might explain why we found no correlation between the CORE agitation subscore and actigraphy.

Although in our analyses we have used the HDRS17 excluding two items on psychomotor functioning as a measure for depression severity, it could have been interesting to rate depression severity according to the melancholia subscale of the HDRS17 (the HDRS6) that has proven to be superior to the HDRS17 in terms of scalability in a recent review of literature (23). However, because retardation is considered to be the most severe symptom of the melancholia subscale (24) and we would exclude this item for calculation of an adapted score (HDRS5), we have chosen to use the full HDRS in our analyses after all. We can confirm a somewhat greater age-controlled correlation between the CORE and the HDRS5 subscale ($r = 0.497$, $p < 0.001$) than between the CORE and the HDRS15 ($r = 0.433$, $p < 0.001$), which is consistent with findings by Caldieraro et al. (25).

A remarkable finding was that smokers showed somewhat milder psychomotor symptoms than non-smokers. A possible explanation for this difference can be found in age, as the smokers were on average younger than the non-smokers, but even controlling for age the CORE retardation subscale and motor component of the drawing task differ significantly for smokers versus non-smokers. This could be a consequence of the positive effect of nicotine on motor abilities (26) or could be explained by another

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Table 2. Regression model of gross motor functioning ($r^2 = 0.45$) and fine motor performance ($r^2 = 0.36$) model versus CORE retardation subscale

		95% Confidence interval		
	Point estimate	Lower limit	Upper limit	*p*-value
Gross motor functioning				
Intercept	2.644	−2.039	7.327	
MW DAL	−0.787	−1.122	−0.454	<.0001
HDRS15	0.124	−0.023	0.271	0.0968
Age	0.045	−0.012	0.102	0.1165
Smoking (0)	1.201	0.347	2.054	0.0065
Fine motor performance				
Intercept	−0.339	−4.855	4.177	
LCT MT	3.252	1.208	5.296	0.0025
HDRS15	0.143	−0.020	0.306	0.0849
Age	−0.008	−0.0694	0.053	0.7889
Smoking (0)	0.675	−0.173	1.523	0.1161

HDRS15, Hamilton Depression Rating Scale, excluding 2 items on psychomotor functioning; LCT MT, Line Copying Task movement time; MW DAL, MotionWatch daytime activity level.

factor in which both groups differ (that we have not registered), such as coffee consumption (27).

Limitations

A limitation of the present study is the amount of dropout (23%) on the task of fine motor functioning due to the complexity of the task. Development of a simplified measure to assess fine motor functioning would be valuable for severely depressed patients, who frequently experience PMD. Because of the limited size of our sample, we did not control for all potential confounders. Although we have looked for differences between patients that did not use antidepressants and those that were on monotherapy or several antidepressants, the use of different combinations of psychotropics could have influenced psychomotor performance and was not accounted for in our analyses. The diagnostic heterogeneity (uni- as well as bipolar, melancholic as well as non-melancholic, both psychotic and non-psychotic depression) can be considered another limitation of this study, as well as the difference in therapy programmes on the wards that could have influenced the DALs that were measured. Besides that, there was a skewed gender distribution for which we have no explanation.

Conclusion

This study involved two domains of psychomotor functioning which were correlated with a well-known scale to measure PMD. Correlations were found that confirm the concept of psychomotor retardation, in part explained by age. These analyses indicate that different measurement methods are required to capture the different aspects of psychomotor functioning. Actigraphy and measurement of fine motor functioning can make a valuable contribution when diagnosing psychomotor retardation.

Suggestions for future research

For future research, we emphasise that actigraphy and drawing tasks do not capture all aspects of PMD, as defined by the CORE. Because of the complexity of the construct, a more extensive test battery would be beneficial. For example, speech and gait analysis could be of added value to obtain more objective information on these items of the CORE.

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Authors' Contribution. L.V.D., D.S. and T.B. designed the study and wrote the study protocol. L.V.D. was responsible for data collection and statistical analyses. S.W. and E.F. contributed to the process of these analyses. L.V.D. wrote the draft of the manuscript and integrated the comments of all other authors. They all contributed to and approved the final version of the manuscript.

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Conflicts of Interest. None.

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