Examining the Impact of Childhood Trauma on Ketamine's Real-World Effectiveness in Treatment-Resistant Depression

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Submitter Danica Johnson

Affiliation University of Toronto

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Abstract: Background: Childhood trauma is a well-established risk factor for the development and persistence of major depressive disorder (MDD), contributing to increased illness severity, chronicity, and resistance to standard antidepressant treatments. Intravenous (IV) ketamine has emerged as a rapid-acting and efficacious intervention for treatment-resistant depression (TRD), but the impact of childhood trauma on its effectiveness remains unclear. This study aimed to examine the impact of trauma load, type, and severity on the antidepressant effectiveness of ketamine in individuals with TRD, addressing a critical gap in the existing literature.

Methods: We conducted a retrospective analysis on adults (n = 83) who received four ketamine infusions at a community clinic to examine whether childhood trauma influences ketamine’s antidepressant effectiveness in TRD. Trauma load (high vs. low) and specific trauma types were assessed using the Childhood Trauma Questionnaire (CTQ). Trauma severity was also rated on a 7-point Likert scale. Depressive symptoms were evaluated using the Quick Inventory of Depressive Symptomatology Self-Report 16-item (QIDS-SR16) at baseline and after each infusion. Linear mixed models (LMMs) assessed the effects of trauma load and specific trauma types on depressive symptom trajectories, while chi-square tests examined response (=50% reduction in QIDS-SR16) and remission rates (QIDS-SR16 =5). Pearson correlation analyses explored the relationship between trauma severity and antidepressant response.

Results: Depressive symptoms decreased significantly across participants over time (mean QIDS-SR16 reduction: 5.7 points, $p < .001$). High trauma load was reported by 55% of participants. Response rates were 25% in the high trauma group and 19% in the low trauma group, while remission rates were 14% and 11%, respectively. LMMs revealed no significant differences in depressive symptom trajectories between high and low trauma load groups ($p = .572$) or between individuals with specific trauma types and those without (all $p > .05$). Similarly, chi-square tests found no significant associations between trauma load and response ($p = .230$) or remission ($p = .397$). Trauma severity, assessed via Likert ratings, was not significantly correlated with

antidepressant response (r= .124, p= .266).

Conclusion: These preliminary findings suggest that ketamine is an effective treatment for TRD, regardless of childhood trauma load, type, or severity. This highlights ketamine's potential utility in addressing depressive symptoms in populations burdened by significant trauma. Future research should focus on replicating these findings and identifying specific mechanisms that mediate ketamine's antidepressant effects in trauma-affected populations to further optimize its therapeutic potential.

Learning Objectives:

Learning Objective 1 Evaluate how childhood trauma load, type, and severity influence the antidepressant response to ketamine in individuals with treatment-resistant depression (TRD).

Learning Objective 2 Discuss the clinical implications of ketamine's antidepressant effectiveness in trauma-affected populations and identify key areas for future research to optimize its therapeutic potential.

DISCLOSURE

Financial Relationships

Disclosure No, I have nothing to disclose.