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Longitudinal associations between melancholic depression and executive function in adult patients with major depressive disorder: a 12-month follow-up study

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ABSTRACT

Major depressive disorder (MDD) is often associated with deficits in executive function, but the long-term cognitive impact of specific depressive subtypes, in particular melancholic depression (MelD), is underexplored. This is the first prospective study aimed at exploring longitudinal associations between MelD and executive function in adult patients with MDD. This is a secondary analysis using data from a larger project with assessments at baseline, 6 and 12 months. MelD was identified using an algorithm derived from a subset of eight items from the Inventory of Depressive Symptomatology-Self Rated, which provides a standardized framework for the identification of this specific depressive subtype. Executive function was assessed using the Cambridge Neuropsychological Test Automated Battery. Longitudinal associations between MelD and executive function, including a global domain, four subdomains (working memory, planning, response inhibition and decision-making), and eight individual variables used to calculate the composite scores of the five (sub)domains, were analyzed using linear mixed-effects models adjusted for demographic and clinical variables and psychomotor speed. One hundred and five patients (20.95 % MelD) were analyzed at baseline, 73 (17.81 % MelD) at 6 months, and 61 (19.67 % MelD) at 12 months. MelD, older age and female sex were significantly associated with worse performance in the global executive function domain, in the working memory subdomain, and in four individual variables within the working memory, planning and decision-making subdomains, independent of other demographic and clinical variables and psychomotor speed. The findings highlight MelD as a distinct risk factor for worse long-term executive function in adult patients with MDD.

1. Introduction

Major depressive disorder (MDD) is a complex psychiatric condition characterized by a wide variety of symptomatic presentations, underscoring its inherently heterogeneous clinical nature (Baumeister and Parker, 2012; Østergaard et al., 2011). Along with distinctive symptoms such as depressed mood and decreased interest or pleasure, cognitive deficits are another central feature of MDD, as captured in its nosological definition (American Psychiatric Association, 2013). These deficits, present during acute episodes and often persisting after remission, mainly affect attention, learning and memory, executive function and processing speed (Roca et al., 2015b; Semkovska et al., 2019). However, a universally accepted general cognitive profile for MDD has not yet been established (Vicent-Gil and Portella, 2021).

Melancholia is a syndrome with a long history and tradition in psychiatry characterized by distinctive psychopathological features (Martino et al., 2019; Parker et al., 2010). It has been proposed as a qualitatively different form of depression or as a more severe type of illness on a depressive continuum (Martino et al., 2021). Research comparing the cognitive profile of melancholic depression (MelD) and

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non-melancholic depression (NMelD) has yielded conflicting results. Most studies have reported worse cognitive performance in patients with MelD compared to patients with NMelD (Austin et al., 1999; Cornell et al., 1984; Day et al., 2015; Exner et al., 2009; Krogh et al., 2012; Lin et al., 2014; Michopoulos et al., 2008, 2006; Pier et al., 2004; Quinn et al., 2012a, 2012b; Roca et al., 2015a; Rogers et al., 2004; Rush et al., 1983; Valerio et al., 2023; Withall et al., 2010). In contrast, some studies have observed the opposite pattern (Lee et al., 2021; Markela-Lerenc et al., 2006) or have found no differences between the two groups (Austin et al., 1992; Gorlyn et al., 2006; Liang et al., 2023). To date, one systematic review (Bosaipo et al., 2017) and two meta-analyses (Valerio et al., 2021; Zaninotto et al., 2016) have synthesized these findings, offering a more comprehensive perspective on the general cognitive profile of MelD.

Bosaipo et al. (2017) conducted a systematic review including 17 studies and found that patients with MelD perform worse than those with NMelD and healthy individuals on psychomotor speed, sustained attention and span, verbal and visual memory, and executive function. The authors concluded that MelD can be qualitatively and quantitatively distinguished from NMelD by cognitive testing. For their part, Zaninotto et al. (2016) meta-analyzed nine studies comprising 522 patients (253 with MelD) and found that patients with MelD perform worse than those with NMelD on processing speed, attention and working memory, visual learning and memory, reasoning and problem solving, and global cognition. However, the authors acknowledged that their study is limited by a broad definition of cognitive domains. Finally, Valerio et al. (2021) meta-analyzed 14 studies involving 1782 patients (729 with MelD) and observed that, during acute episodes, patients with MelD perform worse than those with NMelD in processing speed, attention, working memory, verbal learning and memory, verbal fluency, executive function and global cognition, while after remission the worse performance in verbal fluency persists. The authors noted that the worse cognitive performance of MelD may not simply be due to differences in symptom severity and psychomotor speed but could represent an endophenotype of this depressive subtype (Hasler et al., 2004).

By refining the definition of cognitive domains, Valerio et al. (2021) addressed the main methodological shortcoming of the Zaninotto et al. (2016) study. However, the authors acknowledged that their research remains limited by the paucity of studies examining subdomains of executive function beyond the traditional ones. Traditional subdomains involve "cold," emotionally neutral cognitive processes related to goal-directed behavior, such as working memory, inhibitory control, cognitive flexibility, reasoning, problem solving and planning. In contrast, non-traditional subdomains encompass "hot" cognitive processes that involve emotional and motivational components, such as decision-making and social cognition (Diamond, 2013; Salehinejad et al., 2021). Impaired decision-making, which has recently been identified as longitudinally intertwined with suicidal behavior in adult patients with MDD (Riera-Serra et al., 2023), has not yet been explored in the context of MelD.

In addition, most research to date is based on cross-sectional studies (Austin et al., 1999, 1992; Cornell et al., 1984; Day et al., 2015; Exner et al., 2009; Gorlyn et al., 2006; Krogh et al., 2012; Lee et al., 2021; Liang et al., 2023; Markela-Lerenc et al., 2006; Michopoulos et al., 2008, 2006; Pier et al., 2004; Quinn et al., 2012b, 2012a; Rogers et al., 2004; Rush et al., 1983; Valerio et al., 2023) or longitudinal studies spanning no >6 months (Lin et al., 2014; Roca et al., 2015a; Withall et al., 2010), limiting the ability to draw firm conclusions about possible long-term associations between MelD and executive function in adult patients with MDD. Other questions also remain to be resolved, such as whether these associations are global or subdomain-specific or whether they are independent of symptom severity and psychomotor speed.

The is the first study to address these clinical and research gaps using a prospective design with a 12-month follow-up period. The primary objective was to examine longitudinal associations between MelD and executive function in adult patients with MDD, while controlling for the effects of symptom severity and psychomotor speed. Four key components of executive function, namely working memory, planning, response inhibition and decision-making, were examined, encompassing both traditional "cold" and non-traditional "hot" subdomains. This comprehensive approach also captured the broader complexity of global executive function. The secondary goal was to explore longitudinal associations between MelD and individual executive function variables to uncover subtle patterns of association that might go unnoticed if only broad (sub)domains were analyzed.

2. Methods

2.1. Study design

This is a secondary analysis of a larger prospective non-interventional study with three data collection points: baseline, 6 and 12 months. The original study aimed to examine longitudinal associations between executive function and suicide risk in adult patients with MDD (Roca et al., 2019). Data not related to the specific aims of the present study have been reported in another publication (Riera-Serra et al., 2023).

2.2. Participants

Inclusion criteria were being aged 18–65 years, being diagnosed with MDD according to the criteria of the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 2013), having an active MDD episode defined as a score >17 on the Inventory of Depressive Symptomatology-Self Rated (IDS-SR30) (Gili et al., 2011; Rush et al., 1996) and being an outpatient.

Exclusion criteria were having psychotic symptoms, being under treatment with antipsychotic or mood-stabilizing drugs, being diagnosed with borderline personality disorder, neurological disease or cognitive impairment resulting from other medical conditions, having received electroconvulsive therapy or being unable to understand the study tests.

2.3. Procedure

The study was conducted in Mallorca, Balearic Islands, Spain, from November 2018 to July 2022. All patients provided written informed consent before inclusion. The initial diagnosis of MDD was established using the Spanish version of the MINI International Neuropsychiatric Interview (Ferrando et al., 1998; Sheehan et al., 1998). Patients were recruited, evaluated and followed by a clinical and research team of expert psychiatrists and psychologists, who systematically collected a comprehensive set of demographic, clinical and cognitive data. Assessments and data collection were conducted either at the patients' primary care center or at the Research Institute of Health Sciences of the University of the Balearic Islands. Each evaluation lasted between 90–120 min and was completed in one or two sessions, depending on the patient's level of fatigue. During the study period, none of the patients underwent neurocognitive rehabilitation.

Approval was obtained from the Research Ethics Committee of the Balearic Islands, number IB3687/18PI. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the 1964 Declaration of Helsinki and its subsequent revisions.

2.4. Demographic variables

Data were collected on age, sex (male, female), education (<12 years, ≥12 years), professional status (employed, unemployed) and marital status (married, unmarried).

2.5. Clinical variables

The severity of depression was assessed with the Spanish version of the IDS-SR30 (range 0–84). A higher score indicates more severe depressive symptoms. The depressive episode was considered to be in remission when scores at 6 and 12 months were <14 (Gili et al., 2011). Other variables such as type of MDD episode (first, recurrent), duration of MDD episode (<12 months, ≥12–24 months, >24 months), being on antidepressant treatment (yes, no) and having comorbid psychiatric disorders (yes, no) were extracted from medical records.

MelD was identified using an algorithm based on a subset of eight items from the IDS-SR30 developed by the STAR*D research group, providing a standardized framework for the identification of this depressive subtype (Khan et al., 2006). To meet the MelD criteria, patients had to score 2 or 3 on items of pleasure/enjoyment (i.e. loss of pleasure in all, or almost all, activities) and reactivity of mood responses (i.e. lack of reactivity to usually pleasurable stimuli) –rated on a scale from 0 (symptom not present) to 3 (greater severity of the symptom)– and 1, 2 or 3 on at least three of the following items: mood quality (i.e. distinct quality of depressed mood), mood variation (i.e. depression regularly worse in the morning), early morning insomnia or awakening, psychomotor slowing or agitation, appetite or weight decrease (i.e. significant anorexia or weight loss) and self-outlook (i.e. excessive or inappropriate guilt). Patients not meeting these criteria were classified as NMelD.

2.6. Cognitive variables

Five tasks from the Cambridge Neuropsychological Test Automated Battery (CANTAB) were administered, of which four assessed executive function and one assessed psychomotor speed: 1) Spatial Working Memory, a measure of strategy and working memory errors, 2) One Touch Stockings of Cambridge, a measure of spatial planning and working memory, 3) Stop Signal Task, a measure of response inhibition and impulse control, 4) Cambridge Gambling Task, a measure of decision-making and risk-taking behavior, and 5) Motor Screening Task, a measure of sensorimotor skills (Cambridge Cognition Limited, 2023).

Nine variables were selected from the five CANTAB tasks administered, including: 1) Spatial Working Memory-Between Errors, 2) Spatial Working Memory-Strategy, 3) One Touch Stockings of Cambridge-Problems Solved on First Choice, 4) One Touch Stockings of Cambridge-Median Latency to First Choice, 5) Stop Signal Task-Stop Signal Reaction Time, 6) Cambridge Gambling Task-Delay Aversion Total, 7) Cambridge Gambling Task-Decision Making Quality Total Merged, 8) Cambridge Gambling Task-Risk Adjustment Merged, and 9) Motor Screening Task-Mean Latency. A comprehensive description of these variables and how they were combined to compose a global executive function domain and four executive function subdomains, including: 1) working memory (Spatial Working Memory), 2) planning (One Touch Stockings of Cambridge), 3) response inhibition (Stop Signal Task), and 4) decision making (Cambridge Gambling Task), is provided in Table S1 (Supplementary Material, SM).

In the absence of both normative data for most CANTAB variables (Cambridge Cognition Limited, 2023) and a reference group of healthy individuals in the original data set (Roca et al., 2019), cognitive variables were preprocessed prior to statistical analyses. For this purpose, raw scores were transformed into standardized, demographically corrected z-scores (mean =0, standard deviation [SD] =1), ensuring comparability between MelD and NMelD groups (Andrade, 2021). Following the methodology described by Riera-Serra et al. (2023), raw scores for each cognitive variable were first transformed into standardized z-scores using the mean and SD of the entire patient sample as reference values. Where appropriate, z-scores were inverted (i.e. multiplied by −1) so that higher scores consistently indicated better cognitive performance. The z-scores were then corrected for demographic factors such as age, sex and education. The z-scores for the executive function variables were also corrected for the Motor Screening Task-Mean Latency (psychomotor speed) variable. Finally, the corrected z-scores of the individual variables were combined to compose the scores for the global executive function domain and the four executive function subdomains, as shown in Table S1 (SM).

2.7. Statistical analysis

Data normality was tested by P-P plots and the Shapiro-Wilk test. Descriptive data are shown as mean (SD) or frequency (%). Differences between the MelD and NMelD groups in demographic, clinical and cognitive variables at baseline, 6 and 12 months were analyzed by *t*-tests and Chi-squared tests, as appropriate.

Longitudinal associations between MelD and executive function were analyzed at both the domain and subdomain levels using linear mixed-effects models. To uncover subtle patterns of association that might go unnoticed if only broad (sub)domain scores were analyzed, a series of additional exploratory linear mixed-effects models were conducted to analyze longitudinal associations between MelD and executive function at the level of individual variables (Freemantle et al., 2003; Rothman, 1990). Variables used to improve model fit were selected based on their potential to influence executive function according to previous systematic reviews and meta-analyses (Bosaipo et al., 2017; Valerio et al., 2021; Zaninotto et al., 2016). Following the methodology described by Riera-Serra et al. (2023), the sequential inclusion of the following blocks of covariates and a subject level-random intercept was performed: 1) follow-up time (Model 1), 2) demographic variables (age, sex and education) (Model 2), 3) clinical and cognitive variables (melancholia, remission, type and duration of the MDD episode, antidepressant treatment, psychiatric comorbidities and psychomotor speed) (Model 3), and 4) a time-level random slope (Model 4). The goodness-of-fit of the models was tested using log-likelihood (LL), Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC). Table S2 (SM) shows that, although all but one of Models 4 have a higher LL than Models 3, indicating better model fit, the improvement in model fit is marginal and comes at the cost of increased complexity. Specifically, all but one of Models 4 have higher AIC and BIC values compared to Models 3. This indicates that Models 4, despite providing slightly better LL values, are mostly less parsimonious than Models 3. Given the necessary trade-off between fit (LL) and parsimony (AIC and BIC), Models 3 were selected as the final models, since they mostly achieve a better balance between fit and parsimony, i.e. a competitive fit while avoiding the unnecessary complexity introduced by the time-level random slope in Models 4.

To evaluate the robustness of the results, a sensitivity analysis was conducted on the subset of patients who completed all study time points ($n = 61$). In addition, a dropout pattern analysis was performed. For this analysis, patients were classified into two groups: “completers,” which included patients who completed all study time points ($n = 61$), and “dropouts,” which included patients who dropped out at any time point, either after baseline or 6 months ($n = 44$). Due to sample size limitations, it was not possible to perform a more detailed sensitivity analysis distinguishing the time point of dropout. Both sensitivity analyses were adjusted for the same variables as those in the final Models 3. These analyses allowed us to assess whether the results were influenced by potential biases arising from missing data or participant attrition.

Analyses were performed using STATA v.17.0. Statistical significance was set at $p < 0.05$.

3. Results

3.1. Sample characteristics

A total of 168 patients were screened for eligibility. Of these, 105 were evaluated at baseline, 73 at 6 months, and 61 at 12 months, yielding a total of 239 observations (Fig. 1). Throughout the study,

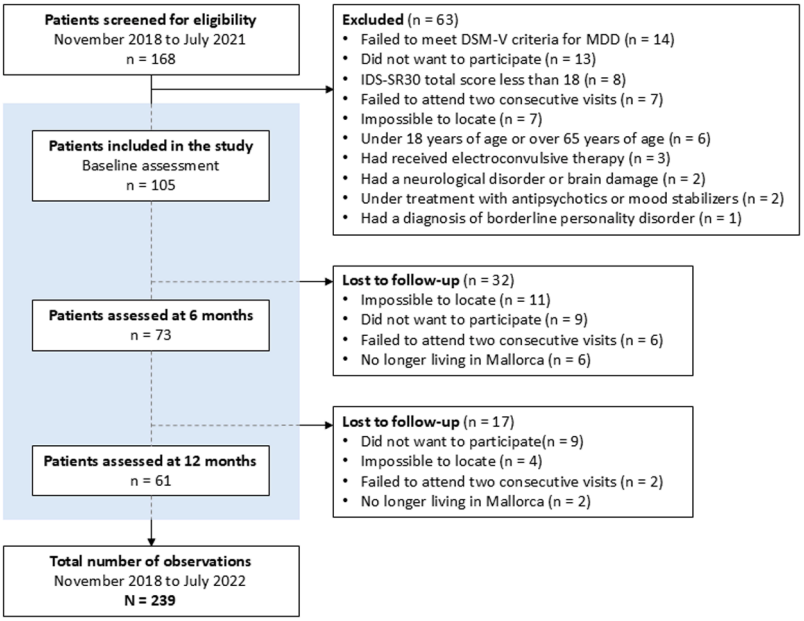

Fig. 1. Flowchart of the study. During the study, 44 (41.90 %, $n = 44/105$) patients were lost to follow-up, 30.48 % ($n = 32$) at 6 months, and 16.19 % ($n = 17$) at 12 months. Five (4.76 %) patients who did not attend follow-up at 6 months completed follow-up at 12 months. Dropout was more frequent in unemployed patients (68.18 % [$n = 30/44$] vs. 47.54 % [$n = 29/61$]; $OR_{(employed)} = 0.423$, 95 % CI: 0.188–0.950, $p = 0.037$), patients with a first episode of MDD (81.82 % [$n = 36/44$] vs. 60.66 % [$n = 37/61$]; $OR_{(recurrent\ episode)} = 0.343$, 95 % CI: 0.136–0.861, $p = 0.023$) and patients with slower reaction time/psychomotor speed (One Touch Stockings of Cambridge-Median Latency to First Choice score: -0.23 ± 0.95 vs. 0.16 ± 0.64; $t = -0.149$, 95 % CI: -0.266 – -0.031, $p = 0.014$; Motor Screening Task-Mean Latency score: -0.20 ± 0.84 vs. 0.14 ± 0.83; $t = -0.116$, 95 % CI: -0.228 – -0.004, $p = 0.043$). No significant differences were found between patients with a first MDD episode and patients with recurrent MDD episodes in demographic, clinical and cognitive variables. DSM-V, Diagnostic and Statistical Manual of Mental Disorders, fifth edition criteria; MDD, major depressive disorder; IDS-SR30, Inventory of Depressive Symptomatology-Self Rated.

approximately 20 % of patients met MelD criteria, with percentages of 20.95 % at baseline, 17.81 % at 6 months and 19.67 % at 12 months. The remaining 80 % were classified as NMelD, with percentages of 79.05 % at baseline, 82.19 % at 6 months and 80.33 % at 12 months.

Table 1 shows the demographic, clinical and cognitive characteristics of the patients at baseline and the differences in these variables between MelD and NMelD groups. The respective figures 6 and 12 months later are shown in Tables S3 and S4 (SM). At baseline, patients with MelD had lower employment rates (22.73 % vs. 49.40 %, $p < 0.025$), more severe depressive symptoms (IDS-SR30 total score: 54.02 $\pm$ 7.65 vs. 39.82 $\pm$ 10.69, $p < 0.001$) and a higher percentage of psychiatric comorbidities (72.73 % vs. 40.96 %, $p = 0.008$) than patients with NMelD. Similar results were obtained 6 and 12 months later, except for current MDD status. Throughout the study, all patients in the MelD group were in an active episode of depression. In contrast, while 100 % of patients in the NMelD group were in an active episode of depression at baseline, 20 % were in remission at 6 months and 26.53 % at 12 months.

3.2. Longitudinal associations between MelD and executive function at the domain and subdomain level

Table 2A and Fig. 2A show that MelD ($p = 0.003$), older age ($p < 0.001$) and female sex ($p = 0.007$) were significantly associated with lower scores on the global executive function domain ($F_{(16,217)} = 72.79$, $p < 0.001$). Table 2B and Fig. 2B show that MelD ($p = 0.005$), older age ($p < 0.001$) and female sex ($p < 0.001$) were significantly associated with lower scores on the working memory subdomain ($F_{(16,229)} = 78.87$, $p < 0.001$). No significant association was found between MelD and the subdomains of planning ($p = 0.301$; $F_{(16,227)} = 59.42$, $p < 0.001$), response inhibition ($p = 0.937$; $F_{(16,220)} = 43.77$, $p < 0.001$) and decision making ($p = 0.111$; $F_{(16,218)} = 16.54$, $p < 0.221$) (Table S5, SM). Details on the goodness-of-fit of the models are shown in Table S2 (SM).

3.3. Exploratory analysis on the longitudinal associations between MelD and executive function at the individual variable level

Table 3A and Fig. 2C show that MelD ($p = 0.003$), older age ($p < 0.001$) and female sex ($p = 0.009$) were significantly associated with lower scores on the Spatial Working Memory-Between Errors variable ($F_{(16,229)} = 71.30$, $p < 0.001$). Table 3B and Fig. 2D show that MelD ($p = 0.042$), older age ($p < 0.001$) and female sex ($p < 0.001$) were significantly associated with lower scores on the Spatial Working Memory-Strategy variable ($F_{(16,229)} = 71.16$, $p < 0.001$). Table 3C and Fig. 2E show that MelD ($p = 0.020$) and older age ($p = 0.004$) were also significantly associated with lower scores on the One Touch Stockings of Cambridge-Problems Solved on First Choice variable ($F_{(16,228)} = 27.88$, $p = 0.009$). Finally, Table 3D and Fig. 2F show that MelD ($p = 0.027$), older age ($p = 0.018$) and female sex ($p = 0.019$) were significantly associated with lower scores on the Cambridge Gambling Task-Risk Adjustment Merged variable ($F_{(16,218)} = 23.47$, $p = 0.036$). No significant association was found between MelD and the individual variables One Touch Stockings of Cambridge-Median Latency to First Choice ($p = 0.354$; $F_{(16,227)} = 62.90$, $p < 0.001$), Cambridge Gambling Task-Delay Aversion Total ($p = 0.522$; $F_{(16,218)} = 9.68$, $p = 0.720$) and Cambridge Gambling Task-Decision Making Quality Total Merged ($p = 0.541$; $F_{(16,218)} = 5.81$, $p = 0.953$) (Table S5, SM). Details on the goodness-of-fit of the models are shown in Table S2 (SM).

3.4. Sensitivity analysis

The main effect of MelD remained consistent in all linear mixed-effects models when the sample was restricted to patients who completed all study time points ($n = 61$) (Table S6, SM). Specifically, MelD remained significantly associated with lower scores on the global executive function domain ($p = 0.003$; $F_{(16,168)} = 70.31$, $p < 0.001$), the working memory subdomain ($p = 0.004$; $F_{(16,175)} = 80.36$, $p < 0.001$) and the individual variables Spatial Working Memory-Between Errors (p

Table 1
Demographic, clinical and cognitive characteristics of patients at baseline.

	All patients	MelD	NMelD	p value
N (%)	105 (100.00)	22 (20.95)	83 (79.05)	N/A
Demographic variables				
Age, years	41.64 (12.99)	42.82 (10.65)	41.33 (13.58)	0.634
Female sex, n (%)	67 (63.81)	13 (59.09)	54 (65.06)	0.604
High education (≥12 years), n (%)	33 (31.43)	5 (22.73)	28 (33.73)	0.323
Professional status (employed), n (%)*	46 (43.81)	5 (22.73)	41 (49.40)	0.025
Marital status (married), n (%)	46 (43.81)	12 (54.55)	34 (40.96)	0.502
Clinical variables				
Active MDD episode (IDS-SR30 total score ≥14), n (%)	105 (100.00)	22 (100.00)	83 (100.00)	N/A
First MDD episode (yes), n (%)	73 (69.52)	12 (54.55)	61 (73.49)	0.086
Depression severity (IDS-SR30 total score)***	42.81 (11.65)	54.09 (7.56)	39.82 (10.69)	<0.001
Duration of the MDD episode, n (%)				0.416
<12 months	60 (57.14)	12 (54.55)	48 (57.83)	
≥12–24 months	15 (14.29)	5 (22.73)	10 (12.05)	
>24 months	30 (28.57)	5 (22.73)	25 (30.12)	
Antidepressant treatment (yes), n (%)	77 (76.24)	18 (85.71)	59 (73.75)	0.252
Psychiatric comorbidities (yes), n (%)**	50 (47.62)	16 (72.73)	34 (40.96)	0.008
Cognitive variables (standardized z-scores)				
Global executive function domain[a]	0.01 (0.48)	−0.14 (0.54)	0.05 (0.46)	0.114
Working memory subdomain (Spatial Working Memory, SWM)[a]	−0.01 (0.78)	−0.15 (0.75)	0.04 (0.79)	0.320
SWM-Between Errors variable[a]	0.01 (0.87)	−0.18 (0.82)	0.05 (0.87)	0.270
SWM-Strategy variable[a]	−0.01 (0.86)	−0.11 (0.82)	0.03 (0.88)	0.486
Planning subdomain (One Touch Stockings of Cambridge, OTS)[a]	0.01 (0.63)	−0.06 (0.78)	0.02 (0.59)	0.615
OTS-Problems Solved on First Choice variable[a]	0.01 (0.91)	−0.29 (1.09)	0.08 (0.85)	0.099
OTS-Median Latency to First Choice variable[a]	0.01 (0.80)	0.17 (0.95)	−0.04 (0.76)	0.279
Response inhibition subdomain (Stop Signal Task)[a,b]	0.01 (0.90)	−0.01 (0.93)	0.01 (0.89)	0.967
Decision-making subdomain (Cambridge Gambling Task, CGT)[a]	−0.01 (0.68)	−0.21 (0.74)	0.06 (0.66)	0.112
CGT-Delay Aversion Total variable[a]	−0.01 (0.98)	−0.15 (1.06)	0.04 (0.96)	0.444
CGT-Decision Making Quality Total Merged variable[a]	−0.01 (0.99)	−0.30 (1.15)	0.08 (0.93)	0.113
CGT-Risk Adjustment Merged variable[a]	−0.01 (0.95)	−0.18 (0.81)	0.05 (0.98)	0.223
Psychomotor speed (Motor Screening Task)[c,d]	−0.01 (0.85)	0.03 (0.92)	−0.01 (0.83)	0.877

Mean (SD) is reported unless otherwise specified.
MelD, melancholic depression; NMelD, non-melancholic depression; N/A, does not apply; MDD, major depressive disorder; IDS-SR30, Inventory of Depressive Symptomatology-Self Rated; SD, standard deviation.
Number of antidepressant treatment observations, $n = 101$; MelD, $n = 21$; NMelD, $n = 80$.
Number of global executive function domain observations, $n = 98$; MelD, $n = 21$; NMelD, $n = 77$.
Number of working memory subdomain observations, $n = 104$; MelD, $n = 22$; NMelD, $n = 82$.
Number of SWM-Between Errors variable observations, $n = 104$; MelD, $n = 22$; NMelD, $n = 82$.
Number of SWM-Strategy variable observations, $n = 104$; MelD, $n = 22$; NMelD, $n = 82$.
Number of planning subdomain observations, $n = 103$; MelD, $n = 22$; NMelD, $n = 81$.
Number of OTS-Problems Solved at First Choice variable observations, $n = 103$; MelD, $n = 22$; NMelD, $n = 81$.
Number of OTS-Median Latency to First Choice variable observations, $n = 103$; MelD, $n = 22$; NMelD, $n = 81$.
Number of response inhibition subdomain observations, $n = 99$, MelD, $n = 21$; NMelD, $n = 78$.
Number of decision-making subdomain observations, $n = 98$; MelD, $n = 21$; NMelD, $n = 77$.
Number of CGT-Delay Aversion Total variable observations, $n = 98$; MelD, $n = 21$; NMelD, $n = 77$.
Number of CGT-Decision Making Quality Total Merged variable observations, $n = 98$; MelD, $n = 21$; NMelD, $n = 77$.
Number of CGT-Risk Adjustment Merged variable observations, $n = 98$; MelD, $n = 21$; NMelD, $n = 77$.
Number of psychomotor speed observations, $n = 104$; MelD, $n = 22$; NMelD, $n = 82$.
[a] Demographically corrected z-scores by age, sex, education and psychomotor speed (Motor Screening Task-Mean Latency).
[b] Stop Signal Task-Stop Signal Reaction Time variable.
[c] Demographically corrected z-scores by age, sex and education.
[d] Motor Screening Task-Mean Latency variable.
*$p < 0.05$. ** $p < 0.01$. *** $p < 0.001$.

$= 0.002$; $F_{(16,175)} = 77.87$, $p < 0.001$), Spatial Working Memory-Strategy ($p = 0.032$; $F_{(16,175)} = 67.79$, $p < 0.001$), One Touch Stockings of Cambridge-Problems Solved on First Choice ($p = 0.040$; $F_{(16,174)} = 29.67$, $p < 0.005$) and Cambridge Gambling Task-Risk Adjustment Merged ($p = 0.043$; $F_{(16,169)} = 20.79$, $p < 0.077$). No significant association was found between MelD and the subdomains of planning ($p = 0.132$; $F_{(16,173)} = 50.46$, $p < 0.001$), response inhibition ($p = 0.587$; $F_{(16,170)} = 37.21$, $p < 0.001$) and decision-making ($p = 0.130$; $F_{(16,169)} = 21.44$, $p < 0.065$), nor with the individual variables One Touch Stockings of Cambridge-Median Latency to First Choice ($p = 0.772$; $F_{(16,173)} = 42.61$, $p < 0.001$), Cambridge Gambling Task-Delay Aversion Total ($p = 0.539$; $F_{(16,169)} = 17.71$, $p = 0.169$) and Cambridge Gambling Task-Decision Making Quality Total Merged ($p = 0.572$; $F_{(16,169)} = 8.69$, $p = 0.796$).

The main effect of MelD also remained consistent when the dropout pattern variable was included as an additional covariate in the linear mixed-effects models (Table S7, SM). Specifically, MelD remained significantly associated with lower scores on the global executive function domain ($p = 0.003$; $F_{(17,217)} = 74.90$, $p < 0.001$), the working memory subdomain ($p = 0.006$; $F_{(17,229)} = 79.71$, $p < 0.001$) and the individual variables Spatial Working Memory-Between Errors ($p = 0.004$; $F_{(17,229)} = 71.48$, $p < 0.001$), Spatial Working Memory-Strategy ($p = 0.045$; $F_{(17,229)} = 72.66$, $p < 0.001$), One Touch Stockings of Cambridge-Problems Solved on First Choice ($p = 0.020$; $F_{(17,228)} = 27.99$, $p = 0.014$) and Cambridge Gambling Task-Risk Adjustment Merged ($p = 0.030$; $F_{(17,218)} = 24.68$, $p = 0.038$). No significant association was found between MelD and the subdomains of planning ($p = 0.313$; $F_{(17,227)} = 61.88$, $p < 0.001$), response inhibition ($p = 0.982$; $F_{(17,220)} = 46.47$, $p < 0.001$) and decision-making ($p = 0.125$; $F_{(17,218)} = 20.33$, $p = 0.120$), nor with the individual variables One Touch Stockings of Cambridge-Median Latency to First Choice ($p = 0.330$; $F_{(17,227)} = 66.76$, $p < 0.001$), Cambridge Gambling Task-Delay Aversion Total ($p = 0.530$; $F_{(17,218)} = 9.82$, $p = 0.775$) and Cambridge Gambling Task-Decision Making Quality Total Merged ($p = 0.613$). The dropout pattern variable was a significant predictor only for the Cambridge Gambling Task-Decision Making Quality Total Merged variable ($p = 0.015$), with patients who dropped out ($n = 44$) scoring approximately

Table 2
Linear mixed-effects models in which MelD showed significant longitudinal associations with executive function at the domain and subdomain level.

	A) Global executive function domain[a]			B) Working memory subdomain (Spatial Working Memory)[a]		
	B	95 % CI	p value	B	95 % CI	p value
Time of the follow-up (ref. baseline)						
6 months	−0.023	−0.115 to 0.068	0.615	−0.016	−0.207 to 0.175	0.869
12 months	0.037	−0.063 to 0.138	0.469	0.077	−0.136 to 0.290	0.477
Age, years	−0.025	−0.032 to −0.018	**< 0.001**	−0.033	−0.044 to −0.023	**< 0.001**
Female sex (ref. male)	−0.256	−0.442 to −0.071	**0.007**	−0.500	−0.763 to −0.237	**< 0.001**
High education (ref. <12 years)	0.099	−0.097 to 0.295	0.323	0.050	−0.229 to 0.329	0.725
MelD (ref. NMelD)	−0.188	−0.311 to −0.064	**0.003**	−0.344	−0.585 to −0.103	**0.005**
Remission (ref. active MDD episode)	0.017	−0.141 to 0.175	0.832	0.097	−0.226 to 0.419	0.557
First MDD episode (ref. recurrent)	−0.022	−0.215 to 0.170	0.820	0.075	−0.194 to 0.344	0.584
Duration of the MDD episode (ref. <12 months)						
≥12–24 months	0.124	−0.133 to 0.382	0.345	0.060	−0.309 to 0.429	0.749
>24 months	0.166	−0.041 to 0.373	0.115	0.228	−0.067 to 0.521	0.129
Antidepressant treatment (ref. no)	0.008	−0.146 to 0.161	0.922	0.216	−0.050 to 0.482	0.112
Psychiatric comorbidities (ref. no)	−0.030	−0.140 to 0.080	0.596	0.013	−0.202 to 0.227	0.907
Psychomotor speed (Motor Screening Task-Mean Latency)	−0.004	−0.053 to 0.046	0.891	0.036	−0.062 to 0.133	0.471
Subject-level random intercept[b]	0.165	0.117 to 0.232		0.250	0.150 to 0.418	

MelD, melancholic depression; CI, confidence interval; NMelD, non-melancholic depression; MDD, major depressive disorder.
[a] Uncorrected standardized z-scores.
[b] Standard deviation and 95 % CI are reported.
Statistically significant results ($p < 0.05$) are highlighted in bold.

0.50 SDs lower on this variable than patients who completed all study time points ($n = 61$). However, the overall model was not significant, as indicated by a non-significant omnibus test ($F_{(17,218)} = 11.93, p = 0.612$), so this result should be interpreted with caution, as it may reflect a spurious finding, potentially due to limited statistical power in a small sample.

4. Discussion

To the authors' knowledge, this prospective study is the first longitudinal investigation with a 12-month follow-up period that has specifically explored the long-term association between MelD and executive function in adult patients with MDD. Patients with MelD performed worse than those with NMelD in the global executive function domain, in the working memory subdomain, and in four individual variables within the working memory, planning and decision-making subdomains, independent of other clinical variables and psychomotor speed. In contrast, no differences were observed in the response inhibition subdomain between the two groups. Importantly, the results did not change after restricting the analysis to the subset of patients who completed all study time points, nor when the dropout pattern variable was included as an additional covariate in the linear mixed-effects models, confirming the robustness of the findings when accounting for potential biases introduced by missing data or participant attrition. The results are consistent with previous research, including a systematic review (Bosaipo et al., 2017) and two meta-analyses (Valerio et al., 2021; Zaninotto et al., 2016), which already linked MelD with worse executive function, particularly in traditional "cold" subdomains such as working memory and planning. The results also contribute to the existing literature by demonstrating for the first time that these associations persisted over the long term and extended to non-traditional "hot" subdomains, such as decision-making. The results further support the view of MelD as a distinct longitudinal risk factor for worse executive function in adult patients with MDD (Hasler et al., 2004).

In a more detailed analysis, MelD was found to be longitudinally associated with worse performance in one of the three traditional "cold" subdomains of executive function assessed, namely working memory, but not planning or response inhibition. This association was also found for the two specific variables Spatial Working Memory-Between Errors, which assesses working memory accuracy, and Spatial Working Memory-Strategy, which assesses the effectiveness of systematic search strategies, indicating that patients with MelD performed worse than those with NMelD on both working memory accuracy and strategic planning. It was also observed that MelD was longitudinally associated with worse performance in the specific variable One Touch Stockings of Cambridge-Problems Solved on First Choice, which assesses accuracy and efficiency in planning and executing the solution to a problem. Importantly, this variable indirectly reflects decision making, as participants must mentally evaluate possible solutions, select the optimal path and commit to their choice with confidence. In contrast, no such association was found with the broad subdomain of planning nor with the specific variable One Touch Stockings of Cambridge-Mean Latency to First Choice, which assesses the time it takes a participant to make a first decision, indicating that patients with MelD performed worse than those with NMelD in problem-solving accuracy –consistent with the result for Spatial Working Memory-Strategy–, but not in speed to initiate actions. The latter, in turn, is consistent with the non-significant relationship between MelD and the specific variable Motor Screening Task-Mean Latency, which measures simple psychomotor speed.

Overall, these results are consistent with most cross-sectional studies (Austin et al., 1999; Cornell et al., 1984; Day et al., 2015; Exner et al., 2009; Krogh et al., 2012; Michopoulos et al., 2008, 2006; Pier et al., 2004; Quinn et al., 2012a, 2012b; Rogers et al., 2004; Rush et al., 1983; Valerio et al., 2023) and shorter-term longitudinal studies (Lin et al., 2014; Roca et al., 2015a; Withall et al., 2010) conducted to date, which similarly compared working memory, planning and response inhibition between MelD and NMelD. However, they are at odds with other studies that found no differences between the two groups (Austin et al., 1992; Gorlyn et al., 2006; Liang et al., 2023) or that found that patients with MelD perform better than those with NMelD (Lee et al., 2021; Markela-Lerenc et al., 2006). One possible explanation for these contradictory results could be the use of different cognitive tests to assess the same executive function variable (e.g. the Stop Signal Task in our study or the Stroop test in others). Variations in test administration methods, such as the computer-based approach used in the present study compared with the paper-and-pencil methods employed in others, may also contribute to discrepancies (Harris et al., 2024). Differences in how the global domain of executive function was defined, along with the overlapping nature of cognitive processes across different subdomains, could also

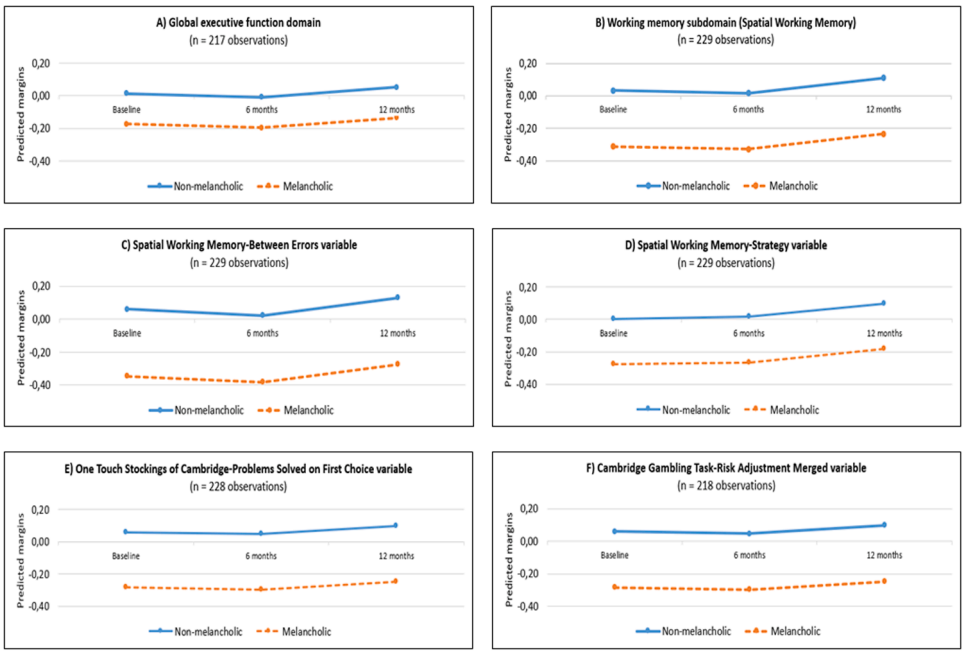

Fig. 2. Plots of significant linear mixed-effects models exploring longitudinal associations between MelD and executive function at the domain, subdomain and individual variable levels. A) Global executive function domain (main effect of MelD, $p = 0.003$). B) Working memory subdomain (main effect of MelD, $p = 0.005$). C) Spatial Working Memory-Between Errors variable (main effect of MelD, $p = 0.003$). D) Spatial Working Memory-Strategy variable (main effect of MelD, $p = 0.042$). E) One Touch Stockings of Cambridge-Problems Solved on First Choice variable (main effect of MelD, $p = 0.020$). F) Cambridge Gambling Task-Risk Adjustment Merged variable (main effect of MelD, $p = 0.027$). MelD, melancholic depression.

result in different approaches to calculating cognitive composites (Willoughby and Hudson, 2021). Achieving consensus on definitions and on the most appropriate cognitive tests and administration formats for assessing executive function could help reduce discrepancies between studies. Successful efforts in this direction have been made in MDD (McIntyre et al., 2017) and bipolar disorder (Miskowiak et al., 2018, 2022).

For the first time, MelD was also found to be longitudinally associated with worse performance in the specific variable Cambridge Gambling Task-Risk Adjustment Merged, which assesses the ability to adapt decision strategies under conditions of fluctuating risk. In contrast, no such association was found with the broad subdomain of decision-making nor with the two specific variables Cambridge Gambling Task-Delay Aversion Total, which assesses preference for immediate versus delayed rewards, and Cambridge Gambling Task-Decision Making Quality Merged, which assesses the overall quality of decision making under conditions of uncertainty, indicating that patients with MelD had more difficulty than those with NMelD in adjusting their decision strategies in response to different levels of risk –consistent with the result for One Touch Stockings of Cambridge-Problems Solved on First Choice– but retained the ability to make decisions without strong delay aversion and consistently maintained the overall quality of decision making. Given that this is the first study to explore the relationship between MelD and non-traditional "hot" subdomains of executive function (i.e. decision making) further studies are needed to confirm this result.

Consistent with previous research (Brito et al., 2023; Wang et al., 2020), older age and female sex were also longitudinally associated with worse performance in the global executive function domain, in the working memory subdomain, and in the three specific variables within the working memory and decision-making subdomains, whereas for the specific variable within the planning subdomain only older age was significant. In contrast, neither clinical remission at 6 or 12 months nor psychomotor speed was significant for executive function. The latter conflicts with the consideration of psychomotor impairment as a hallmark symptom of MelD (American Psychiatric Association, 2013; Martino et al., 2019; Parker et al., 2010). However, it points to worse executive function as a defining feature of this depressive subtype, and not merely a consequence of other cognitive difficulties, such as psychomotor slowness (Snyder, 2013; Valerio et al., 2023). Regarding the absence of a significant association between clinical remission and executive function, this is consistent with previous shorter-term longitudinal studies demonstrating that patients with MelD tend to show slower improvement and incomplete recovery with residual interepisode cognitive deficits, in contrast to patients with NMelD, which tend to show higher rates of both cognitive improvement and recovery after clinical remission (Lin et al., 2014; Roca et al., 2015a; Withall et al., 2010). This result further underscores the importance of considering MelD as a distinct longitudinal risk factor for worse executive function in adult patients with MDD (Hasler et al., 2004).

Finally, it should be noted that patients taking antipsychotics or mood-stabilizing drugs were excluded from the present study and data collection focused only on the number of individuals receiving antidepressant treatment. A recent meta-analysis found that executive function may improve slightly after successful antidepressant treatment (Gudayol-Ferré et al., 2021). However, this finding was not replicated in the present study. This discrepancy could be attributed to the absence of recorded data on specific antidepressants doses, which limits the possibility of further analyses. Similarly, the data available for this secondary analysis was limited to the number of patients with psychiatric comorbidities, with no information on the specific number of co-occurring disorders. The finding that having comorbid psychiatric disorders did not affect executive function aligns with another meta-analysis that reported no difference in effect sizes between studies that excluded patients with comorbid Axis I disorders and those that included such participants (Snyder, 2013). Furthermore, not all patients were in their first depressive episode, nor did they have a uniform episode duration. A critical review found inconsistent findings regarding the impact of previous depressive episodes on executive function (Roca et al., 2015b). Recently, longer duration of depression has been associated with more severe cognitive impairment (Wang et al., 2024), especially in processing speed and executive function (Albert et al., 2018). In

Table 3
Exploratory linear mixed-effects models in which MelD showed significant longitudinal associations with executive function at the individual variable level.

	A) Spatial Working Memory-Between Errors variable[a]			B) Spatial Working Memory-Strategy variable[a]		
	B	95 % CI	B	B	95 % CI	p value
Time of the follow-up (ref. baseline)						
6 months	−0.036	−0.254 to 0.182	0.746	0.011	−0.206 to 0.229	0.920
12 months	0.071	−0.171 to 0.313	0.566	0.095	−0.147 to 0.336	0.442
Age, years	−0.038	−0.049 to −0.027	< **0.001**	−0.029	−0.040 to −0.018	< **0.001**
Female sex (ref. male)	−0.377	−0.661 to −0.093	**0.009**	−0.620	−0.900 to −0.339	< **0.001**
High education (ref. <12 years)	−0.092	−0.393 to 0.209	0.548	0.191	−0.107 to 0.488	0.209
MelD (ref. NMelD)	−0.404	−0.675 to −0.133	**0.003**	−0.280	−0.550 to −0.011	**0.042**
Remission (ref. active MDD episode)	0.140	−0.223 to 0.502	0.450	0.055	−0.306 to 0.416	0.765
First MDD episode (ref. recurrent)	0.084	−0.206 to 0.374	0.572	0.070	−0.216 to 0.357	0.631
Duration of the MDD episode (ref. <12 months)						
≥12–24 months	0.228	−0.170 to 0.625	0.261	−0.104	−0.497 to 0.288	0.603
>24 months	0.227	−0.090 to 0.544	0.161	0.230	−0.084 to 0.544	0.151
Antidepressant treatment (ref. no)	0.226	−0.067 to 0.519	0.131	0.207	−0.083 to 0.498	0.162
Psychiatric comorbidities (ref. no)	−0.033	−0.273 to 0.208	0.792	0.082	−0.158 to 0.322	0.502
Psychomotor speed (Motor Screening Task-Mean Latency)	0.004	−0.105 to 0.114	0.937	0.067	−0.043 to 0.176	0.234
Subject-level random intercept[b]	0.270	0.152 to 0.477		0.260	0.149 to 0.451	

	C) One Touch Stockings of Cambridge-Problems Solved on First Choice variable[a]			D) Cambridge Gambling Task-Risk Adjustment Merged variable[a]		
	B	95 % CI	p value	B	95 % CI	p value
Time of the follow-up (ref. baseline)						
6 months	−0.013	−0.244 to 0.217	0.909	−0.044	−0.275 to 0.186	0.708
12 months	0.037	−0.219 to 0.293	0.777	0.009	−0.245 to 0.263	0.945
Age, years	−0.018	−0.031 to −0.006	**0.004**	−0.016	−0.029 to −0.003	**0.018**
Female sex (ref. male)	−0.249	−0.564 to 0.066	0.121	−0.405	−0.744 to −0.065	**0.019**
High education (ref. <12 years)	0.267	−0.067 to 0.601	0.118	0.220	−0.138 to 0.578	0.228
MelD (ref. NMelD)	−0.344	−0.633 to −0.055	**0.020**	−0.333	−0.629 to −0.037	**0.027**
Remission (ref. active MDD episode)	0.026	−0.361 to 0.412	0.897	−0.178	−0.564 to 0.208	0.366
First MDD episode (ref. recurrent)	−0.078	−0.401 to 0.244	0.634	0.034	−0.318 to 0.385	0.851
Duration of the MDD episode (ref. <12 months)						
≥12–24 months	0.187	−0.254 to 0.628	0.405	0.318	−0.152 to 0.788	0.185
>24 months	0.260	−0.091 to 0.612	0.146	0.229	−0.150 to 0.609	0.236
Antidepressant treatment (ref. no)	−0.134	−0.453 to 0.184	0.408	0.009	−0.325 to 0.343	0.956
Psychiatric comorbidities (ref. no)	0.055	−0.202 to 0.312	0.674	−0.051	−0.311 to 0.210	0.704
Psychomotor speed (Motor Screening Task-Mean Latency)	−0.002	−0.119 to 0.115	0.971	−0.042	−0.162 to 0.078	0.491
Subject-level random intercept[b]	0.358	0.225 to 0.570		0.444	0.290 to 0.679	

MelD, melancholic depression; CI, confidence interval; NMelD, non-melancholic depression; MDD, major depressive disorder.
[a] Uncorrected standardized z-scores.
[b] Standard deviation and 95 % CI are reported.
Statistically significant results ($p < 0.05$) are highlighted in bold.

the present study, neither the type nor the duration of the depressive episode was significant for executive function. These discrepancies underscore the need for further research on how the characteristics of the MDD episode and the age of onset of the disorder may affect executive function in patients with MelD. Finally, education was used as a proxy variable for intelligence quotient (Deary and Johnson, 2010). Like psychomotor speed, education was not significant, ensuring that it did not confound the association between MelD and executive function. Overall, the results are consistent with most research to date, which has shown that MelD may play a more critical role than any other clinical or cognitive variable in explaining executive function (Austin et al., 1999; Day et al., 2015; Exner et al., 2009; Quinn et al., 2012a; Valerio et al., 2023; Withall et al., 2010). This result further supports that in MelD, worse working memory accuracy, strategic planning, problem solving and risk adjustment in decision making are more likely to be syndrome-dependent traits than state-dependent traits (Hasler et al., 2004). Therefore, in daily clinical practice, mental health professionals should closely monitor patients with MDD who present with this executive function profile, as impaired executive function has recently been linked to an increased risk of suicidal behavior (Riera-Serra et al., 2023). Furthermore, the finding that executive function is largely independent of other clinical and cognitive variables beyond MelD emphasizes the potential benefits of cognitive rehabilitation interventions targeting this clinical subpopulation (Legemaat et al., 2021; Vicent-Gil et al., 2022). Such interventions should aim to improve executive function even after clinical remission is achieved.

The present study has several limitations. First, it is a secondary analysis of a larger prospective project (Riera-Serra et al., 2023) that was not originally designed to address the specific objectives of the present study (Roca et al., 2019). Second, the exploratory nature of the secondary objective limits our ability to draw definitive conclusions about the relationship between MelD and individual variables of executive function. Nevertheless, the results provide a basis for generating hypotheses to guide future studies. Third, the absence of normative data for most cognitive variables, as well as the lack of a control group of healthy individuals, makes it difficult to accurately assess the severity of executive dysfunction. Consequently, in this study we were only able to compare executive function between MelD and NMelD groups but could not reliably determine the degree of executive function impairment relative to population norms or healthy individuals. Fourth, the severity of depressive symptoms was assessed using a self-reported measure. Fifth, this study did not evaluate all cognitive domains, such as attention and memory, nor all traditional "cold" and non-traditional "hot" subdomains of executive function, such as cognitive flexibility, verbal fluency and social cognition. For insights into the relationship between MelD and other cognitive domains or traditional "cold" subdomains of executive function not examined here, including attention, memory, cognitive flexibility and verbal fluency, see Bosaipo et al. (2017), Valerio et al. (2021) and Zaninotto et al. (2016). Sixth, prior research has indicated that practice effects in repeated measures designs may confound results, as improved performance may derive from familiarity with the task rather than from actual cognitive changes (Harris et al., 2024; Willoughby and Hudson, 2021). In this regard, it is important to note that the main aim of the present study was to longitudinally compare executive function between MelD and NMelD rather than to assess changes over time. In addition, cognition was assessed using the CANTAB, which is specifically designed to reduce the risk of practice effects through features such as parallel modes and randomized stimuli, thus ensuring the reliability of the results (Cambridge Cognition Limited, 2023). Finally, the small sample size limits the generalizability of the findings to other MDD populations and warrants cautious interpretation of the results.

This study also has several strengths that add value to the findings. First, its longitudinal design enables the establishment of sustained causal relationships between MelD and executive function. Second, MelD was identified using an algorithm based on eight items selected from the IDS-SR30 by the STAR*D research group, which provides a standardized framework for the identification of this depressive subtype (Khan et al., 2006). Third, the statistical analysis employed linear mixed-effects models, which effectively address challenges such as dropouts, missing data, unbalanced groups, and multiple repeated measures. In addition, a sensitivity analysis confirmed the robustness of the findings, as the results remained unchanged both when analyzing only patients who completed all study time points and when including the dropout pattern variable as an additional covariate in the linear mixed-effects models. However, further research is needed with larger samples of patients with MDD and a control group of healthy individuals. To deepen the understanding of the executive function profile of adult patients with MelD, such studies should explore non-traditional "hot" subdomains of executive function that are often overlooked, such as social cognition (Valerio et al., 2021).

In conclusion, the results of the present study show that MelD was characterized by persistent long-term difficulties in executive function, particularly in traditional "cold" subdomains such as working memory and planning, but also in non-traditional "hot" subdomains such as decision-making. Specifically, patients with MelD demonstrated worse accuracy in working memory, strategic planning, problem solving and decision strategy under fluctuating risk conditions, whereas they retained response inhibition, reaction time when making a first decision, and overall quality of decision making without strong delay aversion compared to patients with NMelD. This executive function profile was found to be independent of other clinical and cognitive factors, such as remission of the depressive episode and psychomotor speed, highlighting that MelD may be a distinct longitudinal risk factor for worse executive function in adult patients with MDD. The results also support that MelD can be distinguished both qualitatively and quantitatively through cognitive testing, reinforcing the view of MelD as a distinct form of depression or as a more severe type of illness on a depressive continuum.

Data statement

The data that support the findings of this study are available from the corresponding author, A.C. (a.castro@uib.es), upon reasonable request.

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CRediT authorship contribution statement

Guillem Navarra-Ventura: Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Formal analysis. **Pau Riera-Serra:** Writing – review & editing, Validation, Methodology, Data curation, Investigation. **Adoración Castro:** Writing – review & editing, Investigation. **Juan José Montaño:** Writing – review & editing, Validation, Methodology, Formal analysis. **Miquel Roca:** Conceptualization, Writing – review & editing, Supervision, Resources, Project administration, Investigation, Funding acquisition. **Margalida Gili:** Supervision, Project administration, Writing – review & editing, Resources, Investigation, Conceptualization.

Declaration of competing 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.psychres.2025.116636.

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