

Intranasal esketamine improves depressive symptoms and cognition in elderly patients with treatment-resistant depression

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1 Introduction

Treatment-resistant depression (TRD) in elderly patients represents a clinical challenge, often overlapping with neurodegenerative diseases. Intranasal esketamine has shown potential efficacy in this population. However, few studies have focused on older adults, and none have explored cognitive improvement as a secondary outcome. This study aims to evaluate the tolerability, efficacy, and cognitive effects of intranasal esketamine in elderly patients.

2 Materials and Methods

Eight consecutive elderly patients aged >65 years (median age = 68.8 years) with TRD were treated with intranasal esketamine as an add-on therapy. Depression severity was assessed using the Montgomery-Åsberg Depression Rating Scale (MADRS) and the Hamilton Depression Rating Scale (HDRS) at baseline and after 3 months. Cognitive functioning was evaluated using the Montreal Cognitive Assessment (MoCA) and a comprehensive neuropsychological battery, including social cognition measures (ECAS subtest - Poletti et al. 2016). Tolerability was monitored throughout the treatment period.

3 Results

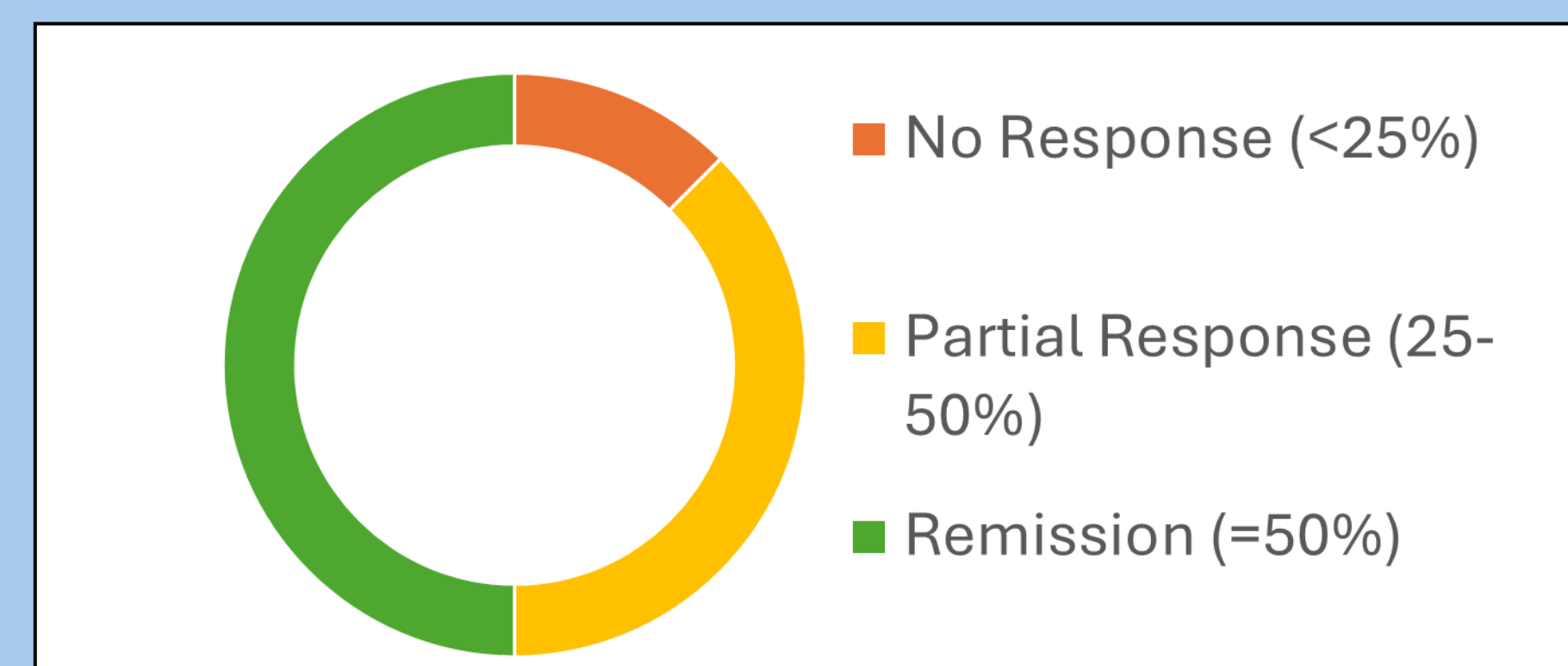
After three months of treatment, 4 patients achieved remission, 3 showed a partial response (defined as a MADRS reduction between 25-50%), and 1 patient showed no change. On average, MADRS and HDRS scores were reduced by 50% across the entire sample. Logistic regression analyses revealed a significant treatment effect for both MADRS ($p=.005$; $p_{\text{MODEL}}<.044$, $\text{adj-R}^2=.40$) and HDRS ($p=0.003$; $p_{\text{MODEL}}<.023$, $\text{adj-R}^2=.47$).

Improvements were observed in immediate prose memory ($p=.018$, $p_{\text{MODEL}}<.001$, $\text{adj-R}^2=.76$) and social cognition ($p=.035$; $p_{\text{MODEL}}<.022$, $\text{adj-R}^2=.48$). Changes in MADRS scores significantly correlated with improvements in verbal fluency and naming tasks ($r=0.7$, $p=.02$). The treatment was well tolerated, with no serious adverse events reported.

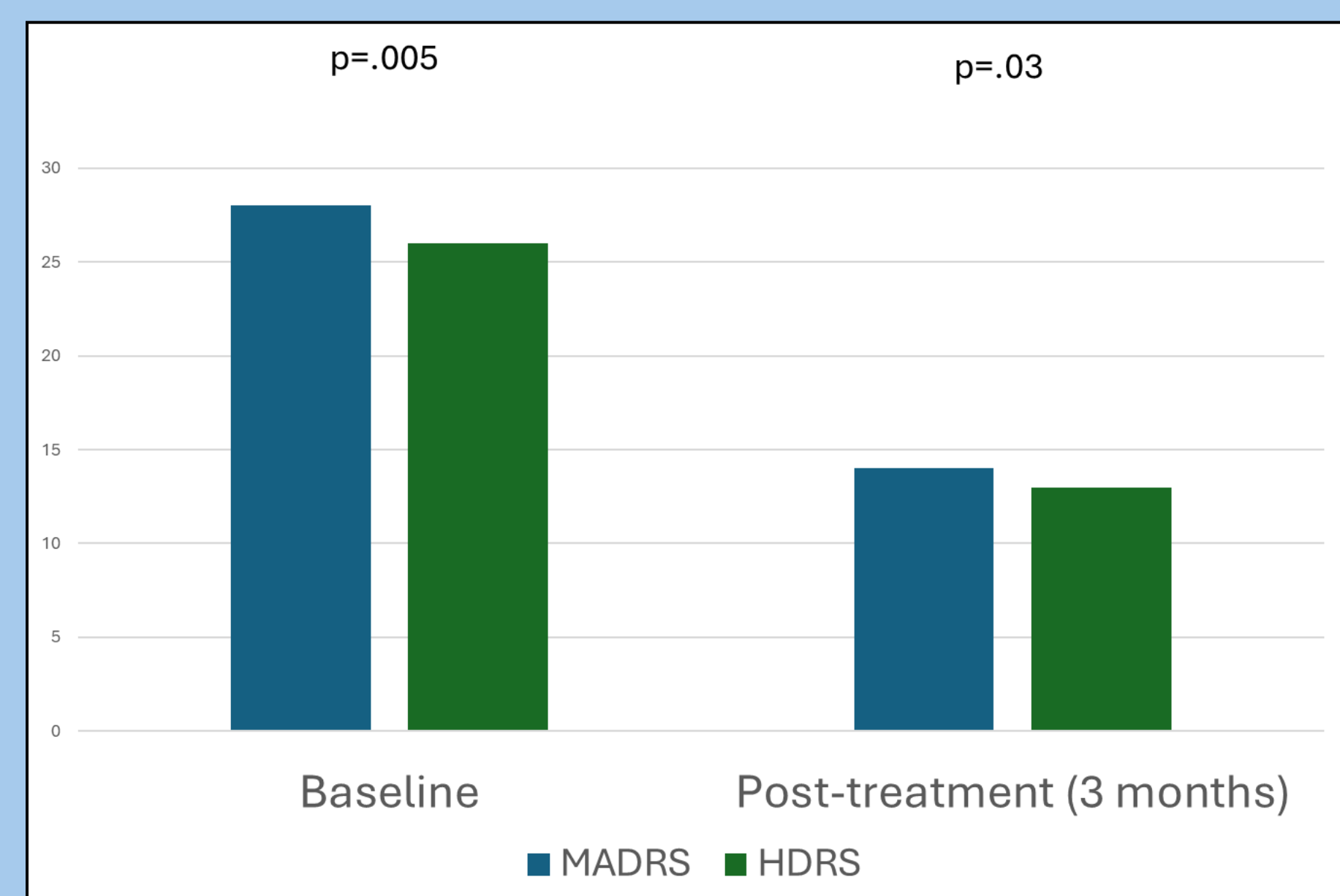
4 Conclusion

Three months of intranasal esketamine treatment significantly reduced depressive symptoms in elderly patients, while also improving immediate memory and social cognition, with good overall tolerability and no serious adverse events.

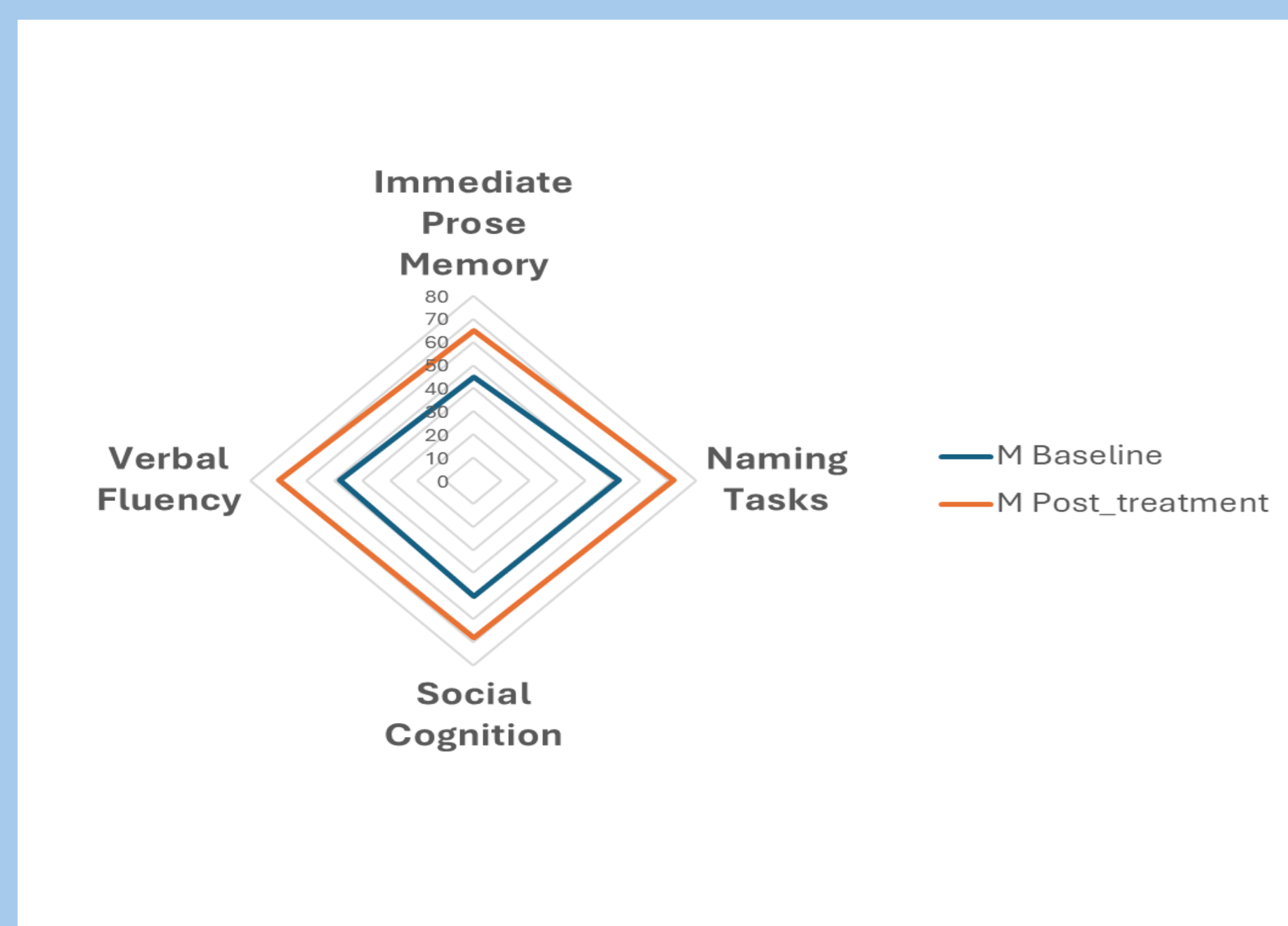
Treatment Response Distribution



MADRS and HDRS Score Reduction



Cognitive Improvements



MADRS and cognitive verbal correlations

