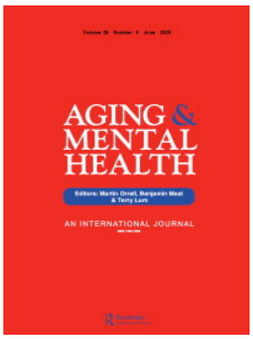

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Repetitive transcranial magnetic stimulation: an effective treatment for resistant depressive episodes in the elderly

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ABSTRACT

Objectives: To evaluate the effectiveness of repetitive transcranial magnetic stimulation (rTMS) in older (≥60 years) versus younger (<60 years) patients with treatment-resistant depression (TRD), and to determine whether age affects clinical outcomes in a naturalistic clinical setting.

Method: A retrospective analysis was conducted on 272 patients with TRD treated with rTMS at a tertiary psychiatric hospital. Depression severity was assessed at baseline, end-of-treatment (V1), and one-month follow-up (V2) using the Montgomery-Åsberg Depression Rating Scale (MADRS) and the Beck Depression Inventory (BDI). Response (≥50% MADRS reduction) and remission (MADRS ≤10) rates were calculated. Repeated measures ANOVA and logistic regression were used to examine the influence of age and treatment protocol.

Results: Both age groups showed significant improvement in depressive symptoms. Older adults had higher remission rates at V1 (36% vs. 23%, $p = 0.033$), although this difference was no longer significant at V2. No interaction between age and protocol was observed. Female sex was the only significant predictor of remission at V2 (OR = 14.25, $p = 0.021$). Sensitivity analyses treating age as a continuous variable yielded consistent findings.

Conclusion: rTMS is an effective treatment for TRD in both older and younger adults. Older patients respond comparably to younger ones, challenging concerns about age-related reductions in neuromodulation efficacy. These findings support the use of rTMS in late-life depression without major protocol adjustments and underscore the need for future studies examining personalized treatment parameters and psychosocial moderators of response.

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KEYWORDS
rTMS; late-life depression; treatment-resistant depression; aging; remission; sex differences

Introduction

Major depressive episode (MDE) is a prevalent and disabling psychiatric condition that affects individuals across the lifespan. In older adults, late-life depression (LLD) – defined as a MDE occurring after age 60 – is particularly challenging to diagnose and treat, due to overlapping somatic symptoms, stigma, and the presence of comorbidities (Alexopoulos, 2019; Husain-Krautter & Ellison, 2021; MacQueen et al., 2016).

Pharmacological treatments are considered first-line but often lead to suboptimal outcomes in this population, with high rates of adverse effects and a considerable proportion of patients failing to respond (Gutsmiedl et al., 2020; Otte et al., 2016; Sobieraj et al., 2019). Treatment-resistant depression (TRD) is therefore common in LLD and calls for alternative therapeutic options (Patrick et al., 2024).

Repetitive transcranial magnetic stimulation (rTMS), a non-invasive neuromodulation technique targeting the dorsolateral prefrontal cortex (DLPFC), has shown efficacy in younger adults with TRD (Brunoni et al., 2017; Mutz et al., 2019). However, its effectiveness in older patients remains debated, with early trials yielding mixed results, partly due to age-related neurobiological changes such as cortical atrophy and reduced neuroplasticity (Kricheldorff et al., 2022; Manes et al., 2001; Mosimann et al., 2004; Oberman & Pascual-Leone, 2013).

Recent evidence, however, indicates that rTMS remains effective in older adults, with clinical and neuroimaging studies showing comparable or even enhanced responses in some cases (Kaster et al., 2018; Leuchter et al., 2024; Zhang et al., 2023). Nevertheless, further naturalistic studies are needed to confirm these findings and guide age-adapted treatment strategies for LLD (Conelea et al., 2017). In fact, naturalistic studies, unlike randomized controlled trials, provide real-world insights into treatment effectiveness in clinical practice. This approach includes a heterogeneous population, thereby increasing the generalizability of findings to everyday psychiatric care.

For these reasons, we conducted a retrospective naturalistic study to compare the efficacy of rTMS in treatment-resistant depression between adults aged over 60 and younger adults. This study utilized a large dataset of patients who received rTMS for depression in a real-world clinical setting at a tertiary referral hospital.

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Method

We revised and analyzed the records of 300 patients with mood disorders, who were treated with rTMS in the Neurostimulation Department of Henri Laborit psychiatric Hospital between September 2014 and February 2024. From the initial dataset of 300 medical records, 28 were excluded due to missing data ($n = 15$), protocol deviations ($n = 9$), or ineligibility based on study criteria ($n = 4$). The final analyzed cohort consisted of 272 patients (81 aged 60 years or older, and 191 younger than 60). Of the 272 patients initially included, 70 (26%) discontinued the study before visit V2. Therefore, 204 participants completed the full protocol. Dropout reasons were not systematically recorded, but no adverse events were reported as causes.

At the last visit, data were available for only 140 patients in the younger patient group and 64 in the older one (Figure 1). Each patient was treated only one time with rTMS.

Consent

A total of 272 patients were retrospectively selected for this study. Prior informed consent for the retrospective use of participants' research data was obtained, ensuring their non-opposition to its utilization in this study. The study was registered on the Health Data Hub platform (N° F20210128152411). Additionally, all patients provided informed written consent for the use of rTMS in clinical settings.

Ethics

Given the retrospective design of this study and the anonymized nature of the data, the National Commission for Information Technology and Civil Liberties (CNIL) did not require further regulatory review beyond the Health Data Hub registration and the collection of patient non-opposition.

Patients

Patients treated with rTMS in our department have fulfilled DSM-IV-TR criteria for major depressive disorder. Diagnosis was made using the Mini International Interview for Neuropsychiatric Disorders (Sheehan et al., 1998) by an experienced psychiatrist. All patients had to be in a current major depressive episode with a MADRS score of more than 20. Exclusion criteria included a DSM-IV-TR Axis I of psychotic disorder, DSM-IV-TR diagnosis of alcohol or substance dependence, significant current active medical problem and known neurological disease or a contra-indication to rTMS (e.g. history of seizure disorder, presence of a pacemaker or metal somewhere in the head other than in the teeth) or to MRI scanning (e.g. aneurysm clips, stents or metal anywhere in the body).

Treatment resistance was defined as non-responsiveness to at least two courses of antidepressant medications for at least 6 weeks (Stage II, Thase and Rush, 1997, definition (Thase and Rush, 1997)), as determined by their primary treating clinician and patient judgment of medication effectiveness. Medications were not allowed to have changed in the 3 wk prior to the beginning of the rTMS treatment or during the rTMS treatment itself.

The inclusion criteria for the retrospective analysis were: rTMS-naïve (only the patient's first treatment with rTMS was considered), primary diagnosis of a depressive disorder (including bipolar disorder currently depressive episode, major depressive disorder, and recurrent depressive disorder), a complete documented MADRS at beginning (baseline), at the end of rTMS treatment (Visite 1, V1), and one month after the end of rTMS treatment

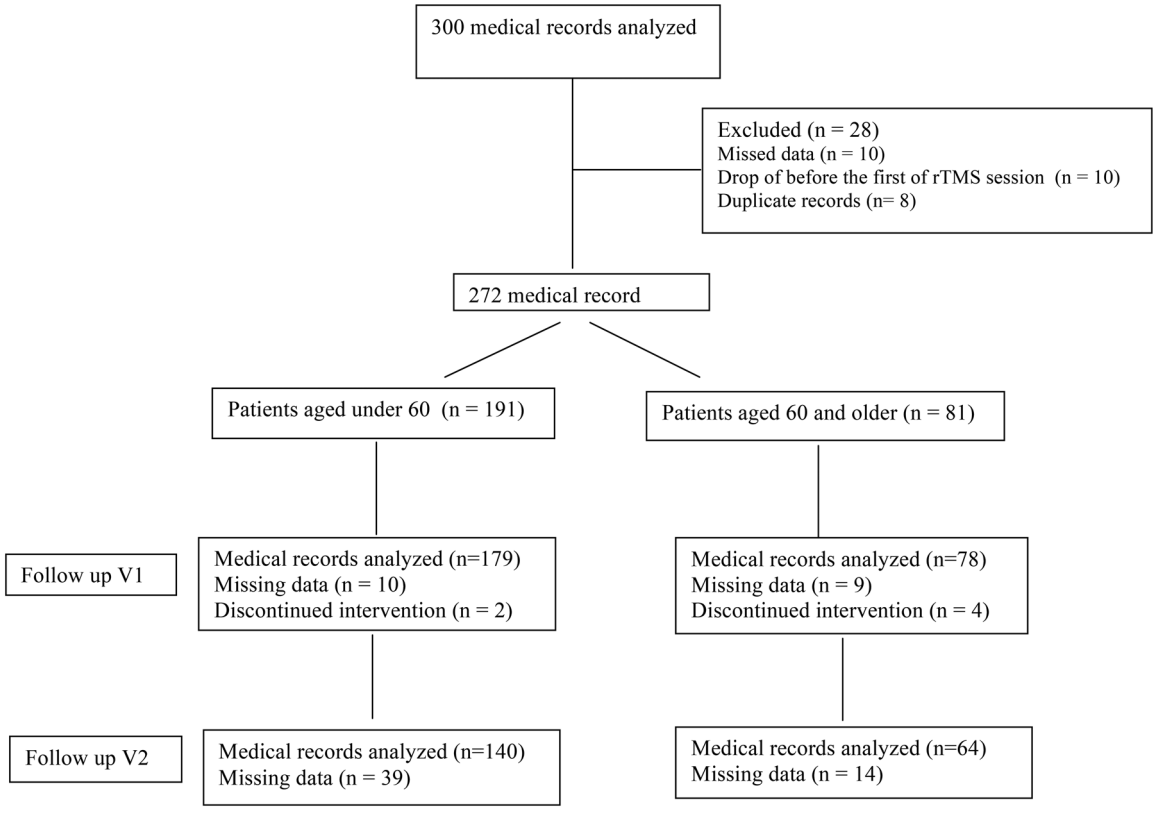

Figure 1. Graphical representation of CONSORT flow diagram.

(Visite 2, V2) the end of rTMS course, absence of a serious somatic illness. Both inpatients and outpatients were included.

Assessment

Trained psychiatrists completed clinical assessments. All assessments included the MADRS and BDI scales. Follow-up assessments were conducted at two fixed time points: V1 (immediately after the completion of rTMS) and V2 (one month post-treatment). V2 was systematically scheduled for all patients at one month following rTMS, ensuring consistency in follow-up timing. The primary outcome measure was the total MADRS score at V1. Responder status was defined as a 50% decrease in MADRS score, and remission was defined as a MADRS score ≤ 10. Response and remission were defined based on MADRS scores, as MADRS is widely recognized in clinical research as a standard, clinician-rated measure of depression severity. Its sensitivity to treatment effects and objective nature make it the preferred scale for evaluating antidepressant interventions. While BDI was included in the study to capture subjective experiences of depression, it is less commonly used to define treatment response in rTMS trials.

Treatment

The coil was positioned to target the left DLPFC or the right DLPFC (neuronavigation system (Syneika One; Syneika)). All patients underwent a baseline and weekly evaluation of the motor cortex excitability by measuring the resting motor threshold (RMT). The rTMS treatment was administered with the MagPro X100 with Option stimulator (MagVenture, Inc) using a Figure 8 coil. Stimulation protocols used are (1, 10, or 20 Hz) (Cotovio et al., 2023; Speer et al., 2000), and Stimulation parameters are presented in Table 1.

Statistical analyses

Statistical analyses were performed using Jamovi version 2.2 (https://www.jamovi.org) and the software R, version 4.1.0 (nlme, sjplot packages; R Foundation for Statistical Computing, Vienna, Austria). We compared the demographic and clinical characteristics at baseline between the younger group and the older group using independent sample *t*-tests (two-tailed) and chi-square tests.

Primary and secondary outcomes were analysed using a series of linear mixed-effects models with time (baseline vs follow-up: V1, V2), group (Younger and older), and their cross-level interaction as independent variables. A significant threshold of $p < 0.05$ was chosen for all tests.

Age was initially included as a categorical variable (≥60 vs. <60). To assess the robustness of this approach, we conducted a sensitivity analysis treating age as a continuous variable. The results showed that age, when modeled continuously, was not a significant predictor of remission ($p = 0.295$). Model fit was slightly better with age categorized (AIC = 158 vs. 160; McFadden's $R^2 = 0.126$ vs. 0.110). Given the possibility of threshold effects in older adults and the slightly better model performance, we retained age as a categorical variable in the final analyses (Supplementary Table 2).

We then conducted a binomial logistic regression to evaluate the predictors of remission. The regression model included predictors like age, baseline depression severity (MADRS and BDI scores), sex, type of depression, history of suicide attempts, use of benzodiazepines, antidepressants, or adjunctive treatments, and the stimulation protocol used (1, 10, or 20 Hz).

Prior to including both MADRS and BDI scores in the regression models, we assessed their correlation and potential multicollinearity. Pearson's correlation between baseline MADRS and BDI was moderate ($r = 0.570$, 95% CI: 0.483–0.646, $p < 0.001$). To evaluate multicollinearity, we calculated the Variance Inflation Factor (VIF) and tolerance values for both predictors. VIF values were 1.49 and tolerance was 0.672 for each, indicating that collinearity was within acceptable limits (VIF < 5). These results supported the inclusion of both MADRS and BDI in the models, as they capture complementary aspects of depressive symptoms without introducing statistical redundancy (Supplementary Table 1).

Comparative analyses were conducted between dropouts and completers to assess potential bias. No significant differences were observed in baseline demographic or clinical characteristics between groups (Supplementary Table 4). Therefore, analyses were conducted on available data without imputation.

Table 1. Parameters of rTMS stimulation protocols used in the study.

Parameter	1 Hz (Cotovio et al. 2023)	10 Hz (Cotovio et al. 2023)	20 Hz (Speer et al. 2000)
Number of pulses per train	60	40	40
Duration of inter-train interval	30 s	26 s	10 s
Number of trains per session	6	75	80
Stimulation intensity	120% of resting motor threshold	120% of resting motor threshold	110% of resting motor threshold
Total number of pulses/ session	360	3000	3200
Total duration of session	8 min	37 min	25 min
Target area	Right DLPFC	Left DLPFC	Left DLPFC
Total number of sessions	20	20	10

Results

Participants

A total of 272 patients were included, with 191 in the younger group and 81 in the older group. The two groups were compared across several baseline characteristics, including sex, type of depression (unipolar vs. bipolar), history of suicide attempts, and treatment protocols (Table 2). There were no significant differences between the age groups in sex distribution ($p = 0.341$), type of depression ($p = 1.00$), or treatment resistance ($p = 0.550$). Similarly, the type of rTMS protocol (1, 10, or 20 Hz) used in the study did not differ significantly between the two age groups ($p = 1.00$).

For the MADRS score, at baseline, no significant difference was found between younger and older patients (27.30 ± 7.57 vs. 26.43 ± 9.14, $p = 0.422$). However, by V1, older patients had a significantly greater reduction in MADRS scores compared to younger patients (15.22 ± 8.82 vs. 17.83 ± 9.59, $p = 0.023$). At V2, no significant difference in MADRS scores was observed between the groups ($p = 0.810$).

For the BDI score, at baseline, older patients had significantly lower BDI scores compared to younger patients (15.48 ± 8.19 vs. 18.43 ± 9.27, $p = 0.014$). At V1, the BDI score was significantly lower in the older group compared to the younger group (9.99 ± 7.93 vs. 13.23 ± 8.48, $p = 0.003$). However, we did not directly compare the magnitude of BDI reduction between

Table 2. Comparison of demographic, clinical, and treatment characteristics between age groups (<60 vs. ≥60 years).

Variable	<60 years ($n = 181$)	≥60 years ($n = 81$)
Age (mean ± SD)	44.6 ± 9.6	67.3 ± 5.33
Sex: Female (%)	115 (60%)	54 (66.6%)
Sex: Male (%)	76 (40%)	27 (33.3%)
Type of depression: Unipolar (%)	86 (77%)	38 (79%)
Type of depression: Bipolar (%)	25 (23%)	10 (21%)
History of suicide attempt (%)	74 (32.5%)	25 (11%)
Resistance stages (1–2) (%)	90 (47%)	36 (44.4%)
Resistance stages (3–5) (%)	79 (43%)	35 (55.5%)
Protocol: 1 Hz (%)	81 (42.4%)	35 (43%)
Protocol: 10 Hz (%)	26 (14%)	11 (4.1%)
Protocol: 20 Hz (%)	82 (45%)	34 (42%)
Treatment: SRI (%)	113 (60%)	48 (60%)
Treatment: Potentiation (%)	98 (54%)	34 (42%)
Treatment: Benzodiazepines (%)	104 (57%)	43 (53%)
MADRS baseline (mean ± SD)	27.30 ± 7.57	26.43 ± 9.14
MADRS V1 (mean ± SD)	17.83 ± 9.59	15.22 ± 8.82
MADRS V2 (mean ± SD)	16.49 ± 10.62	15.55 ± 8.82
BDI baseline (mean ± SD)	18.43 ± 9.27	15.48 ± 8.19
BDI V1 (mean ± SD)	13.23 ± 8.48	9.99 ± 7.93
BDI V2 (mean ± SD)	11.68 ± 9.79	10.02 ± 7.49
Response V1: NR (%)	120 (68%)	44 (56%)
Response V1: R (%)	57 (32%)	34 (44%)
Response V2: NR (%)	77 (55.4%)	32 (50%)
Response V2: R (%)	62 (44.6%)	32 (50%)
Remission V1: NR (%)	138 (77%)	50 (64%)
Remission V1: R (%)	41 (23%)	28 (36%)
Remission V2: NR (%)	93 (66.4%)	43 (67%)
Remission V2: R (%)	47 (33.6%)	21 (33%)

Comparison of demographic, clinical, and treatment characteristics between age groups (<60 years and ≥60 years). Data are presented as mean ± standard deviation (SD) or percentages (%). Statistical comparisons were performed using the chi-square test for categorical variables and the independent samples *t*-test for continuous variables. Abbreviations: MADRS = Montgomery-Åsberg Depression Rating Scale; BDI = Beck Depression Inventory; NR = Non-Responder; R = Responder; SRI = Serotonin Reuptake Inhibitor.

groups, and the observed difference at V1 could be influenced by the baseline differences between the two groups. Since baseline BDI scores were already lower in the older group, the observed difference at V1 might partly reflect this initial difference rather than a greater reduction due to treatment. At V2, no significant difference in BDI scores was noted between the two groups ($p = 0.419$).

Among the 272 patients enrolled, 70 discontinued the study before the final evaluation. Comparative analyses revealed no statistically significant differences between dropouts and completers in terms of age, sex, depression severity, or medication use (Supplementary Table 4).

Concerning treatment tolerance, no specific adverse event questionnaire was administered. However, throughout follow-up visits, no serious adverse events were reported. Moreover, no patients discontinued treatment due to side effects. The only side effects described were mild and transient headaches, which resolved spontaneously.

Response and remission rates

The remission rate was significantly higher in the older group compared to the younger group (36% vs. 23%, $p = 0.033$). At V2, no significant differences were observed in response (50% vs. 44.6%, $p = 0.545$) or remission (33% vs. 33.6%, $p = 1.00$) between the groups (Table 2).

Concerning drop-off patients, response and remission rates were slightly lower among dropouts, suggesting that some attrition may have been linked to lower treatment efficacy

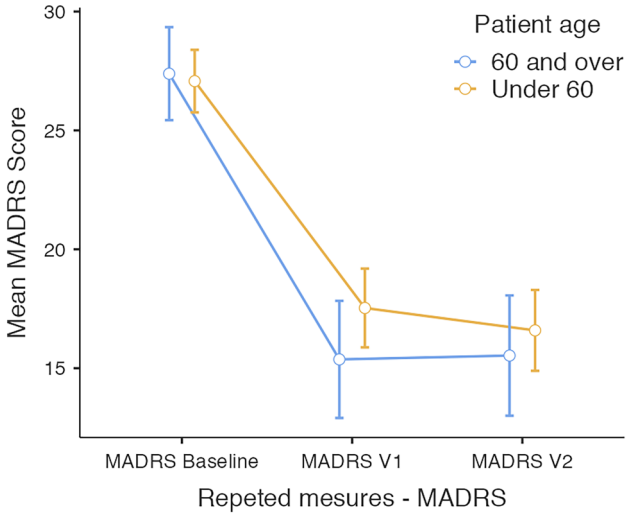

Figure 2. Changes in MADRS scores over time by age group. Mean montgomery–åsberg depression rating scale (MADRS) scores across three time points (baseline, V1, and V2) in patients aged under 60 years (orange line) and 60 years and over (blue line). Error bars represent standard deviations.

perceptions. Importantly, symptom reduction trajectories were similar between groups, indicating that treatment effects remained consistent despite attrition.

Anova

We conducted a repeated-measure ANOVA for MADRS and BDI scores.

A significant reduction in MADRS scores was observed over time across the three assessment points (Figure 2): $F(2, 394) = 144.80$, $p < 0.001$. As the assumption of sphericity was violated, a Greenhouse-Geisser correction was applied: $F(1.92, 378.72) = 144.80$, $p < 0.001$. No significant time × age group interaction was found: $F(2, 394) = 1.39$, $p = 0.251$ (Greenhouse-Geisser corrected: $F(1.92, 378.72) = 1.39$, $p = 0.251$). Additionally, there was no significant main effect of age on MADRS scores.

Concerning the BDI score, there is a significant reduction (Figure 3) over time (across the three measurement points), $F(2, 394) = 90.49$, $p < 0.001$ (Sphericity not assumed: Greenhouse-Geisser correction applied: $F(1.85, 364.45) = 90.49$, $p < 0.001$). No significant interaction effect between age group and time was observed (Timex AgerTMS - Age and rTMS Interaction), $F(2, 394) = 2.48$, $p = 0.085$ (Greenhouse-Geisser correction: $F(1.85, 364.45) = 2.48$, $p = 0.085$). There was no significant main effect of age on BDI scores ($F(1, 197) = 0.444$, $p = 0.506$).

Effect of protocol

Table 3 shows the response (R) and non-response (NR) rates for patients undergoing three different rTMS protocols (1, 10, and 20 Hz). Statistical significance was assessed, and the *p-value* for differences between the protocols was $p = 0.045$, indicating that the response rates to different protocols were significantly different. The 1 Hz protocol shows a relatively balanced outcome, with 44 responders (57%) and 33 non-responders (43%).

We also performed an additional analysis to examine the effects of different rTMS protocols on response and remission across age groups (Supplementary Table 3). The interaction between age and protocol type was not significant, indicating that protocol effects were comparable across younger and older adults.

Regression analysis

Finally, a series of binomial logistic regression models were conducted to examine predictors of treatment response and remission in older patients, using a range of variables including age, baseline MADRS and BDI scores, sex, rTMS treatment protocols, depression subtype, history of suicide attempts, use of benzodiazepines, SSRI treatment, potentiation strategies, and treatment resistance stage.

Both MADRS and BDI scores were included as predictors, given their complementary roles in assessing depressive symptoms. The MADRS offers a clinician-rated evaluation of core mood disturbances, while the BDI captures the patient's subjective experience, particularly cognitive and affective dimensions. These scales demonstrated moderate correlation ($r = 0.570$) and acceptable multicollinearity (VIF < 1.5), supporting their concurrent inclusion in the models.

To further investigate treatment outcomes, four binomial logistic regression models were tested with different dependent variables: (1) response at V1 (2) response at V2, (3) remission at V1, and (4) remission at V2.

Among these, only the remission at V2 model (see Table 4) identified a statistically significant predictor: female sex ($p = 0.021$), indicating that women were significantly more likely to achieve remission. No other predictors—including age group, protocol type, or baseline symptom severity—were statistically associated with remission or response across the models. A summary of model fit indices (AIC, McFadden's R^2) and a predictor significance level is provided in Supplementary Table 5.

The remission at V2 model showed a moderate explanatory power (McFadden's $R^2 = 0.405$), with female sex being the only variable significantly associated with outcome (OR = 14.25).

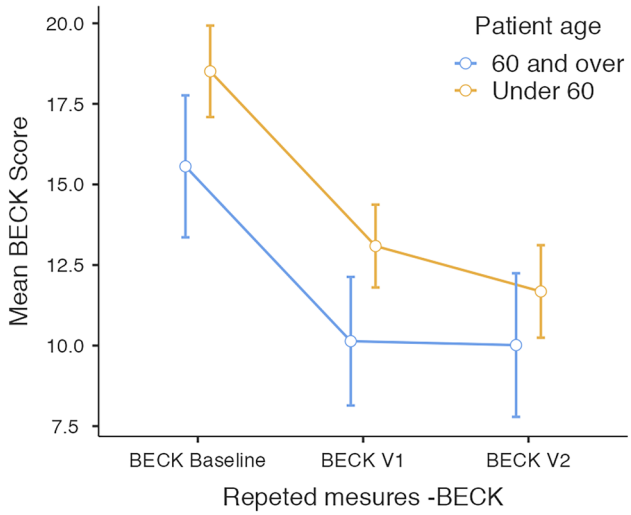

Figure 3. Changes in BDI scores over time by age group. Mean beck depression inventory (BDI) scores across three time points (baseline, V1, and V2) for two age groups: under 60 years (orange line) and 60 years and over (blue line). Error bars represent standard deviations.

Although certain variables (such as bipolar depression or a history of suicide attempt) showed non-significant trends toward increased odds of remission, these did not reach statistical significance. Other variables—such as age, treatment protocol, baseline MADRS/BDI scores, and concurrent psychotropic medication—were not predictive of remission status in this model.

Discussion

This retrospective study evaluated the effects of rTMS on younger and older patients with treatment-resistant depression. A central finding is the absence of significant differences in treatment outcomes between the two age groups, suggesting that rTMS can be applied safely and effectively in older adults without requiring substantial protocol adjustments.

Both groups showed significant improvement in MADRS scores over time, with no significant age × time interaction. This indicates that both younger and older adults benefited similarly from treatment in terms of symptom reduction trajectory. Interestingly, remission was more frequent among older patients at the first post-treatment time point (V1), though this difference was not maintained at V2. While the overall speed of improvement was statistically comparable, this early response in older patients could have clinical implications, especially considering the heightened vulnerability to prolonged depression in this population (Husain-Krautter & Ellison, 2021).

Although concerns have been raised regarding the diminished neuroplasticity associated with aging (Burke & Barnes, 2006), our data support the idea that rTMS remains effective in stimulating cortical circuits in older adults (Freitas et al., 2013). Brain regions such as the DLPFC, commonly targeted in rTMS, may remain receptive to stimulation in this group (Lefaucheur et al., 2020). Moreover, recent findings suggest that age-related changes in prefrontal activity (Ohsugi et al., 2013) might even facilitate early therapeutic responses in LLD. Additionally, daily sessions may provide structure and social interaction that can be particularly beneficial to older adults, whose depression is often exacerbated by isolation (Burke et al., 2019; Wathra et al., 2023). This "care effect" may contribute to outcomes beyond the neurobiological mechanisms of rTMS. We can assume that this effect is minimal in younger populations, as they are generally more socially active and less isolated. However, we acknowledge that this effect may not be exclusive to the older population. In particular, the sampling period of our study spanned nearly a decade, including the COVID-19 pandemic, during which younger individuals may also have experienced significant social isolation. This could have increased the relevance of the care effect in this group as well.

Medication adherence may also play a role (Girone et al., 2024). Unlike oral antidepressants, rTMS ensures consistent dosing in a clinical setting. Older adults – often at risk of missed doses due to cognitive issues – may therefore benefit more from structured, supervised treatments like rTMS (Kok & Reynolds, 2017).

Table 3. Association between rTMS protocol and clinical response at V2.

Protocol	1 Hz	10 Hz	20 Hz	Total	p-value
Non-responder	33 (43%)	17 (63%)	39 (50%)	109 (54%)	0.045
Responder	44 (57%)	10 (37%)	39 (50%)	93 (46%)	
Total	77 (100%)	27 (100%)	78 (100%)	202 (100%)	

This contingency table presents the distribution of responders and non-responders across the three different rTMS protocols (1, 10, and 20 Hz) at the second follow-up (V2). A statistically significant association was observed between protocol type and clinical response ($p = 0.045$), suggesting protocol-dependent variability in treatment outcomes.

Table 4. Binomial logistic regression predicting remission at V2.

Model fit measures				
Model	Deviance		AIC	McFadden's R^2
1	30.6		56.6	0.354
Model coefficients – Remission at V2				
Predictor	Estimate	SE	Z	*P*-value
Intercept	−1.63348	10.2310	−0.15966	0.873
AGE	0.03236	0.1342	0.24120	0.809
MADRS score Baseline	−0.11814	0.0914	−1.29218	0.196
BDI score Baseline	−0.04435	0.0870	−0.51004	0.610
Sex: Female – Male	2.65646	1.2180	2.18108	0.029
Depression type: Bipolar – Unipolar	1.37943	1.3103	1.05273	0.292
History of suicide attempt: No – Yes	0.88610	1.3291	0.66669	0.505
Benzodiazepine treatment: No – Yes	0.92474	1.3437	0.68819	0.491
SRI treatment: No – Yes	−0.27481	1.4881	−0.18467	0.853
Potentiation treatment: No – Yes	0.43681	1.3102	0.33340	0.739
Protocol: 1 Hz – 20 Hz	0.62794	2.6134	0.24028	0.810
Protocol: 10 Hz – 20 Hz	−1.40347	1.7364	−0.80827	0.419
Resistance stage: High – Low	0.00260	1.2387	0.00210	0.998

Note: Estimates represent the log odds of 'Remission at V2 = Yes' versus 'Remission at V2 = No'. Statistical significance is indicated at $p < 0.05$.
This table presents the results of a binomial logistic regression analysis predicting remission at the second follow-up (V2). The model includes fit indices (Deviance, AIC, and McFadden's R^2), along with coefficient estimates (log odds) for predictors including age, baseline MADRS and BDI scores, sex, depression type, history of suicide attempts, concurrent treatments (benzodiazepines, SRI, and potentiation), rTMS protocol (1 Hz, 10 Hz, 20 Hz), and resistance stage.

We also observed lower baseline BDI scores in older adults, a difference that persisted at V1 but not V2. This may reflect different symptom expression in late-life depression, where somatic rather than affective symptoms predominate (Hegeman et al., 2015). Self-report tools like the BDI may thus underestimate depressive severity in older patients, and age-appropriate scales such as the Geriatric Depression Scale (GDS) may be more appropriate.

Several factors have been identified as being associated with better response and remission rates in rTMS treatment for depression. Biological sex is one such factor, with studies showing that females tend to have better response and remission rates compared to males. Research by Kedzior et al. (2014), Sackeim et al. (2020), Leuchter et al. (2024) and Huang et al. (2008) demonstrating higher efficacy of rTMS in women. Several biological differences between the sexes may influence the clinical response to rTMS (Hanlon & McCalley, 2022). This may relate to biological factors such as scalp-to-cortex distance (McCalley & Hanlon, 2021), estrogen-driven cortical excitability (Chung et al., 2019), and regional gray matter differences (Ruigrok et al., 2014). However, not all studies have replicated this effect. A recent study on late-life depression by Göke et al. (2024) found no impact of sex on rTMS outcomes. This study highlighted that other factors, such as lower baseline severity of depression, fewer antidepressant treatment failures, and higher global cognitive functioning, were more strongly associated with better remission rates in older adults.

The impact of the stimulation protocol is a crucial factor in determining the efficacy of rTMS for depression. One commonly used protocol is the 1 Hz stimulation targeting the right dorsolateral prefrontal cortex. This protocol has shown significant effectiveness in patients regardless of age (Van Rooij et al., 2020). In our study, we did not observe a significant interaction between age and protocol type, suggesting that the effects of rTMS protocols were comparable across both younger and older adults. These findings indicate that standard rTMS protocols can be applied effectively in the treatment of LLD without requiring major age-specific modifications.

While this study provides valuable data on the use of rTMS in younger versus older patients, there are some limitations to consider. First, the study's retrospective design may introduce biases related to patient selection and treatment adherence. Additionally, the use of standard rTMS protocols across all patients may not fully account for the need to tailor treatment parameters, such as frequency or intensity. The number of patients, particularly in the older group, is limited, making the statistical analyses less robust. Another limitation of our study is the dropout rate (26%), which may have impacted statistical power. However, dropout analyses did not reveal significant baseline differences between completers and non-completers, suggesting minimal bias. Future research should explore personalized rTMS protocols that account for factors like cognitive function or comorbidities, which may influence response to treatment in older adults. We categorized age as a two-level factor (≥60 years old) based on past literature. However, the cutoff for defining LLD remains somewhat arbitrary and may vary across studies. Finally, we did not stratify our analyses based on the timing of inclusion (pre- vs post-pandemic).

Conclusion

A key finding of this study is the absence of significant differences in treatment outcomes between older and younger patients, suggesting that rTMS can be safely and effectively applied in older adults without requiring major protocol modifications. This supports the growing body of evidence advocating for the use of neuromodulation techniques in geriatric psychiatry. Although we did not directly assess mechanisms such as social engagement, neuroplasticity, or individualized stimulation parameters, these remain promising avenues for future research. Understanding how these factors interact with age could help tailor more precise and personalized interventions for late-life depression.

The favourable response observed in older adults reinforces the potential of rTMS as a valuable and effective treatment option for this population, particularly given their frequent resistance to pharmacological interventions. These results align with recent findings from (Leuchter et al., 2024; Sackeim et al., 2020; Valiengo et al., 2022), who similarly demonstrated that response and remission rates in older adults are comparable to, if not greater than, those in younger patients receiving rTMS.

Further research is essential to consolidate the role of rTMS in managing neuropsychiatric disorders in elderly patients. This includes optimizing stimulation parameters, identifying reliable

predictors of response, and evaluating long-term outcomes to better inform clinical decision-making in this vulnerable population.

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No potential conflict of interest was reported by the authors.

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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