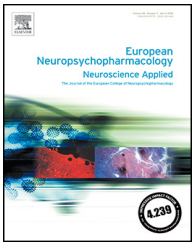
European Neuropsychopharmacology (2019) 29, 46–56



www.elsevier.com/locate/euroneuro

Discrepancy between objective and subjective cognition in major depressive disorder

Maria Serra-Blasco[a], Ivan J. Torres[b,c,*], Muriel Vicent-Gil[a,d], Ximena Goldberg[a], Guillem Navarra-Ventura[a,e], Eva Aguilar[a], Esther Via[a], Maria J Portella[d], Inés Figuereo[a], Diego Palao[a], Raymond W Lam[b], Narcís Cardoner[a,]**

[a] *Mental Health Department, Neuroscience and Mental Health Research Area, Parc Taulí Hospital Universitari, Institut d'Investigació i Innovació Parc Taulí I3PT, Universitat Autònoma de Barcelona, CIBERSAM, Corporació Sanitària Parc Taulí, Sabadell, Barcelona, Spain*
[b] *Department of Psychiatry, University of British Columbia, Room 2C7- 2255 Wesbrook Mall, Vancouver, BC V6T 2A1, Canada*
[c] *BC Psychosis Program: British Columbia Mental Health and Substance Use Services, Vancouver, BC, Canada*
[d] *Department of Psychiatry, Sant Pau Biomedical Research Institute (IIB-Sant Pau), CIBERSAM, Barcelona, Spain*
[e] *Department of Psychiatry and Forensic Medicine, Universitat Autònoma de Barcelona, Barcelona, Spain*

Received 8 August 2018; received in revised form 27 October 2018; accepted 9 November 2018

KEYWORDS
Cognitive functioning;
Depression;
Neurocognition;
Self report;
Affective disorders

Abstract
Objective and subjective cognitive measures are altered in major depressive disorder (MDD), but there is a poor correlation between them. This study aims to explore such discrepancy and the characteristics explaining this phenomenon.
229 patients with MDD subdivided into remitted ($n = 57$), partially remitted ($n = 90$) and acute ($n = 82$) underwent a clinical interview, completed self-report questionnaires and a neuropsychological assessment. The association between objective and subjective cognition was evaluated in the areas of attention and memory. Also, dependent measures of concordance and self-appraisal were calculated for each patient. Potential predictors of these outcomes were

* Corresponding authors at: Department of Psychiatry, University of British Columbia, Room 2C7- 2255 Wesbrook Mall, Vancouver, BC V6T 2A1, Canada.
** Corresponding author.
E-mail addresses: Ivan.Torres@ubc.ca (I.J. Torres), ncardoner@tauli.cat (N. Cardoner).

https://doi.org/10.1016/j.euroneuro.2018.11.1104

evaluated through regression analysis. Depressive symptoms correlated negatively with objective but especially with subjective cognition. Patients in an acute episode showed a significant correlation between objective and subjective attention/memory measures, but also the greatest underestimation of their cognitive performance. In those with fewer depressive symptoms, objective and subjective cognition showed poor correspondence between them. In the regression analyses with the full MDD sample, higher scores on depressive symptoms, intelligence quotient and executive functions predicted lower self-appraisal.
Objective and subjective cognition show poor concordance in MDD patients, especially in those with residual mood symptoms. Higher executive functions also explain this discrepancy. Assessments of both subjective cognitive complaints and objective performance seem necessary as they may be measuring different aspects of cognitive functioning.

1. Introduction

Major Depressive Disorder (MDD) is a common mental health problem (Ferrari et al., 2013) and one of the most disabling conditions in the developed world (Lopez et al., 2006; Vos, 2016). Cognitive symptoms such as forgetfulness, inattention, slowness or indecision have long been thought to be influenced by the depressive state. However, these deficits have also been shown to persist in remitted states (Preiss et al., 2007; Rock et al., 2014) and to exert a negative and independent impact on patients' functionality (Evans et al., 2014). More specifically, cognitive difficulties are a principal mediator of poor occupational functioning (Woo et al., 2016), have a negative impact on work productivity (Clark et al., 2016), and are associated with impairments in quality of life (Cotrena et al., 2016; Shimizu et al., 2013).

While most studies have focused on evaluating objective cognition, the subjective impression of patient's own cognitive abilities, a sort of meta-cognitive process (Klusmann et al., 2011), has been considerably disregarded, despite its potential impact on patients' quality of life (McIntyre et al., 2015) and work-related productivity (Kim et al., 2016). Additionally, patients' self-evaluation of their cognitive performance does not generally correlate with objective cognitive measures (Miskowiak et al., 2016; Mohn and Rund, 2016; Srisurapanont et al., 2017; Svendsen et al., 2012). While this lack of relationship between objective and subjective cognitive measures might be associated with symptoms and/or prognosis, it has been scarcely studied and we have little information on its respect. For example, depressed patients tend to underrate their performance (Farrin et al., 2003), and this phenomenon has been attributed to a distinctive negative cognitive bias. However, this hypothesis originally proposed by Beck (1963); (2008), has not been directly tested in adults with mood disorders until recently. Both in bipolar disorder (Miskowiak et al., 2016) and MDD (Srisurapanont et al., 2017), it has been demonstrated that depressive symptoms negatively influence subjective cognition. This may at least partly explain the discrepancy with objective performance, endorsing the hypothesis of depression severity as a contributor to negative cognitive bias.

Depressive severity, however, only contribute in part to the mentioned discrepancy (Srisurapanont et al., 2017, 2018), and other factors have to be involved. Indeed, intelligence and executive functioning have demonstrated to be related with subjective cognition in healthy volunteers (Mäntylä et al., 2010) and with discrepancy between objective and subjective cognitive measures in psychiatric population. Bipolar patients with higher intelligence quotient (IQ) tended to overestimate their cognitive functioning (Miskowiak et al., 2016). In addition, better performance in executive functioning, which is highly, but not completely, attributable to IQ (Friedman et al., 2006), was related to an overestimation of one's cognitive abilities in healthy volunteers (Burmester et al., 2016). These findings contrast with those supporting a relationship between better performance in executive function and illness awareness (Dias et al., 2008; Yen et al., 2008). Thus, the effects of IQ and executive functioning may be viewed to influence discrepancy in multiple ways, either acting as a compensation for the cognitive impairment (i.e. leading to less subjective complaints) or, conversely, by making the patients more aware of their difficulties when they compare their current with their past performance (i.e. leading to report more cognitive complaints). A better comprehension of the discrepancy between objective and subjective measures of cognitive functioning, taking into account the relation with clinical symptoms and the direction of such disparity (overestimation vs. underestimation) and putative factors associated with this bias, becomes a necessity for future clinical interventions targeting cognitive alterations in MDD.

The aims of the present study are twofold: (I) to study the relationship between objective and subjective measures of cognitive functioning in MDD patients in different clinical states (i.e. remitted, partially remitted and within an acute episode), and (II) to explore the clinical and neuropsychological factors that may have a relevant impact on such associations. For these purposes, we have focused our study on attention and verbal memory, as these cognitive domains can reliably be measured with available objective and subjective measurements, and are highly relevant to mood disorders along with executive functions (Roca et al., 2015). Executive functions were not included as dependent variables given their significant role in the meta-cognitive process (Lysaker et al., 2008; 2005) needed to compare objective and subjective cognitive functioning (Burmester et al., 2016), so they have been introduced as independent variables. Given the known negative influence of depressive state on subjective measures, we hypothesized that the more severe the depressed subgroup the more underestimation of their subjective cognitive functioning. As a

secondary hypothesis, we expected that executive functioning and IQ would have an effect on the concordance and direction (underestimation vs. overestimation) between objective and subjective measures of cognitive functioning.

2. Experimental procedures

2.1. Participants

Two hundred and twenty-nine patients were consecutively recruited from the outpatient unit of the Mental Health Department across 12 months (February 2016 to February 2017). To be selected for the study patients had to meet the following criteria: 18–65 years old, fulfilling criteria for a past or present diagnosis of MDD according to the Diagnostic and Statistical Manual of Mental Disorders 4th Edition (DSM-IV-TR), IQ > 85 and ability to understand and sign the informed consent. Diagnoses were carried out by experienced psychiatrists and double-checked through computerized clinical records. The exclusion criteria were the presence of any neurological, cardiac or respiratory condition with any decompensation in the last year, or the presence of bipolar disorder, schizophrenia, past or present substance abuse or any axis II diagnosis according to the DSM-IV-TR. Written informed consent was collected from all participants following a complete description of the study. The Institutional Review Board of the University Hospital of Parc Taulí-i3PT, Spain approved the study protocol.

2.2. Assessments

After inclusion in the study, participants underwent a single assessment (1.5–2 h duration), which comprised a short clinical interview collecting clinical data and a neuropsychological test battery to measure objective cognition. Finally, patients completed a set of clinical questionnaires including subjective cognitive functioning and depressive symptoms.

2.2.1. Neurocognitive and clinical measures

Objective measures of cognitive functioning

1) Attention: Composite score including Trail Making Test A, TMT-A (Casals-Coll et al., 2013); Digit Span Forward, Wechsler Adult Intelligence Scale 4th edition, WAIS-IV (Wechsler, 2008) and Spatial Span Forward, Wechsler Memory Scale, 3rd edition, WMS-III, (Wechsler, 2004).
2) Memory: Composite score including Rey Auditory Verbal Learning Test, RAVLT Total Score –Trial 1–5– and 30 min delayed recall score(Strauss et al., 2006).

Subjective measures of cognitive functioning

Perceived Deficit Questionnaire (PDQ-20) (Lam et al., 2013; Strober et al., 2016; Sullivan et al., 1990) consists of four subscales identifying specific cognitive domains: attention, retrospective memory, prospective memory, and planning and organisation (Supplement 1). The combined subscales yield a total score ranging from 0 to 80, with a higher score indicating greater perceived cognitive impairment. To test our hypothesis, only attention (0–20) and memory (0–40, retrospective and prospective) subscales were used for this purpose.

2.2.2. Clinical features

Depressive symptomatology was rated with the Hamilton Depressive Rating Scale (HDRS-17,(Hamilton, 1960)). Patient's illness characteristics collected during the clinical interview where: age at first MDD episode, number of previous MDD episodes (including the present) and burden of current psychopharmacological treatment (named medication load) measured following the system code proposed by Sackeim (2001). Comorbid conditions such as anxiety, dysthymia or marked personality traits where also collected from patient's clinical records, as a recent work has found that subjective cognitive impairment following a major depressive episode may be largely driven by the existence of comorbid diagnoses (Schaefer et al., 2017).

2.2.3. Executive functioning and intelligence quotient (EF & IQ)

Executive functions were measured covering: working memory (Digit Span Backward, WAIS-IV; Spatial Span Backward, WMS-III), phonetic fluency (PMR, (Casals-Coll et al., 2013; Pena-Casanova et al., 2009), shifting (Wisconsin Card Sorting Test, WCST and Trail Making Test-B, TMT-B), planning (Tower of London, TOL) and abstraction (Similarities, WAIS-IV). Computerized versions of the WCST and TOL were administered from the Inquisit Test Library (http://www.millisecond.com/download/library/). Premorbid intelligence quotient (IQ) was measured by means of the Vocabulary subtest (WAIS-IV) (Lezak and Lezak, 2004).

2.3. MDD patients' stratification

The whole MDD sample was subdivided according to the HDRS-17 forming three groups with different clinical status: (i) Remission (≤ 7), (ii) Partial remission (8–18) and (iii) Acute episode (> 19) (Paykel, 2008).

2.4. Data pre-processing

All data were analysed using IBM SPSS Statistics (IBM SPSS Statistics for Windows, Version 21.0) except for those procedures not included in the package, for which R Statistical Package (R 3.4.3) was used instead.

First, neuropsychological data from the objective and subjective cognitive assessments were standardized removing the effects of age, gender and educational level (Miskowiak et al., 2017). For TMT-A and B, scores were reverted such that higher scores reflected better performance. The resulting z-scores were averaged to create objective and subjective attention and memory composite values that were z-transformed in reference to the full patient sample. Subjective measures (relative to PDQ) were reverted for easier interpretation; higher scores reflected better-perceived performance.

2.4.1. Self-appraisal

This measure was obtained by subtracting the z-scores of attention and memory neuropsychological tests (objective measures of cognitive functioning) from patient's perspective of their attentional and memory skills in real-word situations (subjective z-scores of cognitive functioning).

Table 1 Demographics and clinical variables of the MDD sample divided by depression severity.

	Remission ($n = 57$)	Partial remission ($n = 90$)	Acute MDD ($n = 82$)	F/χ^2	p
Age	51.09(11.68)	52.42(8.51)	53.99(6.64)	.648	.648
Gender (n = Female %)	35 (61.40%)	61 (67.78%)	59 (71.95%)	1.711	.425
Years of education	11.86(4.83)	10.00(3.92)	9.65(3.74)	8.084	.018[1]
HDRS-17	3.75(2.30)	14.41(3.02)	24.79(4.44)	200.502	<0.001[2]
Age at illness onset	39.70(14.11)	41.36(11.61)	41.99(12.02)	.623	.537
Number of previous MDD episodes	2.21(1.24)	2.21(1.25)	2.37(1.42)	0.331	.848
Comorbidities *n, %*	16(7%)	38(16.7%)	38(16.7%)	4.582	.101
Anxiety disorders, *n, %*	4(1.8%)	9(3.9%)	6(2.6%)	.542	.763
Dysthymia, *n, %*	5(2.2%)	19(8.3%)	26(11.4%)	10.143	.006
Dysfunctional personality traits*, *n, %*	8(3.5%)	14(6.1%)	11(4.8%)	.161	.923
Medication Load (ATHF)	4.07(2.33)	5.27(2.60)	5.78(2.28)	17.444	<0.001[3]
Antidepressants n, %	52(91.2%)	87(96.7%)	81(98.8%)	6.351	.042
Benzodiazepines n, %	18(31.6%)	48(53.3%)	51(62.2%)	13.017	.001
Antipsychotics n, %	11(19.3%)	20(22.2%)	24(29.3%)	2.043	.360
Lithiumn, n, %	2(3.5%)	0	8(9.8%)	9.826	.007
Anticonvulsants n, %	9(15.8)	18(20%)	19(23.2%)	1.138	.566
Premorbid IQ (Vocabulary T-scores)	52.23(7.73)	50.38(7.80)	47.56(7.59)	16.672	<0.001[4]

MDD = Major depressive disorder; HDRS-17 = Hamilton Depression Rating Scale; IQ = Intelligence.
[1] Remission > Partial remission; Remission > Acute MDD (Post Hoc Tests).
[2] Remission < Partial remission; Partial remission < Acute MDD; Remission < Acute MDD.
[3] Remission < Partial remission; Remission < Acute MDD.
[4] Remission < Acute MDD.
* Do not fulfil DSM-IV criteria for Axis II diagnosis.

Negative values indicated that patients rated their real world cognitive functioning below the objective measures taken in the clinic (underestimation), whereas positive ones, that they rated themselves above objective cognitive tests (overestimation). Similar measures have been employed in prior studies in mood disorders (Miskowiak et al., 2016; Srisurapanont et al., 2017; Torres et al., 2016).

2.4.2. Concordance

Concordance or agreement between objective and subjective cognitive measures at a group level was examined using correlation analyses. Individual concordance was examined by calculating the absolute value of self-appraisal scores, which gives the magnitude of individual concordance between objective and subjective cognitive measures, regardless of whether patients under- or over-estimate their cognitive performance. Thus, a score of zero corresponded to maximal concordance, and higher values represented less concordance (Torres et al., 2016). To estimate a proxy of good and poor concordance, a cut-off point ≥ 1 SD under the mean was established.

2.5. Statistical analyses

Data were checked for normality using the Kolmogorov-Smirnov test. One-way ANOVA or Kruskal-Wallis test were run to test differences in demographic, clinical, and neuropsychological data across depressive groups, for variables following and not following a normal distribution, as appropriate based upon distribution of data. To study the relationship between objective and subjective cognitive measures in MDD patients with different clinical status, Pearson correlations were calculated for the full MDD sample as well as for each subgroup, both for attention and for memory domains. Also, to calculate the magnitude and direction of agreement for each individual, self-appraisal and concordance values were computed as described above. Finally, to explore what clinical and neuropsychological factors may have a relevant impact on such agreement/disagreement, clinical and neuropsychological variables (executive functioning measures), and IQ were correlated (Pearson correlations or Kendall's tau_b) with self-appraisal and concordance. Separate hierarchical linear regression models were run with self-appraisal (attention and memory) as dependent variables and clinical characteristics as independent variables in the first block, introducing executive functioning and intelligence quotient in the second block.

3. Results

3.1. Participants

There were no group differences in age, gender, age at MDD onset or number of previous episodes. Patients in remission, however, had more years of education than the two other groups. This was not viewed as problematic given that the effect of education was regressed-out from the cognitive measures. As expected, groups significantly differed in the HDRS-17, which was used to divide the depressive groups. Remitted patients had lower medication load and higher premorbid IQ than the other groups (Table 1). Remitted patients also perfomed better than the other groups in three out of the seven executive function tests (Spatial Span Backward, phonetic fluency and similarities), and better than the group with acute depression in Digit Span Backward, WCST and TMT-B (Bonferroni Post Hoc tests, $p < 0.05$). See further details on Table 2.

Table 2 Executive functions scores by symptom severity group. Statistics refer to T-scores if no otherwise specified.

	Cognitive test	Remitted ($n=57$)	Partial remission ($n=90$)	Acute depression ($n=81$)	F(df)	p
Executive functions	Digit span backward	46.61(10.4)	43.70(8.2)	42.20(9.1)	3.988(2224)	.020
	Spatial span backward	53.23(9)	49.54(8.2)	46.75(9.5)	8.870(2224)	<0.001
	Phonetic fluency (PMR)	47.91(6.7)	42.31(9.3)	41.10(9.1)	11.360(2226)	<0.001
	WCST (Categories achieved)	3.67(2)	3.10(1.8)	2.7(1.7)	4.198(2202)	.016
	TMT-B	50.72(10.5)	45.87(11.1)	41.38(12.5)	9.721(2190)	<0.001
	Tower of London (raw score)	25.84(6.2)	24.90(5.4)	25.32(5.9)	.466(2217)	.628
	Similarities	48.40(9.7)	43.76(11.5)	40.84(11.8)	7.692(2226)	.001

3.2. Cognitive performance between MDD subgroups

Objective and subjective cognitive measures were normally distributed (Kolmogorov-Smirnov test: *P*-levels > 0.09).

For the full sample, the proportion of patients presenting with objective cognitive difficulties (T < 40) was 25.1% in attention (7% Remission, 21.1% Partial remission and 42.5% Active MDD) and 44.9% in memory (28.1% Remission; 45.6% Partial remission and 56.3% Active MDD).

The one-way ANOVA/Kruskal-Wallis analyses of cognitive measures showed significant differences between groups in attention ($F_{(2,225)}=17.076$, $p<.001$) and memory objective composite scores ($F_{(2,225)}=6.977$, $p=.001$) as well as in subjective measures for both domains (attention: $F_{(2,226)}=76.529$, $p<.001$; memory: $F_{(2,226)}=55.373$; $p<.001$). Post-hoc comparisons showed that the acute MDD subgroup scored significantly lower than the remitted and partial remitted subgroups ($p<.05$), except for the objective measure of memory, in which the acute MDD subgroup only scored lower than fully remitted patients.

3.3. Correlation between depressive symptoms and cognitive measures

HDRS-17 scores negatively correlated ($p<.001$) with both objective and subjective cognitive measures (lower scores meaning worse performance/perception, respectively). It is relevant to highlight that correlations with subjective cognition - reversed - (attention: $r=-.635$, memory: $r=-.565$) were significantly higher than correlations with objective cognition (attention: $r=-.360$, memory $r=-.293$) both for attention ($z=-3.96$, $p<.001$) and memory ($z=-3.6$, $p<.001$) using the Fisher r-to-z transformation.

3.4. Correlation between objective and subjective cognitive measures

Objective and subjective cognitive function measures for the attention domain showed a significant correlation ($r=0.374$, $df=1,228$, $p<.001$) for the whole group. For individual patient groups (Fig. 1), there was no significant correlation between objective and subjective attention in the remitted group ($r=0.257$, $df=1,57$, $p=.053$), nor for the partially remitted ($r=0.079$, $df=1,90$, $p=.459$). For the acute MDD subgroup, however, there was a significant correlation between objective and subjective attention ($r=0.341$, $df=1,81$, $p=.002$).

Regarding memory, the whole group showed a statistically significant correlation as well ($r=0.301$, $df=1,228$, $p<.001$). However, in the subgroup analyses, significance was only present in the acute group ($r=0.346$, $df=1,81$, $p=.002$) but not in the remitted ($r=0.051$, $df=1,57$, $p=.706$) or partially remitted patients ($r=0.174$, $df=1,90$, $p=.102$). All correlations were corrected for Bonferroni multiple comparisons (Fig. 1).

3.5. Self-appraisal in MDD subgroups

A significant difference between MDD subgroups was detected both in attention ($F=9.48$, $p<.001$) and in memory ($F=9.16$, $p<.001$) self-appraisal, with the remitted subgroup scoring significantly higher than the other two, after conducting post-hoc comparisons (Fig. 2, Table 3). Thus, remitted patients showed a significantly higher overestimation of their cognitive performance compared to the other groups.

3.5.1. Relationship between self-appraisal, and clinical and EF & IQ measures

Pearson correlations between clinical and executive function and self-appraisal measures for attention showed significant correlations with HDRS-17′ scores ($r=-.240$, $df=1,228$, $p<.001$), Digit Span Backward ($r=-.357$, $df=1,228$, $p<.001$), Spatial Span Backward ($r=-.323$, $df=1,228$, $p<.001$), TMT-B ($r=-.328$, $df=1,193$, $p<.001$), phonetic fluency ($r=-.308$, $df=1,228$, $p<.001$), TOL ($r=-.277$, $df=1,220$, $p<.001$), WCST ($r=-.204$, $df=1,204$, $p=.003$), similarities ($r=-.246$, $df=1,228$, $p<.001$) and IQ ($r=-.267$, $df=1,228$, $p<.001$).

Correlations between memory self-appraisal and clinical and EF & IQ showed significant correlations with HDRS-17 ($r=-.226$, $df=1,228$, $p=.001$), Digit Span Backward ($r=-.222$,$df=1,228$, $p=.001$), Spatial Span Backward ($r=-.181$,$df=1,226$, $p=.006$), TMT-B ($r=-.250$,$df=1,193$, $p<.001$), phonetic fluency ($r=-.228$,$df=1,228$, $p=.001$), TOL ($r=-.239$,$df=1,220$, $p<.001$), WCST ($r=-.155$, $df=1,204$, $p=.027$) similarities ($r=-.240$,$df=1,228$, $p<.001$) and IQ ($r=-.218$,$df=1,228$, $p=.001$).

Table 3 Objective, subjective and *concordance/self-appraisal* measures of attention and memory by symptom severity group. Statistics refer to z-scores for all measures except concordance and appraisal (raw scores).

Objective	Cognitive test	Remitted ($n = 57$)		Partial remission ($n = 90$)		Acute depression ($n = 81$)		F/χ^2	p
		T-score*	z-score	**T-score***	z-score	**T-score***	z-score		
Attention	Digit span forward	45.07(8.8)	.48 (0.0)	41.00(7.7)	.03(0.84)	37.85(8.9)	−0.35(1.0)	12.92	<0.001
	Spatial span forward	51.65(10.6)	.34(0.81)	48.88(11.2)	.17(0.90)	44.04(11.1)	−0.36(0)	11.29	<0.001
	TMT-A (reverse)	49.58(8.5)	.24(0.63)	45.61(10.0)	.17(0.56)	40.29(10.9)	−0.34(1.4)	8.39	<0.001
	Composite	48.77(6.1)	.44(0.74)	45.16(6.5)	.14(0.75)	40.82(8.5)	−0.46(1.2)	17.08	<0.001
Memory	RAVLT – 1–5 trials	43.91(11.6)	.36(0.97)	39.20(11.8)	.032(0.91)	34.43(13.1)	−0.28(1.0)	7.49	.001
	RAVLT – Delayed trial	46.37(9.9)	.33(0.92)	42.49(10.3)	−0.00(0.98)	38.43(11.6)	−0.25(1.0)	5.94	.003
	Composite	45.14(10.2)	.37(0.98)	40.84(10.5)	.01(0.94)	36.75(11.4)	−0.26(1.0)	6.98	.001
Subjective		**Raw score**	z-score	**Raw score**	z-score	**Raw score**	z-score		
Attention	PDQ-20** Attention/concentration	5.67(4.0)	0.98(0.84)	10.79(3.8)	−0.015(0.80)	13.94(3.1)	−0.67(0.67)	76.53	<0.001
Memory	PDQ-20 Retrospective + Prospective Memory	7.17(6.3)	0.87(0.70)	15.51(8.0)	−0.00(0.93)	20.90(6.3)	−0.61(0.76)	55.37	<0.001
Concordance	Attention	.90(0.64)	-	.86(0.63)	-	.87(0.68)	-	.120	.887
	Memory	1.08(0.68)	-	1.02(0.63)	-	0.85(0.66)	-	2.42	.091
Self-appraisal	Attention	.54(0.97)	-	−0.15(1.0)	-	−0.19(1.2)	-	9.48	<0.001
	Memory	.51(1.2)	-	−0.005(1.2)	-	−0.33(1.0)	-	9.16	<0.001

* T-Scores of normative data based on age in general population, (Mean = 50 Standard deviation = 10). See references in the text.
** PDQ-20: The Perceived Deficits Questionnaire.

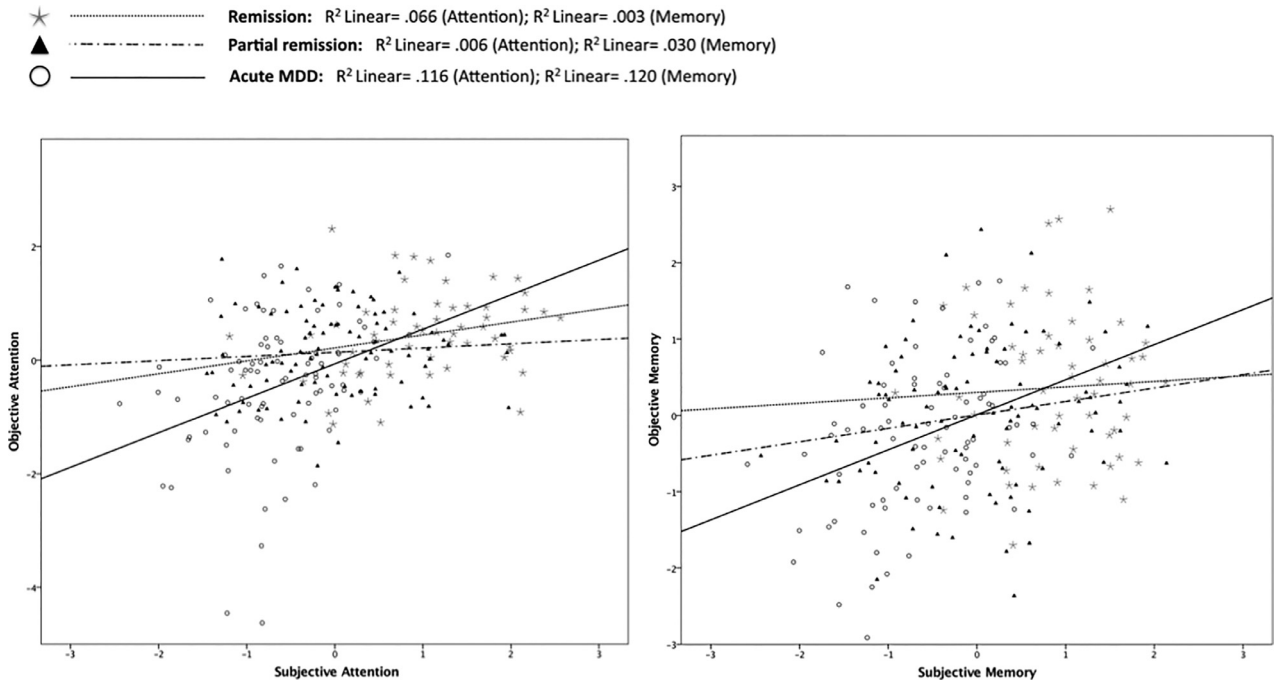


Fig. 1 Correlation between subjective and objective cognition according to depressive subgroup for attention and memory.

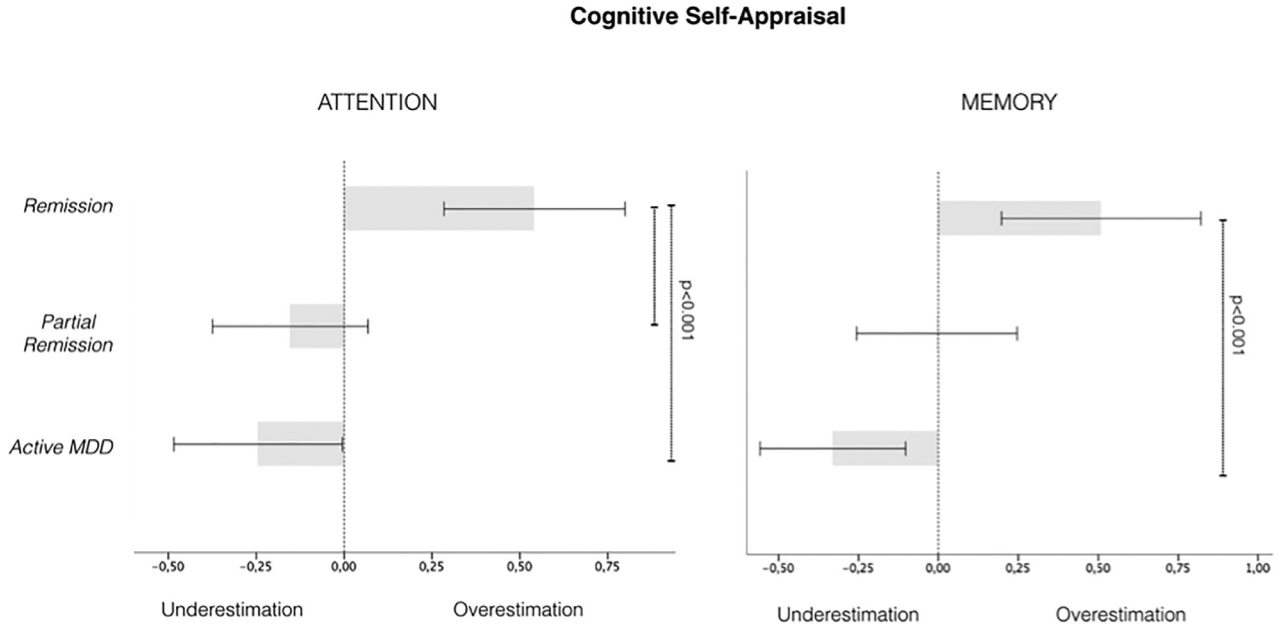


Fig. 2 Mean and confidence intervals (CI-95%) of cognitive self-appraisal for attention and memory domains.

3.5.2. Multiple regression analyses for variables predicting self-appraisal

The model predicting attentional *self-appraisal* explained a 5.9% of the variance in the first block ($R^2 = 0.086$; Adjusted $R^2 = 0.059$; $F_{5,173} = 3.237$; $p < .008$) with HDRS as only significant predicting variable. In the second block, which also included executive functioning and IQ, the variance explained increased to 33% ($R^2 = 0.381$; Adjusted $R^2 = 0.332$; $F_{6,181} = 7.800$; $p < .001$), with higher HDRS-17, Digit Span Backward, Spatial Span Backward and TOL as significant predictors of a lower self-appraisal. By including those executive function measures, the explained variance of the model significantly increased up to 27,3% (R^2-change = 0.295; F-change = 9.826; $p < .001$). Regarding memory *self-appraisal*, the first block was also explained by HDRS solely ($R^2 = 0.067$; Adjusted $R^2 = 0.040$; $F_{5,173} = 2.492$; $p < .033$), whereas in the second, TOL also entered the model ($R^2 = 0.235$; Adjusted $R^2 = 0.175$; $F_{13,165} = 3.902$; $p < .001$), explaining 17.5% of the variance. Along the same line as attention, higher depressive symptoms and TOL scores predicted a lower self-appraisal of memory function. (**See** Table 4 for details)

Table 4 Hierarchical multiple regression analyses for variables predicting self-appraisal for attention (A) and for memory (B) domains. Only significant predictors are reported.

(A) Attention Self-appraisal ($n = 188$)	ß	t	p
First block			
HDRS	−.269	−3.457	.001
Second block			
HDRS	−.412	−5.963	<0.001
Spatial span backwards (z-score)	−.163	−2.095	.038
Digit span backwards (z-score)	−.157	−1.980	.049
TOL (z-score)	−.147	−2.177	.031
(B) Memory Self-appraisal ($n = 189$)			
First Block			
HDRS	−.264	−3.368	<0.001
Second Block			
HDRS	−.363	−4.725	<0.001
TOL (z-score)	−.151	−2.012	.046

3.6. Concordance in MDD subgroups

The absolute values of concordance did not show between-group significant differences in attention or in memory. In the entire sample, 64% of patients with MDD showed good agreement between subjective and objective attention measures, while for memory 55% presented good concordance. Similar rates were detected when the sample was divided in the three clinical subgroups -remitted, partial remitted and acute MDD. Rates were 64.9%, 64.3% and 63% for attention and 45.6%, 54.4% and 63% for memory.

3.6.1. Relationship between concordance, and clinical and EF & IQ measures

Attention and memory concordance were not normally distributed and non-parametric measures were used. There were no significant correlations (Spearman's rho) between concordance and clinical/neuropsychological variables ($p > .05$) and, therefore, the regression analysis with this measure as a dependent variable was not conducted.

4. Discussion

In this study, we have examined the discrepancy between objective cognitive deficits and subjective cognitive complaints in a clinical sample including patients in remission, in partial remission or in an acute MDD episode. Patients in an acute episode, as expected, showed a greater objective and subjective cognitive deficit. However, they were also the only group that showed a significant correlation between both cognitive measures. Furthermore, the measure of self-appraisal, which provides information about the patients' perception of their real word cognitive functioning relative to their objective cognitive performance in the clinic, also showed significant differences between clinical states, both in attention and in memory domains. While patients in an acute phase showed a pattern of underestimation (higher scores in objective measures), remitted patients displayed a bias towards overestimating their attentional and memory skills in real-word. Multiple regression analyses revealed that, in the whole MDD sample, underestimation of both attention and memory were predicted by higher depressive symptoms and better performance on executive function tests. It is worth mentioning that, consistent with prior research (Farrin et al., 2003), depressive symptoms had significantly stronger correlations with subjective than objective cognitive measures. Thus, these findings suggest that, besides depressive symptoms' role in attentional and memory meta-cognitive processes, cognitive executive ability is also important, independently of mood state.

Overall, the majority of patients with MDD (64% for attention and 55% for memory) showed good concordance (the absolute magnitude of discrepancy) between subjective and objective cognitive measures, regardless of subgroup. However, contrary to our hypothesis, the acutely depressed MDD group was the only one that showed a significant correlation between subjective and objective cognition scores. These findings contrast with many other studies that found no correlation between objective and subjective cognitive measures in acute depression (Farrin et al., 2003; Mohn and Rund, 2016; Srisurapanont et al., 2017; Svendsen et al., 2012). A possible explanation for this disparity may come from differences in symptom severity, as our acute subgroup are severely depressed whereas the cited studies present moderate depressive symptoms. In a more severely depressed sample, in which both objective (Brand et al., 1992; Gualtieri et al., 2006) and subjective (Farrin et al., 2003) cognitive measures are markedly impaired, it may be easier to detect a correlation between the two measures.

At the same time, patients with an acute episode are those who most underestimate their performance in the cognitive domains of attention and memory. This suggests that, although their performance is objectively affected, they rated themselves even worse, indicating a high sensitivity to perceiving cognitive problems. Patients in partial remission showed population-based normal values on objective cognitive performance, although memory was in the lowest boundary. Finally, remitted MDD patients showed a very poor self-appraisal in memory (where their performance was poorer than perceived in daily life) and a positive self-appraisal with a trend towards significance regarding attention. Both the partial and remitted groups showed preserved cognitive performance, which may have made detection of the subtle objective cognitive deficits more difficult, and hence showing considerably higher self-ratings of their performance. The better performance of less severe patients could have blurred their capacity to detect subtle cognitive deficits and therefore they rated themselves as more preserved than they may be. This was likely responsible for the poor correlation between objective and subjective cognitive ratings in the remitted group.

The present study has demonstrated that severity of depressive symptoms is a predictor of underestimation of attentional and memory self-appraisal in MDD patients, which is consistent with prior works studying self-evaluation of cognitive performance (Miskowiak et al., 2016; Srisurapanont et al., 2017) but also of their personality (Orchard

and Reynolds, 2018). The underestimation of patients' own abilities has important implications for treatment approaches, especially regarding functionality restoration, where subjective cognition has demonstrated to play a crucial role (Kim et al., 2016; McIntyre et al., 2015). According to the hypothesis that subjective cognition might reflect pre-morbid cognitive functioning (Friedman et al., 2018; Papakostas, 2014; Scult et al., 2017) not captured in objective cross-sectional evaluations, one important treatment target would be patients' acceptance of their actual difficulties based on objective cognitive performance (which might not come back to premorbid levels). Thus, therapies such as cognitive (Bowie et al., 2013) or functional remediation (Torrent et al., 2013) might benefit from including a module focused on subjective cognition. Treatment approaches like Mindfulness (Sanders and Lam, 2010) or cognitive behavioural therapy (Spinhoven et al., 2018) might be used for this purpose, but this field is still scarcely explored (Joormann and Quinn, 2014).

As expected, the discrepancy between objective and subjective cognitive measures is not only explained by depressive symptoms. Indeed, executive functioning had a significant effect on self-appraisal across MDD patients. Specifically, the higher the EF scores, the higher the underestimation of attentional and memory abilities. Such tendency toward "underestimation" may reflect a more accurate assessment of skills, since subjective complaints may reveal the recognition of a decline in patient's baseline performance, which may or may not be captured by the objective cognitive tests. Indeed, it has been found that older people with subjective cognitive complaints but no objective deficits were twice as likely to develop dementia (Mitchell et al., 2014) and to present underlying functional brain changes when explored (Stewart, 2012). Moreover, better executive functioning might be related to better capacity to compare present with past states. Interestingly, the specific executive functions related to the discrepancy in the current study, have been related with higher insight (switching (Burmester et al., 2016)) and greater levels of subjective cognitive complaints (working memory (Bassel et al., 2002)). The fact that executive functioning and depressive symptomatology explained more variance for attentional than for memory self-appraisal may suggest that determinants of our beliefs of our own cognitive functioning may have different influences depending on the cognitive domain. It is also possible that the model explained more variance for attention because the additional significant predictors (spatial and verbal working memory) are more related to attention than to memory. These findings, however, contrast with prior results in bipolar patients (Miskowiak et al., 2016), which found that those with higher verbal IQ tended to overestimate their cognitive skills. One possible explanation for the divergent results, considering the effect that depressive symptomatology has demonstrated to exert on subjective cognition, is that in the mentioned article all patients were euthymic, while in the present sample a significant number of patients show depressive symptomatology. Also, an alternative, but not exclusive, explanation is the existence of a cognitive cost to compensatory activities (i.e. greater fatigability and loss of energy) perceived by the individual, thus leading to report lower functioning. Finally, the mentioned study includes bipolar patients while ours included unipolar patients. In any case, it seems that self-appraisal (or the estimation of one's cognitive abilities vs. their actual performance) is partly explained by executive functions, whereas concordance, although is a good measure of the accuracy, does not capture the capacity for reflective evaluation.

There are some limitations that should be considered when examining the results of the present study. First, without a group of healthy comparison participants, the absolute magnitude of impairment could not be ascertained. Although the present study allows for the analysis of relative differences in self-appraisal across stratified patients based upon their symptom severity, it cannot provide absolute determinations about whether the observed concordance and self-appraisals fall within "normal" ranges in reference to healthy individuals, i.e. free of any psychiatric condition. Thus, it is not clear if the observed tendency of the euthymic patients in this study to over-estimate their cognitive abilities reflects diminished awareness/metacognition, or whether this reflects a previously identified bias to overestimate one's ability in healthy individuals (Kruger and Dunning, 1999). Second, the cross-sectional design does not allow any causal inference. Finally, although current medication effects did not show any correlation with self-appraisal nor concordance, treatment trajectory effects were not ruled out, as patients were not cognitively assessed prior to treatment. Future studies would benefit from a longitudinal study design evaluating the association between changes in executive functions and in subjective impression to further explore whether executive functioning exerts changes in patient's self-appraisal.

Altogether, this data provides novel insights of the involvement of depressive symptoms and executive functions in the discrepancy between subjective and objective cognitive deficits in MDD. The findings have clinical implications as they suggest that it may be necessary to assess both subjective and objective cognition in MDD patients regardless of their clinical status, especially if they are in remission or partially remitted. Finally, pro-cognitive or psychological therapies might be explored to address the negative attentional bias (Beevers et al., 2015), which might underlie the subjective cognitive dysfunction.

Acknowledgements

We thank the staff of the Department of Psychiatry, Hospital Universitari Parc Taulí for their assistance in this study, specifically to Dr Crivillés, Dr Acebillo, Dr Ros and Dr Coronas for their help in patient's recruitment. We also thank the patients who participated in the current study for their kind cooperation.

Conflict of interest

Author I. J. Torres has received consultation fees from Lundbeck Canada and Sumitomo Dainippon. Authors E. Aguilar and I. Figuereo report personal fees from Janssen Cilag and from Lunbeck-Otsuka, outside the submitted work. Author R. W. Lam has received honoraria for ad hoc speaking or advising/consulting, or received research funds,

from: Akili, Allergan, Asia-Pacific Economic Cooperation, BC Leading Edge Foundation, Brain Canada, Canadian Institutes of Health Research, Canadian Depression Research and Intervention Network, Canadian Network for Mood and Anxiety Treatments, Canadian Psychiatric Association, CME Institute, Janssen, Lundbeck, Lundbeck Institute, Medscape, MindHealth Technologies, Otsuka, Pfizer, St. Jude Medical, University Health Network Foundation, Vancouver Coastal Health Research Institute, and VGH Foundation. Author N. Cardoner declares that he has received honoraria as consultant, advisor or CME speaker from, Janssen, Lundbeck, Pfizer, Exeltis and MSD. All other authors confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

Contributors

NC designed the study and wrote the protocol. NC and IJT coordinated the study and supervised the writing. MSB, IJT and NC performed the conceptualization of the study. MSB, MVG, GNV, IF and EA conducted the data collection and MVG, EA and GNV also completed the data curation. MSB, IJT, EV and XG performed the main analysis. MSB and IJT wrote the first draft and NC, EV, MJP and XG assisted in the upcoming writing. NC, IJT, RWL and MJP validated and supervised the manuscript and NC and DP provided the required resources to conduct it. All authors contributed to and have approved the final manuscript.

Role of the funding source

This study was supported by Lundbeck Spain. Lundbeck had no role in the design and conduct of the study, collection, management, analysis, or interpretation of the data, preparation, review, or approval of the manuscript, and decision to submit the manuscript for publication.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.euroneuro.2018.11.1104.

References

Bassel, C., Rourke, S.B., Halman, M.H., Smith, M.Lou, 2002. Working memory performance predicts subjective cognitive complaints in HIV infection. Neuropsychology 16, 400–410.

Beck, A.T., 2008. The evolution of the cognitive model of depression and its neurobiological correlates. Am. J. Psychiatry 165, 969–977.

Beck, A.T., 1963. Thinking and depression. Arch. Gen. Psychiatry 9, 324.

Beevers, C.G., Clasen, P.C., Enock, P.M., Schnyer, D.M., 2015. Attention bias modification for major depressive disorder: effects on attention bias, resting state connectivity, and symptom change. J. Abnorm. Psychol. 124, 463–475.

Bowie, C.R., Gupta, M., Holshausen, K., Jokic, R., Best, M., Milev, R., 2013. Cognitive remediation for treatment-resistant depression. J. Nerv. Ment. Disord. 201, 680–685.

Brand, A.N., Jolles, J., Gispen-de Wied, C., 1992. Recall and recognition memory deficits in depression. J. Affect. Disord. 25, 77–86.

Burmester, B., Leathem, J., Merrick, P., 2016. Subjective cognitive complaints and objective cognitive function in aging: a systematic review and meta-analysis of recent cross-sectional findings. Neuropsychol. Rev. 26, 376–393.

Casals-Coll, M., Sánchez-Benavides, G., Quintana, M., Manero, R.M., Rognoni, T., Calvo, L., Palomo, R., Aranciva, F., Tamayo, F., Peña-Casanova, J., 2013. Estudios normativos españoles en población adulta joven (proyecto NEURONORMA jóvenes): normas para los test de fluencia verbal. Neurologia 28, 33–40.

Clark, M., DiBenedetti, D., Perez, V., 2016. Cognitive dysfunction and work productivity in major depressive disorder. Expert Rev. Pharmacoecon. Outcomes Res. 16, 455–463.

Cotrena, C., Branco, L.D., Kochhann, R., Shansis, F.M., Fonseca, R.P., 2016. Quality of life, functioning and cognition in bipolar disorder and major depression: a latent profile analysis. Psychiatry Res. 241, 289–296.

Dias, V.V., Brissos, S., Carita, A.I., 2008. Clinical and neurocognitive correlates of insight in patients with bipolar I disorder in remission. Acta Psychiatr. Scand. 117, 28–34.

Evans, V.C., Iverson, G.L., Yatham, L.N., Lam, R.W., 2014. The relationship between neurocognitive and psychosocial functioning in major depressive disorder: a systematic review. J. Clin. Psychiatry 75, 1359–1370.

Farrin, L., Hull, L., Unwin, C., Wykes, T., David, A., 2003. Effects of depressed mood on objective and subjective measures of attention. J. Neuropsychiatry Clin. Neurosci. 15, 98–104.

Ferrari, A.J., Somerville, A.J., Baxter, A.J., Norman, R., Patten, S.B., Vos, T., Whiteford, H.A., 2013. Global variation in the prevalence and incidence of major depressive disorder: a systematic review of the epidemiological literature. Psychol. Med. 43 (3), 471–481.

Friedman, N.P., du Pont, A., Corley, R.P., Hewitt, J.K., 2018. Longitudinal relations between depressive symptoms and executive functions from adolescence to early adulthood: a twin study. Clin. Psychol. Sci. 6, 543–560.

Friedman, N.P., Miyake, A., Corley, R.P., Young, S.E., Defries, J.C., Hewitt, J.K., 2006. Not all executive functions are related to intelligence. Psychol. Sci.: J. Am. Psychol. Soc. / APS 17, 172–179.

Gualtieri, C.T., Johnson, L.G., Benedict, K.B., 2006. Neurocognition in depression: patients on and off medication versus healthy comparison subjects. Clin. Res. Rep. 18, 217–255.

Hamilton, M., 1960. Hamilton depression rating scale (HAM-D) instructions for the clinician : HAM-D scoring instructions. J. Neurol. Neurosurg. Psychiatry 23, 56–62 2356-62.

Joormann, J., Quinn, M.E., 2014. Cognitive processes and emotion regulation in depression. Depress. Anxiety 31, 308–315.

Kim, J.M., Chalem, Y., di Nicola, S., Hong, J.P., Won, S.H., Milea, D., 2016. A cross-sectional study of functional disabilities and perceived cognitive dysfunction in patients with major depressive disorder in South Korea: The PERFORM-K study. Psychiatry Res. 239, 353–361.

Klusmann, V., Evers, A., Schwarzer, R., Heuser, I., 2011. A brief questionnaire on metacognition: psychometric properties. Aging Ment. Health 15, 1052–1062.

Kruger, J., Dunning, D., 1999. Unskilled and unaware of it: How difficulties in recognizing one's own incompetence lead to inflated self-assessments. J. Pers. Soc. Psychol. 77, 1121–1134.

Lam, R.W., Saragoussi, D., Danchenko, N., Rive, B., Lamy, F.X., Brevig, T., 2013. Psychometric validation of perceived deficits questionnaire – depression (PDQ-D) in patients with major depressive disorder (MDD). Value Health 16, A330.

Lezak, M.D., Lezak, M.D., 2004. Neuropsychological Assessment. Oxford University Press.

Lopez, A.D., Mathers, C.D., Ezzati, M., Jamison, D.T., Murray, C.J.L., 2006. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. Lancet 367, 1747–1757.

Lysaker, P.H., Carcione, A., Dimaggio, G., Johannesen, J.K., Nicolò, G., Procacci, M., Semerari, A., 2005. Metacognition amidst narratives of self and illness in schizophrenia: associations with neurocognition, symptoms, insight and quality of life. Acta Psychiatr. Scand. 112, 64–71.

Lysaker, P.H., Warman, D.M., Dimaggio, G., Procacci, M., LaRocco, V.A., Clark, L.K., Dike, C.A., Nicolò, G., 2008. Metacognition in schizophrenia: associations with multiple assessments of executive function. J. Nerv. Ment. Disord. 196, 384–389.

Mäntylä, T., Rönnlund, M., Kliegel, M., 2010. Components of executive functioning in metamemory. Appl. Neuropsychol. 17, 289–298.

McIntyre, R.S., Soczynska, J.Z., Woldeyohannes, H.O., Alsuwaidan, M.T., Cha, D.S., Carvalho, A.F., Jerrell, J.M., Dale, R.M., Gallaugher, L.A., Muzina, D.J., Kennedy, S.H., 2015. The impact of cognitive impairment on perceived workforce performance: results from the international mood disorders collaborative project. Compr. Psychiatry 56, 279–282.

Miskowiak, K., Burdick, K., Martinez-Aran, A., Bonnin, C., Bowie, C., Carvalho, A., Gallagher, P., Lafer, B., López-Jaramillo, C., Sumiyoshi, T., McIntyre, R., Schaffer, A., Porter, R., Torres, I., Yatham, L., Young, A., Kessing, L., Vieta, E., 2017. Methodological recommendations for cognition trials in bipolar disorder by the international society for bipolar disorders targeting cognition task force. Bipolar Disord. 19, 614–626.

Miskowiak, K.W., Petersen, J.Z., Ott, C.V., Knorr, U., Kessing, L.V., Gallagher, P., Robinson, L., 2016. Predictors of the discrepancy between objective and subjective cognition in bipolar disorder: a novel methodology. Acta Psychiatr. Scand. 134, 511–521.

Mitchell, A.J., Beaumont, H., Ferguson, D., Yadegarfar, M., Stubbs, B., 2014. Risk of dementia and mild cognitive impairment in older people with subjective memory complaints: meta-analysis. Acta Psychiatr. Scand. 130, 439–451.

Mohn, C., Rund, B.R., 2016. Neurocognitive profile in major depressive disorders: relationship to symptom level and subjective memory complaints. BMC Psychiatry 16, 108.

Orchard, F., Reynolds, S., 2018. The combined influence of cognitions in adolescent depression: biases of interpretation, self-evaluation, and memory. Br. J. Clin. Psychol. 57, 420–435.

Papakostas, G.I., 2014. Cognitive symptoms in patients with major depressive disorder and their implications for clinical practice. J. Clin. Psychiatry 75, 8–14.

Paykel, E.S., 2008. Partial remission, residual symptoms, and relapse in depression. Dialogues Clin. Neurosci. 10, 431–437.

Pena-Casanova, J., Quinones-Ubeda, S., Gramunt-Fombuena, N., Quintana-Aparicio, M., Aguilar, M., Badenes, D., Cerulla, N., Molinuevo, J.L., Ruiz, E., Robles, A., Barquero, M.S., Antunez, C., Martinez-Parra, C., Frank-Garcia, A., Fernandez, M., Alfonso, V., Sol, J.M., Blesa, R., 2009. Spanish multicenter normative studies (NEURONORMA Project): norms for verbal fluency tests. Arch. Clin. Neuropsychol. 24, 395–411.

Preiss, M., Kucerova, H., Stepankova, H., Sos, P., Lukavsky, J., Uceni, T., 2007. Cognitive deficits in unipolar depression during remission - auditory verbal learning test findings. Psychiatrie 11, 79–83.

Roca, M., López-Navarro, E., Monzón, S., Vives, M., García-Toro, M., García-Campayo, J., Harrison, J., Gili, M., 2015. Cognitive impairment in remitted and non-remitted depressive patients: a follow-up comparison between first and recurrent episodes. Eur. Neuropsychopharmacol. 25, 1991–1998.

Rock, P.L., Roiser, J.P., Riedel, W.J., Blackwell, A.D., 2014. Cognitive impairment in depression: a systematic review and meta-analysis. Psychol. Med. 44, 2029–2040.

Sackeim, H.A., 2001. The definition and meaning of treatment-resistant depression. J. Clin. Psychiatry 62 (Suppl 1), 10–17.

Sanders, W.A., Lam, D.H., 2010. Ruminative and mindful self-focused processing modes and their impact on problem solving in dysphoric individuals. Behav. Res. Ther. 48, 747–753.

Scult, M.A., Paulli, A.R., Mazure, E.S., Moffitt, T.E., Hariri, A.R., Strauman, T.J., 2017. The association between cognitive function and subsequent depression: a systematic review and meta-analysis. Psychol. Med. 47, 1–17.

Schaefer, J.D., Scult, M.A., Caspi, A., Arseneault, L., Belsky, D.W., Hariri, A.R., Harrington, H., Houts, R., Ramrakha, S., Poulton, R., Moffitt, T.E., 2017. Is low cognitive functioning a predictor or consequence of major depressive disorder A test in two longitudinal birth cohorts. Dev. Psychopathol. 16, 1–15.

Shimizu, Y., Kitagawa, N., Mitsui, N., Fujii, Y., Toyomaki, A., Hashimoto, N., Kako, Y., Tanaka, T., Asakura, S., Kusumi, I., 2013. Neurocognitive impairments and quality of life in unemployed patients with remitted major depressive disorder. Psychiatry Res. 210, 913–918.

Spinhoven, P., Klein, N., Kennis, M., Cramer, A.O.J., Siegle, G., Cuijpers, P., Ormel, J., Hollon, S.D., Bockting, C.L., 2018. The effects of cognitive-behavior therapy for depression on repetitive negative thinking: a meta-analysis. Behav. Res. Ther. 106, 71–85.

Srisurapanont, M., Suttajit, S., Eurviriyanukul, K., Varnado, P., 2017. Discrepancy between objective and subjective cognition in adults with major depressive disorder. Sci. Rep. 7, 1–7.

Stewart, R., 2012. Subjective cognitive impairment. Curr. Opin. Psychiatry 25, 445–450.

Strauss, E., Sherman, E.M.S., Spreen, O., 2006. A Compendium of Neuropsychological Tests: Administration, Norms, and Commentary. Oxford University Press.

Strober, L.B., Binder, A., Nikelshpur, O.M., Chiaravalloti, N., DeLuca, J., 2016. The perceived deficits questionnaire: perception, deficit, or distress? Int. J. MS Care 18, 183–190.

Sullivan, M., Edgley, K., Dehoux, E., 1990. A survey of multiple sclerosis: I. Perceived cognitive problems and compensatory strategy use. Can. J. Rehabil. 4, 99–105.

Svendsen, A.M., Kessing, L.V., Munkholm, K., Vinberg, M.A.J., Miskowiak, K.W., 2012. Is there an association between subjective and objective measures of cognitive function in patients with affective disorders? Nord J. Psychiatry 66, 248–253.

Torrent, C., Bonnin, C.M, Martínez-Arán, A., Valle, J., Amann, B.L., González-Pinto, A., Salamero, M., Vieta, E., 2013. Efficacy of functional remediation in bipolar disorder: a multicenter randomized controlled study. Am. J. Psychiatry 17, 852–859.

Torres, I.J., Mackala, S.A., Kozicky, J.-M., Yatham, L.N., 2016. Metacognitive knowledge and experience in recently diagnosed patients with bipolar disorder. J. Clin. Exp. Neuropsychol. 38, 730–744.

Vos, T., 2016. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the global burden of disease study 2015. Lancet 388, 1545–1602.

Wechsler, D., 2008. Wechsler Adult Intelligence Scale WAIS-IV; Technical and Interpretive Manual. Pearson.

Wechsler, D., 2004. WMS-III: Escala de Memoria Wechsler-III. TEA ediciones.

Woo, Y.S., Rosenblat, J.D., Kakar, R., Bahk, W.-M., McIntyre, R.S., 2016. Cognitive deficits as a mediator of poor occupational function in remitted major depressive disorder patients. Clin. Psychopharmacol. Neurosci. 14, 1–16.

Yen, C.F., Cheng, C.P., Ko, C.H., Yen, J.Y., Huang, C.F., Chen, C.S., 2008. Relationship between insight and neurocognition in patients with bipolar I disorder in remission. Compr. Psychiatry 49, 335–339.