

Introduction: Esketamine intranasal spray has been approved in both the USA and EU as a novel treatment in patients with treatment-resistant major depression (TRD) and for the management of acute depressive emergencies during the course of major depressive disorder (MDD). Real-world data on the effectiveness and safety of esketamine nasal spray in clinical use are limited.

Objectives: To investigate the clinical effects and safety of esketamine nasal spray on depression severity and suicidal ideation during inpatient treatment in $n=76$ patients in a German university hospital.

Methods: In this retrospective chart review, we analyzed the change in depression severity and safety after a treatment series with esketamine nasal spray combined with treatment-as-usual in patients with treatment-resistant depression (TRD) in inpatient treatment setting of a University Hospital. Depression severity has been rated with the Montgomery–Åsberg Depression Rating Scale (MADRS) as well as with the BDI-II (Beck Depression Inventory-Second Edition) before and after the treatment series. The intensity of suicidal ideation has been evaluated using MADRS item 10 on suicidal thoughts.

Results: A total of 76 patients have been included (women 55.3, $n=42$) in this analysis. Mean BDI-II pre-treatment was 37.6 and mean MADRS was 33.6 corresponding to severe depression. Mean score on item-10 pre-treatment was 2.4 (median 2.0). On average patients received 10.9 sessions (standard deviation 4.2, median 11.0) of esketamine nasal spray (min 1, max. 19 sessions). There was clear improvement after the treatment series in both the BDI-II (mean change -10.1 , $p < 0.001$) as well as in MADRS score (mean reduction -10.0 , $p < 0.001$). Suicidal ideation on item-10 also decreased significantly (-0.9 , $p < 0.001$). The effect sizes were large for all three measures: Cohen's d 1.050 for BDI-II; 0.986 for MADRS and 0.742 for changes in suicidal ideation. Overall, esketamine treatment was well tolerated. In five cases esketamine treatment has been terminated early (after a mean of 3.4 sessions) due to dissociations ($n=4$; 5.3%) or due to non-response ($n=1$).

Conclusions: Esketamine nasal spray is a novel effective and safe treatment option, which leads to significant decrease in depression severity as well as in suicidal ideation. More data from real-world patients are needed to position esketamine in the algorithm of depression treatment. Rate of treatment discontinuation due to side-effects in this study was comparable to those in other esketamine studies (4.2% in Reif et al, NEJM, 2023).

Disclosure of Interest: None Declared

EPP0378

Comparison of Staging Methods for Treatment-Resistant Depression: Chart Review

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Introduction: Treatment-resistant depression (TRD) lacks a universally consistent definition due to varied interpretations despite

attempts to define it based on inadequate response or remission despite sufficient antidepressant treatment. There's a crucial demand for a uniform definition and staging to streamline its effective management amid diverse treatment options and the complex nature of resistance. Five methods have emerged to define and classify treatment resistance reliably.

Objectives: The aim of this study is to compare the five staging methods (Thase&Rush SM (T&R), European Staging Method (ESM), Maudsley Staging Method (MSM), Massachusetts General Hospital Staging Method (MHG-s), Conway Staging Method(Conway)) in assessing treatment resistance within a single sample.

Methods: Retrospective analysis involved medical records of inpatient psychiatry clinic admissions at Hacettepe University between October 2012 and October 2014. Patients with a primary diagnosis of bipolar affective disorder, schizophrenia, other chronic psychotic disorders, dementia or cognitive disorders, alcohol and substance use disorders, and those with missing data were excluded.

Results: Initial screening yielded a total of 115 patients. 64 patients were included in the study, 13 patients were excluded due to missing data, and 38 patients were excluded due to comorbidity.

Characteristic	Total (N=64)	Last Episode Characteristics	Total (N=64)
Female - N(%)	44 (69)	Episode duration – month (mean ± SD)	13.75 ± 16.09
Age – yr (mean ± SD)	48.39 ± 18.81	Psychotic symptoms – N(%)	20 (31)
Married – N(%)	41 (64)	Anxiety symptoms – N(%)	24 (38)
Secondary school and over – N(%)	38 (59)	Suicidal attempt – N(%)	19 (30)
Employed – N(%)	16 (25)		

TRD definition and staging method (N=55)	T&R	ESM	MSM	MGH-S	Conway
Not resistant by this method	26 (47.3)	45 (81.8)	0 (0)	27 (49.1)	43 (78.2)
Identified by this method	29 (52.7)	10 (18.2)	55 (100)	28 (50.9)	12 (21.8)
Exclusively identified by this method	0 (0)	0 (0)	21 (38.2)	0 (0)	0 (0)
By this and one other method	27 (49.1)	0 (0)	11 (20)	5 (9.1)	0 (0)
By all methods	10 (18.2)	10 (18.2)	10 (18.2)	10 (18.2)	10 (18.2)
<i>Identified as TRD</i>					
Age of onset (mean ± SD)	40.28 ± 17.42	35.6 ± 18.27	40.44 ± 18.38	40.07 ± 17.9	38.17 ± 17.71
ATHF score (mean ± SD)	7.55 ± 5.46	12.1 ± 6.51	4.93 ± 4.98	7.43 ± 5.69	11.08 ± 6.47
Last episode duration (month) (mean ± SD)	17.11 ± 17.25	22.10 ± 20.96	14.22 ± 17.08	16.33 ± 17.66	20.83 ± 19.25

Conclusions: There is no universally agreed-upon definition for treatment resistance. In this sample, different definition and staging methods were employed to examine the similarities and differences in the clinical and treatment related characteristics of groups with TRD identified with each. The reasons and possible implication of concurrence and discordance between the methods will be discussed.

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EPP0379

Exploring the Interplay Between Early Maladaptive Schemas and Depression: A Comparative Analysis

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Introduction: Depression, a pervasive mood disorder, significantly impairs one's quality of life. Early Maladaptive Schemas (EMS), ingrained thought patterns stemming from early life experiences, play a pivotal role in shaping adult beliefs and behaviors. This study delves into the relevance of specific EMS domains—Emotional Inhibition (EI), Negativity/Pessimism (NP), and Social Isolation/Alienation (SI)—in influencing the severity of depression among medical students and diagnosed patients.

Objectives: Our primary goal was to assess the correlation between specific EMS domains and depression severity in medical students and clinically diagnosed patients. We aimed to elucidate whether these schemas could serve as indicators for potential depressive tendencies or if they had a stronger association in those already diagnosed with depression.

Methods: We conducted a prospective cross-sectional analysis involving 73 medical students and 61 diagnosed depression patients (aged 18-32). Four key variables—Depression, EI, NP, and SI—were measured using the Beck Depression Inventory-2 and The Young Schema Questionnaire-Short-form-3 in the Romanian context. Statistical analyses, including correlation coefficients and t-tests, were employed to explore the relationships between EMS domains and depression severity.

Results: In the non-clinical sample, we identified moderate, statistically significant correlations between depression and EI ($r=0.63$), NP ($r=0.71$), and SI ($r=0.59$). Conversely, the clinical sample exhibited slightly weaker, yet significant correlations (EI- $r=0.42$, NP- $r=0.39$, SI- $r=0.29$). Notably, significant differences emerged between the groups in all measured variables. These findings imply that while a positive correlation between EMS variables and depression exists in both samples, the association weakens in diagnosed patients, indicating that these schemas may be less predictive in this population.

Conclusions: Our study underscores the importance of understanding EMS domains in assessing depression severity. While specific schemas—EI, NP, and SI—correlate with depression in both medical students and diagnosed patients, this link is notably weaker in the latter group. Elevated EMS variables suggest a potential for future subclinical depression in medical students, but they

might not strongly predict depression in those already diagnosed. These nuanced insights have implications for preventive interventions and therapeutic approaches tailored to individuals at different stages of depression, thereby enhancing targeted mental health care strategies.

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EPP0380

DNA methylation signatures support the role of neutrophils and monocytes in depression

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Introduction: Research repeatedly linked inflammation with major depressive disorder (MDD). The presence of an inflammatory subtype of depression is supported by molecular findings as well as imaging reports. We investigated the cell type composition estimated by using epigenome-wide DNA methylation markers in a sample of depressed individuals showing high or low inflammation levels measured by hsCRP. We aimed to understand the connection between depression and inflammation, specifically differences in cell type compositions between high and low inflammation groups at baseline.

Objectives: 119 individuals with MDD were included for this analysis. Following quality control procedures, 113 participants were included in the analysis ($M_{age}=47$ years, 57.98% women). The sample consisted of 37 individuals with high hsCRP (hsCRP > 1.5, $M_{age}=45$, $M_{hsCRP}=8.2$, $M_{MADRS}=28$, 70% women) and 76 individuals with low hsCRP (hsCRP < 1.5, $M_{age}=44$, $M_{hsCRP}=0.99$, $M_{MADRS}=28$, 49% women).

Methods: The Illumina Infinium MethylationEPIC 850k BeadChip was used for analyzing whole blood derived DNA. Data processing and cell type estimation was conducted using the RnBeads package. We applied the Houseman method to estimate cell type composition through epigenome-wide DNA methylation signatures, resulting in six cell types: neutrophils, natural killer cells, B cells, CD4+ T cells, CD8+ T cells and monocytes. Comparisons between both groups were tested using ANOVA.

Results: High and low hsCRP groups were compared for each of the six cell types estimated. A statistically significant difference was seen for monocytes ($p=0.0316$) and a trend for neutrophils ($p=0.0742$). The mean values for neutrophils in patients without inflammation were found to be 60%, while in patients with inflammation, it was 63%. For monocytes, the mean values for patients without inflammation and those with inflammation were 10% and 9.4%, respectively, with a smaller range (4.5%-14.3%) for individuals with inflammation as compared to patients without inflammation (5.3%-20.7%). None of the other four cell types showed a statistically significant difference.

Conclusions: We identified differences in the cell type composition between groups of depressed patients with high versus low inflammation. These results align with the existing body of knowledge reported in established academic literature. Our study